National Study of Reproductive Tract Infections and Sexually Transmitted Infections

Proposed Research Strategy and Study Design

Prepared by the London School of Hygiene & Tropical Medicine, the Population Council and the Aga Khan University for the UK Department for International Development.

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Summary

1. Background

Currently, Pakistan has very low levels of HIV infection but the country is considered to be at high potential risk for a number of reasons. In particular, there are large concentrations, particularly in the major cities, of individuals with behaviours that make them extremely vulnerable to rapid spread of HIV and of classical sexually transmitted infections (STIs) such as chlamydia, syphilis and gonorrhoea. These individuals include male and female commercial sex workers, men who have (unprotected) sex with men (MSM), hijras or transvestites, injecting drug users and highly mobile occupational groups, such as truckers. It is likely that Pakistan’s HIV epidemic will start in one or more of these groups and then spread to the general population through individuals who have contact both with high-risk groups and the general population. In epidemiological parlance, individuals who spread the infection from concentrated high-risk groups to the general heterosexual population are termed the bridging group (or population). Typically these are married or unmarried men who are clients of sex workers, or bisexuals, or share needles with injecting drug users. Rather little is known about the sexual conduct of men in Pakistan but the available evidence suggests that both pre-marital and extra-marital sexual contacts – either homosexual or heterosexual – are sufficiently common to create and sustain a generalised HIV epidemic. Immediate and effective action is needed to avert the threat of an HIV epidemic in Pakistan.

While some classical STIs are reproductive tract infections (RTIs), other RTIs are not, or not primarily, transmitted by sexual intercourse. They can be acquired iatrogenically such as during the insertion of intra-uterine devices (IUDs) or abortion. They may also arise endogenously due to proliferation of organisms normally present in the body.

Among the RTIs, bacterial vaginosis (BV) has become increasingly recognised as a major public health concern especially in countries where maternal and child health outcomes are poor such as Pakistan. The recognition of BV over the past decade as a major underlying cause of MCH morbidity offers great potential for developing intervention strategies to improve the health of both women and children. If left untreated, BV can lead to problems in pregnancy, low birth weight babies, and intrauterine infections. Evidence now shows that BV is perhaps the most common RTI. Approximately 22% of Asian women may be affected. There is no related
health science literature from Pakistan though a plausible baseline prevalence of approximately 15% is suggested.

The Ministry of Health (MOH) is well aware of the growing challenge of HIV/AIDS in Pakistan and has elaborated policies and programmes for its prevention and control. A National AIDS Prevention and Control programme (NACP) has been created, with provincial implementations units. The Ministry of Population Welfare has framed a Reproductive Health Policy in light of the Declaration of the International Conference on Population and Development 1994 (ICPD) held in Cairo that is waiting Federal Cabinet’s approval. This policy calls for more active intervention in areas of reproductive and sexual health, including the reduction of RTIs and STIs and improving the reproductive health of men and women.

As the number of reported HIV infections and AIDS cases is steadily on the rise in all provinces, the MOH has drafted an Expanded Response Programme of about US$ 40 million with the assistance of the World Bank and other funding agencies to be implemented over next five years. The objective is to prevent HIV from becoming established in vulnerable populations and spreading to the general adult population. Two key aims of the Expanded Response Programme are to achieve:

- Increased prevalence of safe behaviours and improved availability of STI services among vulnerable populations
- Improved knowledge and practice of HIV preventive measures including use of high quality STI services by the general population

The Pakistan Reproductive Health Services Package (RHSP) jointly developed by the MOH and MOPW in 1999 also includes as components: (a) prevention and management of RTIs/STDs and HIV/AIDS, and (b) management of reproductive health related problems and issues in women and men. The Pakistan Reproductive Health Project (RHP) to be launched in 2002 with the support of the Asian Development Bank will focus on these service delivery components and will also benefit from the proposed study.

Hence, on part of the Government, there is visible commitment to the ICPD plan of action regarding RTIs and STIs and also for limiting the spread of an HIV/AIDS epidemic in Pakistan. However, there is lack of data needed for sound programme planning and monitoring of
progress. MOH and NACP envisage that the proposed National Study of Reproductive Tract and Sexually Transmitted Infections will provide the benchmarks for monitoring the progress of the Expanded Response Programme.

2. Objectives of the National Study
As stated in the Original Terms of Reference the goal was to design a national survey of RTIs and STIs with outcomes that would have applications in terms of policy development and programme planning. The objectives were stated as follows:

- Obtain estimates of the prevalence of selected RTIs/STIs from samples that can defensibly construed as nationally and provincially representative, using the most reliable epidemiological and laboratory techniques that can practically be applied.

- Gather from all study participants a limited range of information about clinical symptoms, knowledge, beliefs, attitudes, and behaviours related to STDs;

- Examine in greater depth, from sub-samples within the above sampling framework: knowledge, beliefs, attitudes, and behaviours associated with risk practices and with health seeking behaviours; and

- Acquire estimates of prevalence of selected RTIs/STIs and associated behavioural factors from purposive samples of known or suspected high-risk groups.

3. Overall Study Design
To meet the objectives in the original Terms of Reference and epidemiological considerations outlined above, the Study Design Team in consultation with national experts recommends that high-risk groups, the bridging population and the general population be studied as three distinct population groups in three separate studies.

The choice of high-risk groups to study is more a matter of judgement than science. After much discussion, it was decided to focus attention on the following five groups: female sex workers, male sex workers, hijrays, injecting drug users and truckers
Whereas high-risk groups are easy to define and distinguish - in principle if not in practice - there can be no easily distinguishable **bridging population**. Indeed it is more appropriate to think in terms of bridging behaviours (i.e. pathways along which HIV and other STIs may spread from high-risk groups to the general population) rather than a discrete population. A consideration of bridging behaviours, such as use of sex workers and homosexual contacts by married persons, suggests that men rather than women are implicated. Moreover as urban, migrant men are particularly susceptible to bridging behaviours, we recommend that this stratum of the population be taken to represent the bridging population.

The third population to be studied is the **general (or low risk) population**. As noted earlier, the original Terms of Reference clearly call for an assessment of disease burden in the general population. This component of the overall study will provide much needed information on the prevalence of non-sexually transmitted RTIs (together with coping strategies and treatment patterns) in women.

The general, or low risk, population includes, of course, both men and women. The inclusion of women is indispensable for estimation of RTI prevalence. The inclusion of men, though desirable, was not considered to be sufficiently important to justify the implicit near-doubling of costs. Because the infectivity of classical STIs is high, levels of infection in married women are a sound indicator of levels of infection in their husbands and thus very little is lost by excluding men in terms of estimating disease prevalence.

These considerations led the Design Team to propose a study of currently or formerly married women as the most cost-effective approximation to the general population. The exclusion of unmarried women is justified on the ground that STIs will be very rare, together with severe anticipated difficulties of obtaining compliance to intrusive biological data collection.

4. **Hallmarks of the Proposed Research Strategy**

4.1 **Policy and Programme Relevance**

In the recent past, the Government of Pakistan has recognized the importance of RTIs and STIs in many of its new initiatives such as the formulation of its Reproductive Health and Population policies. These infections are adding to the burden of disease, therefore becoming more central
to health concerns as well as leading to dire economic and social consequences for certain sub-populations. This study has direct relevance for policies such as the National Plan for Action of the Ministry of Women Development and the Poverty Reduction Strategy of the Ministry of Finance due to the close link between RTI/STIs and gender related issues, such as autonomy of women, communication between spousal partners and poverty of households and individuals.

The government's medium term health strategy has a sharp focus on preventive and control programmes especially in the area of communicable and infectious diseases, reproductive health, child health, and nutrient deficiencies. It has especially highlighted the importance of additional programs including adoption of DOTS strategy against TB; RBM approach in combating malaria; measures for preventing the spread of Hepatitis B, HIV and AIDS through immunization and public health campaigns. The importance of “raising the curtain on STIs” was one of the highlights of the Secretary Health’s presentation to the consortium of donors during the Human Development Forum in January 2002.

The jointly developed Reproductive Health Package of the two Ministries of Health and Population Welfare developed in 2000 calls for service delivery institutions to train and retrain staff to provide various levels of RTI/STI services according to their levels of competence.

This study will assist in the implementation of these policies and programmes because its findings will:

- Provide baseline information for evaluation of intervention strategies to reduce RTI/STIs prevalence
- Assess the relative importance of specific RTI and STIs in the context of Pakistan, in terms of morbidity, treatment costs, loss of economic productivity etc.
- Assess the levels of prevalence of RTIs and STIs among men and women and sub groups according to economic status and geographic location in order to apportion resources more appropriately and judiciously
- Document the type and degree of symptoms reported by women and men related to RTIs and STIs so that providers may be able to assess and accordingly manage the treatment of these infections
- Inform programme personnel about health-seeking behaviour (which is influenced by facilitating and inhibiting factors) among various risk groups and therefore assist in designing appropriate services for different cadres of providers
• Develop capacities in the laboratories and among select service providers (in locations where the survey is to take place) to deal with RTI/STI diagnosis and treatment
• Contribute towards the development of second-generation surveillance programs being planned for in the near future.
• Assist in developing culturally sensitive and effective RTI/STI awareness campaigns

4.2 Scientific rigour and value for money
In addition to policy and programme relevance, the main principles underlying the proposed study design include scientific rigour and value for money. The need for scientific rigour requires particular emphasis. It is the view of the Design Team that any study that does not aspire to meet the best international standards represents a poor investment because the results will be open to doubt and challenge. Hitherto, most HIV-related research in Pakistan has been well below best international standards. Samples have been small and unrepresentative in nature and little attempt at quality assurance of laboratory results has been made. The net result is that the scientific evidence base available to NACP and other organisations with a mandate to improve reproductive and sexual health is incomplete, fragmentary and unreliable. It is essential, in our view, that the National Study yields findings of the highest possible quality that will command respect from all stakeholders and set the standard for future work in this area. At the same time, the Design Team has kept in mind that funds for the study are not unlimited and that donors have to be convinced that their investment will be cost-effective, when judged against alternative investments. The need for cost-containment has been kept in mind, leading, for instance, to suggest different options and to restrict sample sizes to the minimum required and similarly to restrict laboratory tests to priority infections.

4.3 Quality control and assurance
The creation of quality in all aspects of study implementation, its maintenance and assurance and its verification have been a foremost consideration during the design phase. Ultimately, the quality of the study will be largely determined by the implementing agencies. At the design phase, however, it is possible to recommend procedures that if followed systematically, will ensure that the findings are of high quality.

Detailed procedures for day-to-day supervision and higher level supervision of data collection teams have been specified. Each team will be accompanied by appropriate laboratory technicians and a cold chain specialist, with adequate equipment and a dedicated vehicle to
ensure the integrity of the cold chain. Laboratories participating in the study should be required
to meet objective performance criteria for each diagnostic test and will require training in
standard operating procedures. All results will be double-checked by a pre-designated
reference laboratory on a 10% sub-sample basis.

4.4 Local capacity strengthening
One of the main priorities in the Design Phase was to assess local capacity for undertaking the
National Study and to identify training or other capacity strengthening that would be needed for
successful execution of the proposed study design. The underlying assumption was that all
components of the National Study should be conducted primarily (though not necessarily
exclusively) by institutions based in Pakistan.

4.5 Public-private partnerships
The proposed study offers considerable potential for strengthening public-private partnerships,
especially in relation to health science and policy development. The proposed study offers an
opportunity to develop a new level of partnership between public and private sectors especially
in the area of laboratory capacity development: building new capacity where justifiable and
sustainable, combining capacities where these are already complementary, and utilizing existing
capacities in new roles such as the proposed designation of reference laboratories. The same
principle applies to the development of behavioural sciences, epidemiology and data
management capacities in Pakistan.

4.6 Link to future surveillance systems
NACP is currently re-designing its HIV/STI surveillance system and it was impossible therefore
to demonstrate in detail how the National Study might be linked to ongoing surveillance. The
importance of this link and the related issue of replicability cannot be overemphasised because
the value of the National Study will be greatly enhanced if it is seen as baseline for future
monitoring of HIV and STI infections and their associated behaviours. Furthermore, in the
context of survey and surveillance development in settings with low HIV prevalence, capturing
trends in behavioural risk factors and other STIs, has been advocated with particular reference
to Pakistan.
4.7 Adherence to high ethical standards

Detailed recommendations have been made with regard to three key ethical dimensions. A step-wise approach to ensuring informed consent is recommended. Information needs to be conveyed to the selected communities in advance of the main data collection activities; informed consent from individual subjects for the behavioural interview is needed; and finally, informed consent is required for the biological data collection.

With regard to privacy and confidentiality, the behavioural interviews and collection of specimens should be conducted in privacy, out of the hearing of other people. Confidentiality will be maintained by the use of personal identification numbers (PINS). These will be issued to subjects following the completion of the behavioural interviews and used as the only means of identification for bio-medical data collection.

The recommended treatment protocol for all components of the study is to maximise front line treatment at time of data collection but nevertheless develop a notification strategy for subjects found to be infected by laboratory tests and NOT already treated approximately. Front line treatment will be performed by paramedics or medical doctors at time of biological data collection, using the recently revised WHO guidelines for syndromic management. Other members of the communities will be offered treatment for acute conditions.

Each component of the National Study should be subject to ethical review. Some institutions in Pakistan have their own ethical review boards but no national board exists. It is strongly recommended that such a national board be constituted and involved in the review of the STI/RTI study. Nonetheless, it is a recognised norm internationally that all institutions engaged in research should have their own ethical review processes in place, and are normally required to obtain approval from their own boards, regardless of approval from external boards.

4.8 Effective dissemination of results

The dissemination strategy should address the diverse needs of different audiences. The latter include federal policy makers and managers, provincial mangers, NGOs, donors, the private sector, the general public, the Pakistan and international research community.

Specifically it is recommended that the implementing agency be required to produce key descriptive results, together with information on compliance and any other caveats regarding
data quality, within eight weeks of the completion of data entry, editing and cleaning. Dissemination workshops should be held.

Some six months after release of the preliminary findings, the implementing agencies should be required to present an analytic report of some 30-50 pages of text together with detailed results. A one-day symposium is recommended at this stage.

4.9 Data ownership, access & storage
We recommend that best practice in international medical research be followed in regard to data ownership and access. In essence, the scientific team who collect and analyse data should be allowed exclusive access to them for a relatively short period of time but that, thereafter, the data should be made freely available to bona fide research groups. In practical terms, this strategy would allow the implementing team exclusive access until publication of the analytical report, which is likely to be about 12 months following completion of fieldwork. Following the release of the report, ownership of the data should be vested in another organisation such as NACP or in a committee who would have a mandate to release the data to all genuine research organisations and departments in Pakistan.

4.10 Partners & stakeholders for implementations
Many institutions and agencies working at national level have shown interest in the undertaking of the proposed study. Recruitment should be through a transparent bidding process. It is expected that organisations will form partnerships to bring together relevant skills for executing these studies. These organisations will have to define very clear management structures and responsibilities of each partner.

One advantage of the proposed study design is that it comprises at least three distinct studies and thereby permits different agencies to bid for specific components. However, it is essential that the research be of the same high standard across all studies. This is particularly true of the laboratory component.

5. Study of the General Population

Objectives: The general population survey has the following main objectives:
- Measure the prevalence of key RTIs and STIs
• Assess self-reported symptoms of RTIs/STIs, associated treatment-seeking behaviour, and the subjective burden of such symptoms in women
• Measure knowledge of STIs, including HIV, and means of avoiding infection
• Determine risk and protective behaviours
• Examine variations in disease prevalence, self-reported symptoms, treatment seeking and knowledge across major strata of the population

This information will meet the needs of a variety of stakeholders, policies and programmes. Specifically it will:

• Provide baseline data to NACP for future STI/HIV surveillance
• Inform decisions on the nature of future surveillance, particularly on the key issue of whether facility-based surveillance (e.g. ante-natal clinic attenders) is adequate.
• Allow MOH, MPW and other providers of health and family planning services in NGO and private-sectors to assess the need for improving mechanisms for creating awareness regarding RTI/STI's and also to design programs that allow providers to be able to better assess and manage these conditions.

Options: Two main options are proposed for the survey of the general population. Option 1 will yield nationally representative results on a relatively small sample of 4000 women and is designed to maximise the potential for it to be repeated at regular intervals and thus form part of an ongoing surveillance system for RTIs/STIs. Option 1 will permit estimation of results separately for the urban and rural population and for Punjab, the most populous province. However it will not permit estimation of results (with a useful degree of precision) for other provinces or administrative areas.

Option 2a, based on a larger sample of 6000, will yield similar results but at a provincial level as well as the national level. This was stated by both provincial and national representatives during the design process, as being highly desirable for the evidence-based development of provincial programs. However, Option 2a, because of its higher cost and because the general population is not currently considered an intervention priority by the NACP, may have less potential to be repeated. It is therefore most appropriately viewed as an assessment of the burden of RTIs/STIs (and associated behaviours and coping mechanisms) with sufficient statistical power to enable comparisons of the magnitude and nature of this burden between provinces.

Option 2b is similar to option 2a but contains an additional sample of 1000 women from FATA/AJK. AJK and FANA are federally dependent territories that have been excluded from
most national surveys. They are of special interest in relation to RTIs/STIs because of the special circumstances of men and women in these areas. Specially, these are areas of major out-migration of men (many of them married) for employment in the South, while, simultaneously, they are host to large numbers of men from elsewhere in the country, in service of the military. Such large movements of men have clear potential implications for STI transmission.

The great merit of options 2a and 2b is that they will provide data for policy and programmes for use by provincial health officials and will permit identification of major differences between provinces in the nature of the problem. It is impossible to gauge the probability that major differences in RTI/STI prevalence and associated behaviours exist at the province level but this is plausible and it can be argued forcefully that it is important to find out. The choice between the options involves financial, political, policy and scientific considerations. Obviously options 2a and 2b provide information at the appropriate level, i.e. the province or administrative area, where many health investment decisions are made and are thus preferable to option 1.

**Eligibility Criteria:** The study population is defined as all ever-married women aged 20 to 39 years who have spent the previous night in the randomly selected households. Female visitors to selected households will be included if they resided in the household on the night prior to enumeration. Conversely, usual residents who are away from home at the time of the survey will not be regarded as eligible. The number of women meeting the selection criteria is expected to be around 0.9 per household.

**Sample Size:** Under Option 1 It is proposed to select 4000 individuals using a nationally representative sample (excluding FANA, AJK and restricted areas). If a sample of the same size was repeated in say 5 years, it would be able to detect (with statistical confidence) a change over time in bacterial vaginosis prevalence from 15% to 11.4%, or a change in prevalence of chlamydia from 5% to 3.2%. The 95% confidence intervals of a 15% estimate of bacterial vaginosis would be 13.1% to 16.9%. The confidence intervals for a chlamydia estimate of 5% would be 4% to 6%.

Under Option 2a It is proposed to select 1500 households/individuals in each of the 4 provinces. The overall sample size would therefore be 6000. At provincial level the 95% confidence intervals for a 15% estimate of bacterial vaginosis would be 12% to 18%, whereas at national
level it would be 12.6% to 17.4%. At provincial level the 95% confidence intervals of a 5% estimate of chlamydia would be 3.1% to 6.9%, whereas at national level they would be 3.7% to 6.3%.

Under Option 2b It is proposed to select 1500 households/individuals in each of the 4 provincial strata and 1000 individuals for the AJK + FANA stratum. This sample allocation would have the power to detect with statistical confidence a difference of ±4% in the prevalence of chlamydia in AJK/FANA from the expected level of 5% in the four provinces.

**Behavioural and biological data:** Information of a social, demographic and behavioural nature will be obtained from home interviews with eligible women by specially trained female lay interviewers. These interviews will be conducted before the biological data collection. Each interview is expected to last on average about 25-30 minutes.

It is proposed that biological data collection be performed by specially trained female paramedical staff at temporary clinics in each selected cluster. The biological samples to be collected are blood, urine and vaginal swabs. It is proposed to study the two most important classical STIs - chlamydia, and syphilis - and the two most common RTIs that are not primarily transmitted via sexual intercourse - bacterial vaginosis and candidiasis.

6. **Study of the Bridging Population**

**Objectives:** The survey of the bridging population (male, urban migrants living away from home) has the following main objectives

- Measure the prevalence of STIs
- Measure behaviours that modify the risk of STI with an emphasis on sexual behaviour and condom use
- Assess self-reported STI symptoms and associated treatment-seeking behaviour
- Measure knowledge of STIs, including HIV and means of avoiding infection
- Measure perceived risk of STI/HIV infection
- Examine variations in the above across major strata of this population

This information will meet the needs of a variety of stakeholders, policies and programmes. Specifically it will
• Provide baseline data to NACP for future STI/HIV surveillance
• Establish the need for enhanced STI services in urban areas
• Identify priorities for information and education campaigns for STI/HIV prevention
• Assess the need for strengthened social marketing of condoms in urban areas

**Eligibility Criteria:** The study population is defined as married or single men aged 20-49 years living in major urban centres, who have spent most of the past six months away from their natal or marital homes.

**Geographical Coverage:** The cities to be selected are the ones included in the Federal Bureau of Statistics (FBS) “major urban” stratum. It includes Islamabad, Karachi, Hyderabad, Lahore, Multan, Rawalpindi, Sialkot, Gujranwala, Faisalabad, Sargodha, Quetta, and Peshawar. It is expected that these cities will provide information about men from all over Pakistan. Altogether these 12 cities represent 18% of total population and 57% of the urban population.

**Sample Size:** The proposed sample size of 4,000 would have the power to detect a fall in STI prevalence from 7% to 4.4% if repeated in 5 years time, for instance. The 95% confidence intervals for an estimate of 7% would be 5.7%-8.3% and for an estimate of 3% (e.g. for a specific STI) would be 2.1%-3.9%. The proposed sample size can also be justified in terms of its power to detect behavioural change with statistical confidence.

**Behavioural and biological data:** Information of a social, demographic and behavioural nature will be obtained from home interviews with eligible men by specially trained male lay interviewers. These interviews will be conducted before the biological data collection. Each interview is expected to last about 30-40 minutes on average.

The contents of the questionnaire should cover the indicators recommended by UNAIDS for second-generation HIV surveillance, with a focus on sexual risk behaviour, condom use, STI symptoms and HIV-related knowledge.

Biological specimens will be collected by phlebotomists at the homes of participants or by doctors in temporary clinics. The samples to be collected are blood and urine. It is proposed to assess the prevalence of chlamydia, syphilis and gonorrhoea, the three most important STIs.
7. **Study of High-risk groups**

**Objectives:** Surveys of high risk groups have the following main objectives:

- Measure the prevalence of HIV
- Measure the prevalence of classical STIs
- Measure behaviours that modify the risk of STI/HIV infection
- Assess self-reported STI symptoms and associated treatment-seeking behaviour
- Measure knowledge of STIs and HIV and means of avoiding infection
- Measure perceived risk of STI/HIV infection

The information will meet the need of a variety of stakeholders, policies and programmes. Specifically it will

- Provide baseline data to NACP for future STI/HIV surveillance
- Assess the current state of the HIV epidemic in Pakistan
- Assess the need for enhanced focussed interventions by NACP, NGOs and others
- Identify priorities among different groups for urgent preventive measures
- Identify priority areas for action within each group

**Eligibility Criteria:** Definitions of precise eligibility criteria for each group require an in-depth understanding of the various sub-populations’ demographic and behavioural features. These definitions will have to be developed by the implementing agency during the initial phase of social reconnaissance with the help of NGOs working with specific groups and in consultation with NACP.

**Geographical Coverage:** The vulnerable groups are thought to be widely spread in urban areas of Pakistan. In preparation for expanded HIV surveillance, the NACP is currently conducting a rapid assessment and mapping exercise of these groups in 16 major cities of Pakistan that is likely to be completed by July 2002.

The geographical coverage of the studies of high risk groups should be responsive to epidemiological probabilities. The rapid spread of HIV in vulnerable groups, if and when it occurs, will be geographically focussed, almost certainly in one or more of the major cities. In India, for instance, the course of HIV epidemics has varied widely from city to city.
appropriate response in terms of research and surveillance, therefore, is not to propose a widely dispersed sample (as for the study of the general population) but rather to focus attention on a relatively small number of sites where rapid HIV transmission is most likely to occur. Before the results of NACP’s current social exercise are known, it is premature to designate these priority sites and, of course, they may be different for particular high risk groups. However, the two major cities, Karachi and Lahore, are likely to be selected for most, if not all, groups.

**Sample size:** It is recommended that, in each site, a total of 400 individuals from a vulnerable group should be sampled, except for the truckers, where it is recommended to include 400 drivers and 400 attendants/cleaners. This sample size is rather small for obtaining precise estimates or for detecting change. For instance, a prevalence of 20% (e.g. condom use at last sexual act or infection with any STI) would have 95% confidence intervals of 17% to 23%. Similarly, if a survey of the same size was repeated, a rise in prevalence from 20% to 26% could be established with 95% statistical confidence, but any smaller change could not be established with such certainty.

However pragmatic and scientific reasons exist for proposing a relatively small sample size per study site. With effectively six high risk groups (counting truckers and helpers as separate groups), a study design with one site only for each group would imply an overall sample of 6 x 400 = 2400 subjects. This is a considerable number. Raising the number of study sites to two per group obviously doubles the overall sample size to 4800. Clearly, further raising the number of subjects per site quickly encounters budgetary as well as logistical constraints.

The scientific justification for proposing a relatively small sample per group per site is twofold. First, an exceptionally wide range of biological and behavioural data will be collected. Indicators of the direction of change can thus be measured in a variety of ways (e.g. condom use, number of partners, anal sex, prevalence of STIs, treatment). If data of sound quality are collected, change in these indicators should be mutually consistent and such consistency greatly enhances the interpretative weight that can be placed on results, even if the trend for any one indicator, taken in isolation, is not statistically significant at the 95% confidence level. (It may be noted, at this juncture, that 95% has no 'magic' qualities. Most programmatic decisions are based on evidence that is far less secure.) The second scientific justification is that results from a series of repeated surveys can be averaged in ways (eg., 3-year moving averages) that increase the operational stability and statistical precision of results.
Behavioural and biological data: Information on social, demographic and behavioural characteristics will be obtained from all five of the high-risk groups by specially trained lay interviewers. In addition, detailed information has to be obtained regarding risk and protective factors such as condom use, blood and needle use, drug use and hygiene. This again will be part of a quantitative questionnaire.

More detailed information on certain topics will be obtained through in depth interviews following the survey with a selected sub group of persons from each risk category. The main topics to be covered are:

- Health seeking behaviour: sequence of providers contacted, kind of help sought
- Providers contacted as related to perceptions of and severity of symptoms
- Social and communication networks within and across the high risk groups
- Perceptions of self risk and knowledge of protective and risk behaviours
- Consequences of experiencing RTI/STI symptoms and infections
- Power relations within the groups and how and to the extent to which protective measures can be adopted by group members to protect themselves against infection

It is proposed that trained staff, such as laboratory technicians or health technicians will collect biological samples from males and Hijray, while LHV will collect from female sex workers. The biological samples to be collected are a combination of blood, urine, vaginal swabs and anal swabs depending on the group. The recommendation is to study HIV, chlamydia, syphilis and gonorrhoea in all groups, to study bacterial vaginosis for female sex workers and Hepatitis C for injecting drug users. HIV testing will be done on an anonymous, unlinked basis.
Chapter 1
BACKGROUND

1.1 Demographic and Health Characteristics of Pakistan

Pakistan covers an area of about 796,000 square kilometers and comprises the provinces of Balochistan, North West Frontier (NWFP), Punjab and Sindh and the Federally Administered Tribal Areas (FATA). The current population is over 140 million with a sex ratio of 108 males per 100 females. Punjab is the most densely populated province with 56% of total population, followed by Sindh (23%), NWFP including FATA (16%), Balochistan (5%). Islamabad, the federal capital has less than 1% population. The very uneven distribution of the population across provinces and other administrative territories poses difficulties for sample design that will be discussed later. The overall urban: rural distribution of the population is 33:67 (Population and Housing Census, 1998).

