HIV-1 trends, risk factors and growth in India

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It is certain that the epidemic of human immunodeficiency virus type 1 (HIV-1) in India will increase. However, there remains considerable uncertainty about the prevalence and incidence of HIV-1 infection, and the determinants of infection. The future growth of HIV-1 also remains uncertain.

Currently, the official prevalence is estimated at just below 1% of the adult (15–49 years) population, based on data from female antenatal clinic (ANC) attendees.[1] The official National AIDS Control Organization (NACO) estimates suggest that 50 lakh adults are infected. The estimated prevalence is roughly double this figure in the southern States. Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu, and the north-eastern States of Nagaland and Manipur together comprise over 75% of all infections, even though they have less than 30% of the adult population.

Surveillance is central to HIV-1 control programmes. However, surveillance in general and high-risk populations has been limited to date. This report provides a systematic overview of several key sources of data, including all ANC data from 1998 to 2003, the national behavioural surveillance surveys, and published literature on risk factors for HIV-1. New mathematical modelling of the growth of HIV-1 for the next two decades is also provided.

These interim analyses will be followed by more complete analyses of all the data later in 2005. Specifically, primary data from ANC and sexually transmitted infection (STI) surveillance in 2004, and the primary data from behavioural surveillance have not yet been made available for analyses.

Objectives

- Study the current levels and recent trends (1998–2003) of HIV-1 in general populations based on ANCs.
- Describe what is known about the determinants of HIV-1 infection in general populations based on a meta-analysis of the literature and behavioural surveillance surveys.
- Provide projection data for HIV-1 in various risk groups based on mathematical models.
- Provide estimates of reduction in growth of HIV-1 from various prevention and treatment interventions.

Definition and sources of data

Definition of transmission dynamics

Transmission dynamics reveal how HIV-1 spreads in the population. We provide a brief review of transmission dynamics, as understanding this is central to the design of control programmes, choice of interventions and monitoring changes in transmission.

Sexual behaviour and HIV-1 infection are not evenly distributed in the population. Core groups of highly sexually active people drive the rate of transmission in HIV-1 epidemics. The basic reproductive rate, R_0, is the average number of infectious contacts by one infected individual. An infectious contact is a person who would transmit the infection if his/her partner is uninfected. For an epidemic to occur, each infected individual must on an average make infectious contacts with more than one individual (R_0 must exceed 1). The R_0 must be reduced to lower the prevalence of the infection, and brought below 1 to eradicate it from a population.[2]

R_0 is the product of three factors:

- transmissibility (β),
- rate of partner change (C), and
- duration of infection (D).

Each of these factors in turn depends on physiological and sociological events. The transmissibility, β, varies with the number of sexual acts per individual as well as the probability of infection. The rate of partner change, C, is dependent on the average number of unprotected partners and how much variation there is from the average.[2]

Thus, interventions can be directed at any aspect of these parameters.

1. Interventions *directed at* β enhance resistance to infection or decrease susceptibility. Barrier methods such as

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condoms, treatment of co-existent STIs, antiretrovirals that decrease transmission, circumcision and HIV-1 vaccines would reduce β.

2. Interventions *directed at C* aim to alter sexual behaviour, including decreasing the rate of partner change, decreasing concurrency (more than one partner at once), lengthening the time gap between serial partners, increasing the age of initiation of sexual activity, or decreasing high-risk behaviour.
3. Interventions *directed at D* aim to reduce the period of infectivity by the use of antimicrobials and antiretrovirals or via contact tracing or partner notification.

For HIV-1, the contribution of each individual to the value of R_0 is not proportional to his/her number of (unprotected) sex partners but to the approximate square of that number.[2] The average rate in the mean population is not high enough to sustain HIV-1 epidemics. However, C can be high enough in vulnerable groups (i.e. $C>1/\beta D$) to increase the epidemic above an R_0 of 1. Historically, there is little doubt that 'core transmitters' are central to the epidemiology of any STI including HIV-1.[3] This is not always well understood, and occasions much debate about the importance of such vulnerable groups, especially at high levels of the epidemic.[4,5]

Sources of data

Antenatal clinics and sexually transmitted infection sentinel sites

Data here refer to individual-level data from 319,097 visits of women to 266 public ANCs and 130,233 visits of men and women to public STI clinics from all 36 States and Union Territories in India from 1998 to 2003.

