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ST. MICHAEL'S HOSPITAL  
A teaching hospital affiliated with the University of Toronto



CENTRE FOR GLOBAL  
HEALTH RESEARCH

## HIV/AIDS RELATED RESEARCH

### Research Plan: Epidemiological studies of the causes of HIV-1 in low income countries

Epidemiological studies on the consequences of HIV-1 infection are required to raise public knowledge and to guide control programs. Targeted interventions must be knowledge based; the evidence from these epidemiological studies will guide these programs to be more efficient and effective in decreasing HIV-1 transmission.

"With a population of 1 billion, large numbers of commercial sex workers, mobile male workers, a high prevalence of STDs, low reported condom use with non-regular partners and a low prevalence of male circumcision, India is set to experience an explosion of HIV-1 cases." (CMAJ, 2004). Our efforts are therefore geared towards understanding the transmission dynamics and providing evidence for targeted interventions. We have used data from a variety of sources including antenatal clinics (ANCs), Voluntary counseling and treatment clinics (VCTCs), sexually transmitted infection clinics (STIs), and surveys including the Reproductive and Child Health Rapid Household Survey (RCH), and the Behavioural Surveillance Survey (BSS).

Below is a list of the studies we have completed or are in the process of completing.

#### A. Population levels, trends and determinants of HIV prevalence

##### 1. Trends in HIV among 300,000 antenatal clinic attendees in North and South India.

This study was published in the Lancet in March 2006 and is the world's largest published study of HIV among a routine resting population. The study documents a 30% decline in HIV prevalence from 2000 to 2004 among young women in the South. This is most likely due to increased condom usage between male clients of female sex workers.

##### 2. HIV prevalence among urban and rural antenatal clinics in North and South India.

This study will examine differences in HIV levels, trends and determinants of infection between urban (n=100,000) and rural (n=49,000) India using two different definitions of residence; one site-based and one individual-based.

##### 3. Trends in HIV prevalence among 120,000 male and female sexually transmitted infection (STI) clinic attendees in North and South India.

This study documents changes in HIV prevalence among males with genital ulcer from 2000 to 2004. Genital ulcer among male STI clinic attendees is a marker for recent high-risk sex contact and helps document changes in male sexual behaviour.

##### 4. Geographic analysis of HIV in 115 districts of South India.

There is a substantial geographical heterogeneity of HIV prevalence existing within the 115 districts of the 4 states analyzed. Our findings are robust with respect to the specification of the prior distribution. Prevalence of STDs in the previous year and average age at marriage are significantly associated with district-wise HIV infection. Spatial mapping will be used to quantify locality and risk of HIV infection.

##### 5. Ecological Study of HIV-1 in 115 Districts in 4 Southern States of India

This study examined the differing risk factors on an ecological level in 115 districts in 4 high prevalence southern states of India: Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu.

##### 6. Measurement of AIDS mortality from a large scale representative community-based national household survey.

Part of a much larger cohort study called the "Million Death Study" that aims to document causes of death in 1.3 million households (approximately 7.6 million people) from 2004 to 2014

## **7. Meta-analysis of behavioural and sexual risk factors for HIV in Africa**

The study synthesizes evidence from 79 studies done in African countries and provides strong evidence that commercial sex work multiple sex partners, HSV-2 and male lack of circumcision were significantly associated with HIV infection. The meta-analysis will be expanded to Asia. (link to be posted soon)

## **8. Review of Behavioural Surveys in India.**

We have systematically analyzed data from over 25 behavioural surveys covering more than 100,000 adults at high-risk of HIV infection (female sex workers and their male clients) and at lower risk (general population). These analyses will help us better understand sexual networks in India. (link to be posted soon)

## **B. Improved tools for population-based HIV measurement**

### **9. Risk of HSV-2 infection among general population survey subjects.**

We aim to use HSV-2 as a marker for high-risk sexual activity in our general population survey of 3,000 adults to improve validity of sexual behavioural surveys. We are in talks with biotech firms to develop a "risk chip". This bloodspot-based technology would yield results for an individual's HIV status, including incident versus prevalent infection, and status of an STI such as HSV-2.

### **10. Comparative study of demographics of ANC attendees and the Indian general population from the reproductive child health survey.**

A large proportion of women in India utilize private ANC services. HIV sentinel surveillance among pregnant women in India draws from only public ANCs. We are studying ANC public versus private usage behaviour among general population women in India to assess validity of HIV estimates of prevalence and trends.

### **11. Audio-assisted confidential voting interview to improve validity of data on sexual risk taking behaviour from community based surveys.**

In low literacy setting, audio assisted confidential voting interview method may extract more valid information related to sexuality than the conventional face to face interview or the self administered questionnaire.

### **12. HIV prevalence and risk factors among 30,000 voluntary counselling and testing centre (VCTC) attendees in Tamil Nadu, India.**

A descriptive analysis of the population attending VCTC services. Marked heterogeneity exists in reason for attending. We are attempting to characterize HIV risk sub groups within this high-risk self-selected population.