Pakistan is predominantly an agricultural country with about 50% of the work force employed in agricultural occupations. The average per capita income is Rs 24,528. The average rural monthly income per household is about one-third lower than the urban income. The adult literacy rate is 58% and 28% for males and females respectively (UNICEF 2002). The low literacy level has implications for the ethical dimension of research on sensitive issues.

The current growth rate is 2.1% resulting in a net addition of about 8500 persons every day. The estimated doubling time of the population is 33 years. The contraceptive prevalence rate in 2001 was 28%, with 49% women reporting having received prenatal care during last birth (NIPS 2001). This low coverage of antenatal services complicates the development of a sound HIV surveillance system that in many settings is largely based on antenatal clinic attenders. The estimate for Maternal Mortality Ratio (MMR) continues to remain high, ranging between 340-700 per 100,000 live births (UNFPA 2002).
1.2 Sexually Transmitted Infections (including HIV) in Developing Countries and in Pakistan

The World Health Organisation (WHO) considers sexually transmitted infections (STIs) to be a major health problem that carries a heavy health burden. STIs are transmitted from person-to-person through sexual contact and over 30 different infecting organisms can be transmitted in this manner (Population Council, 1999). Beside these, the HIV/AIDS pandemic has spread all over the world, and it is estimated that over forty million people are currently infected, 90% of whom live in developing countries.

The significance of STIs lies not only in morbidity or their potential for asymptomatic transmission, but also in their propensity for causing infection of the upper reproductive tract, i.e. pelvic inflammatory disease or PID (Westrom and Mardh, 1989). Although only 10-20% of STIs result in PID leading to chronic complications, these episodes increase the risk of tubal infertility, ectopic pregnancy, chronic pain, menstrual irregularities or another episode of PID (Brabin, 1993; Elias, 1991). Untreated STIs are also thought to increase the chances of contracting HIV by three to five times (Natraj, 1994; Faundes, 1994). In addition, untreated STIs are thought to account for 10 – 15% of fetal wastage and 30 – 50% of prenatal infections and are linked to cervical cancer and ectopic pregnancy (Abraham et al 1996 cited in Maitra et al 2001). STIs are also associated with primary and secondary infertility, Elias et al [(1993) cited in Jejeebhoy and Koenig (2002)] suggest that 15-40% of infertility in Asia is due to STIs.

Information about STI prevalence in Pakistan is limited and comes largely from poorly designed small-scale studies. Information has mostly been gathered through interviews and only a few studies have carried out serological assessment or other laboratory investigations. The results have shown very high levels of self-reported symptoms in women, both in rural (74%) and urban (63%) areas (MCWAP, 1995; Rozina Khalid, 1999; ADB TA 3387, 2001). The few studies that performed biological testing found substantially lower levels of infection (KRHP, 1997).

STI prevalence is an indicator of the vulnerability of a population to an HIV epidemic because classical STIs and HIV share the same main transmission mode, namely unprotected sexual intercourse. Moreover, as already mentioned, infection with some
STIs increases the risk of HIV transmission. Surveillance of STIs and associated behaviours has been advocated as a proxy for HIV risk, especially in countries where HIV prevalence is low, as in Pakistan (Nanan et al., 2000). The National AIDS Control Programme conducted an STI prevalence study in 2001 on 2400 women (1600 antenatal clinic attendees and 800 gynaecological patients) equally distributed between tertiary care hospital in Islamabad, Karachi, Lahore and Peshawar. Clinical examination revealed 78% women with “pathological” discharge, 29% with pelvic tenderness, 17% with cervical ulcers and 3% with vesicles on genitalia. Laboratory examination confirmed Chlamydia trachomatis in 7.8% (NACP, 2002). Other smaller scale studies of clinic populations have found lower levels of STI infection, for instance 4.3% for Trichomoniasis and 0.2% each for syphilis gonorrhoea and chlamydia (KRHP 1997). Policy makers thus face considerable uncertainty in estimates of the current burden of ill health caused by RTIs/STIs.

In Pakistan, the first HIV case was diagnosed in 1986. While a number of studies of mostly high risk groups have been reported, as in the case of RTI studies more generally, these suffer from being of generally small scale, and subject to a range of biases that have been described elsewhere (Nanan et al., 2000). The WHO/UNAIDS EPI model estimates that currently 70,000 to 80,000 i.e. 0.1% of the adult population is living with HIV/AIDS. The sentinel surveillance system established by the National AIDS Control Program (NACP) reveals a very low overall HIV prevalence – 222 AIDS cases and 1664 HIV cases detected from 3.136 million tests carried out from 1986 to 31 December 2001 (fax from NACP, 2002). The surveillance reports and studies from other hospitals show that the infection has mainly affected men (above 85% cases), heterosexual transmission being the leading contributor to the pool of cases as evident from Table 1.1 (Iqbal and Rehan, 1996 Baqi, 1997; Shah et al, 1999; Akhtar et al, 2001; Memon, 2001).
Table 1.1: Distribution of HIV and AIDS cases by December 2001 as reported by NACP (Absolute Numbers)

<table>
<thead>
<tr>
<th>Modes of Transmission</th>
<th>AIDS</th>
<th>HIV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterosexual</td>
<td>141</td>
<td>675</td>
<td>816</td>
</tr>
<tr>
<td>Men having sex with men</td>
<td>13</td>
<td>36</td>
<td>49</td>
</tr>
<tr>
<td>Bisexual</td>
<td>-</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Blood/blood products</td>
<td>16</td>
<td>280</td>
<td>296</td>
</tr>
<tr>
<td>Injecting drug use</td>
<td>02</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>Mother to child</td>
<td>07</td>
<td>24</td>
<td>31</td>
</tr>
<tr>
<td>Unknown</td>
<td>43</td>
<td>570</td>
<td>613</td>
</tr>
<tr>
<td>Total</td>
<td>222</td>
<td>1664</td>
<td>1886</td>
</tr>
<tr>
<td>Percent</td>
<td>12</td>
<td>88</td>
<td>100</td>
</tr>
</tbody>
</table>

However, low national HIV prevalence provides no justification for complacency. The world has seen rapidly emerging epidemics in several countries that had previously recorded low rates of HIV infection – proof that epidemics can spread quickly and unexpectedly, and that no society is immune. For example, in the largest Muslim country, Indonesia, where recorded infection rates were negligible until very recently there has been a striking increase in HIV infection levels (Data from FHI, Bangkok, 2002).
Currently, Pakistan is placed in a “high-risk/low-prevalence” status as were several other Asian countries in the 1980s and early 1990s (NACP and UNAIDS, 2000). However, in many of these countries the status changed rapidly to high-risk/high-prevalence due to a relaxed response to the epidemic.

Pakistan is classified to be at high potential risk for a number of reasons. There are large concentrations, particularly in the major cities, of individuals with behaviours that make them extremely vulnerable to rapid HIV transmission. These include male and female commercial sex workers, men who have (unprotected) sex with men (MSM), hijras or transvestites, injecting drug users and highly mobile occupational groups, such
as truckers. It is likely that Pakistan’s HIV epidemic will start in one or more of these
groups and then spread to the general population through individuals who have contact
both with high-risk groups and the general population. In epidemiological parlance,
individuals who spread the infection from concentrated high-risk groups to the general
heterosexual population are termed the bridging group (or population). Typically these
are married or unmarried men who are clients of sex workers, or bisexuals, or share
needles with injecting drug users. Rather little is known about the sexual conduct of
men in Pakistan but the available evidence suggests that both pre-marital and extra-
marital sexual contacts – either homosexual or heterosexual – are sufficiently common
to create and sustain a generalised HIV epidemic. (Ahmed et al., 1995; SOCH, 1995,
Agha, 1999; Mirza and Hasnain, 1995; Baqi, et al., 1999; Laghari, et al., 1999; pretest of
the study).

Two longstanding demographic changes have probably served to increase Pakistan’s
vulnerability to the threat of HIV. First, age at first marriage has been rising steadily for
the past half-century and now averages over 26 years for males. Thus the typical male,
following puberty, faces a decade of potential risk and temptation before he marries.
Second, the ever increasing pace of internal and international migration implies that a
growing fraction of unmarried and married men live away from their natal or marital
home. Abundant international evidence shows that such migrant men are more likely to
engage in high risk sexual activities than men living at home.

It may be inferred, therefore, that the country faces a potential threat of a serious HIV
epidemic that may overwhelm the capacity of health services and may further constrain
the fragile economy of Pakistan as the majority of HIV/AIDS cases (currently 71%) are in
the most economically productive years of life i.e. 20-49 years. Pakistan’s present low-
prevalence status presents a special opportunity for averting large numbers of future
infections.

1.3 Reproductive Tract Infections that are Not Transmitted Sexually

Reproductive tract infections (RTIs) that are not, or not primarily, transmitted by sexual
intercourse, can be acquired iatrogenically such as during the insertion of intra-uterine
devices (IUDs) or abortion. They may also arise endogenously due to proliferation of organisms normally present in the body.

International evidence shows that many of the major RTIs, though described in the medical literature for over a century, have only recently achieved recognition as major reproductive health conditions that can lead to major gynaecological morbidities as well as threatening maternal and child well being in both the developed as well as developing countries.

Reproductive tract infections, specifically bacterial vaginosis (BV) and candidiasis, are important in relation to their consequences (clinical and social); hence their related public health burden should be taken into consideration as a significant indicator for their relative priority in health policy decisions. RTIs are not just a clinical or epidemiological problem but encompass larger psychosocial ramifications—mental, economic, political and social factors that are embedded deep in the web of causation (ICWH, 1991). These problems have devastating personal effects and ultimately lead to social ostracism, and compromised economic and social security (Brabin, 1993; Elias, 1991). This has major social and potential marital and economic implications for women in a setting like Pakistan. In addition, women’s routine domestic and other responsibilities, such as cooking and praying, are affected by minor reproductive ill health such as menstrual irregularities or vaginal discharge – these can have a substantial impact on the quality of their daily life.

Among the RTIs, BV has become increasingly recognized as a major public health concern especially in countries where maternal and child health outcomes are poor such as Pakistan (Tinker, 1998). Women with BV have a two-fold risk increase in the risk of pre-term delivery that has serious consequences for child survival. The recognition of BV over the past decade as a major underlying cause of MCH morbidity offers great potential for developing intervention strategies to improve the health of both women and children. If left untreated BV can lead to problems in pregnancy, low birth weight babies, and intrauterine infections (Nugent et al., 1991 Amsel et al., 1983). Evidence now shows that BV is perhaps the most common RTI. Approximately 22% of Asian pregnant women may be affected (Stoll, 1997). In a recent Bangladesh study, the background rate among women attending MCH and family planning clinics was somewhat lower
(<19%) (Hawkes, et al., 1999). There is no related health science literature from Pakistan though based on the latter findings a plausible baseline prevalence of approximately 15% is suggested. As the etiology of BV is not well clarified, especially in developing countries where it is apparently highly prevalent, there is an urgent need for epidemiological and related behavioural studies. Factors related to personal hygiene, sexual practices, reproductive history, and health care could be implicated. While BV may underlie a wide range of non-specific signs and symptoms in some women the concern is particularly relevant to birth outcomes and child survival.

There are no consistent prevalence patterns across countries or even within the same continent to indicate which groups of women are likely to be most in need of services (Westrom and Mardh, 1989). Although women in the general population are considered to be at “low risk” of STIs, the prevalence of non-sexually transmitted RTIs in this group have been reported to be very similar to high-risk populations (ICWH, 1991). This may be due to high frequency of asymptomatic disease and long duration of infectiousness (Brabin, 1993; Tsui, 1997; Wasserheit and Holmes, 1992).

While most RTIs can be clinically managed, treated, and cured, numerous challenges prevent widespread control of these infections. Evidence from the developed countries that would also hold true for Pakistan point to challenges that include patient, provider, and health care system issues. Providers due to their lack of training in this particularly sensitive area, fail to accurately diagnose or provide appropriate treatment. Many women do not understand their conditions and are often likely to accept the symptoms as normal or use inappropriate over the counter medications, some women are also hesitant to discuss vaginal conditions with their providers. The health care system has also failed to recognize the gravity of the problem and has not responded by developing preventive programmes.

1.4 Policies and Programmes

The Ministry of Health (MOH) is well aware of the growing challenge of HIV/AIDS in Pakistan and has an elaborate policy and programme for its prevention and control. The Ministry of Population Welfare has framed a Reproductive Health Policy in light of the
Declaration of the International Conference on Population and Development 1994 (ICPD) held in Cairo that is waiting Federal Cabinet's approval. This policy calls for more active intervention in areas of reproductive and sexual health, including reducing reproductive tract and sexually transmitted infections and improving reproductive health of men and women.

The programme for prevention and control of AIDS was initiated on a small scale in 1987 after the detection of the first case of AIDS in Pakistan, and has gained impetus since 1994, especially under Social Action Programmes I and II. Programme expenditures showed a marked increase from Rs. 25 million in 1997 to Rs. 67 million in 2000. Currently, it is a Federal Programme designated as the National AIDS Prevention and Control Programme (NACP). It has Provincial Implementation Units and a network of surveillance centres. The Programme has been successful in sensitisation of key influential persons and decision makers, raising awareness about AIDS in the general public through mass media communication and improving screening of donors' blood in public sector hospitals. However, it has not been very successful in reaching vulnerable populations (NACP, 2002).

As the number of reported HIV infections and AIDS cases is steadily on the rise in all provinces, the MOH has drafted an Expanded Response Programme of about US$ 40 million with the assistance of the World Bank and other funding agencies to be implemented over next five years. The objective is to prevent HIV from becoming established in vulnerable populations and spreading to the general adult population. Two key aims of the Expanded Response Programme are to achieve:

- Increased prevalence of safe behaviours and improved availability of STI services among vulnerable populations
- Improved knowledge and practice of HIV preventive measures including use of high quality STI services by the general population

The Pakistan Reproductive Health Services Package (RHSP) jointly developed by the MOH and MOPW in 1999 also includes as components: (a) prevention and management of RTIs/STDs and HIV/AIDS, and (b) management of reproductive health related problems and issues in women and men (MOH and MOPW, 1999). The Pakistan
Reproductive Health Project (RHP) to be launched in 2002 with the support of the Asian Development Bank will focus on these service delivery components and will also benefit from the proposed study.

Hence, on part of the Government, there is visible commitment to the ICPD plan of action and also for limiting the spread of an HIV/AIDS epidemic in Pakistan. However, there is lack of data needed for sound programme planning and monitoring of progress. MOH and NACP envisage that the proposed National Study of Reproductive Tract and Sexually Transmitted Infections will provide the benchmarks for monitoring the progress of the Expanded Response Programme.

1.5 Information Needs to Inform and Guide Policies and Programs

The literature review for this study has confirmed that the available data about prevalence of RTIs/STIs including HIV/AIDS and associated behaviours are very limited, sporadic and scanty and are not sufficient to help MOH and MOPW formulate sound policies and programmes. The known facts are that Pakistan is the seventh most populous country in the world with people having remarkable array of risk behaviours, significant levels of RTIs/STIs, a low level of confirmed HIV infection in high risk groups and close proximity to the rapidly accelerating HIV/AIDS epidemic in India. In order to plan effective programmes, MOH requires more representative and reliable data about the current status of RTIs/STIs and risk behaviours in high-risk groups, the general population and the population that plays the bridging role between them. This study will support the government’s efforts by providing data that are reliable, valid and representative and gathered in ways that can be replicated.

1.6 Goal and Objectives of the Study Design phase

In response to the RTI/STI situation in Pakistan and the dearth of relevant information to guide policy and programmes, DFID asked the London School of Hygiene & Tropical Medicine, in partnership with the Population Council and the Aga Khan University, to prepare a detailed proposal for programme-relevant research. This document is the outcome of that request.
References


Fax from NACP dated 2nd April 2002.


Chapter 2

GOAL, OBJECTIVES AND OVERALL STUDY DESIGN

2.1 Goal and Objectives

As stated in the Original Terms of Reference the goal was to design a national survey of RTIs and STIs with outcomes that would have applications in terms of policy development and programme planning. The objectives were stated as follows:

- Obtain estimates of the prevalence of selected RTIs/STIs from samples that can defensibly construed as nationally and provincially representative, using the most reliable epidemiological and laboratory techniques that can practically be applied.

- Gather from all study participants a limited range of information about clinical symptoms, knowledge, beliefs, attitudes, and behaviours related to STDs;

- Examine in greater depth, from sub-samples within the above sampling framework: knowledge, beliefs, attitudes, and behaviours associated with risk practices and with health seeking behaviours; and

- Acquire estimates of prevalence of selected RTIs/STIs and associated behavioural factors from purposive samples of known or suspected high-risk groups.

Though the design team maintained a clear focus on the original Terms of Reference, the importance of other considerations - specifically cost and replicability - was increasingly recognised. The requirement to design a study that would yield provincially representative results (with acceptable precision) was endorsed by experts as highly desirable but the cost implications of this strategy are considerable. The design team
therefore decided to present two main options for the study of the general population, one that maintained the requirement of yielding provincially representative results and one that will yield nationally representative results only.

The second important consideration - replicability - had a major influence on design decisions. A national Survey of RTIs and STIs can be justified as single-round exercise in needs assessment that will permit priority setting. However the utility of results is greatly enhanced if the entire study, or elements of it, can be repeated at regular intervals in order to monitor changes in disease prevalence and associated behaviours and to assess the impact of HIV-prevention and RTI-control programmes. An analogy with the regular series of fertility and family planning surveys conducted in Pakistan is appropriate. These have proved invaluable in assessing progress towards achieving the goals of Pakistan's population policy. A regular series of HIV-related studies will be similarly valuable.

NACP is currently re-designing its HIV/STI surveillance system and it was therefore impossible to specify the links between the National Survey and the future surveillance system. However in its work the Design Team has given priority to replicability of studies. This criterion implies proper and well documented sampling of subjects, an emphasis on scientific rigour and quality control at all stages, and cost-containment.

2.2 Methods and Processes of the Design Phase

The design phase of the study was conducted from July 2001 to April 2002:

It began with the collection and review of relevant literature about the prevalence of RTIs/STIs and relevant behavioural studies in Pakistan, the epidemiology of RTIs and STIs, the available laboratory tests and behaviour research design.

Simultaneously, NGOs and institutions were approached to seek their expression of interest to be facilitative partners in the implementation phase; to ascertain their current activities, target groups and geographical access; and to assess their capacity in terms of human resources and logistics. Initially, preliminary data about the NGOs was collected from different sources such as UNAIDS publications, National and Provincial
AIDS Control Programme Offices and other project reports. This led to the identification of 68 NGOs and institutions that were contacted through correspondence. Major ones were visited. These visits also helped to develop an understanding of the dynamics of community-based interventions, especially about the high risk groups.

The Core Team, consisting of the Principal Investigator Prof. John Cleland, Co-investigators Prof. Franklin White and Dr. Zeba Sathar, Project Manager Dr. Arjumand Faisel, and Deputy Project Coordinator Dr Guy Morineau was scheduled to assemble in mid September with other international project consultants. However, this could not be achieved due to the events that followed 11 September 2001. The design phase suffered from uncertainties for several weeks.

The First Steering Committee was held on 15 October 2001, at which proposed design phase activities and schedule was approved. This was followed by extensive consultation between the three partners of the design phase, with NACP and national experts.

Five workshops were conducted between December and April to use the best available national and international human resources for the development of the design. These included Laboratory Issues Workshop in December 2001, Study Design and Behaviour Issues Workshop in January 2002, Design Review Workshop in March 202 and Ethical Issues Workshop in April 2002. These occasions provided an opportunity for extensive consultations between the team and leading national experts from diverse backgrounds.

The progress of the design phase was regularly reported to the National Steering Committee including the presentation of the first draft. The DFID health specialist in Islamabad was also kept regularly informed about the developments and inputs were welcomed and given due consideration.

The proposed methodologies for studies were pretested in the Karachi, Lahore and Peshawar to assess their feasibility and expected compliance among women for vaginal swab specimens and among men for providing sexual histories, and blood and urine specimens.
The overall process has been interactive, participatory and this report is the outcome of the collaborative efforts of the Design Team, other internal and external consultants, the counterpart Government departments and the donor.

2.3 Three Studies to Meet the Objectives and its Rationale

To meet the objectives in the original Terms of Reference and additional considerations, the Core Design Team in consultation with national experts recommends that high-risk groups, the bridging population and the general population be studied as three distinct population groups in three separate studies.

The rationale for this approach is that Pakistan currently falls under low-level HIV epidemic state as per UNAIDS and WHO classification (i.e. HIV prevalence has not consistently exceeded 5% in any defined sub-population) (AIDS, 2001). In low-level epidemics, infections are largely confined to individuals with high risk behaviour, often among groups such as sex workers, drug injectors and men who have sex with men (MSM). Their behaviour exposes them to especially high risks of acquiring or passing on HIV. The extent to which HIV will spread among these sub-populations depends on the success of interventions to promote safer practices such as condom use and prompt treatment of classical STIs. The choice of high-risk groups to study is more a matter of judgement than science. After much discussion at the first Design Review Workshop, it was decided to focus attention on the following groups: female and male sex workers; hijras; injecting drug users; and truckers.

To limit the spread of HIV, it is imperative not only to identify high risk groups and their behaviours likely to spread HIV, but also to identify the bridging population and their behaviours that have the potential to carry HIV infection from high risk populations into the general population. This information could then be used to design appropriate interventions aimed at a wider spectrum of society.

Whereas high-risk groups are easy to define and distinguish - in principle if not in practice - there can be no easily distinguishable bridging population. Indeed it is more appropriate to think in terms of bridging behaviours (i.e. pathways along which HIV and other STIs may spread from high-risk groups to the general population) rather than a
discrete population. A consideration of bridging behaviours, such as use of sex workers and homosexual contacts by married persons, suggests that men rather than women are implicated.

To study bridging behaviours by men, one option is to draw a representative sample of all adult men. Though this strategy is the safest because it makes no assumptions about the distribution of risk behaviour or infection, it would not be cost-effective because the majority of the sample would have no infection and report no relevant behaviours. Another strategy would be to study a mosaic of "occupational" groups such as factory workers, government servants, armed forces, students etc. This option is feasible but was rejected on the grounds that (a) it might be difficult to replicate; (b) only a small number of occupations could be studied within the bounds of a reasonable overall sample size; (c) the majority of adult males in Pakistan would be omitted because they belong to no easily identifiable and accessible occupational grouping.

Our final recommendation is to study a stratum of men who, on the basis of common-sense expectations and scientific evidence from other countries, are particularly likely to engage in bridging behaviours. This stratum is defined as married or single urban migrants living away from their marital or natal homes and thus exposed to the sexual opportunities of urban life without the constraints of close family members. It is not possible to estimate the size of this stratum but consideration of urban and rural sex-ratios suggests that it constitutes at any one time a sizeable fraction of all adult men in Pakistan, ranging from about 15% to 20%. We thus propose and have designed a study of these "men on the move" or MOMS that will be cost-effective, and replicable.

The third population to be studied is the general (or low risk) population. As noted earlier, the original Terms of Reference clearly call for an assessment of disease burden in the general population. This component of the overall study will provide much needed information on the prevalence of non-sexually transmitted RTIs (together with coping strategies and treatment patterns) in women. Until reliable evidence on these infections is obtained, sensible priorities in the development of integrated reproductive health services cannot be set. The general population survey also provides an opportunity to establish whether or not classical STIs are sufficiently prevalent to warrant the strengthening of service provision (e.g. routine syphilis testing of pregnant women) or
educational activities. As mentioned earlier, past studies of STIs in the general population are few in number and have given very different indications of the magnitude of the problem. This uncertainty will persist until results are obtained from a scientifically rigorous survey on a representative sample.

The general, or low risk, population includes, of course, both men and women. The inclusion of women is indispensable for estimation of RTI prevalence. The inclusion of men, though desirable, was not considered to be sufficiently important to justify the implicit near-doubling of costs. Because the infectivity of classical STIs is high, levels of infection in married women are a sound indicator of levels of infection in their husbands and thus very little is lost by excluding men in terms of estimating disease prevalence.

These considerations led the Design Team to propose a study of currently or formerly married women as the most cost-effective approximation to the general population. The exclusion of unmarried women is justified on the ground that STIs will be very rare, together with severe anticipated difficulties of obtaining compliance to intrusive biological data collection.

In summary, it is proposed that the National Study be composed of three distinct components: high-risk groups, bridging population (or behaviours) composed of MOMS, and the general population as represented by married women. This proposal has the great practical advantage of allowing different research groups to be involved in specific components, though it is essential that all component studies aspire to the same high standards of execution and use identical diagnostic procedures for the detection of infections.

2.4 Principles Underlying the Proposed Design

2.4.1 Policy and Programme Relevance

In the recent past, the Government of Pakistan has recognized the importance of RTIs and STIs in many of its new initiatives such as the formulation of its Reproductive Health and Population policies. These infections are adding to the burden of disease, therefore
becoming more central to health concerns as well as leading to dire economic and social consequences for certain sub-populations. This study has direct relevance for policies such as the National Plan for Action of the Ministry of Women Development and the Poverty Reduction Strategy of the Ministry of Finance due to the close link between RTI/STIs and gender related issues, such as autonomy of women, communication between spousal partners and poverty of households and individuals.

The government's medium term health strategy has a sharp focus on preventive and control programmes especially in the area of communicable and infectious diseases, reproductive health, child health, and nutrient deficiencies. It has especially highlighted the importance of additional programs including adoption of DOTS strategy against TB; RBM approach in combating malaria; measures for preventing the spread of Hepatitis B, HIV and AIDS through immunization and public health campaigns. The importance of “raising the curtain on STIs” was one of the highlights of the Secretary Health’s presentation to the consortium of donors during the Human Development Forum in January 2002.

The jointly developed Reproductive Health Package of the two Ministries of Health and Population Welfare developed in 2000 calls for service delivery institutions to train and retrain staff to provide various levels of RTI/STI services according to their levels of competence.

This study will assist in the implementation of these policies and programmes because its findings will:

- Provide baseline information for evaluation of intervention strategies to reduce RII/STIs prevalence
- Assess the relative importance of specific RTI and STIs in the context of Pakistan, in terms of morbidity, treatment costs, loss of economic productivity etc.
- Assess the levels of prevalence of RTIs and STIs among men and women and sub groups according to economic status and geographic location in order to apportion resources more appropriately and judiciously

- 20 -
- Document the type and degree of symptoms reported by women and men related to RTIs and STIs so that providers may be able to assess and accordingly manage the treatment of these infections
- Inform programme personnel about health-seeking behaviour (which is influenced by facilitating and inhibiting factors) among various risk groups and therefore assist in designing appropriate services for different cadres of providers
- Develop capacities in the laboratories and among select service providers (in locations where the survey is to take place) to deal with RTI/STI diagnosis and treatment
- Contribute towards the development of second-generation surveillance programs being planned for in the near future.
- Assist in developing culturally sensitive and effective RTI/STI awareness campaigns

As intimated above, each of the three proposed component studies will provide results and will be implemented through processes that are directly relevant to policies and programmes of the Ministry of Health (MOH) and Ministry of Population Welfare (MOPW). Table 2.1 summarises the relevance of each study to policies and programmes of these ministries and of other stakeholders.