For 12 consecutive weeks, twice a year, unlinked, anonymous testing is done among 400 ANC and 250 STI clinic attendees from each ANC or STI clinic. HIV-1 status is measured in ANC and STI clinic attendees, following the World Health Organization (WHO) protocol for confirming HIV-1 status in a developing country: two positive HIV-1/2 enzyme immunoassays results confirm HIV-1/2 seroprevalence, while two negative tests confirm negative HIV-1/2 status.[1]

ANC-based HIV-1 data are used to monitor trends in HIV-1 prevalence over time among general populations. ANC attendees provide a large annual sampling frame, the characteristics of which stay relatively constant.[6–8] ANC attendees are assumed to be representative of the general population. However, ANC-based HIV-1 surveillance has been questionable in estimating prevalence in the general population as both over- and underestimation have been reported, when compared to population-based surveys.[9,10]

The major weakness in the ANC data is, however, the poor coverage. The number of sites has increased from 36 in 1998, 63 in 1999, 107 in 2000, 167 in 2001, 191 in 2002 to 266 in 2003. Only half the sites have been open for more than three years, making projections of trends unreliable before 2000/2001.

Changes in HIV-1 prevalence in the general population are approximated by trends in HIV-1 seroprevalence among ANC attendees aged 15–49 years. HIV prevalence among 15–24-year-old women attending ANCs has been selected by UNAIDS and WHO as a key indicator for the monitoring of HIV-1 prevention programmes.[11,12] While ANC data are valuable, several issues concerning selection biases for ANC data have been identified and must be taken into consideration when using them to estimate HIV-1 prevalence or incidence in the general population.[13–18]

ANCs provide care for expectant women. Ideal ANC care includes three or more visits—with at least one in the first trimester, two or more tetanus toxoid injections, and iron and folic acid supplements for at least three or more months. Women attending ANCs are supposed to receive a range of medical tests and counselling.

The population attending ANCs in India is diverse and thought to be, by and large, representative of the general population. The mean and median age of the attendees is 23 years. Public ANC coverage, defined as women having ever used a public ANC or been visited by a health worker prior to a birth, is approximately 65% nationally.[19] Women are less likely to visit an ANC if they are older, have high parity, are from scheduled tribes, illiterate, or poor.[19]

STI clinics provide care for persons with symptoms of STI or who are concerned about possible exposure. Persons attending STI clinics receive a physical examination for genital ulcerative/non-ulcerative disease and a Venereal Disease Research Laboratory (VDRL) slide test. STI clinic attendees are not representative of the general population. The mean and median age of STI clinic attendees during this time period is 28 years.

All results for ANC and STI populations are age-standardized to the 2001 Census.

Behavioural surveillance in general populations

NACO carried out two Behavioural Surveillance Surveys (BSS) in 2001 and 2002. One of the surveys assessed the behaviour of people from the general public. The general population BSS surveyed a total of 84,478 people, 42,125 of whom (49.9%) were residing in urban areas while 42,263 (50.01%) came from rural areas. Among the interviewed respondents, 42,631 were females (50.5%) while 41,847 were males (49.5%).[20] The median age of the respondents was 29 years for females and 30 years for males. The general population BSS used 22 sampling units from 35 States and Union Territories. Characteristics of those who did not agree to participate are not provided.

NACO also conducted BSS for high-risk people among 5572 commercial sex workers (CSWs) and 5648 of their clients. The median age of CSWs in the study was 27 years with a range of 11–49 years. The median age of clients of CSWs was 27 years with a range of 15–49 years. The high-risk study was conducted in 21 sampling units in 32 States and Union Territories of the country. The study was not undertaken in areas of the country where the number of sex workers was considered to be insignificant. For various reasons, including those of study quality, the BSS for high-risk populations are not reported further here, but will be part of a forthcoming report examining all BSS among high-risk groups (Salil *et al.,* unpublished).