## **C. Policy and programmatic impact**

### **13. Comprehensive mathematical model of HIV transmission in India**

Our comprehensive model suggests almost all of the new HIV-1 infections arise from first or second generation exposure to FSWs. The most practical and effective intervention is to increase the rate of condom use. We are currently working on modeling the effects of a HIV-1 vaccine, with and without disinhibition, a Herpes Simplex Virus 2 (HSV-2) vaccine, male circumcision and the population impact of antiretroviral roll-out.

### **14. Monitoring and evaluation of HIV sentinel surveillance system expansion in India**

A pilot project in five sentinel surveillance sites in both the north and south of India to evaluate ways in which a few simple low cost improvements to the surveillance system in the behavioural questionnaire and biological testing could greatly improve explanatory power of routinely collected data

### **15. Qualitative examination of uptake of information from the Ecological Study**

This study aims to determine whether the provision of evidence for preventative HIV interventions to policy makers and program officers at the district and state level translates into programmatic changes. The study also includes a two day Workshop aimed at information dissemination to key policy makers and NGOs involved in targeted interventions in India.

## MILLION DEATH STUDY – II PHASE

### Rationale

In Phase I of India's "Million Death Study" (NIH Grant# RWA TW05991), we have shown that tobacco smoking is a major cause of premature adult mortality in Indian men. Because tobacco use patterns and disease patterns vary considerably within India, the expected consequences of prolonged tobacco use will also likely vary in India's large and heterogeneous population. Considerably more research is needed in order to document the links of smoking and tuberculosis, respiratory mortality among non-smoking females and children in relation to passive exposure to smoke and indoor air pollution, the joint risks of tobacco use with other chronic disease risk factors and the impact of tobacco control policies and individual knowledge on cessation of tobacco use.

### Aims

This prospective study will investigate all-cause mortality and cause-specific mortality (tuberculosis, vascular disease, asthma, chronic obstructive pulmonary disease, cancer, childhood respiratory diseases, and other causes) by age, gender and socio-economic group in relation to tobacco use among 1.3 million homes in India. We will relate the following exposures and outcomes:

Exposures	Outcomes	Sample Sizes
Male bidi and cigarette smoking and tobacco chewing	Relative and absolute risks of tuberculosis, myocardial infarction and other chronic diseases	98,000 male deaths and 65,000 female deaths at ages 25-69 (2006-2012)
Female tobacco chewing		
Household male smoking with/without indoor air pollution exposure	Adult female and child respiratory mortality	7,500 female deaths at ages 25-69 and 3,500 child deaths at ages 1-4 (2006-2012)
Local and national control policies	Male and female smoking or chewing prevalence and ex-smoking or ex-chewing rates	About 0.6 million male smokers, 0.5 million male chewers and 0.2 million female chewers in 2004
Smoking or chewing tobacco and other risk factors	Other risk factors: body mass, blood pressure, blood lipids (apo B/A1 ratios), diabetes (self-reported and HgA1C)	10,000 adults age 18 or older

### Methods

We will monitor the mortality caused by tobacco use among 1.3 million households (or about 7.6 million people) who are already enrolled in the Indian Sample Registration System (SRS), and who will be re-surveyed every six months until 2014. India's SRS is a large continuous demographic survey of 7,597 small areas (4,433 rural and 3,164 urban) randomly selected from the 2001 Census. The follow up will be through computerised linkage to determine the vital status (alive/dead) of the individual and, if dead, the cause of death, using a nine-digit unique identity number. Such linkage will establish the relationship of total mortality with smoking. In order to establish the relationship with cause-specific mortality, a team of 800 trained interviewers will visit all the houses to determine, retrospectively, the cause of death using a well-validated field instrument for deaths from 2004-2014 (i.e. 0.7 million deaths over ten years, of which this project will document about 0.42 million deaths occurring from 2006-2012). Home visits will be subjected to random re-sampling, and each death report will be adjudicated centrally for cause by two trained physicians.

Sub-samples will be used to re-measure exposures (smoking and indoor air pollution) using re-interviews and biological measurements (breathalyser carbon monoxide measurements and machines to measure household particulate matter) in order to check validity and to adjust for the regression dilution bias. A sub-sample of 10,000 adults in representative regions will be surveyed for the chronic disease risk factors including body mass (height, weight and waist-hip ratio), blood pressure, peak respiratory flow, and lipid and diabetic factors measured on dried blood spots. Various precautions will ensure strict quality control of the fieldwork, coding, entry of data, and statistical analyses. Specific cessation surveys will track the levels and correlates of adult quitting, and substantial "knowledge translation" and training opportunities will be provided.

### Impact

The project is among the world's largest prospective investigations of premature mortality. It builds sustainable capacity to monitor diverse tobacco hazards in a population of one billion at a unique scale. Leverage of Government of India and other resources permits the study to be very low-cost (< \$1/person/year). The blood-based pilot studies should enable large, representative and reliable genetic and biological epidemiological studies of premature mortality in the near future.