**Table 2.1: Relevance of Each Study to the Policies and Programmes of MOH and MOPW**

<table>
<thead>
<tr>
<th>Policy and Programmes of MOH and MOPW</th>
<th>Study of General Population</th>
<th>Study of Bridging Population</th>
<th>Study of High Risk Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capacity building for health policy monitoring</td>
<td>Steering Committee formed to guide implementation of these studies will provide the forum for policy monitoring. In addition, it could play an important role in strengthening programmes related to reproductive health, sexual health and HIV control for both women and men in Pakistan.</td>
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<tr>
<td>Develop a multisectoral approach to addressing the health and population problem involving different ministries and departments of the government</td>
<td>The results will have far reaching implications, and will be beneficial for MOH, MOPW, Ministry of Finance. They are likely to lead to a wider collaboration among above mentioned ministries and program and also Ministry of Education and Ministry of Information and Media Development</td>
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<tr>
<td>Address inadequacies in primary/secondary health care services</td>
<td>Protocols developed for training of doctors and female paramedics for treating RTIs/STIs will be useful for public sector doctors and paramedics.</td>
<td>Ensure equity in terms of access and affordability of services, especially for the poorest and most vulnerable segments of the population.</td>
<td>Women of all ethnic groups and of all income levels will have equal chance to be selected as respondents and also equal opportunity to receive treatment for defined illnesses without charges</td>
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<tr>
<td>Ensure equity in terms of access and affordability of services, especially for the poorest and most vulnerable segments of the population.</td>
<td>Promote gender equity in the health sector</td>
<td>Gender inequities in the household and couple decisions regarding health care and access to health care to be assessed</td>
<td>Men's sexual health to be addressed in urban areas on a large scale for the first time</td>
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<tr>
<td>Actively support, promote and recognize the role of the non-governmental sector</td>
<td>Gender inequities in the household and couple decisions regarding health care and access to health care to be assessed</td>
<td>NGO and private sector role in providing RTI services and awareness promotion to be better informed</td>
<td>NGO and private sector role in providing STI services, social marketing of condoms and IEC to be better informed</td>
</tr>
<tr>
<td>Conduct advocacy to create an enabling environment</td>
<td>REI-related treatment seeking constraints to be highlighted and a more enabling environment at home and in the health sector</td>
<td>Results will help to sensitise key policy and decision makers and opinion leaders</td>
<td>Results will help to sensitise key policy and decision makers and opinion leaders</td>
</tr>
<tr>
<td>Reduce the prevalence of communicable diseases</td>
<td>Results will help MOH and MOPW to launch specific programmes for reducing RTIs/STIs in general population.</td>
<td>Results will help MOH and MOPW to launch specific programmes for reducing RTIs/STIs in general population.</td>
<td>Results will help NACP to plan STI control programme in urban areas</td>
</tr>
<tr>
<td>Enhance availability, quality and range of RH services to meet the minimum standard. Improve and expand management of RTI/STI cases</td>
<td>Will provide data for treatment needs and help to launch training programs for health care providers</td>
<td>Will provide data for treatment needs and help to launch training programmes for the health care</td>
<td>Will provide data for treatment needs and help to launch training programmes for the health care</td>
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<tr>
<td>Initiative</td>
<td>Results</td>
<td>Survey and services are being planned with sound ethical considerations of confidentiality, privacy and rights of the clients.</td>
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<tr>
<td>Heighten public awareness about RH and HIV/AIDS and create effective demand for information</td>
<td>Results will help to develop focused IEC campaigns for the general population</td>
<td>Behavioural information will help to develop specific awareness campaigns</td>
<td></td>
</tr>
<tr>
<td>Ensure the dissemination of knowledge and provision of services respecting all human rights including the right to decide and the right to choose.</td>
<td>Survey and services are being planned with sound ethical considerations of confidentiality, privacy and rights of the clients.</td>
<td>Behavioural information will help to develop specific awareness campaigns</td>
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</tr>
<tr>
<td>Support Expanded Response to HIV/AIDS</td>
<td>Will provide baseline about prevalence of RTIs/STIs. STIs will serve as a marker for risk behaviours</td>
<td>Will provide data about current behaviours and help to develop BCC strategy for general adult population</td>
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<tr>
<td>Enhance behaviour change communication (BCC) for issues related to STIs, including HIV</td>
<td>Will provide data about current behaviours and help to streamline BCC strategy for general adult population</td>
<td>Will provide data about current behaviours and help to develop BCC strategy for this sub-population</td>
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<tr>
<td>Initiate Social Marketing of condoms for disease prevention</td>
<td>Ability of women to use condoms with husbands for protection to be assessed and promoted</td>
<td>Concerned organisations will use the study results for effective social marketing</td>
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<tr>
<td>Reduce Vulnerability of Migrant Labour</td>
<td>Women to be altered to risks attached to unprotected sex with husbands working away from home</td>
<td>Concerned organisations will use the study results for effective social marketing</td>
<td></td>
</tr>
<tr>
<td>Expand Surveillance and Research</td>
<td>One option will be amenable to replication and surveillance. Will provide national data</td>
<td>Will provide rigorous data that could be used as benchmark for surveillance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Will provide rigorous data that could be used as benchmark for surveillance</td>
<td>Will provide rigorous data that could be used as benchmark for surveillance</td>
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<td></td>
<td>Laboratory component of the study will develop QA system. This could be used as a guide for QA system for blood transfusion in designated labs.</td>
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<tr>
<td><strong>Capacity building</strong></td>
<td>Will enhance capacity of implementing institutions, referral and reference laboratories.</td>
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<tr>
<td><strong>Implementation of Quality Assurance System for blood transfusion</strong></td>
<td>Will enhance capacity of implementing institutions, referral and reference laboratories and participating NGOs.</td>
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<tr>
<td><strong>Ethics</strong></td>
<td>The emphasis on ethical dimensions in the design phase should stimulate the development of systematic ethical reviews systems for future research. The Secretary and DG Health has shown immense interest in the process and have decided to create a National Research Ethics Committee.</td>
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### 2.4.2 Scientific Rigour and Value for Money

In addition to policy and programme relevance, the main principles underlying the proposed study design include scientific rigour and value for money. The need for scientific rigour requires particular emphasis. It is the view of the Design Team that any study that does not aspire to meet the best international standards represents a poor investment because the results will be open to doubt and challenge. Hitherto, most HIV-related research in Pakistan has been well below best international standards. Samples have been small and unrepresentative in nature and little attempt at quality assurance of laboratory results has been made. The net result is that the scientific evidence base available to NACP and other organisations with a mandate to improve reproductive and sexual health is incomplete, fragmentary and unreliable. It is essential, in our view, that the National Study yields findings of the highest possible quality that will command respect from all stakeholders and set the standard for future work in this area.

The need for scientific rigour is partly a matter of putting in place systems of supervision and quality control that do not add greatly to costs. Other aspects of achieving rigour, however, do have financial implications. Samples have to be properly drawn to ensure representatively and have to be sufficiently large to monitor changes with statistical confidence. Laboratory tests need to make use of recent technological advances that
improve sensitivity and specificity and that reduce the possibility of laboratory and human errors. Quality control and assurance issues are discussed in more detail in the next section. At the same time, the Design Team has kept in mind that funds for the study are not unlimited and that donors have to be convinced that their investment will be cost-effective, when judged against alternative investments. The need for cost-containment has been kept in mind, leading, for instance, to suggest different options and to restrict sample sizes to the minimum required and similarly to restrict laboratory tests to priority infections.

2.4.3 Quality Control and Assurance

The creation of quality in all aspects of study implementation, its maintenance and assurance and its verification have been a foremost consideration during the design phase. It is not difficult to identify, though invidious to mention, complex and ambitious studies in Pakistan (such as the National RTI/STI study will be), that have failed to fulfil their potential because of defective implementation. Ultimately, the quality of the study will be largely determined by the implementing agencies. At the design phase, however, it is possible to recommend procedures, that if followed systematically, will ensure that the findings are of high quality.

The recommended quality control steps are specified in detail for each study. In summary they include the following essential components:

- Standardised training of behavioural interviewers, field laboratory staff and laboratory staff
- Careful preparation pre-testing in the field of all questionnaires and biomedical protocols
- Constant supervision of field teams by a team leader or co-ordinator
- Higher-level checks that field teams are rigorously adhering to specified procedures by regional, provincial or city co-ordinators and similar checking of the work of participating laboratories by a reference laboratory
- Careful pre-planning of the data processing phase and the application of data editing procedures
- Checking of laboratory results on sub-samples of specimens by a pre-designated reference laboratory in Pakistan
• Checking of selected laboratory results on sub-samples of particular types of testing that utilise advanced technologies, by an international laboratory.

2.4.4 Local Research Capability and Capacity Strengthening

One of the main priorities in the Design Phase was to assess local capacity for undertaking the National Study and to identify training or other capacity strengthening that would be needed for successful execution of the proposed study design. The underlying assumption was that all components of the National Study should be conducted primarily (though not necessarily exclusively) by institutions based in Pakistan. These issues were discussed extensively at all Workshops and explored further by site visits to 13 laboratories in four provincial centres and the federal capital.

Pakistan has a long and successful tradition of conducting large-scale nationally representative interview-surveys on demographic, social and economic topics. Among institutions with the greatest experience are the Federal Bureau of Statistics (FBS), National Institute of Population Studies (NIPS), the Population Council and the Pakistan Institute for Development Studies (PIDE). The mechanics of conducting such surveys (sample design, instrument design, training, field logistics) thus pose no particular problems and require no special efforts at capacity strengthening. When problems have arisen in the past, they have usually concerned data entry, data processing and analysis. Relatively few research institutions have a good record of fast and efficient processing of large survey data sets, and high quality analytical skills, as elsewhere, are in short supply. The net consequence is that publications of results are delayed or never appear. The problems with data processing reflect poor planning, organisation and management rather than lack of technical expertise. The issue here is that contractors for implementation of the study need to convince sponsors that they can handle the considerable task of data entry, editing, linking and analysis.

The behavioural component of the proposed studies goes beyond survey research with structured questionnaires. For the high risk groups, non-survey methods, such as social mapping, focus group discussions, key informant interviews and unstructured intensive interviews, have been proposed. The necessary skills for successful application of these social science techniques are in very short supply in Pakistan. Full and rigorous analysis of qualitative data (which may use computer-assisted methods) is a particular
weakness. Accordingly, in the studies of the high risk groups, we have budgeted £5000 to allow for international training.

In terms of large scale field collection of biological data, Pakistan also possesses highly relevant recent experience in the form of the National Health Survey and the National Nutrition Survey, both of which were more ambitious in scope than the proposed STI/RTI study. Expertise thus exists in the country with the practicalities of collecting and storing biological specimens in the field, of maintaining a cold chain and of transport to laboratories. The main emphasis on these aspects of the study has to be on rigorous and systematic application of standard procedures.

The need for capacity strengthening of laboratories themselves depends very largely on the actual selection of laboratories proposed by implementers. Nearly all the tests proposed for the study are already routinely performed by several laboratories, in both private and public sectors. The performance of these particular tests is therefore a strong criterion for selection of laboratories for the STI/RTI study, with obvious advantages. A number of laboratories (e.g. NIH, AKU, PIMS and AFIP) have Quality Assurance (QA) mechanisms in place and NACP has its own guidelines for internal and external QA. In addition, the WHO has conducted a series of workshops on QA which included information on standard operating procedures (SOPS).

The broad verdicts reached following the site visits to laboratories are that:

- SOPS need to be developed for each test and associated training is required for all participating laboratories.
- Specific training is required in the use of Nugent scoring criteria for diagnosis of bacterial vaginosis.
- All participating laboratories should be required to meet performance standards prior to commencement of study. For some tests, well established international methods of proficiency testing exist and these should be used.
- A reference laboratory be proposed for each test.

Subject to these pre-requisites, the Design Team is confident that at least one laboratory can be located in each of the four provinces to participate in the study at the standard
required, at least for some organisms. Nonetheless, if any laboratory is proposed by an implementer to perform tests with which it is not currently familiar, provision will have to be made for related capacity strengthening in order to achieve proficiency and meet performance standards. In the event that such capacity strengthening may be required for any given laboratory, this will have budget implications, but could be viewed as an investment as long as the capacity so developed is not simply utilised by the study, but will have some ongoing, sustainable value. More fundamentally however, participation by laboratories that currently have no QA mechanisms in place, will gain capacity in terms of enhanced quality improvement procedures as a result of the proficiency testing activities as already noted.

2.4.5 Public-Private partnerships
The proposed study offers considerable potential for strengthening public-private partnerships, especially in relation to health science and policy development. The options analysis itself, reflected by this report, illustrates a range of public and private sector consultation and participation. The underlying reality is that the public sector in Pakistan delivers only about 20% of the health service, and that health comprises significantly less than 1% of all government expenditures, much lower than most countries. As a result, capacity development for the health of Pakistanis depends to a greater extent overall on private sector initiatives. While both public and private sectors require strengthening, this process needs to be viewed as complementary and collaborative, not as competitive. The proposed study offers an opportunity to develop a new level of partnership between public and private sectors especially in the area of laboratory capacity development: building new capacity where justifiable and sustainable, combining capacities where these are already complementary, and utilizing existing capacities in new roles such as the proposed designation of reference laboratories. The same principle applies to the development of behavioural sciences, epidemiology and data management capacities in Pakistan. Beyond these more technical needs, further engagement of private sector organizations in public policy development should be encouraged. There is a great opportunity for this principle to be demonstrated through the study of reproductive and sexually transmitted infections.
2.4.6 Link to Future Surveillance Systems and Replicability

As mentioned earlier, NACP is currently re-designing its HIV/STI surveillance system and it was impossible therefore to demonstrate in detail how the National Study might be linked to ongoing surveillance. The importance of this link and the related issue of replicability cannot be overemphasised because the value of the National Study will be greatly enhanced if it is seen as baseline for future monitoring of HIV and STI infections and their associated behaviours. Furthermore, in the context of survey and surveillance development in settings with low HIV prevalence, capturing trends in behavioural risk factors and other STIs, has been advocated with particular reference to Pakistan (Nanan et al., 2000).

The frequency of repetition of study components is of course a matter for NACP and other stakeholders. Moreover firm decisions should not be made in advance of the key results. Higher than expected levels of risk or infection among, for instance, the general population or MOMS would argue for more frequent repetition. Lower levels would argue the opposite. Similarly results for the high-risk groups should permit prioritisation in terms of their vulnerability to rapid spread of HIV, with more intensive monitoring among the most vulnerable.

Nevertheless, drawing on international experience and recommendations, it is possible to suggest in broad outline an appropriate strategy for repetition. Infection and behaviour in high-risk groups need to be monitored rather closely (ie., more frequently), both to assess the impact of focussed interventions and also to serve as an early warning system of an impending HIV epidemic. Repeat surveys every year or every two years is appropriate. For the MOMS, less frequent monitoring is indicated: a repeat survey every five years would be a sensible strategy at this stage.

The proposed study of the general, or low risk, population is the most expensive single component of the National Study, particularly the options that provide provincial-level results. The need for repetition hinges on whether or not studies of clinic populations (such as antenatal clinic attenders) can be used as a reasonable substitute for representative population-based surveys. This is the internationally recommended strategy for HIV-surveillance systems and is certainly a much cheaper option than population-based surveys. The limitation in the context of Pakistan is the rather low,
albeit increasing, uptake of antenatal services, particularly in rural areas. The results of
the proposed study of the general population will allow comparison of STI/RTI
prevalence of women who have recently used antenatal services and those who have
not. This information will serve as an invaluable guide for future HIV/STI surveillance in
Pakistan. If infection levels between the two categories of women are similar, then
confidence in clinic-based surveillance will be enhanced. If they are dissimilar, the case
for repetition of population-based surveys is strengthened.

2.4.7 Ethical Principles
The complex ethical issues surrounding community-based studies of RTIs/STIs were
discussed by experts at a one-day workshop. While the general principles underlying
the ethics of medical research are well established, practical applications in field studies
vary widely, as do the views of ethical review committees. Much of the detail is a matter
of judgement, based on knowledge of local circumstances. Recommendations
concerning the key issues - informed consent, confidentiality and privacy and treatment
of subjects - are described below.

Informed Consent: A step-wise approach to ensuring informed consent is
recommended. Information needs to be conveyed to the selected communities in
advance of the main data collection activities; informed consent from individual subjects
for the behavioural interview is needed; and finally, informed consent is required for the
biological data collection.

Informing communities in advance about the nature and scope of the study is particularly
important for close-knit communities, such as rural clusters in the survey of the general
population, and for high-risk groups such as hijras and brothel-based sex workers. In
the general population survey, and in the study of urban migrant men, advance
information can be given to communities at the time of sample preparation. For the
studies of high-risk groups it should be performed during the preliminary phase of social
reconnaissance.

Behavioural interviews with selected subjects will be conducted by trained staff, in
conditions of privacy, usually at the person’s dwelling. Interviewers will be required to
describe in outline the contents of the interview, the purpose of the study and the
approximate length of the interview. The confidentiality of answers will be stressed and
the voluntary nature of participation will be emphasised. The implementing agency
should be required to develop an informed consent protocol for use prior to behavioural interviews. Clarity and simplicity are key elements. It is recommended that verbal consent be accepted.

A similar but more lengthy and formalised informed consent procedure is required prior to biological data collection. Again the implementing agency should be required to develop a protocol that clearly describes the biomedical steps, their purpose, the nature of frontline treatment and notification of laboratory results. In the case of the general population survey, it is recommended that women be informed about the biological component at least one day in advance so that they have the opportunity to consult family members, including husbands. A male member of the team in this study will be available to talk to husbands as and when desired. For the study of men and high risk groups, such advance notice is considered unnecessary and impractical.

It is proposed that participants be given the choice between the following four methods of endorsing their consent to bio-medical procedures: consent with signature, consent by fingerprint, oral consent with a witness or oral consent recorded by audiotape. Witnesses should not be members of the research team but they may be other participants. They need not be literate.

The special case of subjects under the legal age of majority (18 years) was discussed at the Ethics Workshop. This situation will only arise in the studies of high risk groups. National guidelines on informed consent for minors vary widely and no internationally recommended guidelines exist. Participants at the workshop and members of the design team thought that a differential informed consent procedure based on chronological age was unhelpful. Minors engaged, for instance, in trucking, sex work or injecting drug use have clearly entered the adult world (either voluntarily or involuntarily) and should be deemed capable of giving their own informed consent without recourse to parents, guardians or other gatekeepers.

**Privacy and Confidentiality:** The behavioural interviews should be conducted in privacy, out of the hearing of other people with the exception of small children. When these conditions cannot be obtained, interviewers will offer an alternative venue or time.
At the temporary clinics, adequate auditory and visual privacy should be available, particularly for collection of specimens, syndromic management and counselling.

Confidentiality will be maintained by the use of personal identification numbers (PINS). These will be issued to subjects following the completion of the behavioural interviews and used as the means of identification for bio-medical data collection. The master list of names, addresses and matching PINS will be collected at the end of each day's work and kept under lock and key by the team supervisor. Similarly, the consent forms which may also contain names and PINS, will be collected and stored securely. Results from laboratory tests will also be identified only via PINS and therefore can only be released to participants in possession of their PINS. It is essential the PINS be durable, unalterable and sufficiently large in minimise their loss.

**Medical Care of Subjects:** Treatment of subjects found to be infected by means of laboratory tests is known to be unsatisfactory. Active case and contact tracing in the case of STIs is extremely stigmatising because it inevitably singles out infected individuals and is ethically unacceptable for this reason in a study of this nature. A more passive mode of treatment whereby individuals are requested to collect laboratory results and receive treatment from a pre-determined local health facility or private medical practitioner is preferable but also beset with problems. In view of the delay of several weeks between data collection and availability of laboratory results, it can be anticipated that many will not remember or bother to seek them out. Moreover, it is probable that the majority who do make the effort to obtain results will receive negative reports. This represents a large aggregate expenditure by subjects in time and travel costs for a small return. A further complication for STI positive cases is partner notification and treatment, without which treatment of the infected individual is unlikely to be effective. Partner notification has to be left to the discretion of subjects. To do otherwise might place them (particularly wives) in physical jeopardy. Cases with STIs should certainly be instructed to inform partners and advised about condom use. However, it remains uncertain how many with STIs will inform their partners and persuade them to take antibiotics.

For these reasons, community-based studies of STIs increasingly rely on frontline treatment at time of data collection. Some do not feed-back laboratory results at all and have received ethical clearance in this regard. However, participants at the Ethics
Workshop regarded this strategy as unacceptable because it would leave some individuals with potentially serious but asymptomatic infections, such as chlamydia, with no chance of notification and treatment.

The recommended treatment protocol for all components of the study is to maximise front line treatment at time of data collection but nevertheless develop a notification strategy for subjects found to be infected by laboratory tests and NOT already treated approximately. Front line treatment will be performed by paramedics or medical doctors at time of biological data collection, using the recently revised WHO guidelines for syndromic management. This will result in very considerable over treatment of uninfected cases but the cost will not be high and is justified both by ethical considerations and by its beneficial effect on participation and community relations. In addition it is proposed to use a rapid test for diagnosis of active syphilis (results available within an hour or so) and to treat infected cases on the spot.

In addition to the syndromic management of RTIs/STIs (including syphilis), paramedical and medical staff will also offer free treatment of other acute conditions. Cases of chronic illness will be referred to a pre-selected public sector health facility (or to a private or NGO facility in some cases). Fees for referral and treatment of chronic conditions will not be covered by the study.

Feedback of laboratory tests requires careful identification of a medical facility or practitioner within, or close by, each selected PSU or research site. Selected staff will be briefed about the study and provided with standard protocols for treatment of RTIs/STIs. Where no competent facility or practitioner can be located within a reasonable distance (e.g. 5 kms) of the primary sampling unit (PSU), the research team will need to make special provision for feedback of laboratory results.

Subjects will be told where they can obtain laboratory results and a date after which they will be available. This date should make generous provision for logistical delays in laboratory processing and communication of results in order to minimise wasted visits. As stated earlier, results will be identified only by PINS and will be released only to subjects in possession of their PINS.

**Medical Care of Community Members:** The treatment of members of selected communities who are not themselves selected as subjects presents a severe dilemma
for community-based health research. A generous approach may result in a deluge of presenting cases that is impossible to handle. An excessively restrictive approach, on the other hand, may jeopardise good relations with the community. No ideal solution exists. Our recommended approach is entirely pragmatic. Non-selected individuals should not be encouraged to seek treatment from the data collection teams nor should they be abruptly dismissed if and when they do seek advice or treatment. Medical care of acute cases should be given within the constraints of staff availability and budgeting provision has been made for such treatment.

**HIV Testing:** HIV testing will be performed on high risk groups. Fully informed consent will be required but testing will be unlinked and anonymous.

**National Ethics Review Panel:** Each component of the National Study should be subject to ethical review. Some institutions in Pakistan have their own ethical review boards but no national board exists. It is strongly recommended that such a national board be constituted and involved in the review of the STI/RTI study. Nonetheless, it is a recognized norm internationally that all institutions engaged in research should have their own ethical review processes in place, and are normally required to obtain approval from their own boards, regardless of approval from external boards.

### 2.5 Dissemination of Results

The dissemination strategy should address the diverse needs of different audiences. The latter include federal policy makers and managers, provincial managers, NGOs, donors, the private sector, the general public, the Pakistan and international research community.

Specifically it is recommended that the implementing agency be required to produce key descriptive results, together with information on compliance and any other caveats regarding data quality, within eight weeks of the completion of data entry, editing and cleaning. These key results will comprise the prevalence of specific infections (with 95% confidence intervals) and of key behavioural indicators, disaggregated by selected background characteristics of the sample. Illustrations are given in relation to each study in later sections. A short text of 10-20 pages should accompany the preliminary statistical results, outlining methods, interpreting results and spelling out major implications.
Dissemination workshops should be planned for Islamabad and (for federal staff and donors in particular) and should be repeated in Lahore, Karachi, Peshawar and Quetta for provincial audiences. About 100 copies of the preliminary report should be mailed to a pre-prepared list of appropriate institutions. To meet the needs of the lay public, assistance should be given to selected journalists for dissemination in print media.

Some six months after release of the preliminary findings, the implementing agencies should be required to present an analytic report of some 30-50 pages of text together with detailed results. The main emphasis in this report will be the exploration of relationships, for instance between socio-economic factors and behaviour, between behaviour and biological evidence of infection, between self-reported symptoms of infection and treatment seeking. This will require both bivariate and multivariate techniques of analysis. In the case of reports on high risk groups, qualitative as well as numerical evidence should be presented.

It is suggested that the issue of the analytical report should be accompanied by a one-day scientific symposium with nationwide participation of up to 200 scientists, policymakers and programme managers. If possible, this report should be accessible on a local website and about 50 copies should be sent to appropriate institutions. To meet the needs of the international scientific community, the implementing agency should be encouraged to submit articles to peer-reviewed journals.

### 2.6 Data Ownership, Access and Storage

We recommend that best practice in international medical research be followed in regard to data ownership and access. In essence, the scientific team who collect and analyse data should be allowed exclusive access to them for a relatively short period of time but that, thereafter, the data should be made freely available to bona fide research groups. In practical terms, this strategy would allow the implementing team exclusive access until publication of the analytical report, which is likely to be about 12 months following completion of fieldwork. Following the release of the report, ownership of the data should be vested in another organisation such as NACP or in a committee who would have a mandate to release the data to all genuine research organisations and departments in Pakistan (and perhaps to selected institutions outside of Pakistan). An alternative more liberal approach would be to allow automatic access to everyone, as was the case of the 1991 Pakistan Demographic and Health Survey. This alternative
may appear hazardous because of the possibility of irresponsible or malign use of the data, though international experience suggests that such misuse is rare.

Use of the study data sets by others requires that the implementing agency prepares well documented files containing both behavioural and linked biological data, together with weighting factors. All publications emerging from the study must appropriately acknowledge the implementing agency, the funding agency and the role of the Government of Pakistan.

Laboratory techniques for diagnosis of STIs/RTIs are changing rapidly. Moreover the specimens collected in the study have potential uses beyond those proposed. The study team strongly recommends that all biological specimens be stored at a single laboratory for a minimum of five years. Access to the specimens for re-analysis or new analysis should be controlled by an organisation or committee, perhaps the same one that controls access to the electronic data. If testing and analyses are proposed that go beyond the scope of the original ethical approvals, new approvals for these activities must be sought in advance at that time.

2.7 Partners and Stakeholders for Implementation

Many institutions and agencies working at national level have shown interest in the undertaking of the proposed study. Information about some of these organisations is presented in an annexe as an illustration of the interest and capacities. Recruitment should be through a transparent bidding process. It is expected that organisations will form partnerships to bring together relevant skills for executing these studies. These organisations will have to define very clear management structures and responsibilities of each partner.

One advantage of the proposed study design is that it comprises at least three distinct studies and thereby permits different agencies to bid for specific components. However, it is essential that the research be of the same high standard across all studies. This is particularly true of the laboratory component.
It is suggested that the selection is done in collaboration with NACP and it is mandated that the implementing agency carries out the study as designed in close consultation with NACP, the counterpart Government department for RTI/STI and HIV control programme. For effective utilisation of the study results, the NACP should closely involve all PACPs at every important level.

NACP should also involve other stakeholders in the public sector such as Ministry of Education, Ministry of Information and Media Development, Ministry of Labour, MoPW, leading NGOs and medical professional bodies such as Pakistan Medical Association, College of Family Physicians. These could be brought into a network as members of steering committee.