Review and meta-analysis of studies on risk factors for HIV-1 infection

We conducted a systematic review of existing epidemiological studies on risk factors for HIV-1 infection (Chen *et al.*, in preparation). The literature included in this study consisted of journal articles as well as reports and conference abstracts. We also contacted key control officers and non-governmental organizations (NGOs) to glean further information on risk factors. From 43 studies identified, we included 7 studies from 3 south Indian States with a total of 4212 adults as meeting the search criteria (having HIV-1 negative and HIV-1 positive populations, and also measured risk factors). Most studies drew their populations from STI clinics. We analysed the following risk factors: risky behaviour (paid sex, no condom use and history of STI), genital ulcer disease (GUD), lack of male circumcision and alcohol use. Standard statistical methods for analyses, chiefly pooled Mantel–Haenzel estimates, apply.

Dynamic compartment modelling for growth of HIV-1 and impact of interventions

We created a discrete, compartmental model incorporating high- and low-risk groups for HIV transmission (Weiss *et al.,* in preparation). High-risk groups included sex workers and men who often or sometimes visit them.

Low-risk groups comprised men who never visit sex workers and their wives. HIV spreads between these risk groups due to mixing; low-risk individuals can become high-risk by engaging in risky behaviour themselves (e.g. by becoming a sex worker), a high-risk individual can become low-risk as well (e.g. trucker chooses another profession). Different physiological and sociological characteristics of men and women are included in the model: condom use and efficacy, the presence of other STIs, the number of sexual contacts, and population growth with sex selection to favour male children.

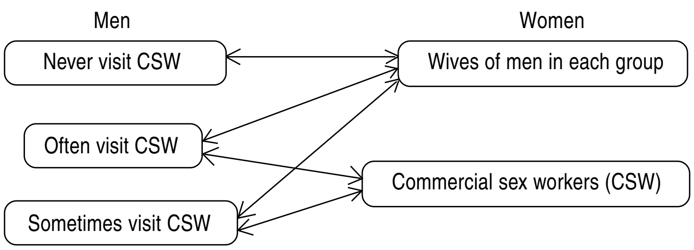


Fig. 1 Centre for Global Health Research (CGHR) mathematical model of HIV-1 spread

The data used for the dynamic compartment model draw on a careful review of all national data on HIV-1 transmission parameters, including various surveys (BSS), mapping studies, and other literature. They use conservative assumptions throughout, focused on modest HIV-1 growth, and have internal consistency checks on mathematical assumptions. The studies also included comparison to existing results, and a sensitivity analyses.

The equation to describe transmission is given in Fig. 2. Here, β is the probability that individual y, in risk group r, infects his/her partner x. The transmissibility, h, depends on the sex of the uninfected individual. The number of contacts per year for individual x is n. Both ulcerative (subscript 1, 3) and non-ulcerative (subscript 2, 4) STIs were considered in the model; STIs increase both the rate of transmission and acquisition of HIV. Above, w_x is the proportion of a given STI in the subgroup x, and m is the multiplication factor for a given STI. The transmission of HIV also depends on condom efficacy, E, and the frequency, f, of condom use between y and x. The proportion of partnering that occurs between individuals in group x and group y (with risk level r) is P_{yr}. The population of infected individuals in risk group yr is y_{ir}. When an uninfected individual becomes infected, through sexual contact with an infected individual, they move to the infected compartment with the same risk state and sex as before infection. Individuals can also move between risk levels.

Results of the routine ANC and STI surveillance from 1998 to 2003

Trends and variation of HIV-1 prevalence among ANC attendees

These were studied among 320,000 women attending ANCs from 1998–2003. Table 1 provides the overall results from 1998 to 2003 in the national ANC results. This shows steady but slow increases from 1998. The 2002 ANC HIV-1 prevalence is notably higher but this may reflect the rapid expansion of new sites in that year.

Figures 3a and 3b provide the ANC prevalence trends by high-prevalence States (Andhra Pradesh [AP], Karnataka, Maharashtra and Tamil Nadu [TN]) and the north-eastern

$$\beta_{yr\to x} = h_{yr\to x} \bullet n_x \bullet (w_x + w_{x1} \bullet m_1 + w_{x2} \bullet m_2) \bullet \left[(w_y + w_{yr1} \bullet m_3 + w_{yr2} \bullet m_4) \bullet (1 - E \bullet f_{yr\to x}) \bullet P_{yr} \bullet \frac{y_{ir}}{y_r} \right]$$