Funding agencies involved in supporting RTI/STI and HIV control programs such as the World Bank, CIDA, UNFPA should also be the members of the steering committee to avoid duplication of efforts and to supplement technical and financial assistance.
References


Chapter 3

GENERAL POPULATION SURVEY: RESEARCH STRATEGY AND METHODS

3.1 Restatement of Objectives and Programmatic Relevance

The general population survey has the following main objectives:

- Measure the prevalence of key RTIs and STIs
- Assess self-reported symptoms of RTIs/STIs, associated treatment-seeking behaviour, and the subjective burden of such symptoms in women
- Measure knowledge of STIs, including HIV, and means of avoiding infection
- Determine risk and protective behaviours
- Examine variations in disease prevalence, self-reported symptoms, treatment seeking and knowledge across major strata of the population

This information will meet the needs of a variety of stakeholders, policies and programmes. Specifically it will:

- Provide baseline data to NACP for future STI/HIV surveillance
- Inform decisions on the nature of future surveillance, particularly on the key issue of whether facility-based surveillance (e.g. ante-natal clinic attenders) is adequate.
- Allow MOH, MPW and other providers of health and family planning services in NGO and private-sectors to assess the need for improve RTI/STI information and services, to assess the need for awareness campaigns and also to design protocols to enable health providers to better manage these conditions.

The study will provide information on RTIs that are not primarily transmitted by sexual intercourse. Indeed this survey of the general population is the only component of the overall study that addresses RTIs per se, as distinct from STIs. It is anticipated that the prevalence of these RTIs will be markedly higher than that of STIs. Data on RTI prevalence, and coping and health-seeking consequences, are badly needed for the development of more comprehensive reproductive health services in Pakistan. It is
known from previous research that RTI symptoms are commonly reported by Pakistani women and thus form an important part of the subjective burden of illness. However, it is also well established from research studies in South Asia and elsewhere that self-reported symptoms correlate poorly with bio-medical evidence of infection or pathology (Sloan et al., 2000; Bhatia and Cleland, 2000; Gaag et al., 2001). The development of a sound medical strategy to address RTIs in women cannot be sensibly started in the absence of accurate data on magnitude and nature of bio-medically defined infections.

The study will also yield estimates of the prevalence of key STIs in women, which can also be taken as a good approximation of the level of infection in their husbands. The small amount of information on STI prevalence in Pakistan comes mainly from facility-based studies. Estimates of infection have varied widely and it remains uncertain whether this variation is genuine and reflects the difference due to sample selection procedures or whether it is an artefact of different diagnostic techniques. In the current state of knowledge, it is impossible for policy makers to make informed decisions on whether or not the problem of STIs in the general population should be addressed. The proposed study of the general population will provide invaluable guidance in this regard.

**Options**

Two main options are proposed for the survey of the general population. Option 1 will yield nationally representative results on a relatively small sample of 4000 women and is designed to maximise the potential for it to be repeated at regular intervals and thus form part of an ongoing surveillance system for RTIs/STIs. Option 1 will permit estimation of results separately for the urban and rural population and for Punjab, the most populous province. However it will not permit estimation of results (with a useful degree of precision) for other provinces or administrative areas.

Option 2a, based on a larger sample of 6000, will yield similar results but at a provincial level as well as the national level. This was stated by both provincial and national representatives during the design process, as being highly desirable for the evidence-based development of provincial programs. However, Option 2a, because of its higher cost and because the general population is not currently considered an intervention priority by the NACP, may have less potential to be repeated. It is therefore most
appropriately viewed as an assessment of the burden of RTIs/STIs (and associated behaviours and coping mechanisms) with sufficient statistical power to enable comparisons of the magnitude and nature of this burden between provinces.

Option 2b is similar to option 2a but contains an additional sample of 1000 women from FATA/AJK. AJK and FANA are federally dependent territories that have been excluded from most national surveys. They are of special interest in relation to RTIs/STIs because of the special circumstances of men and women in these areas. Specially, these are areas of major out-migration of men (many of them married) for employment in the South, while, simultaneously, they are host to large numbers of men from elsewhere in the country, in service of the military. Such large movements of men have clear potential implications for STI transmission.

The great merit of options 2a and 2b is that they will provide data for policy and programmes for use by provincial health officials and will permit identification of major differences between provinces in the nature of the problem. It is impossible to gauge the probability that major differences in RTI/STI prevalence and associated behaviours exist at the province level but this is plausible and it can be argued forcefully that it is important to find out. The choice between the options involves financial, political, policy and scientific considerations. Obviously options 2a and 2b provide information at the appropriate level, i.e. the province or administrative area, where many health investment decisions are made and are thus preferable to option 1. The additional cost of option 2a over option 1 is estimated to £___, and the additional cost of option 2b over 2a is £_____. JAWAD TO ADD

3.2 Eligibility Criteria

The study population is defined as all ever-married women aged 20 to 39 years who have spent the previous night in the randomly selected households. Female visitors to selected households will be included if they resided in the household on the night prior to enumeration. Conversely, usual residents who are away from home at the time of the survey will not be regarded as eligible. The number of women meeting the selection criteria is expected to be around 0.9 per household. Selected households with no eligible women will not be replaced. Similarly, refusals will not be replaced. However an effort
will be made to recruit women who initially decline for the reason that they do not wish to be examined during menses, to the extent that it is possible to defer such examination while the field team is sited in the community.

The age band has been kept narrower than the usual range for women of reproductive age (15 to 49). Focusing on the younger more sexually active age groups, who are likely to have higher prevalence of STIs than older women, allows for a smaller sample size without compromising the precision of the prevalence estimates. It should also be noted that all women below the age of 20 will be excluded. In Pakistan 79% of females aged below 20 are unmarried and are predominantly virgins (1998 Census). The inclusion of the minority of married women under age 20 would be feasible but would add rather little to the value of the results.

It is proposed that divorced, separated and widowed women will be included, because of the possibility that disease prevalence or behaviour may differ from those of currently married women.

3.3 Geographical Coverage

Option 1

The universe will consist of all urban and rural areas of the four provinces of Pakistan including the federal capital (Islamabad). The Federally Administered Tribal Areas (FATA), the Federally Administered Northern Area (FANA), the Azad Jammu Kashmir (AJK), the military restricted areas, and the protected areas of North West Frontier Province (NWFP) will be excluded from the sample frame for this option. The populations living in the excluded areas represent 2.4% of the combined population of Pakistan and these independent territories.

It is suggested that Islamabad will be included in Punjab for the sampling design and reporting of results.

Options 2a and 2b

Option 2a will have the same geographical coverage as option 1 but the sample will be allocated equally across provinces rather than allocated according to population size. Under option 2b, a sample will be drawn from FATA/AJK because of the special circumstances of these areas, as described earlier.
3.4 Sample Design

The proposed sample design will be a `classical' multi-stage, stratified, clustered design. Such designs are routinely used for drawing representative samples of the general population in Pakistan and elsewhere. The National Institute for Population Studies used such designs in all its recent national surveys on fertility and family planning. At the first stage, a random sample of enumeration blocks, or clusters, will be selected. Households within each selected cluster will be listed, prior to systematic selection of a sample of households. Finally, all eligible women in each selected household will be canvassed.

The urban sample will be drawn from the most recent master sample frame prepared by the Federal Bureau of Statistics (FBS) and updated with input from the Population Census Organization (PCO). The FBS sampling frame has been developed by dividing each city/town into enumeration blocks of approximately 200-250 households with detailed maps and clearly recognisable boundaries. Each enumeration block has been classified as residential, commercial, and industrial in accordance with the predominance of activity therein. It was updated last in 1995 and there are 22674 enumeration blocks in all urban areas of provinces of Pakistan.

The rural sample will be drawn from the enumeration blocks of the sampling frame of the Population Census Organization updated according to the 1998 Population Census. Each block has about 1500 individuals (or 300 households) from one or a cluster of villages.

The Primary Sampling Units (PSUs) or clusters in the urban and rural areas will be the enumeration blocks. The PSUs will be selected by random sampling from geographically ordered lists within urban-rural strata within each province.

The Secondary Sampling Units (SSUs) are the households. The households will be listed by the survey team in each PSU and will be selected through systematic sampling with a random start. Geographical variations of behaviours and disease prevalence are expected to be less important in rural than in urban areas. Moreover, the logistical and cost benefits of clustering are less important in urban areas. Accordingly, it is proposed
to select 39 households per cluster in the urban stratum, and 55 households per cluster in the rural stratum. As the ratio of households to eligible women is 0.9, the sample design will yield 35 eligible women per urban cluster and 50 per rural cluster.

### 3.5 Sample Size

Sample size calculation methodology is detailed in annexe 1. The calculation is based on a 15% expected prevalence of bacterial vaginosis, the most important non-sexually transmitted RTI, and a 5% expected prevalence of chlamydial infection. The justification for these assumptions may be found in annexe 1. The compliance to urine collection for chlamydia diagnosis is expected to be 80% based on the experience of the National Nutrition Survey. Compliance to vaginal swabs for bacterial vaginosis is expected to be 60%, based on the pre-tests conducted during the design phase. (see annexe 4). The design effect (which takes into account the increase in standard errors due to clustering) is set at 1.7. This design effect is based on typical values found in demographic surveys that have used similar sample designs (Verma et al., 1980).

**Option 1: nationally representative sample**

It is proposed to select 4000 individuals using a nationally representative sample (excluding FANA, AJK and restricted areas). If a sample of the same size was repeated in say 5 years, it would be able to detect (with statistical confidence) a change over time in bacterial vaginosis prevalence from 15% to 11.4%, or a change in prevalence of chlamydia from 5% to 3.2%. The 95% confidence intervals of a 15% estimate of bacterial vaginosis would be 13.1% to 16.9%. In other words, it could be stated with near-certainty that the true value lies between 13.1% and 16.9%. The confidence intervals for a chlamydia estimate of 5% would be 4% to 6%.

Compliance to behavioural interviews is expected to be 90%, to collection of blood and urine 80% and to collection of vaginal swabs 60%. Thus a selected sample of 4000 women would yield the following approximate numbers for analysis.
Behavioural interviews 3600
Urine/blood samples 3200
Vaginal swabs 2400

The approximate provincial breakdown of sample numbers, on the basis of sample allocation proportionate to population size (with slight overrepresentation of Balochistan) is shown in Table 3.1 below.

Table 3.1 Expected Number of Interviews and Specimens: General Population Survey, Option 1

<table>
<thead>
<tr>
<th></th>
<th>Balochistan</th>
<th>NWFP</th>
<th>Punjab</th>
<th>Sindh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interviews</td>
<td>360</td>
<td>550</td>
<td>1890</td>
<td>800</td>
</tr>
<tr>
<td>Urine/blood specimens</td>
<td>320</td>
<td>500</td>
<td>1680</td>
<td>700</td>
</tr>
<tr>
<td>Vaginal swabs</td>
<td>240</td>
<td>360</td>
<td>1270</td>
<td>530</td>
</tr>
</tbody>
</table>

Option 2a: provincially representative sample

It is proposed to select 1500 households/individuals in each of the 4 provinces. The overall sample size would therefore be 6000. At provincial level the 95% confidence intervals for a 15% estimate of bacterial vaginosis would be 12% to 18%, whereas at national level it would be 12.6% to 17.4%. At provincial level the 95% confidence intervals of a 5% estimate of chlamydia would be 3.1% to 6.9%, whereas at national level they would be 3.7% to 6.3%. Note that the confidence intervals for the national estimates take into account the heavy overrepresentation of the less populous provinces and underrepresentation of the more populous provinces. For presentation of national estimates these differences in selection probabilities have to be corrected by introducing weights during the analysis, which increases the standard errors of the national estimates.
Option 2b: provincially representative sample including AJK and FANA

It is proposed to select 1500 households/individuals in each of the 4 provincial strata and 1000 individuals for the AJK + FANA stratum. AJK and FANA are federally administrated areas with circumstances that make the population of special interest as already intimated. This sample allocation would have the power to detect with statistical confidence a difference of ±4% in the prevalence of chlamydia in AJK/FANA from the expected level of 5% in the four provinces.

3.6 Socio-demographic and behavioural data

Information of a social, demographic and behavioural nature will be obtained from home interviews with eligible women by specially trained female lay interviewers. These interviews will be conducted before the biological data collection, under conditions of informed consent and optimal privacy. Each interview is expected to last on average about 25-30 minutes.

The matrix below shows the recommended minimum list of variables/topics to be included in the questionnaire. These topics have been covered in many South Asian community-based surveys (Oomman, 2000) and conform to recommended best practice for community-based studies of RTIs (Cleland and Harlow, in press). Nevertheless prior to designing an interview schedule in the four major languages, it is recommended that a short phase of qualitative investigation be conducted in various parts of the country to establish the appropriate vocabulary for asking questions about RTI symptoms. This should be followed by pre-tests of the draft instrument on opportunistic samples of about 50 women from each major linguistic group.
<table>
<thead>
<tr>
<th>Minimum List of Variables/Topics proposed for the Survey of the General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background Characteristics of Women and Spouse</strong></td>
</tr>
<tr>
<td>Age, education, marital status, duration of marriage,</td>
</tr>
<tr>
<td>employment, occupation, SES, number of children ever born,</td>
</tr>
<tr>
<td>date of most recent birth.</td>
</tr>
<tr>
<td><strong>Migration Patterns of Spouse</strong></td>
</tr>
<tr>
<td>Current residence, duration, frequency, place of visits away</td>
</tr>
<tr>
<td>from home.</td>
</tr>
<tr>
<td><strong>Use of ante-natal and family planning services</strong></td>
</tr>
<tr>
<td>Place of receipt of ANC (if any) for most recent birth and</td>
</tr>
<tr>
<td>number of visits.</td>
</tr>
<tr>
<td>Ever-use and current use of modern methods of FP, plus source</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Presence of recent RTI/STI symptoms</strong></td>
</tr>
<tr>
<td>Focus on vaginal discharge, pain during urination/sex,</td>
</tr>
<tr>
<td>sores/ulcers in genital area.</td>
</tr>
<tr>
<td>Measures of perceived severity, duration and functional</td>
</tr>
<tr>
<td>disability associated with each reported symptom.</td>
</tr>
<tr>
<td><strong>Treatment-seeking for RTI/STI Symptoms</strong></td>
</tr>
<tr>
<td>Types of care, counselling received (if any) and cost</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Risk Factors</strong></td>
</tr>
<tr>
<td>Iatrogenic (e.g. place of last delivery, abortion, IUD,</td>
</tr>
<tr>
<td>receipt of injections, blood transfusion).</td>
</tr>
<tr>
<td>Sexual (frequency of intercourse, condom use, indirect</td>
</tr>
<tr>
<td>questions on perceived behaviour of husband).</td>
</tr>
<tr>
<td><strong>Knowledge/recognition of RTI/STIs (incl. HIV) symptoms and</strong></td>
</tr>
<tr>
<td>protective means</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Experience in most Asian countries shows that married women report very little behaviour that carries the risk of STI infection (e.g. Carael et al., 1995). Little purpose would be served by including questions on non-marital sexual conduct. For this reason, many of the behavioural indicators recommended by UNAIDS/WHO for HIV-surveillance will not be ascertained in the general population survey. Cognitive and health-care indicators, however, can and should be collected. The implementing agency should ensure that all appropriate indictors are included and measured in ways that yield internationally comparable results.

3.7 Biological Data Collection

The range of pathogens to be assessed in the general population survey were extensively discussed at both Design Workshops. A full rationale for the final recommendation is shown in annexe 2 and summarised in the display below. It is proposed to study the two most important classical STIs - chlamydia, and syphilis - and the two most common RTIs that are not primarily transmitted via sexual intercourse - bacterial vaginosis and candidiasis.

It is proposed that biological data collection be performed by specially trained female para-medical staff at temporary clinics in each selected cluster. The biological samples to be collected are blood, urine and vaginal swabs. Blood and urine samples have been collected in previous national surveys in Pakistan, with reasonably high compliance and with no special problems. However, there is no prior experience with the field collection of vaginal swabs, a much more intrusive procedure. Accordingly, the Design Team organised field tests in areas served by NGOs and in other areas (see annexe 4). This experience showed that collection is feasible, with an expected compliance conservatively estimated at 60%. This level of compliance, though far from ideal, was considered acceptable. Possible bias can be assessed because the behavioural survey data will be available for most women who refuse vaginal swabs and urine/blood and samples will be available for some of them. Comparison of women who agree to vaginal swabs and those who do not on these dimensions will permit estimation of the likely direction and magnitude of non-response bias.
<table>
<thead>
<tr>
<th>Pathogen/disease</th>
<th>Sample</th>
<th>Test</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial vaginosis</td>
<td>Vaginal swabs</td>
<td>Gram stain + microscopy + Nugent score</td>
<td>Common disease and curable Perinatal outcomes + gynaecological complications. Curable.</td>
</tr>
<tr>
<td>Candida</td>
<td>Vaginal swabs</td>
<td>Gram stain + Microscopy</td>
<td>Common condition Curable.</td>
</tr>
</tbody>
</table>

*Rationale for Inclusions and Tests*

**Chlamydia** is likely to be one of the most common STIs in Pakistan. Untreated infections can cause Pelvic Inflammatory Disease, leading to infertility. PCR testing on urine samples is recommended over more traditional methods of diagnosis based on cultures from vaginal swabs for several reasons: higher sensitivity; less vulnerability to human error; higher compliance for urine collection than for vaginal swabs, hence results are more representative; greater ease of replication in repeat-surveys (Quinn, 1996). To reduce costs, it is recommended that urine samples be pooled in batches of four for initial testing. This is the optimal pool size for the range of prevalence expected (Kacena, 1998). Specimens in pools testing positive will be tested individually. PCR testing is routinely performed at several public and private sector laboratories in Pakistan.

**Syphilis** is one of the most prevalent and harmful STIs worldwide. No estimates of its likely prevalence in the general population exist. Such estimates are needed in order to assess whether or not routine testing and treatment of pregnant women is a cost-effective strategy. Syphilis will be tested and treated in the field on blood samples using RPR, a quick and simple test that is now routinely used in community-based STI studies (Nadarajah, 1990; Phaaasavasdi, 1989). Field tests, however, are more error-prone than tests in the laboratory and possess little scientific credibility. Therefore all sera will be
re-tested in a laboratory with RPR. As RPR has only moderate specificity, all positive specimens will be confirmed by TPHA, a highly specific test. TPHA is the recommended confirmatory test for syphilis (D'Errico, 1996). Neither test is commonly used in Pakistan but both are straightforward and can be introduced with ease.

The testing strategy will not distinguish between active cases and life-time infections (see annexe 2 for further discussion).

**Bacterial vaginosis** is a top priority for inclusion because of expected high prevalence and important post-natal outcomes (e.g. low birth weight, increased neonatal mortality). The proposed test is a standard one (gram strain + miscoscopy) but training in the application of Nugent's criteria for assessing severity will be required.

**Candidasis** is expected to be a common infection. It has no known serious sequelae but causes discomfort and anxiety. It can be tested using the same specimen and at the same time as bacterial vaginosis. The cost of its inclusion is therefore close to zero.

**Rationale for Exclusions**

**Gonorrhoea** is usually concentrated in high risk groups and its prevalence in the general population is expected to be low. Related to this, it is also not considered by the NACP to be a current priority for public health action in the general population. It can be tested on urine samples from women by LCR with high sensitivity and specificity but this technique is not yet available in Pakistan. Testing on urine by PCR is possible but various studies have shown mediocre sensitivity, resulting in unacceptably low positive predictive values (Mukenge-Tshibaka, 2000; Farrel, 2001; Tabrizi, 1998)). Moreover, pooling of samples is not possible and therefore costs of testing are high. PCR techniques could be applied to vaginal swabs with acceptable sensitivity and specificity (Van Dyck, 2001; Tabrizi, 1998). The estimated extra cost would be about £33,000. However, in the event that a decision were to be made to re-include gonorrhoea in the general survey, because vaginal swabs would result in lower compliance than urine testing, further consideration of LCR (the test of choice scientifically) should be made. The additional cost of testing gonorrhoea with LCR is estimated to be about £12,000. The decision of the Design Team to recommend the exclusion of gonorrhoea from the general population study of women therefore is a finely balanced and difficult one.
HIV prevalence is very low in Pakistan (below 0.3%). In their early phases, epidemics are not homogeneously distributed throughout the population but concentrated in core groups or geographical areas. The inclusion of HIV testing in the study of the general population would capture only a few cases, and would create findings of little epidemiological significance. It is therefore not recommended.

**Hepatitis B virus (HBV)** can be sexually transmitted, but is not included in the proposed study, partly because estimates would have little programmatic implication for HIV prevention. Moreover estimates from other studies are considered sufficient for HBV control programmes. Nevertheless its inclusion would provide an opportunity to assess prevalence in strictly representative samples of women from the general population. Such estimates would be useful to assess the need for, and of planning preventive programmes especially with regard to mother to child transmission of HBV. As with gonorrhoea, the decision is difficult and expert opinions differ. The cost of its inclusion is estimated to be £12,600 for option 1, £18,800 for option 2a and £22,000 for option 2b.

**Trichomonas vaginalis** is sexually transmitted with an expected prevalence higher than chlamydia or syphilis but it is a minor cause of complications. While high prevalence nonetheless may lead to high attributable risk, this pathogen has not been included in the study because of constraints related to its diagnosis by microscopy, and because it is not a key element within any existing or proposed public health strategies. Diagnosis by microscopy has a low sensitivity (44%) (Van Dyck, 1999); it has to be done on a live specimen in the field, thus increasing the potential for error. The only alternative would be to detect it by PCR from vaginal swabs, with sensitivity of 87% (Lawing, 2000). This is not justifiable in relation to the relatively low personal and public health importance of this pathogen, compared with other being proposed.
3.8 Ethical Considerations

Informed Consent

A multi-layered approach to ensuring informed consent is recommended. Information needs to be conveyed to the selected communities in advance of the arrival of the main data collection team; it is advisable to inform in advance households, or families, that have been selected; informed consent from individual women for the behavioural interview is needed; and finally, informed consent is required for the biological data collection.

It is proposed that information to communities about the nature and purpose of the study be given by the advance listing/mobilisation team who will start the task of listing and then selecting households several days before the arrival of the main team. Information at this stage should include a contact source who is competent to answer queries that might arise\(^1\).

The behavioural interview will be conducted at women's homes by specially trained female lay interviewers. It is recommended that interviewers be trained to describe in outline the scope of the interview, its approximate length and to stress that participation is entirely voluntary. It is recommended that verbal consent should suffice for this component of the study.

Following the interview, subjects will be invited to attend the clinic or camp on the following day for the bio-medical component. The procedures will be described to subjects, their purpose will be outlined as well as opportunities for front-line treatment and secondary treatment when laboratory results are known.

This proposed strategy of fully informing subjects about the nature of the bio-medical component on the day before attendance at the temporary clinic has several

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\(^1\) Some participants at the Ethics Review Workshop suggested that selected households be informed in advance of the behavioural interview and provided with user-friendly information about the study. Others felt that the tactic might arouse anxiety and provide excessive opportunity for husbands or older in-laws to dissuade women from participation. This issue needs to be considered by the implementing organisation.
advantages. It permits women to reflect on the decision whether or not to attend and an opportunity to consult husbands or other family members. It should be stressed that no incentive in kind or cash will be offered for participation, other than treatment and, in exceptional cases, assistance with transport.

On arrival at the clinic, full understanding of the procedures will be re-confirmed by paramedical staff\(^2\). Participants will be given the choice between the following four methods of endorsing their consent to bio-medical procedures: consent with signature, consent by fingerprint, oral consent with a witness or oral consent recorded by audiotape. Witnesses should not be members of the research team but they may be other participants. They need not be literate.

**Privacy and Confidentiality**

The behavioural interviews should be conducted in privacy, out of the hearing of other people with the exception of small children. When these conditions cannot be obtained, interviewers will offer an alternative venue or time. At the temporary clinics, adequate auditory and visual privacy should be available, particularly for collection of vaginal swabs, syndromic management and counselling.

Confidentiality will be maintained by the use of personal identification numbers (PINS). These will be issued to women following the completion of the behavioural interviews and used as the means of identification for bio-medical data collection. The master list of names, addresses and matching PINS will be collected at the end of each day's work and kept under lock and key by the team supervisor. Similarly, the consent forms which may also contain names and PINS, will be collected and stored securely. Results from laboratory tests will also be identified only via PINS and therefore can only be released to women in possession of their PINS. It is essential that PINS be durable, unalterable and sufficiently large to minimise their loss.

\(^2\) Some participants at the Ethics Workshop recommended the administration of a short comprehension test with those failing being given the necessary information and asked to return the following day. Others felt that this was excessive and would result in unnecessarily low participation by inarticulate women. This is a second issue to be resolved by the implementing agency.
**Treatment**

Based on the discussion in Chapter 2, the recommended treatment protocol for the study of the general population is to maximise front line treatment at time of data collection but nevertheless develop a notification strategy for women found to be infected by laboratory tests and NOT already treated approximately. Front line treatment will be performed by female paramedics at time of biological data collection, using the recently revised WHO guidelines for syndromic management (WHO, 2001). This will result in very considerable over treatment of uninfected cases but the cost will not be high and is justified both by ethical considerations and by its beneficial effect on participation and community relations. In addition it is proposed to use a rapid test for diagnosis of syphilis (results available within an hour or so) and to treat infected cases on the spot.

In addition to syndromic management of RTIs/STIs (including syphilis), paramedical staff will also offer free treatment of other acute conditions. Cases of chronic illness will be referred to a pre-selected public sector health facility (or to a private or NGO facility in some cases). Fees for referral and treatment of chronic conditions will not be covered by the study.

Feedback of laboratory tests requires careful identification of a medical facility or practitioner within, or close by, each selected PSU. They will be briefed about the study and provided with standard protocols for treatment of RTIs/STIs. Where no competent facility or practitioner can be located within a reasonable distance of the PSU (e.g. 5 kms), the research team will need to make special provision for feedback of laboratory results.

Women will be told where they can obtain laboratory results and a date after which they will be available. This date should make generous provision for logistical delays in laboratory processing and communication of results in order to minimise wasted visits by women. As stated earlier, results will be identified only by PIN and will be released only to women in possession of their PIN.
In addition to treatment of study participants, non-selected members of communities who present at the temporary clinic will be examined and treated as far as this can be done within constraints of time.

Ethical review of the final study protocol by an independent review board is essential. Such a national board does not exist in Pakistan but is urgently needed.

3.9 Field Strategy
3.9.1 Team Composition

Based on the successful experience of National Health Survey of Pakistan (NHSP) and National Nutrition Survey (NNS), it has been recommended to send an advance team to each PSU at least 4 days before the survey.

- The composition of the advance team is recommended to be as follow:
  - Logistics assistant: 1
  - Regional FBS staff member for listing: 1
  - Male mobiliser: 1

The composition of the data collection team is recommended to be as follows:

- Male Team Coordinator (mobiliser): 1
- Senior LHV/Supervisor: 1
- LHVs: 2
- Interviewers: 3
- Laboratory technician: 1
- Cold chain technician: 1

- The male mobilizers recruited for the study will play a key role in ensuring compliance at the community level. The pre-test studies have shown that married women aged above thirty years of age were successful at mobilising women for participation in the study. The task of encouraging selected women to participate will be largely the responsibility of the female interviewers most of whom will be mature, married women. Help from the local Lady Health Worker (LHW), Dai or any NGO working in the area may also be sought for developing rapport with the community and the selected households.
The lack of female doctors available for field studies justifies the choice of Lady Health Visitors (LHVs) for the data collection team. In addition to their availability, LHVs were found to promote participation among general population in previous national studies. The senior LHV will act as supervisor for both the LHVs and the interviewers. She will therefore require training in both sets of skills. The male team co-ordinator will be responsible for community relations and logistical matters.

3.9.2 Sequence of Activities

The advance team will inform the community leaders (local councillor and village elders) about the study process and objectives, identify a place for the medical camp, identify the boundaries of the cluster, enumerate the households and proceed to the sampling of households. The advance team will eventually present the selected households to the data collection team.

The medical camp will be set-up in a two rooms apartment situated in the cluster. The place should provide the confidentiality required for the medical examination. Past experience suggests that the usual occupants graciously will be willing to lend the rooms for the duration of the study.

The data collection teams will stay in a nearby village/sub-urban area providing safety and accommodation. They will travel to the PSU every morning and leave it in the evening.

The senior LHV will make contact with local medical practitioners and/or LHVs in order to identify the alternatives for referral and feedback to participants. She will keep phone contact with and report to the monitoring team.

The female interviewers will visit selected households and interview all eligible women. The duration of the questionnaire on behaviours will not exceed 25-30 minutes. When privacy is lacking, an alternative place of interview will be proposed to the participants, or the participants will be asked to come to the medical camp for interview and medical examination at the same time. Following the interview, women will be invited to the medical camp for collection of biological samples. The male co-ordinator will be in
charge of giving information to the husbands of the selected women, when required by the female interviewers.

At the medical camp the senior LHV will ensure selected women’s understanding of the study and their willingness to participate, and confirm the informed consent. The LHV will then conduct a general examination and pelvic examination where indicated. Following this, the women will be requested to give a vaginal swab, a urine sample and a blood sample for biological check. The LHV will code the sample and give them to the laboratory technician. They will provide single dose treatments based on the syndromic management of RTIs/STIs. Counselling for partner notification will be provided and treatment for partner provided. Syphilis cases will be treated immediately.

The second LHV of the team will provide medical care to all other women and children from non-sampled households who spontaneously present for treatment, in so far as time permits.

The laboratory technician will control the quality of the coding of the samples, centrifuge the blood, prepare three aliquots of urine and three aliquots of sera for each sample, test the sera for RPR, and prepare the gram stained slides.

The cold chain technician will control the quality of coding of the aliquots and ensure their proper storage. He will monitor the temperature of the sample and reagents. He will be responsible for the samples until their delivery at the designated laboratories.

A diagram of the phasing of work by team is presented in Figure 3.1. The advance team will spend 3 days in each PSU. The data collection team will arrive on the second day following the arrival of the advance team. There will be one day overlapping between the advance team and the data collection team. The data collection team will need to stay 6 days in each PSU.
The interviewers will conduct 3 to 4 interviews per day. The first day will be spent to identify the houses and set-up the medical camp. The data will be collected during the five following days. The team will take two-days rest in between each PSU. Hence, the data collection team will need 10 days per PSU. Because the two days rest of the data collection team is covered by work of the advanced team in the next cluster, each PSU will require a total of 10 days for the whole sampling and data collection process.

3.9.3  **Phasing by province, time frame: option 1**

In order to ensure the quality of the monitoring process and the mobilisation of staff from the referral laboratory, it is proposed to collect the data in one province at a time. There should not be any overlapping of activities from one province to another. Table 3.2 proposes an option for the number of teams to be involved in each province and figure 3.2 presents the corresponding time frame for data collection of such design.

For options 2a and 2b, provincial phasing should be retained but more teams and a longer span of fieldwork (perhaps 12 months) will be required.

<table>
<thead>
<tr>
<th></th>
<th>Population proportion according to 1998 census:</th>
<th>Sampling proportion</th>
<th>Urban proportion (1998 census):</th>
<th>Number of urban clusters</th>
<th>Number of rural clusters</th>
<th>Total number of clusters</th>
<th>Number of teams proposed</th>
<th>Number of days of data collection per team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Islamabad</td>
<td>1</td>
<td>1.0</td>
<td>16.9</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Punjab</td>
<td>56</td>
<td>52.0</td>
<td>31.3</td>
<td>19</td>
<td>29</td>
<td>48</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>Balochistan</td>
<td>5</td>
<td>10.0</td>
<td>2.7</td>
<td>0</td>
<td>8</td>
<td>8</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>Sindh</td>
<td>23</td>
<td>23.5</td>
<td>48.8</td>
<td>13</td>
<td>10</td>
<td>23</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>NWFP</td>
<td>13</td>
<td>13.3</td>
<td>23.9</td>
<td>4</td>
<td>8</td>
<td>12</td>
<td>4</td>
<td>30</td>
</tr>
</tbody>
</table>
3.9.4 Logistics Arrangement: storage and transport of Samples

Blood and urine samples and vaginal swabs will be taken at the medical camp by the LHV. It is preferred that a single blood sample is taken using vacuettes, and to place into Gel tubes. These tubes allow sera to separate over the next few hours (about 6 hours).³

<table>
<thead>
<tr>
<th>Figure 3.2: Phasing of the team work by province</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punjab + Islamabad</td>
</tr>
<tr>
<td>NWFP</td>
</tr>
<tr>
<td>Sindh</td>
</tr>
<tr>
<td>Balochistan</td>
</tr>
</tbody>
</table>

The separated sera will be tested for Syphilis through RPR. The remaining sera will be divided and stored into 3 aliquots, one each for testing, quality control measures and longer-term storage at the designated labs.

Urine samples will be collected in sealable sterile containers. Three aliquots will be prepared and frozen at −20C within a few hours of collection. A clear process for labelling and identification of the aliquoted samples will need to be defined by the implementing agency to meet confidentiality requirements.

Fixed slides will be prepared from the vaginal swabs by drying in air on the spot and they will be stored at room temperature in slide boxes. Frosted slides will be used for the purpose as they allow clear labelling.

For maintaining the cold chain, a cold chain technician (CCT) will also be a member of each Data Collection Team. To guarantee proper storage and timely transport to the laboratories the CCT will have a dedicated vehicle and driver. The vehicle is essential

³ Another option is to collect blood in glass tubes and centrifuge to separate sera within 10-20 minutes. This would decrease the cost of tube from Rs. 5 for Gel tube to Rs. 1 for glass tube (estimated saving of Rs. 2000), while increasing the cost for provision of centrifuge by Rs. 10,000 (an overall effect of Rs. 8,000 per team only). Centrifugation of Gel tubes is also an option for quicker processing of sera. The opinions of medical microbiologists vary on the merits of these methods. The implementing agency will have to make the decision according to the experience and expertise of the medical microbiologist in the team.
as it will carry the cold chain equipment (special freezers, generator, supplies needed for maintenance and ice boxes), the test reagents and transport media kits, which also require refrigeration.

The cold chain mechanism is outlined in Figure 3.3. The aliquoted blood and urine samples will be stored at −20°C in special ice-lined freezers, which are able to maintain the required temperature for at least 48-72 hours in the event of electricity failure. Generators and stabilizers will also be provided to overcome frequent electricity failures and fluctuations, experienced even in cities.

Long-range iceboxes with ice packs (or the freezers) will be used for transporting the samples from the field laboratory to the referral and reference laboratories taking care that samples do not thaw\(^4\). Temperatures at each stage will be monitored through special lab and recording thermometers to ascertain maintenance of the cold chain.

Aliquots will be stored at −70°C at the referral labs. After completion of the study, all samples will be transported at the designated lab for long-term storage.

\(^4\) Transportation using dry ice for road and air transport is not being recommended due to limited availability and high cost.
Figure 3.3 Sample Transport and Cold Chain Mechanism

FIELD
Sample Collection:
- Blood in Gel Tube
- Urine in sterile container

FIELD LAB
- Aliquoting by trained lab technician
- Slide preparation/fixing

TRANSPORT TO PROVINCIAL CAPITAL/REFERRAL LABS
- Transport in Freezer w/ Generator
- Transport in Long Range Ice Boxes with Ice Packs
- Temperatures to be recorded by recording thermometers

TRANSPORT BY AIR
- Transport in Long range Ice Boxes with sufficient Ice Packs
- Temperatures to be recorded by recording thermometers

REFERENCE LABS
- Receiving/labeling
- Freezing of samples at-20C/-70 C

FIELD
Storage by Cold Chain Technician at–20C or direct transport to Referral Labs
- Freezer with Generator
- Temperature monitoring by recording thermometers
3.10 **Reporting of results and feedback**

Participants to the study will be given a PIN and will be offered the opportunity to collect their results at a designated health service situated in or nearby the PSU. Treatment will be provided free of charge to those who will collect their results. Advice on partner notification and on condom use be given as appropriate. Free treatment for partners will also be available. Result should be available as quickly as possible (i.e. within 4-6 weeks of data collection).

Participants and community leaders will be given a phone number to contact the study organisers for any query or complaint.

3.11 **Laboratories to be used**

For Option 1 three to five referral laboratories will be required for the testing of the pathogens. The quality control of each type of test will be ensured by a specific national reference laboratory.\(^5\)

Referral laboratories should be selected according to the following criteria:

- Willingness to participate
- Technical capacity to supervise and conduct the study:
  - Qualification of technical staff
  - Routine performance of the relevant test
  - Quality control programmes in place
  - Facility for disposal of infectious waste
- Capacity to sustain tests introduced by the study
- Willingness to undertake objective performance tests
- Location in different provinces

PCR tests should be performed only at laboratories that already use this technology. Reference laboratories should be selected on the basis that they already use the specific technique both routinely and for research.

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\(^5\) A more centralised system was considered but rejected because of the overriding need to enhance laboratory capacity over the entire country.
3.12 Data Entry, Processing and Analysis

About 3600 forms will be entered. Data entry will be done using “SPSS Data Builder version. 1” or “PC-edit” package, as they have features to minimise errors. Data entry will require eight staff for one month. Whichever package is used, range, filter and skip checks should be applied and errors resolved. Data entry should start soon after receipt of the first batch of questionnaires from the field.

Data analysis will be done in an appropriate Pakistani institution, which may require some capacity building. SPSS, the most widely available analysis package in Pakistan cannot be used because it does not take into account the clustering of the sample when computing standard errors. Instead, a package such as SAS or STATA will have to be used. A senior statistician, or bio-statistician should be involved in the analysis.

Key results should be available within eight weeks after the completion of data entry and editing. It is envisaged that the biological results will be reported in terms of prevalence and 95% confidence intervals (CIs), disaggregated by relevant characteristics, as illustrated below. Behavioural results should be presented similarly.
Illustrative Presentation of Key Results

<table>
<thead>
<tr>
<th>Infection Type</th>
<th>Chlamydia</th>
<th>Syphilis</th>
<th>Either STI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N.</td>
<td>Prev.</td>
<td>95% C.I.</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever married</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etc</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A detailed analytical report would probably take an additional six months to complete. Further discussion of dissemination may be found in Chapter 2.

3.13 Quality Control/Accuracy

Quality Control will have to be created and maintained at all the levels i.e. fieldwork, transport of samples, laboratories and data analysis. Recommendations are summarised below.

Training

- Interviewers be trained for two weeks
- Biomedical and field lab. staff be trained for at least 4 days
- Laboratory staff be trained in Standard Operating Procedures (SOPS) by the reference laboratory (see annexe 7 for an example)
- Special training be given in the use of Nugents Scoring System for diagnosis of bacterial vaginosis (see annexe 6).
Pre-Testing of Instruments

- The development of behavioural questionnaires be preceded by small scale qualitative work and drafts should be pretested in all four major languages
- A full-scale 'dress rehearsal' of fieldwork (both behavioural and biomedical) be tested in one cluster to identify residual problems

Supervision

- Day-to-day supervision will be the responsibility of the senior LHV
- Questionnaires will be checked for completeness and consistency each day
- Occasional spot-checks will be make on interviewers by re-visiting women at home
- The work of LHVs will be checked by direct observation
- The male team co-ordinator will take responsibility for ensuring that no problems arise with transport of samples
- Higher level supervision will be exercised by provincial co-ordinators and other senior members of the research team
- The reference laboratory will check by site-visits that SOPs are being rigorously applied by collaborating laboratories.

Quality Checks and Quality Assurance of Laboratory Work

- All participating laboratories should agree to meet pre-set performance criteria for each test prior to start of the study
- For serology, well established international systems of performance testing exist and should be used
- The reference laboratories should retest a 10% sub-sample of each test performed by each participating laboratory
- Discrepancies exceeding a pre-determined level should result in complete re-testing of the relevant batch
- For tests involving microscopy, the 10% re-test should be applied to each reader
- For PCR tests, a sub-sample of positives and a smaller sub-sample of negatives should be re-tested by an international laboratory
Data Processing and Reporting

- Range, skip and filter checks should be applied and errors resolved
- The system of linking behavioural and biomedical data should be closely monitored
- The main analytical report should be reviewed by international experts before release.

3.14 Management Structure

The precise management structure is the responsibility of the implementing agency. It is recommended that the study team should include one National Co-ordinator, or principle investigator, who will take overall responsibility for the conduct of the study. Regional, or provincial co-ordinators will also be needed for high-level supervision of fieldwork in order to ensure standardisation of procedures and adherence to protocols. They will focus on quality of data collection, storage of samples, treatment, and adherence to ethical standards. For the larger provinces, provincial co-ordinators will require field inspectors to assist them.

Clearly, successfully implementation depends on close collaboration between behavioural scientists and biomedical scientists, between field staff and laboratory staff and between different participating laboratories. The implementing agency will need to consider carefully how best these can achieved.
References


Chapter 4

STUDY OF THE BRIDGING POPULATION: RESEARCH STRATEGY AND METHODS

4.1 Restatement of Objectives of the Study and Programmatic Relevance

The survey of the bridging population (male, urban migrants living away from home) has the following main objectives

- Measure the prevalence of STIs
- Measure behaviours that modify the risk of STIs with an emphasis on sexual behaviour and condom use
- Assess self-reported STI symptoms and associated treatment-seeking behaviour
- Measure knowledge of STIs, including HIV and means of avoiding infection
- Measure perceived risk of STI/HIV infection
- Examine variations in the above across major strata of this population

This information will meet the needs of a variety of stakeholders, policies and programmes. Specifically it will

- Provide baseline data to NACP for future STI/HIV surveillance
- Establish the need for enhanced STI services in urban areas
- Identify priorities for information and education campaigns for STI/HIV prevention
- Assess the need for strengthened social marketing of condoms in urban areas

For a comprehensive understanding of the dynamics of any future HIV epidemic in Pakistan, it is essential not only to study high risk groups and the general, or low risk, population but also to focus attention on ways in which infection may spread from one to the other. In epidemiological terms, these pathways of transmission are defined as bridging behaviours and the individuals responsible bridging groups or population. There are many possible ways of attempting to identify the bridging population. In the
context of Pakistan, one of the most systematic and cost-effective approaches is to focus attention on urban migrant males living away from home.

The 1998 Census shows that the sex ratio for the age group 20-59 years in urban areas is 118:100 while in rural areas it is 102:100, indicating that a large number of men reside in urban areas away from their homes. Consideration of these sex-ratios suggests that this stratum constitutes at any one time a sizeable fraction of all adult men in Pakistan, ranging from about 15% to 20%. As described in Chapter 2, living away from the natal or marital home exposes men to a relatively free environment without the constraints of close family members, and provides opportunities for paid and unpaid sexual activity with different partners. Hence migrant men have a relatively high potential of mixing with high risk groups, becoming infected and transmitting infections to current or future wives (e.g. Jochelson et al., 1991).

We thus propose and have designed a study of these "men on the move" or MOMs that will be cost-effective and replicable. Collection of information from this sub-population can act as baseline for subsequent tracking of changes over time in prevalence of STIs and HIV, and in associated behaviours. Results will also inform information and education campaigns and will permit an assessment of the need to upgrade urban STI treatment facilities.

4.2 Eligibility Criteria

- Men living in major urban centres:
  - Aged 20 to 49 years
  - Living away from marital home for married men for most of past 6 months
  - Living away from natal home for single men for most of past 6 months
  - Resident in the selected dwelling on the night prior to enumeration

- Exclusion criteria:
  - Any individual belonging to the following high-risk groups of the study i.e. sex-workers, transvestites, IVDUs, and truckers.
This study group will include married and single men from different occupations including those working in the informal sector and are unemployed. It will have representation from most linguistic groups since migration to cities is likely to originate in almost any part of the country.

The proposed age band takes into account that many males under age 20 will be virgins and therefore have little of interest to contribute to the objectives of the study. The upper boundary reflects the near-universal finding that men's risk behaviour declines from about age 30 and reaches very low levels by age 50 (Carael et al., 1995).

The proposed restriction to men who have been living away from home for most of the past six months is arbitrary but is intended to ensure a reasonable length of exposure to urban opportunities. It should be noted that men living with relatives other than parents or spouse will be eligible.

4.3 Geographical Coverage

The cities to be selected are the ones included in the Federal Bureau of Statistics (FBS) “major urban” stratum. It includes Islamabad, Karachi, Hyderabad, Lahore, Multan, Rawalpindi, Sialkot, Gujranwala, Faisalabad, Sargodha, Quetta, and Peshawar. It is expected that these cities will provide information about men from all over Pakistan. For example in Karachi, men from NWFP, AJK, Balochistan and Punjab, as well as from interior Sindh will be found. Altogether these 12 cities represent 18% of total population and 57% of the urban population.
4.4  Sample Design

The most cost-effective way of identifying MOMS is proposed\(^6\). The de facto counts of population from the 1998 census permit the calculation of sex ratios for the adult population by block. It is therefore possible to rank blocks in each of the 12 cities by sex ratio and then systematically sample blocks with high sex ratios. These blocks contained a disproportionately large percent of MOMs in 1998 and the situation is unlikely to have changed radically in the past four years. The precise definition of ‘high’ may vary from city to city but preliminary inspection of sex ratios suggests that a boundary point of 120 males per 100 females might be appropriate for most cities. The details of implementation are relatively unimportant. However, clear documentation is vital to permit replicability.

All structures in each selected block will then be listed, together with an approximate estimate of the number of MOMs (if any) in each structure. The number of residential structures together with the estimated total number of MOMS in the block will permit an estimation of the number of structures that need to be selected to obtain a sample of 40 MOMs. Note that, in boarding houses and such like, each room will count as a separate residential structure. The required number of structures will then be selected by systematic sampling. All MOMs at each selected structure who slept there on the night before initial contact with interviewers will be eligible for inclusion.

One important exception to this sample design is needed. Rooms containing more than five MOMs (such as hostels) need to be listed separately and a sub-sampling rule applied. This exception is required to avoid inclusion of large numbers of men from the same room who probably possess similar characteristics. At the analysis stage, weights can be applied to such institutional MOMs in order to reassert the representative nature of the sample.

\(^6\) Alternatives were carefully discussed. Opportunistic, snowball and other informal ways of recruiting subjects were assessed but rejected on the grounds that there would be no way of ensuring the representative nature of the sample nor of repeating it in the future. The ideal way of drawing a sample of MOMS would be to select a random sample of urban blocks or clusters and then systematically sample eligible men within each block. This strategy, however, would be expensive: the ratio of listed dwellings/men to eligible subjects would be high.
4.5 Sample Size

Sample size methodology is detailed in annexe 1. The calculations are based on a conservative expected 7% prevalence of any tested STI (chlamydia, gonorrhoea, syphilis). The justification is given in annexe 1. Expected compliance to biological data collection is 70% based on results of the pre-tests (see annexe 4). The design effect (which takes into account the increase in standard errors due to clustering) is set at 2.0. This value reflects the expected geographic heterogeneity of infection and behaviour in urban areas and is based on experience with standard errors estimated for urban strata in demographic surveys (Verma et al., 1980).

The proposed sample size of 4,000 would have the power to detect a fall in STI prevalence from 7% to 4.4% if repeated in five years time, for instance. The 95% confidence intervals for an estimate of 7% would be 5.7%-8.3% and for an estimate of 3% (e.g. for a specific STI) would be 2.1%-3.9%. The proposed sample size can also be justified in terms of its power to detect behavioural change with statistical confidence. In the pre-tests conducted during the Design Phase, the prevalence of condom use was 2%. A sample of 4,000 men, if repeated, would have the power to detect a rise from 2% to 3.9%.

Sample surveys of men inevitably record lower participation than surveys of women, because men are less likely to be contactable at home and more likely to refuse. Though interviewers will be instructed to work at night and to make at least three call-backs, participation in behavioural interviews is expected to be no higher than 80%. Thus a sample of 4,000 will yield approximately 3,200 interviews and 2,800 urine and blood samples. Assuming sampling probabilities proportionate to the size of each city, and that a minimum of two blocks is to be selected in each city, the allocation of the sample is expected to be as follows:
Table 4.1 Sample Allocation by City: Survey of Bridging Population

<table>
<thead>
<tr>
<th>City</th>
<th>Male population (1998 census)</th>
<th>No. Blocks Selected</th>
<th>No. selected</th>
<th>Men selected</th>
<th>No. of Completed Interviews</th>
<th>No. biological specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karachi</td>
<td>5,029,900</td>
<td>38</td>
<td>1520</td>
<td>1216</td>
<td>1064</td>
<td></td>
</tr>
<tr>
<td>Lahore</td>
<td>2,707,220</td>
<td>21</td>
<td>840</td>
<td>672</td>
<td>588</td>
<td></td>
</tr>
<tr>
<td>Faisalabad</td>
<td>1,053,085</td>
<td>8</td>
<td>320</td>
<td>256</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>Rawalpindi</td>
<td>750,530</td>
<td>6</td>
<td>240</td>
<td>192</td>
<td>160</td>
<td></td>
</tr>
<tr>
<td>Multan</td>
<td>637,911</td>
<td>5</td>
<td>200</td>
<td>160</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Hyderabad</td>
<td>612,283</td>
<td>5</td>
<td>200</td>
<td>160</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Gujranwala</td>
<td>588,512</td>
<td>5</td>
<td>200</td>
<td>160</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Peshawar</td>
<td>521,901</td>
<td>4</td>
<td>160</td>
<td>128</td>
<td>112</td>
<td></td>
</tr>
<tr>
<td>Quetta</td>
<td>307,759</td>
<td>2</td>
<td>80</td>
<td>64</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Islamabad</td>
<td>290,717</td>
<td>2</td>
<td>80</td>
<td>64</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Sialkot</td>
<td>227,398</td>
<td>2</td>
<td>80</td>
<td>64</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>

4.6 Socio-demographic-behavioural data

Information of a social, demographic and behavioural nature will be obtained from home interviews with eligible men by specially trained male lay interviewers. These interviews will be conducted before the biological data collection, under conditions of informed consent and optimal privacy. Each interview is expected to last about 30-40 minutes on average.

The contents of the questionnaire should cover the indicators recommended by UNAIDS for second-generation HIV surveillance. The matrix below shows the minimum list of essential topics that should be included, together with a rationale for inclusion. An illustrative questionnaire may be found in annexe 5. As may be seen, the main focus is on sexual risk behaviour. Promoted by the advent of the HIV pandemic, surveys on sexual behaviour in developing countries have become common (Cleland and Ferry, 1995). If conducted by well trained interviewers, no severe problems of compliance have been encountered. Many successful studies have also been completed in India.
(Pelto, 2000). While little experience exists in Pakistan, the pre-tests conducted during the design phase suggests that Pakistani men are willing to respond to intimate and sensitive questions on heterosexual and homosexual contacts.

The implementing agency will need to pilot and pre-test the questionnaire. Prior to designing an interview schedule in the four major languages, it is recommended that a short phase of qualitative investigation be carried out in several cities to establish appropriate vocabulary for questions about sexual conduct and STI symptoms. This should be followed by pre-test of the draft instrument on opportunistic samples of 50 men in each of two cities.
# Minimum List of Variables/Topics Proposed

<table>
<thead>
<tr>
<th><strong>Background Characteristics of Man and Spouse (if any)</strong></th>
<th><strong>Rationale</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, education, marital status, date of marriage, SES, employment, occupation, place of natal/marital home, current living arrangements</td>
<td>Allows basic descriptive disaggregation of results</td>
</tr>
</tbody>
</table>

**Mobility**

| Frequency and duration of home visits, date of last visit | Establishes link to general population study |

**General Health and Lifestyle Questions**

May be advisable to increase rapport before introduction of sensitive questions

**Heterosexual Conduct**

- **Married men:** number of sexual partners before/after marriage.
- **Single men:** ever had intercourse, number of partners
- **All (non-virgins):** number/nature of sexual partners in past 12 months, use of condoms with each partner

Provides information on patterns of heterosexual mixing, importance of sex workers and extent of protection by condom. Provides link to study of high risk groups.

**Homosexual Conduct**

- **Married men:** number of sexual partners before/after marriage.
- **Single men:** ever had intercourse, number of partners
- **All (non-virgins):** number/nature of sexual partners in past 12 months, use of condoms with each partner

Provides information on patterns of homosexual mixing, importance of sex workers and extent of protection by condom. Provides link to study of high risk groups.

**Iatrogenic Risk Factors**

Receipt of injections, blood transfusion

Cannot be linked to STIs but will reveal potential exposure to HIV and HEP B/C

**Presence of recent STI symptoms**

Focus on urethral discharge, pain during urination, genital ulcers, sores.

Measures perceived STI morbidity and is essential for treatment-seeking
Treatment Seeking for recent STI Symptoms

Type of care, counselling received (if any) and cost

Describes current patterns of health-seeking (allopathic v other: public v private sector). Needed for planning of service

Knowledge/recognition of STIs (incl. HIV)

Symptoms and Protective Means

Provides baseline measures of knowledge to monitor impact of future IEC campaigns.

4.7 Biological Data

It is proposed to assess the prevalence of chlamydia, syphilis and gonorrhoea, the three most important STIs, as shown below. A detailed rationale for this choice may be found in annexe 2. Biological specimens will be collected by phlebotomists at the homes of participants or by doctors in temporary clinics. The samples to be collected are blood and urine. Blood and urine samples have been collected in previous national surveys in Pakistan with reasonably high compliance and no special problems. Moreover, the pre-tests conducted in the design phase shows that collection is feasible among MOMs.

<table>
<thead>
<tr>
<th>Pathogen/disease</th>
<th>Sample</th>
<th>Test</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>Urine</td>
<td>PCR</td>
<td>Most common STI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>STI marker of sexual risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Co-factor of HIV transmission.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Preventable &amp; curable.</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Blood</td>
<td>RPR + TPHA confirmation for positive cases</td>
<td>STI marker of sexual risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Co-factor of HIV transmission.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Preventable &amp; curable.</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>Urine</td>
<td>PCR</td>
<td>STI marker of sexual risk co-factor of HIV transmission</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Preventable and curable.</td>
</tr>
</tbody>
</table>
Rationale for Inclusions and Tests

**Chlamydia** is likely to be one of the most common STIs in Pakistan. Untreated infections in men can cause epididymitis, infertility and Reiter's syndrome. PCR testing on urine samples is recommended over more traditional methods of diagnosis for several reasons: higher sensitivity; less vulnerability to human error; high compliance for urine collection, hence results are more representative; greater ease of replication in repeat-surveys (Palladino, 1999). To reduce costs, it is recommended that urine samples be pooled in batches of four for initial testing. This is the optimal pool size for the range of prevalence expected (Kacena, 1998). Specimens in pools testing positive will be tested individually. PCR testing is routinely performed at several public and private sector laboratories in Pakistan.

**Syphilis** is one of the most prevalent and harmful STIs worldwide. No estimates of its likely prevalence in urban Pakistani men exist. Syphilis will be tested and treated in the field on blood samples using RPR, a quick and simple test that is now routinely used in community-based STI studies (Nadarajah, 1990; Phaosavasdi, 1989). Field tests, however, are more error-prone than tests in the laboratory and possess little scientific credibility. Therefore all sera will be re-tested in a laboratory with RPR. As RPR has only moderate specificity, all positive specimens will be confirmed by TPHA, a highly specific test. TPHA is the recommended confirmatory test for syphilis. (D'Errico, 1996). Neither of these tests is commonly used in Pakistan but both are simple and can be introduced with relative ease.

The testing strategy will not distinguish between active cases and life-time infections (see annexe 2 for further discussion).

**Gonorrhoea** is usually concentrated in high risk groups and its likely prevalence among MOMs is difficult to gauge. It can be tested on urine samples from men (though not from women) by PCR with acceptable sensitivity and specificity (Palladino, 1999). However, pooling of samples is not possible and therefore costs of testing are relatively high. Testing by LCR would permit pooling but this technique is not yet available in Pakistan. For MOMs therefore, it is reasonable to recognise either PCR without pooling, or LCR with pooling as acceptable alternatives, the latter subject to availability. (LCR is being
actively considered for introduction by AKU at present for an unrelated study involving urine from women, for which LCR is strongly established as the preferred choice of test for gonorrhoea, as outlined in Chapter 3). If LCR were used the cost saving would amount to about £2,600.

**Rationale for Exclusions**

**HIV** prevalence is very low in Pakistan (below 0.3%). In their early phases, epidemics are not homogeneously distributed throughout the population but concentrated in core groups or geographical areas. The inclusion of HIV testing in the study of MOMs would capture only a few cases, and would create findings of little epidemiological significance. It is therefore not recommended.

**Hepatitis B virus (HBV)** can be sexually transmitted, but is not included in the proposed study, partly because estimates would have little programmatic implication for HIV prevention. Moreover estimates from other studies are considered sufficient for HBV control programmes.

**Trichomonas vaginalis** is sexually transmitted with an expected prevalence higher than chlamydia or syphilis but it is a minor cause of complications. This pathogen has not been included in the study because of constraints related to its diagnosis by microscopy. Diagnosis by microscopy has a low sensitivity (44%) (Van Dyck, 1999); it has to be done on a live specimen in the field, thus increasing the potential for error. The only alternative would be to detect it by PCR from urethral swabs, with sensitivity of 87% (Van der Schee, 1999). This is not justifiable in relation to the relatively low personal and public health importance of this pathogen, compared with others being proposed.

**4.8 Ethical considerations**

**Informed Consent**

Two phases of informed consent are required: first to the behavioural interview, and second to the biological data collection. Informed consent to the interview will be the responsibility of the male interviewers. It is recommended that interviewers be trained to describe in outline the scope and purpose of the interview, its approximate length and to stress that participation is entirely voluntary. Mention should be made of the bio-medical
component but subjects will be told that participation in the interview does not imply participation for blood and urine collection. It is suggested that verbal consent suffice for the interview.

Following the interview, a more detailed description of the bio-medical component will be given. The procedures will be described to subjects, their purpose will be outlined as well as opportunities for front-line treatment and secondary treatment when laboratory result's are known. The confidentiality of medical results will be stressed. At this stage, participants will be given four main options to confirm consent: consent by signature; consent by fingerprint; oral consent with a witness; or oral consent recorded by audiotape. The witness should not be a member of the research team.

**Privacy and Confidentiality**

The behavioural interviews should be conducted in privacy, out of the hearing of other people. When these conditions cannot be obtained, interviewers will offer an alternative venue or time. At the clinics, adequate auditory and visual privacy should be available, particularly for syndromic management and counselling.

Confidentiality will be maintained by the use of personal identification numbers (PINS). These will be issued to men following the completion of the behavioural interviews and used as the means of identification for bio-medical data collection. The master list of names, addresses and matching PINS will be collected at the end of each day's work and kept under lock and key by the team supervisor. Similarly, the consent forms, which may also contain names and PINS, will be collected and stored securely. Results from laboratory tests will also be identified only via PINS and therefore can only be released to men in possession of their PINS. It is essential that PINS be durable, unalterable and sufficiently large to minimise their loss.

**Treatment**

Syndromic management of STIs following WHO guidelines and of other acute conditions will be offered by doctors at the clinic (WHO, 2001). In addition leukocyte esterase tests will be applied by the phlebomist on urine samples. Gonorrhoea and chlamydia are commonly asymptomatic and are the most frequent cause of urethritis in men.
Leukocyte esterase test detects 90% of cases of urethritis by dipping a stick into a glass of urine for two minutes and reading the colour scale (REFERENCE). Despite a low specificity (54%) that leads to over-treatment, it is a recommended method to improve syndromic management of STIs (see annexe 2). Leukocyte esterase tests will be performed when collecting urine, and positive cases will be referred to the doctor of the team for treatment for gonorrhoea and chlamydia. Those who refuse to attend the doctor will not get the benefit of treatment. Out of the 70% of participants who will give blood and urine, it is estimated that 20% will be treated for suspected STIs by syndromic management. Altogether it is estimated that about 560 participants in the study will receive STIs treatments.

Syphilis will be tested on the spot and the participants will be free to collect their result from the doctor the next day. Tracing of positive cases is not recommended because it is a threat to confidentiality and it would expose the positive cases to stigmatisation. Wherever possible, feedback of laboratory results will be done through a near-by public health facility. In the absence of such, a private practitioner or facility will be used. Men will be told both where and when the results of tests will be available. The date for collection of results should make generous provision for logistical delays. Results will be identified only by PINS and will be released only to men in possession of their PIN.

Ethical review of the final study protocol by an independent review board is essential. Such a national board does not exist in Pakistan but is urgently needed.

4.9 Field Strategy

4.9.1 Team Composition

The survey team will comprise an enumeration team and a data collection team. The enumeration will consist of:

- PCO staff: 1
- Enumerators: 2

The data collection team will consist of:

- Medical Research officer/Supervisor: 1
- Interviewers: 4
- Phlebotomists/laboratory technicians: 2
- Cold Chain Technician: 1

It is anticipated that all staff will be male and that some or all of the enumerators will also be interviewers. The medical research officer ideally should be a young medical doctor trained in community health and with an interest in research. He should be trained in both behavioural and biomedical components of the study.\(^7\)

### 4.9.2 Sequence of Activities

The enumeration team will identify the clusters and produce the sampling frame. PCO staff will demarcate the geographical boundaries of the selected PSU. The two enumerators will list all structures in the PSU and gather information about their residents. They will visit each structure (house, mosque, shop, school, hostels or any other place where a person can live) in the selected PSU and fill a form. From each structure, information about the number of persons living in the structure, male and female members, and men living away from their marital and natal home will be collected. Structures will be marked/numbered so that none of the structures are missed or duplicated and so that selected ones can be identified easily at the data collection phase. Information about locked structures will be obtained from neighbours. In the case of hostels and hotels, each room will be treated as a structure and persons living in it will be listed per room. If the people are found living in tents in a compound then each tent will be treated as one structure and marked accordingly. Based on the pre-test experience, the enumeration team will spend 3.5 days on average in each PSU. The enumeration team will also identify possible structures that could serve as a temporary clinic and inform local community leaders about the nature and purpose of the study.

Sampling of structures with MOMs will be done by senior members of the research team within each city. At this stage, any unsuitable PSUs (e.g. those containing very few MOMS or those experiencing widespread demolition/rebuilding) will be replaced by new PSUs. As described in section 4.4, sub-sampling procedures for structures containing five or more MOMS will be applied.

\(^7\) The alternative of recruiting local medical practitioners to take responsibility for relevant parts of this study was discussed but rejected on the grounds that adequate quality control would be difficult.
The data collection team will spend 3.5 days for data collection. The team supervisor will be responsible for community relations, by providing further information to the concerned authorities and to allay misconceptions and fear among the members of the community. He will also make logistic arrangements for setting up the medical facility in the PSU and for the data collection team. The interviewers will visit selected structures and interview MOMs using a structured questionnaire. As they will be wholly or partly the same staff who did the listing, problems of locating structures will be avoided. It is estimated that it will take on an average 30-40 minutes to take informed consent and complete one interview. Due to the repeated visits needed in order to reach MOMs at their residence, it is expected that each interviewer will conduct little more than three interviews per day on average. Three days data collection will be necessary to complete data collection in each cluster, and the last half day will be spent to allow MOMs to collect the result of their syphilis test.

During the pre-test exercise, it was learnt that most of the men living away from home are available in the evening between 8 pm to 11 pm. However, some are available in the morning before 11 am. This suggests that fieldwork hours will have to be flexible depending on the situation in each selected cluster. Men living away from home should ideally be interviewed at their residences. However, if they are available at the workplace near their residence, they could also be interviewed at their convenience.

After each interview, the interviewer will explain in more detail the biomedical procedures, elicit informed consent and request the respondent for the sample of blood and urine. He will then call in the phlebotomist who will be waiting close by and also offer the individual a medical examination to be carried out by the doctor. The recommendation for 'door-step' collection of blood and urine by phlebotomists is based on pre-test experience when it was found that many men were reluctant to visit a doctor in a clinic, even when the distance was short. Furthermore the pre-tests also indicated that a ratio of one phlebotomist to two interviewers would suffice.

The team medical doctor will conduct the medical examination at the temporary clinic. This will be set-up in a two room apartment situated in the enumeration block. The place should provide the confidentiality required for the medical examination. Based on
experience of past surveys, it is expected that the usual occupants will graciously lend the rooms for the duration of the study. The doctor will also be responsible for controlling the proper storage of samples by the cold chain technician and their transportation to the required centre.

One of the phlebotomists will control the quality of the coding of the samples, centrifuge the blood, prepare three aliquots of urine and three aliquots of sera for each sample, and test the sera for RPR. Three aliquots will be prepared: one for testing and confirmation, one for quality control, and one for storage.

The cold chain technician will control the quality of coding of the aliquots and ensure their appropriate storage. He will monitor the temperature of the sample and reagents. He will be responsible for the samples until their delivery at the designated laboratories.

4.9.3 Phasing by City

It is recommended that the fieldwork in the 12 selected cities should be divided into three regions: South (Karachi, Hyderabad and Quetta), Central (Lahore, Multan, Rawalpindi, Sialkot, Gujranwala, Faisalabad, Sargodha), and North (Peshawar). The number of teams proposed for each region allows for the recruitment and training of team members fluent in the spoken language of each region/city. The number of teams and the duration of fieldwork required in each region is presented in table 4.2.

<table>
<thead>
<tr>
<th>Region</th>
<th>No Blocks</th>
<th>No Teams</th>
<th>No Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>51</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>South</td>
<td>45</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>North</td>
<td>4</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>
The study should be undertaken in one region after another. The overall data collection phase should take less than four months as presented in Figure 4.1.

<table>
<thead>
<tr>
<th>Figure 4.1: Phasing of the data collection by region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Region</td>
</tr>
<tr>
<td>Month 1</td>
</tr>
<tr>
<td>Month 2</td>
</tr>
<tr>
<td>Month 3</td>
</tr>
<tr>
<td>Month 4</td>
</tr>
<tr>
<td>South Region</td>
</tr>
<tr>
<td>North Region</td>
</tr>
</tbody>
</table>

4.9.4 Logistics Arrangement: storage and transport of samples

Blood and urine samples will be taken in the field after the interview or at the temporary clinic. It is preferred that a single blood sample is taken using vacuettees, and to place into Gel tubes. These tubes allow sera to separate over the next few hours (about 6 hours)\(^8\).

The separated sera will be tested for Syphilis through RPR. The remaining sera will be divided and stored into 3 aliquots, one each for testing and quality control measures and one for longer-term storage at the designated labs. A clear process for labeling and identification of the aliquoted samples will need to be defined by the implementing agency taking for meeting confidentiality requirements.

Urine samples will be collected in sealable sterile containers. Three aliquots will be prepared and frozen at –20C within a few hours of collection.

For maintaining the cold chain, a cold chain technician (CCT) will also be a member of each Data Collection Team. It is proposed that the CCT has a dedicated vehicle with driver to keep the cold chain mechanism independent to guarantee proper storage and timely transport to the laboratories. The vehicle is essential as it will carry the cold chain

\(^8\) Another option is to collect blood in glass tubes and centrifuge to separate sera within 10-20 minutes. This would decrease the cost of tube from Rs. 5 for Gel tube to Rs. 1 for glass tube (estimated saving of Rs. 2000), while increasing the cost for provision of centrifuge for Rs. 10,000 (an overall effect of Rs. 8,000 per team). Centrifugation of Gel tubes is also an option for quicker processing of sera. The opinions of medical microbiologists vary on the merits of these methods. The implementing agency will have to make the decision according to the experience and expertise of the medical microbiologist in the team.
equipment (special freezers, generator, supplies needed for maintenance and ice boxes), the test reagents and transport media kits, which too require refrigeration.

The cold chain mechanism is described in Figure 4.2. The samples collected at the field will be placed in ice boxes with ice packs to ensure an ambient temperature. These will then be transferred to the field laboratory where the blood and urine samples will be aliquoted by the technician. The aliquoted samples will be stored at –20°C in special ice-lined freezers, which are able to maintain the required temperature for at least 48-72 hours in the event of electricity failure. Generators and stabilizers will also be provided to overcome frequent electricity failures and fluctuations, experienced even in cities.

Long-range iceboxes with ice packs (or the freezers) will be used for transporting the samples from the field laboratory to the referral and reference laboratories taking care that samples do not thaw. Temperatures at each stage will be monitored through special laboratory and recording thermometers to ascertain maintenance of the cold chain.\(^9\)

Aliquots will be stored at –70°C at the referral labs. After completion of the study, all samples will be transported to the designated laboratory for long-term storage.

\(^9\) Transportation using dry ice for road and air transport is not being recommended due to limited availability and high cost.
Figure 4.2. : Sample Transport and Cold Chain Mechanism

FIELD
Sample Collection:
• Blood in Gel Tube
• Urine in sterile container

FIELD LAB
• Aliquoting by trained lab technician
• Slide preparation/fixing

FIELD
Storage by Cold Chain Technician at -20C or direct transport to Referral Labs
• Freezer with Generator
• Temperature monitoring by recording thermometers

TRANSPORT TO PROVINCIAL CAPITAL/ REFERRAL LABS
• Transport in Freezer w/ Generator
• Transport in Long Range Ice Boxes with Ice Packs
• Temperatures to be recorded by recording thermometers

TRANSPORT BY AIR
• Transport in Long range Ice Boxes with sufficient Ice Packs
• Temperatures to be recorded by recording thermometers

REFERENCE LABS
• Receiving/labeling
• Freezing of samples at -20C/ -70 C
4.10 Reporting of results and feedback

All the respondents will be offered the opportunity to receive their results from a pre-selected location during a fixed period after the survey. This could be a public or private sector facility, such as a Basic Health Unit, Health Centre, private clinic, or any other medical institution. The regional/city co-ordinators will ensure mailing of results to the identified place through a reputable courier service. The implementing agency will arrange for smooth delivery of the results to each PSU. A fee for service should be provided to the person in charge or to the facility taking responsibility for provision of this service. The persons involved in this activity will have to be oriented about the ethical aspects of this service, with especial focus on maintaining confidentiality of those collecting results and of cordial attitude in delivering the results. Positive cases will be offered treatment, advice about partner notification and advice about condom use.

4.11 Laboratories to be used

At least three referral laboratories will be required for the testing of the pathogens. The laboratory quality control of each type of test will be ensured by a specific national reference laboratory.

Referral laboratories should be selected according to the following criteria:

- Willingness to participate
- Technical capacity to supervise and conduct the study:
  - Qualification of technical staff
  - Routine performance of the relevant test
  - Quality assurance programmes in place
  - Facility for disposal of infectious waste

---

10 The group working on the ethical issues has recommended strengthening the health public sector facilities to provide free treatment for STIs. This will require training of the male medical officers in the identified facilities. Alternatively the activity could be subcontracted to NGOs with experience of training doctors in management of sexual health.

11 A more centralised system was considered but rejected because of the overriding need to enhance laboratory capacity in more than one place.
- Capacity to sustain tests introduced by the study
- Willingness to undertake objective performance tests
- Location in cities with largest sample allocation (Karachi and Lahore)

*PCR tests should be performed only at laboratories that already use this technology. Reference laboratories should be selected among the ones who already use the specific technique both routinely and for research purposes.*

### 4.12 Data entry, processing and analysis

Data analysis will be done in an appropriate Pakistani institution, which may require some capacity building. It is proposed that the data are entered electronically using “SPSS Data Builder version 1” or “PC-edit” package, as they have features to minimise data entry errors. Whichever package is used, range, skip and filter checks should be applied and errors resolved. Data entry should start soon after receipt of the first batches of questionnaires from the field. For analysis, SPSS, the software package widely available in Pakistan, cannot be used because it does not take into account the clustering of the sample when computing standard errors. Instead, a package such as SAS or STATA will have to be used. A senior statistician, or biostatistician, should be involved in the analysis.

It is estimated that 60 questionnaires can be entered per day per person. About 60 person-days will be required to enter the data. Two data editors and two coders will be required for editing of the questionnaires and for coding of any open-ended questions in the questionnaire.

Key results should be available within eight weeks of the completion of data entry and editing and linking behavioural to biological data. It is envisaged that the biological results will be reported in terms of prevalence and 95% confidence intervals (CIs), disaggregated by relevant characteristics, as illustrated below.
### Illustrative Presentation of Key Results

#### Infection Type

<table>
<thead>
<tr>
<th></th>
<th>Chlamydia</th>
<th>Gonorrhoea</th>
<th>Syphilis</th>
<th>Any STI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.</td>
<td>N.</td>
<td>N.</td>
<td>N.</td>
<td>Pre.</td>
</tr>
<tr>
<td>Prev.</td>
<td>95% C.I.</td>
<td>Prev.</td>
<td>95% C.I.</td>
<td>Prev.</td>
</tr>
</tbody>
</table>

#### Age

- 20-29
- 30-39
- 40-49

#### Marital Status

- Single
- Ever married

#### Education

- None
- Primary
- Secondary+
- Etc

Similarly, key behavioural indicators, such as percentage any reporting non-marital sexual partner in past 12 months, and percentage who used condom at most recent non-marital intercourse, would be presented, with 95% confidence intervals. A detailed more analytical report would probably take an additional six months to complete.

Further discussion of dissemination may be found in Chapter 2.

### 4.13 Quality Control/Assurance

Quality Control will have to be created and maintained at all the levels i.e. fieldwork, transport of samples, laboratories and data analysis. Recommendations are summarised below.

#### Training

- Interviewers be trained for two weeks
- Biomedical and field laboratory staff be trained for at least 4 days
- Laboratory staff be trained in Standard Operating Procedures (SOPS) by the reference laboratory (see annexe 7 for an example)
• Special training be given in the use of Nugents Scoring System for diagnosis of bacterial vaginosis (see annexe 6).

Pre-Testing of Instruments
• The development of behavioural questionnaires be preceded by small scale qualitative work and drafts should be pretested in all 4 major languages
• A full-scale 'dress rehearsal' of fieldwork (both behavioural and biomedical) be tested in one cluster to identify residual problems

Supervision
• Day-to-day supervision will be the responsibility of the team supervisor
• Questionnaires will be checked for completeness and consistency each day
• Occasional spot-checks will be make on interviewers by re-visiting men at home
• The work of laboratory technicians will be checked by direct observation
• The team supervisor will take responsibility for ensuring that no problems arise with transport of samples
• Higher level supervision will be exercised by regional/city co-ordinators and other senior members of the research team
• The reference laboratory will check by site-visits that SOPs are being rigorously applied by collaborating laboratories.

Quality Checks and Quality Assurance of Laboratory Work
• All participating laboratories should agree to meet pre-set performance criteria for each test prior to start of the study
• For serology, well established international systems of performance testing exist and should be used
• The reference laboratories should retest a 10% sub-sample of each test performed by each participating laboratory
• Discrepancies exceeding a pre-determined level should result in complete re-testing of the relevant batch
For PCR tests, a sub-sample of positives and a smaller sub-sample of negatives should be re-tested by an international laboratory

Data Processing and Reporting

- Range, skip and filter checks should be applied and errors resolved
- The system of linking behavioral and biomedical data should be closely monitored
- The main analytical report should be reviewed by international experts before release.

4.14 Management Structure

The precise management structure will depend on the implementing agency. It is recommended that the study will have one National Coordinator, three Regional Coordinators to supervise the field teams and their activities. Clearly, successful implementation depends on close collaboration between behavioural scientists and biomedical scientists, between field staff and laboratory staff and between different participating laboratories. The implementing agency will need to consider carefully how best these can be achieved.

References:


Chapter 5

STUDY OF THE VULNERABLE OR HIGH RISK GROUPS: RESEARCH STRATEGY AND METHODS

5.1 Restatement of Objectives of the Study and Programmatic Implications

Surveys of high risk groups have the following main objectives:

- Measure the prevalence of HIV
- Measure the prevalence of classical STIs
- Measure behaviours that modify the risk of STI/HIV infection
- Assess self-reported STI symptoms and associated treatment-seeking behaviour
- Measure knowledge of STIs and HIV and means of avoiding infection
- Measure perceived risk of STI/HIV infection

The information will meet the need of a variety of stakeholders, policies and programmes. Specifically it will

- Provide baseline data to NACP for future STI/HIV surveillance
- Assess the current state of the HIV epidemic in Pakistan
- Assess the need for enhanced focussed interventions by NACP, NGOs and others
- Identify priorities among different groups for urgent preventive measures
- Identify priority areas for action within each group

The HIV epidemic in Pakistan is currently classified as ‘low-level’ because HIV prevalence has not consistently exceeded 5% in any defined sub-population (AIDS, 2001). In low-level epidemics, infections are largely confined to individuals with high-risk behaviour, often among groups such as sex workers, drug injectors and men having sex with men (MSM). Their behaviour exposes them to elevated risks of acquiring or passing on HIV. In several Asian countries, HIV has spread explosively among these sub-populations and subsequently to the general population, changing the HIV profile of the country initially to concentrated epidemic-status and later to generalised epidemic-
status. The example of the largest Muslim country, Indonesia, has been cited in chapter 2, indicating that no society is immune.

Regular monitoring of infection and behaviour in high risk groups is a top priority for HIV surveillance in Pakistan because such information can act as an early warning of an impending acceleration in the spread of HIV. Moreover, careful study of these groups can both guide focussed intervention and assess their impact. The proposed studies of high risk groups thus serve several purposes.

After deliberations during the design review workshops, consensus was reached to include the following: female and male sex workers, Hijray, injecting drug users and truckers. Sex workers have been implicated in many Asian HIV epidemics and constitute the most vulnerable group. A large proportion of Hijray act as paid sex workers and the common practice of anal sex in this group defines them as highly vulnerable to HIV transmission. Truckers in Pakistan, as in India and elsewhere (Saini et al., 1998) are known to include many individuals who exhibit high risk behaviour and the size of this group, coupled with their mobility, make them of special relevance.

In Pakistan, information about the number of individuals in each vulnerable group and prevalence of STIs and HIV among them is meagre and mostly comes from small-scale studies, often done with unsatisfactory study designs (Nanan et al., 2000). Little is known about specific risk behaviours of the vulnerable groups and benchmarks are not available to monitor changes or for comparisons between different risk groups and with other countries in the region.

The known facts about the selected vulnerable groups are summarised on the following pages.

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12 A concentrated epidemic is defined as one where HIV prevalence is consistently over 5% in at least one defined sub-population but below 1% in pregnant women in urban areas. A Generalized epidemic is one with HIV prevalence over 1% in pregnant women nation-wide.

13 The selection of high risk groups for study was discussed extensively at Study Design Workshops. Prisoners, the armed forces, street children, Khepias and other groups were considered for inclusion but it was clearly necessary for practical reasons to select a relatively small number of high priority groups. These groups were therefore omitted.
Female Sex Workers (FSWs)

It is estimated that 16,000 workers live in the red light area of Lahore alone and it is probable that similar concentrations are to be found in other major cities. Commercial sex work is illegal but venues for commercial sex exist in almost every city and town.

FSWs in Pakistan can be classified into four categories: 1) brothel-based workers, 2) street-workers, 3) family-girls or housewives, 4) high class call-girls. The brothel-based workers and street-girls receive several clients per night who mostly belong to the lower income groups. Family-girls or married women indulge in paid sexual activity much less often, mostly through an “Aunty”. They provide services to males of middle or upper income group. Call-girls cater mostly to wealthier clients in hotels (World Bank, 2001).

Information about prevalence of STIs and HIV among FSWs is very limited. Two studies done in Karachi and Multan showed variable STI prevalence, rare condom use and three positive cases of HIV (Baqi et al, 1998; Rizvi, 1998). Similarly, knowledge, attitude and practice studies in Karachi and Lahore have shown differing levels of knowledge about AIDS, which is especially low concerning mode of transmission (Pakistan AIDS Prevention Society, 1983) and little adoption of safe sex practices (Manzoor et al., 1995; Tahir, n.d.). Only one study, which used a structured questionnaire for interviewing 100 FSWs in the red light area of Lahore, showed high knowledge about AIDS and safe sex practices. This study reported use of condoms by 80% of FSWs as a measure to prevent AIDS (Saqlain, n.d.). These significant variations in findings further highlight the need for reliable and valid data.

During the design process, NGOs have been identified that were or are working with vulnerable groups including FSWs. Information about them is presented in annexe 8. They are cited for each vulnerable group only for illustrative purposes. Further NGOs and CBOs working with these selected groups are likely to be identified during the current mapping exercise being undertaken by NACP in 14 cities of Pakistan.

NGOs working with FSWs have been identified in three provinces: Punjab, NWFP and Sindh. In Punjab, MESSAGE has worked in Multan with FSWs through a dispensary in the red light area for four years with UNICEF support. This area is estimated to have
about 4000 FSWs. The dispensary closed down about five months ago, after withdrawal of funding. MESSAGE however is still able to help research teams in Multan. MESSAGE is also working in Lahore, but the work is at a preliminary stage. Vite-n-Hope has more experience of working with FSWs in Lahore and has worked for them from time to time since 1993. They also carried out a UNICEF-funded project through peer educators, which ended in 1999. They have access to 500 FSWs through peer educators. AMAL can reach about 100 FSWs in the same area. Mohib-e-Watan, in Rawalpindi, have experience of working on a UNAIDS project for FSWs in the city, and has access to about 100 of them.

Gender and Reproductive Health Forum has stated that they could facilitate the study team to reach 2000 FSWs in Karachi, Hyderabad and Nawabshah. AWARD would help to access about 1000 FSWs in Swat and Peshawar in NWFP.

**Male Sex Workers (MSWs)**

Detailed studies on MSWs in Pakistan could not be identified; hence there is a wide gap in knowledge about this vulnerable group in Pakistan. A few years ago, The Herald, a leading monthly magazine reported that young boys operate as MSWs under the protection of pimps and police on different roads and spots of Karachi. In addition, male masseurs were also found to be active in this business, both as active and passive partners. During the design process, it was learnt that MSWs are hired for sex by males and also by females.

One study conducted in Islamabad and Rawalpindi interviewed 100 homosexual and bisexual respondents, of whom 33 were MSWs, 16 masseurs, 25 Hijray and 26 other individuals. Males from all groups showed high risk behaviours. In the preceding three months, 61% had 11 or more sexual encounters. Only one individual reported using condoms in all encounters while 67% had never used them (Mirza and Hasnain, 1995). Thus the small amount of available evidence suggests that MSWs may be common in Pakistan and that they and their clients are probably extremely vulnerable to STI/HIV transmission.
A few NGOs have been identified who currently reach MSWs. Vite-n-Hope has identified the “dens” and “cruising places” of MSWs in Lahore. This exercise took about 6-8 months and currently they are providing treatment services to them, and have developed good relationships with the “mentors” of these MSWs. Vite-n-Hope has given an assurance that if they are approached by the study team they would help to reach 200-500 MSWs. They have also offered to identify contacts in D.I. Khan in NWFP. Also in NWFP, AWARD could help reach 500 masseurs and MSWs, while Amal could help to reach about 20. Gender and Reproductive Health Forum has contact with 1000 in Karachi and Hyderabad, while Pakistan Society in Karachi has given a figure of 150.

**Hijray**

Hijray in Pakistan can be classified into three categories. *Transvestites*, include those who are born as males but present themselves as females. *Transsexuals* are male by birth but are castrated, either voluntarily or involuntarily. The cost of the procedure is Rs. 5,000 to 10,000 and is available in special clinics. *Hermaphrodites* have congenital abnormalities of their sexual organs and are very limited in number. More information is available about Hijray than MSWs.

Hijray work as singers, dancers and a very large number of them act as commercial sex workers. They usually live in groups or under the patronage of a group and mostly have low socio-economic status. However, they are accepted in society and are invited to wedding ceremonies and other festivities to entertain. Studies among Hijray have identified that they have high risk practices: unprotected receptive anal intercourse and fellatio with multiple male partners (frequency of 4-5 new clients on an average per week). Thus they are a highly vulnerable population for HIV and STIs.

A study conducted in a big cluster of Hijray in Taxilla city about 40 km from Islamabad found that the majority of them have heard about AIDS and almost all of them know about condoms, but less than one-fourth believed that condoms could be used for HIV prevention and even fewer had used them. In fact there was a misperception among some that condoms can spread diseases. Seroprevalence studies among this group have showed 2.6% positive cases for HIV (Khan, 1996).
Another seroprevalence study of 208 Hijray in Karachi showed high prevalence of syphilis and HBV but no case of HIV (Baqi et al., 1999). The age range of this group was 15-70 years, with mean age of 26.6 years. They had experienced their first consensual intercourse at an average age of 12 years. Less than one third of the study participants had heard of STIs but most had heard of AIDS. Ninety three percent of them reported a preference for receptive anal sex. The stated range of partners during the last month was 2 to 10. The majority of these activities were unprotected sexual acts; less than 10% of clients had used a condom in the last sexual intercourse. Fourteen percent of Hijray also reported selling blood.

On the basis of the above information, Hijray could be considered as a very high risk group for acquiring and spreading STIs, including HIV.

Seven NGOs were identified working with Hijray. MESSAGE is confident that they could help the team to reach 500 transvestites in Multan, as they have a good relationship with their Guru, and estimates access to 100 in Lahore. Mohib-e-Watan claimed to have good relations with a Guru in Rawalpindi who is the ‘leader’ of 200 Hijray. In Punjab and Sindh, Amal could take the team to 50 transvestites. Gender and Reproductive Health Forum could access more than 800 in Karachi and Quetta, and the Pakistan Society about 100 in Karachi. AWARD would help to access about 300 in NWFP and DARES about 150 in three cities of Balochistan.

**Injecting Drug Users (IDUs)**

Parenteral transmission is the second most frequent route of HIV infection in Pakistan as identified by the Surveillance Centres of the NACP. Hence, it is a high priority to study the behaviours of injecting drug users (IDUs) as there are thought to be over 3 million drug addicts in the country.

A study conducted in 1994 in Karachi among 100 drug users showed that 98% of them were injecting heroin intravenously. Multiple use of the syringe was observed among 91%. Sharing of syringes was reported by 82% of IDUs, and 64% of the respondents were not aware of AIDS (Pakistan Society, 1994). Another study in 1997-98 in Karachi
among 500 heroin addicts showed that 83% of them shared syringes (Pakistan Society, 1998).

In 1996, a study in Karachi checked the sera of 258 drug users and found one positive for HIV (Parviz et al., n.d.). Fourteen percent of these individuals also reported sexual intercourse and most of them did not use a condom with their partner. Hence, it could be inferred that HIV has been introduced into this group and has a potential for explosive spread. The Pakistan Society could help in reaching at least 2000 IDUs in Karachi. Another NGO, Nai Zindagi, could also play a leading role in assisting the implementing agency to help reach IDUs in different provinces. Gender and Reproductive Health Forum could support access to 400 IDUs in Sindh and Balochistan, while Amal could assist in accessing about 100 IDUs in Sindh, Balochistan and Punjab through its network of NGOs and CBOs. Mohib-e-Watan in Rawalpindi may also help to access about 100.

**Truckers and Helpers**

The role of long-distance truck drivers in the spread of HIV was first recognised in sub-Saharan Africa, including the association of geographic spread with major road transportation routes. Their role has also been documented in India during the rise in HIV positive cases that occurred in the mid-1990s. It was noted that more than 70% of cases were truck drivers. Earlier, in 1992, a study of a representative sample of truck drivers in Delhi also showed 1% prevalence of HIV. Furthermore, the truck drivers of Chennai showed an increase in prevalence from 2% in 1995 to 8% in 1996 (Saini et al., 1998).

In Pakistan, according to the National Transport Research Centre, there are 128,000 licensed trucks and one million truck drivers. Studies conducted in Pakistan have also shown that a very high percentage of long-distance truck drivers indulge in unsafe sexual relationships with sex workers (both males and females), Hijray and with their occupational partners, such as other drivers and truck cleaners.
The first study with truck drivers was conducted at the Mauripur truck stand in Karachi, in 1994. It is the largest truck stand in Sindh province and from here trucks move from Karachi to all parts of the country and also to neighbouring countries. The turnover rate at this stand ranges from 500-1000 trucks per day. In a day camp, 29 truck drivers and 6 cleaners of the truck were enrolled for the study. Ethnically, all of them were Pathans. Out of these 35 subjects, 25 (71%) reported ever having sexual contacts with FSWs, and 24 (69%) mentioned homosexual activities. Furthermore 61% were bisexuals and had multiple partners. However, none of them were positive for HIV (Ahmed et al., 1995).

In the following year, a study was conducted in Badami Bagh truck stand in Lahore, probably the largest truck stand in Pakistan, to assess the awareness level of AIDS. One hundred truck drivers were interviewed and only half of them had heard about AIDS. It was reported that less than one-third of respondents had knowledge about the modes of transmission of HIV (SOCH, 1995).

In 1998, another study with a much larger sample size was conducted in Lahore at three truck stands. According to toll tax offices about 2500 to 3000 trucks enter Lahore everyday with, on an average, two drivers and one helper. The study identified several brothels around the major truck stands where sex workers were available. These sex workers included women, young boys and Hijray. In the study 300 truck drivers and their helpers were interviewed and 49% reported having ever had sex with a male, 34% with a FSW and 11% with a Hijra. It also revealed that many of the owners of the goods companies have sex with the truck drivers, and sex also occurs between drivers and their helpers who are usually in their twenties. The study showed that nearly all interviewees have heard about AIDS, but most of them did not believe that it exists in Pakistan, and hence did not consider themselves at risk of infection. The percentage of condom use in their last sex was only 6% with a FSW, 5% with a male and 3% with a Hijra. The majority of respondents (89%) in this study were also Pathans (Agha, 1999).

It may be concluded that long distance truck drivers, their helpers and owner of goods companies have behaviours that carry high risks of acquiring and spreading sexually transmitted infections in Pakistan. Furthermore, opening of routes for trade with India or
Indian trade with Central Asian States through Pakistan could have hazardous consequences for the spread of HIV.

In summary, significant levels of classical STIs have been reported among vulnerable groups; such infections facilitate the acquisition and transmission of HIV. Furthermore, in small-scale studies, HIV has been detected in high-risk groups in Pakistan, putting the country at a potential risk of concentrated epidemics, possibly to be followed by a generalised epidemic. Pakistan's current low-prevalence status presents a special challenge to MOH, which has accepted the challenge of averting large numbers of future infections. One of the key programme interventions is directed to prevent HIV from becoming established in vulnerable populations and spreading to the general adult population.

5.2 Study Groups and Eligibility Criteria

As mentioned above, those involved in the design process discussed the merits and demerits for inclusion and exclusion of different vulnerable groups in the study. After thoughtful consideration it has been recommended to study the following five groups:

- female sex workers
- male sex workers
- Hijray (transvestites)
- injecting drug users
- truck drivers and their crew

Definition of precise eligibility criteria for each group requires an in-depth understanding of the various sub-populations' demographic and behavioural features. These definitions will have to be developed by the implementing agency during the initial phase of social reconnaissance with the help of NGOs working with specific groups and in consultation with NACP.
5.3 Geographical Coverage

The vulnerable groups are thought to be widely spread in urban areas of Pakistan. In preparation for expanded HIV surveillance, the NACP is currently conducting a rapid assessment and mapping exercise of these groups in 16 major cities of Pakistan that is likely to be completed by July 2002.

The geographical coverage of the studies of high risk groups should be responsive to epidemiological probabilities. The rapid spread of HIV in vulnerable groups, if and when it occurs, will be geographically focussed, almost certainly in one or more of the major cities. In India, for instance, the course of HIV epidemics has varied widely from city to city. The appropriate response in terms of research and surveillance, therefore, is not to propose a widely dispersed sample (as for the study of the general population) but rather to focus attention on a relatively small number of sites where rapid HIV transmission is most likely to occur. Before the results of NACP's current social exercise are known, it is premature to designate these priority sites and, of course, they may be different for particular high risk groups. However, the two major cities, Karachi and Lahore, are likely to be selected for most, if not all, groups.

5.4 Sample Design

5.4.1 Introduction

For some groups in selected study sites, it may be possible to use rigorous probability sampling (i.e. construct a list of eligible subjects and then select a sample systematically from the list). For instance, well organised communities of Hijray, institutional sex workers and perhaps truckers may be amenable to such sampling. More commonly, however, it will not be possible to apply the techniques of formal probability sampling. Instead a variety of more pragmatic sampling methods will be needed to generate samples. The latter include: snowball or chain referral sampling (Heckathorn, 1997; Erickson 1979), and targeted sampling (Watters and Biernack 1989).
**Snowball or chain referral sampling** is the most commonly used method. An initial selection of members of the study group, reflecting a range of characteristics, is initially contacted, often by means of local NGOs or health facilities. These initial contacts are then asked to provide the names and enlist the co-operation of other eligible subjects known to them, and so on in an ever-widening network. Key elements in the successful use of this technique include: ensuring that the initial contacts represent the important sub-groups of the study population; avoidance of reliance on a small number of initial contacts; and avoidance of repeated data collection from the same individual (usually this is only a problem when incentives are used).

**Targeted sampling** involves an initial geographic mapping of places where subjects live or congregate, followed by recruitment of a specified number of subjects from each location.

Both methods can and perhaps should be used in tandem but, in advance of social mapping, initial exploratory ethnographic research and identification of local NGOs, key informants or other entry points, it is impossible to specify in detail how best samples can be generated at each study site. In the following pages, we attempt to spell out the practical steps that need to be taken but we cannot do this in a detailed, prescriptive manner.

### 5.4.2 Social Mapping of the Vulnerable Groups and Selection of Sites

The first step is to have social maps of the vulnerable groups, with information on their geographical and physical locations to identify “hot spots” in the country. NACP has contracted out studies to perform this task in 16 cities of Pakistan, which are likely to have concentrations of the vulnerable groups.

The maps that will be prepared will indicate the sites with highest concentrations of the vulnerable groups. This information should be used for selection of the sites, determining the universe and drawing the sample. For each risk group, a list of all key sites together with estimates of the approximate number of subjects should be prepared.
From this list, and in consultation with NACP and other stakeholders, sites should be chosen for the study. The number of sites depend on the needs and capacity of the Programme and the availability of funding. This choice can only be made sensibly after the results of the mapping exercise are available.

5.4.3 Identification of NGOs or other Entry Points

The next step will be the identification of NGOs or individuals working with vulnerable groups at each selected site. The discussion with key informants, national experts and the NACP has highlighted the fact that accessing high-risk groups directly by the study team will be almost impossible without the mediation of organisations or individuals who have already gained the trust of at least some components of the study group. A long time is required to win the trust of the vulnerable populations. NGOs that already have established relationships with these groups appear to be the most appropriate channel for facilitating access by the study team. Moreover, this strategy will minimise the possibility of harming the selected groups or damaging ongoing activities of NACP. The main exception to this strategy is truckers.

The design team has contacted over 60 NGOs and has identified several working with the selected groups. Their expressions of interest (EOI) to work as facilitative partners of the study are attached in annexe 8. The implementing agency will be able to make use of information provided in the EOI and may also identify other NGOs or CBOs working at the selected sites.

The implementing research agency will need to consider carefully the relationship with partner NGOs. It is important to ensure that NGOs do not control access to the study population. Each study should attempt to recruit beyond the individuals who are already in contact with NGOs, because such 'unserved' members of vulnerable groups may have different needs and behaviours from those already in contact with NGOs.

5.4.4 Social Reconnaissance and Recruitment of Members of Target Groups

Once study sites and facilitative partners have been chosen, it is recommended that the research team spend about two months in initial social reconnaissance. During this phase, further mapping will be conducted where necessary, key informants will be
approached and interviewed and arrangements for the bio-medical component of the study made.

International experience with research on vulnerable groups of the population suggest that it may be advisable to recruit members of the study group (or ex-members) as part time members of the research team. Such recruits can act as invaluable bridges between the team and community and thereby enhance participation. However, the feasibility of this approach in Pakistan will have to be assessed.

Qualitative research is also required at this stage and is discussed below.

5.4.5 Selection of Subjects

As discussed earlier, the process for selection of sites and respondents in each vulnerable group may differ and will depend on the available information from the mapping exercise. Snowball and targeted sampling techniques, together with probability sampling where possible, will be used. It is essential that sampling procedures be thoroughly documented so that comparable repeat surveys can be conducted. Currently available information about the social mapping and practical aspects of selection of respondents from each vulnerable group is described below.

Female Sex Workers (FSWs)

The ongoing mapping of FSWs shows that it is possible to identify and list brothels (*kothay*) and brothel-based workers. Conversely it may not be possible to list those who are operating on streets, from houses (*kothis*), from residential colonies and those operating in hotels. Hence the available information will pertain to those relatively easily accessible, who are likely to differ from less accessible workers, as they may have received counselling or services, and may have more control over sexual transactions due to the “protective” environment of the brothel.

Brothel-based FSWs are certainly a priority sub-group for study, with the added advantage that selection procedures are relatively straightforward and replicable.
Brothels can be selected from a list with probability proportionate to the number of workers and then the same number of workers can be sampled from each selected brothel. This arrangement would yield an approximately representative sample of FSWs (i.e. self-weighting). However, experience in Thailand and elsewhere indicates that informal, unorganised FSWs may be more vulnerable to unsafe sex and STI/HIV transmission than brothel-based workers. It is thus recommended that the research team does not opt for the easiest choice but, instead, makes an effort to establish links with and recruit FSWs who are operating on the streets.

**Male Sex Workers (MSWs)**

Male commercial sex work, is more heavily stigmatised than female sex work. MSWs do not operate from brothels. However, some NGOs have been able to identify their “dens” and “cruising” places and are working with them to promote safer sex practices or to provide treatment of STIs. To conduct geographical mapping of this group in major cities, NACP has hired the services of NGOs or firms that have links with NGOs reaching MSWs. They are expected to identify areas where MSWs assemble to seek clients and other possible working places, with approximate estimates of the number of individuals operating at each site. This information should be used for choosing the site(s) for the study. Targeted sampling, as defined earlier, is thus appropriate. Recruitment of individuals in this study will be a difficult process and may require the incorporation of a few MSWs into the research team.

**Hijray**

The geographical mapping of Hijray will be much easier than that for MSWs and is likely to provide more comprehensive information as they mostly live in groups, and their residential places are known and are not concealed or illicit. Hence it will be comparatively easy to identify study sites. Initial approaches should be made to community leaders, the reason being that Hijray are mostly under the command of their “Guru”, who makes decisions for individuals. During the selection of respondents, the survey team will have to ensure that each individual participates in the study voluntarily and without coercion.
**Injecting Drug Users (IDUs)**

In contrast to other core groups who can be approached in specific areas, IDUs have no specific meeting places. They comprise a heterogeneous group, made up of individuals from each of the other sub-populations of the study. They are organised in small independent networks linked to one or more drug dealers. Those who purchase their heroin in a group tend to share needles and paraphernalia. Due to the criminalisation of drug dealing it is practically impossible to identify IDUs though sellers. For similar reasons, drug users do not stay in shooting galleries after receiving their injection. Moreover it is not feasible to establish contact with individuals when they are missing drugs (before injection) or high on drugs (after injection). Therefore contact with IDUs can only be initiated through detoxification centres and extended by networking. Heroin detoxification is a long process and usually each patient undergoes a couple of relapses before being free from drugs. Around the world relapse rates vary from 60% to 95% within one year. There is therefore little bias in selecting IDUs in rehabilitation centres, provided that access to these structures is equitable and widely available. Due to these constraints it is recommended that IDUs be recruited through rehabilitation centres, centres distributing free syringes, or NGOs providing services to this population. Information about these facilities will be provided by the mapping exercise.

**Truckers and Helpers**

The NACP mapping of truckers will provide reliable information about the Truck Addas (truck stands) and estimated numbers of long- and short- distance truck drivers and cleaners/attendants. In the mapping the number of truck stands in the selected cities are being recorded. Some of these addas have registered forwarding agencies but others operate without them. The Munshi (manager) of the forwarding agencies are providing information to the mapping teams about the number of trucks owned or hired by the agency and the estimated number of long-distance and local truck drivers employed or hired by them. According to the preliminary reports of the mapping exercise the estimated number of cleaners/attendants is equivalent to the estimated number of long-distance truck drivers as at least one cleaner accompanies each long distance truck driver. The estimation of numbers of truck drivers and their
attendants/cleaners will be less reliable from addas where forwarding agencies are not operating.

The results of the mapping exercise will guide the selection of addas that should be considered for drawing the sample. In addas with forwarding agencies, random sampling of agencies could be done with probabilities proportionate to the number of truckers (e.g. preliminary reports shows that there are 700 forwarding agencies in three addas in Karachi). It may then be possible to obtain lists of truckers and helpers and sample from this list. However, though scientifically rigorous and replicable, this strategy may not be feasible and may prove too expensive. An alternative approach would be to select addas with probability proportionate to number of truck arrivals per day and select an equal number of truckers from each adda, using a quota sampling approach. With quota sampling, it is established in advance how many truckers of different types should be selected (e.g. young v old, long distance v short distance etc). Field staff are then instructed to recruit the specified numbers. A final component of good practice would be to ensure that subject recruitment takes place on all days of the working week and at all times of the working day to avoid possible biases.

**Sample Size**

It is recommended that, in each site, a total of 400 individuals from a vulnerable group should be sampled, except for the truckers, where it is recommended to include 400 drivers and 400 attendants/cleaners. More details and rationale about the sample size are given in annexe 1.

This sample size is rather small for obtaining precise estimates or for detecting change. For instance, a prevalence of 20% (e.g. condom use at last sexual act or infection with any STI) would have 95% confidence intervals of 17% to 23%. Similarly, if a survey of the same size was repeated, a rise in prevalence from 20% to 26% could be established with 95% statistical confidence, but any smaller change could not be established with such certainty.

However pragmatic and scientific reasons exist for proposing a relatively small sample size per study site. With effectively six high risk groups (counting truckers and helpers
as separate groups), a study design with one site only for each group would imply an overall sample of $6 \times 400 = 2400$ subjects. This is a considerable number. Raising the number of study sites to two per group obviously doubles the overall sample size to 4800. Clearly, further raising the number of subjects per site quickly encounters budgetary as well as logistical constraints.

The scientific justification for proposing a relatively small sample per group per site is twofold. First, an exceptionally wide range of biological and behavioural data will be collected. Indicators of the direction of change can thus be measured in a variety of ways (e.g. condom use, number of partners, anal sex, prevalence of STIs, treatment). If data of sound quality are collected, change in these indicators should be mutually consistent and such consistency greatly enhances the interpretative weight that can be placed on results, even if the trend for any one indicator, taken in isolation, is not statistically significant at the 95% confidence level. (It may be noted, at this juncture, that 95% has no 'magic' qualities. Most programmatic decisions are based on evidence that is far less secure.) The second scientific justification is that results from a series of repeated surveys can be averaged in ways (e.g., 3-year moving averages) that increase the operational stability and statistical precision of results.

5.5 Socio-demographic-behavioural data

The behavioural component of this group is critical for tracking current levels of associated risks and their changes over time. The five “high risk” groups selected for study, despite some distinct patterns of behaviour, are interlinked and comprise permeable categories. Furthermore, their behaviours are of crucial importance as these groups are a major source of transmission of infection to the general population through the intermediary or bridging population. For example, truckers can have relationships with both male and female sex workers and similarly the IDUs can be in contact with both types of sex workers while they may also be married. The nexus between the high risk groups and the general population has also been established through studies that have documented a high prevalence of Hepatitis B and C in the IDUs who are known to be professional donors. These donors could perhaps be a conduit for the spread of both kinds of Hepatitis within the general population, about 30-40% of whom have been exposed to the virus and about 4-10% have become chronic carriers. Transmission of
Hepatitis B has also been established through sexual routes, and Hepatitis C may be similarly transmitted.

A review of literature demonstrates the paucity of social research that has been done in Pakistan to document the knowledge, perceptions and practices of sub-groups who indulge in practices that place them at a greater risk of acquiring sexually transmitted infections. The limited evidence that is available shows considerable variations in practices amongst these high risk groups based on their geographical location.

The measurement of risky sexual and drug taking behaviours has become an important part of efforts to track HIV epidemics. This is especially true in areas where the virus itself is not yet well established in the general population. In these situations, efforts to measure risky behaviour should concentrate on quantifying levels of risk in sub-populations, enquiring about high-risk behaviours, identifying links to other populations and tracking trends over time. These activities can help in planning appropriate prevention programmes and assist in their monitoring and evaluation.

The behavioural research will be multi-staged with a round of qualitative research to be followed by a quantitative survey (in conjunction with the biological test) and finally another round of qualitative research. The first phase of qualitative research will be formative research which will be undertaken to assess terminology to be utilised and range of topics to be explored in the case of each of the high-risk groups. In particular, the behaviours of group members may differ according to living arrangements, work patterns, communication and social networks. These need to be explored in advance of the quantitative measurement of behaviours and biological testing. This phase of qualitative research is also required at very initial stages to identify sub-groups and establish clear eligibility criteria for each of the groups. Mainly focus groups discussions and informal unstructured interviews will be conducted within each of the high risk groups and the findings will be used in conjunction with those regarding locations of the high risk groups from the mapping exercises, to be completed by then.

The next phase of the behavioural research will be the quantitative enquiry whereby basic information on social, demographic and behavioural characteristics will be obtained from all five high-risk groups. This can be directly linked to the laboratory tests
to be performed. A basic questionnaire which would take about 20 minutes to answer will be administered to respondents from the high risk groups (illustrative questionnaires are attached in annexe 5) at the same time as the urine and blood samples (and vaginal swabs in the case of FSWs) are to be collected. This basic information will include risk and protective factors such as condom, blood, needle and drug use, sexual behaviour and hygiene from all groups.

The last phase of qualitative research through in depth interviews will gather more detailed information on certain topics with a select sub group of persons from each risk category. The main topics to be covered in greater breath than possible in the brief quantitative questionnaires are:

- Health seeking behaviour: sequence of providers contacted, kind to help sought
- Perceptions of and severity of symptoms: health care and related communication with spouses and others
- Social and communication networks: linkages within and across the high-risk groups
- Perceptions of self risk: knowledge of protective and risk behaviours
- Consequences of RTI/STIs: experience with symptoms and with actual infections
- Power relations within the groups: extent to which groupmembers can protect themselves against infection.

The recommended minimum lists of topics/variables to be collected in the quantitative surveys of each group are shown below.
Minimum list of Variables/Topics proposed for the survey of Female Sex Workers

<table>
<thead>
<tr>
<th>INDICATORS</th>
<th>RATIONALE</th>
</tr>
</thead>
</table>
| **Background Characteristics of respondent (and spouse of any)**  
  Age, education, marital status, duration of marriage, other source of income, SES, ethnicity, migration pattern, length of time as FSW. | Allows basic descriptive disaggregation of results                        |
| **Commercial Sexual Activities**                |                                                                           |
| Number and type of clients, venues used, number of sexual encounters during last one week, condom use, frequency, anal intercourse, condom use | Provide information about risk behaviour                                  |
| **Non-commercial Sexual Activities**            |                                                                           |
| Number and type of partners, condom use         | Information about non-commercial risk behaviour                           |
| **Iatrogenic Risk factors**                     |                                                                           |
| Receipt of injection, blood transfusion, selling of blood, needle sharing for IV drug use | Can not be linked to STI but will reveal potential exposure to HIV and HEP B/C |
| **Presence of recent RTI/STI Symptoms**         |                                                                           |
| Focus on vaginal discharge, pain during sex/urination, sores/ulcers in genital area  
  Measures of perceived severity, duration and functional disability associated with each reported symptoms | Assesses subjective burden of illness                                     |
| **Treatment-seeking for RTI/STI symptoms**      |                                                                           |
| Types of care, counselling received (if any) and cost | Describe current pattern of health seeking (allopatic vs. others, Public vs. Private). Needed for planning of services. |
| **Knowledge/recognition of STIs (including HIV) symptoms and protective means** | Provides baseline measures of knowledge to monitor impact of future IEC campaigns |
Minimum list of Variables/Topics proposed for the survey of IDUs

<table>
<thead>
<tr>
<th>INDICATORS</th>
<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background characteristics of respondent and spouse</td>
<td>Allows basic descriptive of disaggregation of results</td>
</tr>
<tr>
<td>Age, education, gender, marital status, duration of marriage, SES, place of natal marital home, occupational details</td>
<td></td>
</tr>
<tr>
<td><strong>Mobility</strong></td>
<td></td>
</tr>
<tr>
<td>Frequency and Duration of home visits, date of last visit</td>
<td>Established link to general population</td>
</tr>
<tr>
<td><strong>General health and lifestyle questions</strong></td>
<td>May be advisable to increase rapport before introduction of sensitive questions</td>
</tr>
<tr>
<td><strong>Heterosexual Conduct</strong></td>
<td></td>
</tr>
<tr>
<td>Married respondent: number of sexual partners before/after marriage, use of condom</td>
<td>Provides information on patterns of heterosexual mixing, importance of sex workers and extent of protection by condom. Provides link to study of high risk group</td>
</tr>
<tr>
<td>Single respondent: ever had intercourse, number of partners, use of condom</td>
<td></td>
</tr>
<tr>
<td><strong>Homosexual Conduct</strong></td>
<td></td>
</tr>
<tr>
<td>Married respondent: Number sexual partners before/after marriage, use of condom</td>
<td>Provides information on patterns of homosexual mixing, importance of sex workers and extent of protection by condom. Provides link to study of high risk group</td>
</tr>
<tr>
<td>Single respondent: ever had intercourse, number of partners, use of condom</td>
<td></td>
</tr>
<tr>
<td>Selling sex for money, use of condom</td>
<td></td>
</tr>
<tr>
<td><strong>Iatrogenic risk Factors</strong></td>
<td>Cannot be linked to STIs but will reveal potential exposure to HIV and Hep B/C</td>
</tr>
<tr>
<td>Receipt of injections, blood transfusion, selling blood, frequency of drug use, use of new syringes, sharing needles, number of persons,</td>
<td></td>
</tr>
<tr>
<td><strong>Presence of recent STI symptoms</strong></td>
<td>Measures perceived STI morbidity and is essential for treatment-seeking</td>
</tr>
<tr>
<td>Focus on urethral discharge, pain during urination, genital ulcers, sores</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment seeking for recent STI symptoms</strong></td>
<td>Describes current patterns of health-seeking acre (allopathic vs. others, Private vs. public), needed for planning of services</td>
</tr>
<tr>
<td>Type of care, counselling received (if any) and cost</td>
<td></td>
</tr>
<tr>
<td><strong>Knowledge/ recognition of STIs (including HIV) symptoms and protective means</strong></td>
<td>Provides baseline measures of knowledge to monitor impact of future IEC campaigns</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Minimum list of Variables/Topics proposed for the survey of Male Sex Workers/Hijray

<table>
<thead>
<tr>
<th>INDICATORS</th>
<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background Characteristics of respondent</td>
<td>Allows basic descriptive disaggregation of results</td>
</tr>
<tr>
<td>Age, education, marital status, duration of</td>
<td></td>
</tr>
<tr>
<td>marriage, other source of income, SES,</td>
<td></td>
</tr>
<tr>
<td>ethnicity, migration pattern, length of time</td>
<td></td>
</tr>
<tr>
<td>as MSM/Hijray</td>
<td></td>
</tr>
<tr>
<td>Commercial Sexual Activities</td>
<td></td>
</tr>
<tr>
<td>Number and type of clients, venues used,</td>
<td></td>
</tr>
<tr>
<td>number of sexual encounters during last one</td>
<td></td>
</tr>
<tr>
<td>week, condom use, vaginal intercourse with</td>
<td></td>
</tr>
<tr>
<td>sex workers, condom use</td>
<td></td>
</tr>
<tr>
<td>Provide information about risky behaviour</td>
<td></td>
</tr>
<tr>
<td>Non-Commercial Sexual Activities</td>
<td>Information about non-commercial risk behaviour</td>
</tr>
<tr>
<td>Number and type of partners, condom use</td>
<td></td>
</tr>
<tr>
<td>Iatrogenic Risk factors</td>
<td>Cannot be linked to STI but will reveal potential exposure to HIV and HEP B/C</td>
</tr>
<tr>
<td>Receipt of injection, blood transfusion,</td>
<td></td>
</tr>
<tr>
<td>selling of blood, needle sharing for IV drug</td>
<td></td>
</tr>
<tr>
<td>use</td>
<td></td>
</tr>
<tr>
<td>Presence of recent RTI/STI Symptoms</td>
<td>Assesses subjective burden of illness</td>
</tr>
<tr>
<td>Focus on pain during urination, sores/ulcers in</td>
<td></td>
</tr>
<tr>
<td>genital area</td>
<td></td>
</tr>
<tr>
<td>Measures of perceived severity, duration and</td>
<td></td>
</tr>
<tr>
<td>functional disability associated with each</td>
<td></td>
</tr>
<tr>
<td>reported symptoms</td>
<td></td>
</tr>
<tr>
<td>Treatment-seeking for RTI/STI symptoms</td>
<td>Describe current pattern of health seeking</td>
</tr>
<tr>
<td>Types of care, counselling received (if any)</td>
<td>(allopathic vs. others, Public vs. Private).</td>
</tr>
<tr>
<td>and cost</td>
<td>Needed for planning of services.</td>
</tr>
<tr>
<td>Knowledge/recognition of STIs (including HIV)</td>
<td>Provides baseline measures of knowledge</td>
</tr>
<tr>
<td>symptoms and protective means</td>
<td>to monitor impact of future IEC campaigns</td>
</tr>
</tbody>
</table>
## Minimum list of Variables/Topics proposed for the survey of Truckers and Helpers

<table>
<thead>
<tr>
<th>INDICATORS</th>
<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background characteristics of respondent and spouse</strong>&lt;br&gt;Age education, marital status, duration of marriage, SES, place of natal/marital home, occupational details</td>
<td>Allows basic descriptive disaggregation of results</td>
</tr>
<tr>
<td><strong>Mobility</strong>&lt;br&gt;Frequency and Duration of home visits, date of last visit</td>
<td>Established link to general population</td>
</tr>
<tr>
<td><strong>General health and lifestyle questions</strong></td>
<td>May be advisable to increase rapport before introduction of sensitive questions</td>
</tr>
<tr>
<td><strong>Heterosexual Conduct</strong>&lt;br&gt;Married respondent: number of sexual partners before/after marriage&lt;br&gt;Single respondent: ever had intercourse, number of partners</td>
<td>Provides information on patterns of heterosexual mixing, importance of sex workers and extent of protection by condom.</td>
</tr>
<tr>
<td><strong>Homosexual Conduct</strong>&lt;br&gt;Married respondent: Number sexual partners before/after marriage&lt;br&gt;Single respondent: ever had intercourse, number of partners</td>
<td>Provides information on patterns of homosexual mixing, importance of sex workers and extent of protection by condom. Provides link to study of high risk group</td>
</tr>
<tr>
<td><strong>Iatrogenic risk Factors</strong>&lt;br&gt;Receipt of injections, blood transfusion</td>
<td>Cannot be linked to STIs but will reveal potential exposure to HIV and Hep B/C</td>
</tr>
<tr>
<td><strong>Presence of recent STI symptoms</strong>&lt;br&gt;Focus on urethral discharge, pain during urination, genital ulcers, sores</td>
<td>Measures perceived STI morbidity and is essential for treatment-seeking</td>
</tr>
<tr>
<td><strong>Treatment seeking for recent STI symptoms</strong>&lt;br&gt;Type of care, counselling received (if any) and cost</td>
<td>Describes current patterns of health-seeking acre (allopathic vs. others, Private vs. public), needed for planning of services</td>
</tr>
<tr>
<td><strong>Knowledge/recognition of STIs (including HIV) symptoms and protective means</strong></td>
<td>Provides baseline measures of knowledge to monitor impact of future IEC campaigns</td>
</tr>
</tbody>
</table>
5.6 Biological Data

Both design workshops and the laboratory issues workshop extensively discussed the range of pathogens to be assessed in the survey. The recommendation is to study HIV, chlamydia, syphilis and gonorrhoea in all groups, to study bacterial vaginosis for FSWs and Hepatitis C for IDUs. The rationale for the inclusions and exclusions are described in annexe 2 and summarised below.

It is proposed that trained staff, such as laboratory technicians or health technicians will collect biological samples from males and Hijray, while LHV's will collect from FSWs. The biological samples to be collected are a combination of blood, urine and vaginal swabs or anal swabs depending on the group as shown in the matrix below, which also mentions the organisms to be tested. Blood and urine samples have been collected in previous small-scale studies, with reasonably high compliance and with no special problems. However, there is no prior experience with the field collection of vaginal swabs and anal swabs, a much more intrusive procedure. Field tests conducted during the design process among rural and urban women belonging to the general population showed that collection of vaginal swabs is feasible, with an expected compliance of 60%. It is assumed that compliance among FSWs to vaginal swabs and compliance among MSWs and Hijray to anal swabs will be similar.
### Recommended Biological Tests, Samples and Methods for Testing for Each High-Risk Group

<table>
<thead>
<tr>
<th>Disease and Samples</th>
<th>Risk Groups and Specimens</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Vaginosis</strong></td>
<td>FSWs</td>
<td>MSWs</td>
</tr>
<tr>
<td><strong>Chlamydia</strong></td>
<td>LCR</td>
<td>PCR</td>
</tr>
<tr>
<td><strong>Gonorrhoea</strong></td>
<td>LCR</td>
<td>PCR</td>
</tr>
<tr>
<td>Urine + anal swab for MSWs and Hijray</td>
<td></td>
<td>STI marker of sexual risk. Co-factor of HIV transmission. Preventable &amp; curable.</td>
</tr>
<tr>
<td><strong>Syphilis</strong></td>
<td>Serum</td>
<td>Serum</td>
</tr>
<tr>
<td>(Blood)</td>
<td></td>
<td>As a marker of syringe exchange</td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>Serum</td>
<td>Serum</td>
</tr>
<tr>
<td>(Blood)</td>
<td></td>
<td>To ascertain prevalence</td>
</tr>
<tr>
<td><strong>HIV</strong></td>
<td>Serum</td>
<td>Serum</td>
</tr>
</tbody>
</table>

#### Rationale for Inclusion and Tests

HIV testing is required to provide baseline measures for continued HIV surveillance. It will be tested anonymously and unlinked. Unlinked anonymous testing is the testing of specimens for markers of infection after elimination (delinking) of all personal identifying information from each specimen. Unlinked HIV seroprevalence studies ("blind studies") rely on HIV tests conducted on blood specimens drawn for another purpose. Personal identifiers are stripped from the blood so the results of the test cannot be linked to the individual. Unlinked anonymous surveillance screening, has gained popularity in the
recent years because it reduces participation bias. In the case of HIV testing it also alleviates the ethical issues related to the management of positive cases. The rationale for and the data collection methodology of this test, however, will be fully explained during the informed consent process. All serum will first be tested with one ELISA. Any serum found reactive on the first assay will be re-tested with a second ELISA which is based on a different antigen preparation and/or different test principle (e.g. indirect versus competitive).

**Chlamydia** is likely to be one of the most common STIs in Pakistan. Untreated infections in women can cause Pelvic Inflammatory Disease, leading to infertility. PCR testing on urine samples is recommended over more traditional methods of diagnosis based on cultures from vaginal swabs for several reasons: higher sensitivity; less vulnerability to human error; higher compliance for urine collection than for vaginal swabs, hence results are more representative; greater ease of replication in repeat-surveys (Quinn, 1996). At the expected levels of infection (20%+) pooling of samples for laboratory analysis is not recommended (Karena, 1998). PCR testing is routinely performed at several public and private sector laboratories in Pakistan.

**Syphilis** is one of the most prevalent and harmful STIs worldwide. Syphilis will be tested and treated in the field on blood samples using RRR, a quick and simple test that is now routinely used in community-based STI studies (Nadarajah, 1990; Phaosavasdi, 1989). Field tests, however, are more error-prone than tests in the laboratory and possess little scientific credibility. Therefore all sera will be re-tested in a laboratory with RPR. As RPR has only moderate specificity, all positive specimens will be confirmed by TPHA, a highly specific test. TPHA is the recommended confirmatory test for syphilis. (D'Errico, 1996). Neither RPR nor TPHA is commonly used in Pakistan but both are simple tests and thus the training implications of this recommendation are minor.

The testing strategy will not distinguish between active cases and life-time infections (see annexe 2 for further discussion).

**Gonorrhoea** is usually concentrated in high risk groups and is therefore a high priority. For truckers/helpers and IDUs, PCR testing on urine is recommended. This test has
high sensitivity in men (90%+) but not in women for whom the positive predictive value is very low even in high risk groups (a large majority of positive tests are false positives, as outlined in Chapter 3). For FSWs we therefore recommend LCR testing of urine which has high sensitivity, specificity and positive predictive value in women (Tabrizi, 1997; Mukenge-Tshibaka, 2000). LCR is not yet available in Pakistan but is very likely to be in use in at least one laboratory and possibly more by the time of execution of the study. It is recommended over more traditional tests based on vaginal swabs, because LCR is likely to become routinely used in future STI/HIV surveillance of FSWs. It is thus important that the baseline measure uses the same diagnostic method that is likely to be used in future. For men who practice receptive anal intercourse (MSWs and Hijray), PCR (or LCR) testing of anal swabs is the appropriate anatomical site for the assessment of gonorrhoea.

**Hepatitis C** will be tested among IDUs only, because this group is particularly susceptible to infection. It will be tested by EIA (enzyme immunoassay) which is the screening test normally done in blood banks. EIA has advantages of ease of use, low variability and relatively low cost. Although false-positives remains a problem with EIA testing in low prevalence settings, the accuracy of the EIA-2 test is very good in high prevalence settings (Jeffrey, 2001). As HCV prevalence is usually above 70% in IDUs, supplemental more sensitive anti-HCV tests may not be necessary. These tests cost about US $100 per patient.

**Bacterial vaginosis** will be tested in FSWs only. Its prevalence is expected to be high and it has important post-natal outcomes (e.g. low birth weight, increased neo-natal mortality). Some evidence suggests that it may be transmitted sexually (Morris et al., 2001). The proposed test is a standard one (gram stain + microscopy) but training in the application of Nugent's criteria for assessing severity will be required. This pathogen is far less important than other pathogens proposed for FSWs, especially in contrast to its much greater importance in the general population study of women, and the recommendation to include it is a finely balanced one.
Rationale for Exclusions

Candidiasis is not known to be associated with sexual conduct and has no known serious sequelae.

Hepatitis B virus (HBV) can be sexually transmitted, but is not included in the proposed study, partly because estimates would have little programmatic implication for HIV prevention. Moreover estimates from other studies are considered sufficient for HBV control programmes.

Trichomonas vaginalis is a sexually transmitted organism but it is a minor cause of complications. While high prevalence in women nonetheless may lead to high attributable risk, this pathogen has not been included in the study because of constraints related to its diagnosis by microscopy. Diagnosis by microscopy has a low sensitivity (44%) (Wiese, 2000); it has to be done on a live specimen in the field, thus increasing the potential for error. The only alternative would be to detect it by PCR from vaginal swabs with sensitivity of 87% (Madico, 1998). This is not justifiable in relation to the relatively low personal and public health importance of this pathogen, compared with others being proposed.
5.7 Ethical Considerations

Informed Consent

A step-wise approach to ensuring informed consent is recommended. Information needs to be conveyed to the selected communities of the vulnerable groups well in advance of the arrival of the main data collection team; informed consent from individuals for the behavioural interview is needed; and finally, informed consent is required for the biological data collection.

It is proposed that information to communities about the nature and purpose of the study be given by researchers who will be conducting the initial two months of social reconnaissance and qualitative enquiry.

The behavioural interview will be conducted at an appropriate place for the respondent and by trained interviewers. It is recommended that interviewers be trained to describe in outline the scope of the interview, its approximate length and to stress that participation is entirely voluntary. It is recommended that verbal consent should suffice for this component of the study.

Following the interview, subjects will be invited to attend the clinic or camp for the biomedical component on the same or next day depending on the mobility of the respondent. The procedures will be described to subjects, their purpose will be outlined as well as opportunities for front-line treatment and secondary treatment when laboratory results are known.

It should be stressed that no incentive in kind or cash will be offered for participation, other than treatment and, in exceptional cases, assistance with transport, except perhaps for IDUs.¹⁴

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¹⁴ The members of Ethical Review Committee suggested that at least one meal be provided to the IDUs as an incentive, as it is an exceptionally difficult group to recruit. However, NACP staff have concerns about this suggestion. This is an issue to be resolved by the implementing agency.
On arrival at the clinic, full understanding of the procedures will be re-confirmed by medical or paramedical staff.\textsuperscript{15} Participants will be asked to endorse their consent to bio-medical procedures in one of the following ways: (1) consent with signature; (2) consent by fingerprint; (3) oral consent with a witness; and (4) oral consent recorded on audiotape. Witnesses should not be members of the research team but they may be other participants. They need not be literate.

\textit{Privacy and Confidentiality}

The behavioural interviews should be conducted in privacy, out of the hearing of other people. When these conditions cannot be obtained, interviewers will offer an alternative venue or time. At the temporary clinics, adequate auditory and visual privacy should be available, particularly for collection of vaginal and anal swabs, syndromic management and counselling.

Confidentiality will be maintained by the use of personal identification numbers (PINS). These will be issued to respondents following the completion of the behavioural interviews and used as the means of identification for bio-medical data collection. The master list of names, addresses and matching PINS will be collected at the end of each day’s work and kept under lock and key by the doctor or senior LHV who will be the team supervisors. Similarly, the consent forms, which may also contain names and PINS, will be collected and stored securely. Results from laboratory tests will also be identified only via PINS and therefore can only be released to respondents in possession of their PINS. It is essential that PINS be durable, unalterable and sufficiently large to minimise their loss.

\textit{Treatment}

For reasons discussed in Chapter 2, the recommended treatment protocol for the study of the high risk population is to maximise front line treatment at time of data collection but nevertheless develop a notification strategy for respondents found to be infected by

\textsuperscript{15} Some participants at the Ethics Workshop recommended the administration of a short comprehension test with those failing being given the necessary information and asked to return the following day. Others felt that this was excessive and would result in unnecessarily low participation. This is a second issue to be resolved by the implementing agency.
laboratory tests and NOT already treated appropriately. Front line treatment will be performed by the doctor or paramedic at time of biological data collection, using the recently revised WHO guidelines for syndromic management. This will result in over treatment of uninfected cases but the cost will not be high and is justified both by ethical considerations and by its beneficial effect on participation and community relations. In addition it is proposed to use a rapid test for diagnosis of active syphilis (results available within few hours) and to treat infected cases on the spot.

In addition to syndromic management of STIs (including syphilis), medical or paramedical staff will also offer free treatment of other acute conditions. Cases of chronic illness will be referred to a pre-selected public sector health facility (or to a private or NGO facility in some cases). Fees for referral and treatment of chronic conditions will not be covered by the study.

Feedback of laboratory tests requires careful identification of a medical facility or practitioner within, or close by, each selected study site. It is expected that a partner NGO typically will fulfil this function. Staff will be briefed about the study and provided with standard protocols for treatment of STIs.

Respondents will be told where they can obtain laboratory results and a date after which they will be available. This date should make generous provision for logistical delays in laboratory processing and communication of results in order to minimise wasted visits. As stated earlier, results will be identified only by PINS and will be released only to respondents in possession of their PIN.

In addition to treatment of study participants, non-selected members of communities who present at the clinic will be examined and treated as far as this can be done within constraints of time.

Ethical review of the final study protocol by an independent review board is essential. Such a national board does not exist in Pakistan but is urgently needed.
5.8 Field Strategy

5.9.1 Team Composition

It is expected that the initial two months of exploratory work might be conducted by a Preparatory Team, though much depends on local circumstances:

- 2 persons from the partner NGOs
- 2 members of the study community
- 2 social researchers, trained in qualitative methods

The general composition of the Data Collection Team is likely to be:

- 4 well trained interviewers
- 2 male phlebotomists technicians (or 2 LHV s for FSWs) for collecting blood, urine (or swab samples) in the field
- 1 medical doctor or senior LHV for providing treatment (also the team supervisor)
- 1 laboratory technician for aliquoting and RPR
- 1 cold chain technician
- All members of the advance team

5.9.2 Phasing of Work

It is proposed that the study is carried out in one site with a single vulnerable group at a time. The order of selection of groups is to be determined by the implementing agency or agencies in consultation with the NACP.

5.9.3 Sequence of Activities

The duties of the exploratory or preparatory team include the following:

- Establish good working relationship between research and NGO staff
- Identify and recruit member of the study population, where possible
- Conduct additional social mapping where necessary
- Interview key informants
- Identify sub-groups within the study population, contact them and engage their support
- Design an appropriate sampling approach
- Conduct unstructured interviews with 10-20 members of the study population and (where appropriate) four or more focus group discussion
- Set up an appropriate clinic for biological testing and treatment

After the completion of the task of this phase, the Data Collection Team will join the Preparatory Team. It is estimated that each of the four interviewers will carry out four interviews per day and request subjects to visit the clinic either on the same or next day depending on the mobility of the respondent. This will require 25 working days (one month) to complete the tasks. However, in view of the possibility of unanticipated problems, the period of 1.5 month is proposed for the activity. Finally, it is recommended that a further two weeks of in-depth interviewing is conducted by the two social scientists on the team. About 20 such interviews should be conducted, with the purpose of providing greater explanatory insights into the beliefs and behaviours of the study population.

**Figure 5.1: Duration of Study at One Site for 400 Respondents from one Vulnerable Group**

<table>
<thead>
<tr>
<th>Exploratory and preparatory Phase</th>
<th>Data Collection</th>
<th>Further Qualitative Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>1.5 months</td>
<td>0.5 months</td>
</tr>
</tbody>
</table>

**Total period**

| 4 months |

5.9.4 *Logistics Arrangements*

Blood and urine samples would be taken in the field after the behavioural interview or, if the subject prefers, at the clinic. Phlebotomists or LHV's will accompany each interviewer for collection of blood and urine. It was observed during the pretests that the compliance among urban men for giving biological samples increased dramatically when
phlebotomists accompanied the interviewers. It is reasonable to assume that this holds true with members of high-risk groups. At the clinic the doctor or the senior LHV will examine the respondents and collect vaginal/anal swabs and also blood and urine (if preferred by the respondent).

It is preferred that a single blood sample is taken using vacuettes, to be placed into Gel tubes. These tubes allow sera to separate over the next few hours (about 6 hours).\footnote{Another option is to collect blood in glass tubes and centrifuges to separate sera within 10-20 minutes. This would decrease the cost of tube from Rs. 5 for Gel tube to Rs. 1 for glass tube (estimated saving of Rs. 2000), while increasing the cost for provision of centrifuge by Rs. 10,000 (an overall effect of Rs. 8,000 only). Opinions of medical microbiologists vary on the relative merits of the two approaches. The implementing agency will have to make the decision according to the experience and expertise of the medical microbiologist in the team.}

The separated sera will be tested for Syphilis through RPR. The remaining sera will be divided and stored into three aliquots, one each for testing and confirmation, and one for longer-term storage at the designated labs. A clear process for labelling and identification of the aliquoted samples will need to be defined by the implementing agency for meeting confidentiality requirements.

Urine samples will be collected in sealable sterile containers. Three aliquots will be prepared and frozen at –20C within few hours of collection.

Fixed slides will be prepared from the vaginal or anal swabs by drying in air on the spot and will be stored at room temperature in slide boxes. Frosted slides will be used for the purpose as they allow clear labelling.

For maintaining the cold chain, a cold chain technician (CCT) will also be a member of each Data Collection Team. It is proposed to have a vehicle with driver, accompanied by the CCT to keep the cold chain mechanism independent and thus to guarantee proper storage and timely transport to the labs. The vehicle is essential as it will carry the cold chain equipment (special freezers, generator, supplies needed for maintenance and ice boxes).
The cold chain mechanism is described in Figure 5.2. The samples collected at the field will be placed in ice boxes with ice packs to ensure an ambient temperature. These will then be transferred to the field laboratory where the blood and urine samples will be aliquoted by the laboratory technician. The aliquoted samples will be stored at –20°C in special ice-lined freezers, which are able to maintain the required temperature for at least 48-72 hours in the event of electricity failure. Generators and stabilisers will also be provided to overcome frequent electricity failures and fluctuations, experienced even in cities.

Long range ice boxes with ice packs (or the freezers) will be used for transporting the samples from the field laboratory to the referral and reference laboratories taking care that samples do not thaw. Temperatures at each stage will be monitored through special laboratory and recording thermometers to ascertain maintenance of the cold chain.

Aliquots will be stored at –70°C at the referral labs. After completion of the study, all samples will be transported to the designated laboratory for long term storage.

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17 Transportation using dry ice for road and air transport is not being recommended due to limited availability and high cost.
Figure 5.2: Sample Transport and Cold Chain Mechanism

**FIELD**
- Sample Collection:
  - Blood in Gel Tube
  - Urine in sterile container

**FIELD LAB**
- Aliquoting by trained lab technician
- Slide preparation/fixing

**FIELD**
Storage by Cold Chain Technician at –20C or direct transport to Referral Labs
- Freezer with Generator
- Temperature monitoring by recording thermometers

**TRANSPORT TO PROVINCIAL CAPITAL/REFERRAL LABS**
- Transport in Freezer w/ Generator
- Transport in Long Range Ice Boxes with Ice Packs
- Temperatures to be recorded by recording thermometers

**TRANSPORT BY AIR**
- Transport in Long range Ice Boxes with sufficient Ice Packs
- Temperatures to be recorded by recording thermometers

**REFERENCE LABS**
- Receiving/labeling
- Freezing of samples at –20C/ -70 C
5.9.5 Reporting of results and feedback to subjects

All respondents will be encouraged to receive the results of the laboratory tests from a pre-selected location during a fixed period after the survey. The study co-ordinator will ensure mailing (or other means of conveying) of results to the identified place through a reputable courier service. The research team and its partner NGO will have to identify this location and arrange for smooth delivery of the results. This location should preferably be a health centre, public or private. It may also be facility run by the partner NGO. A fee for service will be provided to the person in charge or to the facility responsible for delivering results to the respondents, and for providing treatment. The persons involved in this activity will have to be trained in the ethical aspects of this service, with especial focus on maintaining confidentiality of those collecting results and on treating subjects with respect.

The results will have to be written in clear and simple language. Treatment of infected cases should ideally be arranged at the centre responsible for feedback of results.

5.9.6 Laboratories to be used

The selection of laboratories for each study will be determined largely by the location of the study sites. There are obvious advantages in choosing laboratories that are located in the same city as the research site. For instance substantial cost savings may be made by removing the need for cold-chain mechanisms. Nevertheless referral laboratories should be selected according to the following criteria:

- Willingness to participate
- Technical capacity to supervise and conduct the study:
  - Qualification of technical staff
  - Routine performance of the relevant test
  - Quality assurance programme in place
  - Facility for disposal of infectious waste
- Capacity to sustain tests introduced by the study
- Willingness to undertake objective performance tests
LCR/PCR test should be performed only at laboratories that already use this technology. Where several laboratories are involved in the study, a reference laboratory should be selected for each test. This may be the same laboratory for all tests or, alternatively, a different reference laboratory could be used for each test.

5.9.7 **Data entry, processing and analysis**

Data analysis will be done in an appropriate Pakistani institution, which may require some capacity building. It is proposed that the data is entered in computer using “SPSS Data Builder version. 1” or “PC-edit” package, as they have features to minimise data entry errors. STATA, SAS, or SPSS should be used for data analysis.

It is estimated that about 10 person-days will be required for data editing, cleaning and double data entry. It is recommended that data entry should be done under the close supervision of a data analyst. One data editor and one coder will be required for editing of the questionnaires and for coding of the open-ended questions in the questionnaire. Analysis of the qualitative data should be conducted by the social scientists, based on field notes and tape-recordings.

Key results should be available within eight weeks of the completion and data entry and editing and linking behavioural to biological data. It is envisaged that biological results and behavioural results will be reported in terms of prevalence and means, with 95% confidence intervals (CIs) as illustrated below.
Illustrative Presentation of Key Results

<table>
<thead>
<tr>
<th>Biological</th>
<th>Number of Tests/Interviews</th>
<th>% Positive (mean)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Syphilis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhoea</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### Behavioural

**FSWs:**
- Mean clients last 7 days
- % used condom last time with client
- % used condom last time with spouse/pimp.
- etc

A more detailed analytical report would probably take an additional six months to complete. It should contain quantitative and qualitative findings. Further details on dissemination may be found in chapter 2.

### 5.9.8 Quality Control/Accuracy

Quality Control will have to be created and maintained at all the levels i.e. fieldwork, transport of samples, laboratories and data analysis. Recommendations are summarised below.

**Training**
- Special international training in qualitative techniques may be required
- Interviewers be trained for two weeks
- Biomedical and field laboratory staff be trained for at least 4 days
- Laboratory staff be trained in Standard Operating Procedures (SOPS) by the reference laboratory (see annexe 6 for an example)
- Special training be given in the use of Nugents Scoring System for diagnosis of bacterial vaginosis (see annexe 5).
Pre-Testing of Instruments
- The development of behavioral questionnaires be preceded by extensive qualitative work and drafts should be pretested in the appropriate language

Supervision
- Day-to-day supervision will be the responsibility of the team supervisor
- Questionnaires will be checked for completeness and consistency each day
- Occasional spot-checks will be make on interviewers by re-visiting subjects, where possible
- The work of laboratory technicians will be checked by direct observation
- The team supervisor will take responsibility for ensuring that no problems arise with transport of samples
- Higher level supervision will be exercised by senior members of the research team
- The reference laboratory will check by site-visits that SOPs are being rigorously applied by collaborating laboratories.

Quality Checks and Quality Assurance of Laboratory Work
- All participating laboratories should agree to meet pre-set performance criteria for each test prior to start of the study
- For serology, well established international systems of performance testing exist and should be used
- The reference laboratory should retest a 10% sub-sample of each test performed by each participating laboratory
- Discrepancies exceeding a pre-determined level should result in complete re-testing of the relevant batch
- For LCR and PCR tests, a sub-sample of positives and a smaller sub-sample of negatives should be re-tested by an international laboratory

Data Processing and Reporting
- Range, skip and filter checks should be applied and errors resolved
- The system of linking behavioral and biomedical data should be closely monitored
• The main analytical report should be reviewed by international experts before release.

5.9 Management Structure

The management structure will depend on the way in which these studies are allocated between different implementing agencies. It is proposed that the study will have one Study Co-ordinator to supervise the field teams and their activities. Each team will have one supervisor, who will be responsible for carrying out the study according to the prescribed guidelines and for the quality of data. Their roles and duties have been mentioned in the section on quality control/assurance. In addition, the co-ordinator will also have to organise independent external monitoring in the field.
References


Daud Saqlain. No date. Impact study on HIV/AIDS Awareness among CSWs Project. AIDS Awareness Group, Lahore.


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