Fig. 2 Mathematical equation to describe the transmission of HIV-1

Table 1. Trends in HIV-1 prevalence among ANC attendees from 1998 to 2003

Year	Number positive/number tested	Prevalence %*	95% CI
1998	106/12,610	0.67	0.49–0.84
1999	205/24,241	0.68	0.48–0.89
2000	376/40,414	0.76	0.60–0.93
2001	492/64,568	0.75	0.60–0.90
2002	648/73,544	1.05	0.66–1.44
2003	897/103,452	0.80	0.69–0.91
All	2724/318,829		

ANC: antenatal clinic
*Age-standardized to the Indian 2001 Census

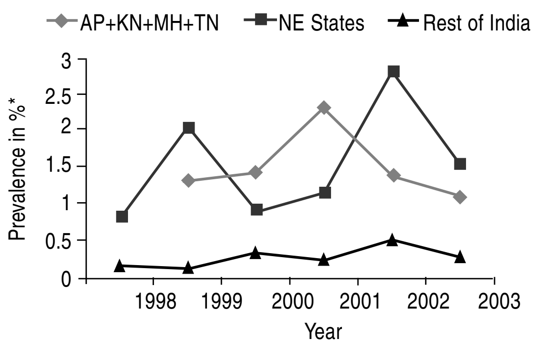
States (Manipur and Nagaland) and the rest of India, as well as within the high-prevalence States.

Marked variability in levels is seen from year to year, reflecting both the expansion of new ANC sites, as well as the small number of positives that need to occur to generate such variations. However, it is worth noting that levels in the high-prevalence States and the north-east are about 4–5-fold higher than those for the rest of India.[1] The important caveat is that the coverage in north India is limited to certain metropolitan cities. Figure 3b also suggests that, in contrast to much more marked variability (presumably reflecting an early, labile stage of the epidemic in Maharashtra, Karnataka and AP), there are lower levels of infection in TN, including some declines over the past few years.

Figures 4a, b and c provide the variation in HIV-1 prevalence in ANCs by education level, migration status and residence. There is a clear inverse association, with lower education levels having a 2–6-fold higher prevalence. The modest upward trend is seen most clearly in those with secondary or graduate education, narrowing the gap between education groups over time. There is little variation between migrant and non-migrant populations or by rural/urban residence.

Figure 5 shows the State-level extrapolations of prevalence in ANCs. This is the standard method used by NACO and others to create State-level estimates. As noted above, the geographical coverage of ANCs even in the high-prevalence States has been limited. Moreover, there is marked variation within a particular State. A more precise way of examining the ANC data is by 'focal-hot spots', as shown on the right side of Fig. 5. This implies that HIV-1 'hot spots' are localized to the following areas:

- The Mumbai–Karnataka corridor comprising about 6–7 districts
- Nagpur area of Maharashtra
- Nammakkal district of Tamil Nadu



*Age-standardized to the Indian 2001 Census

Fig. 3a Variation in HIV-1 prevalence in ANCs for major regions

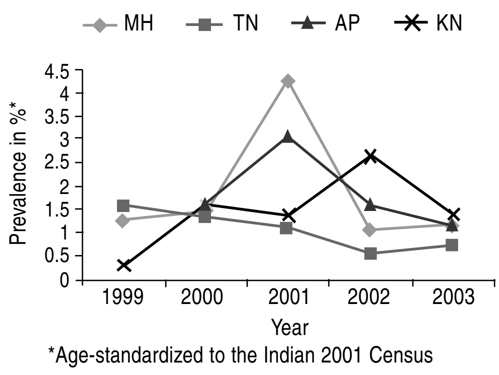


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Fig. 3b Variation in HIV-1 prevalence in ANCs for selected States

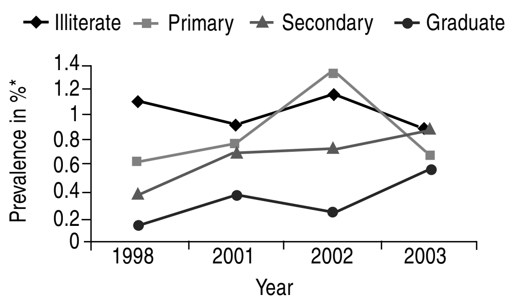

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Fig. 4a Variation in HIV-1 prevalence in ANCs by education

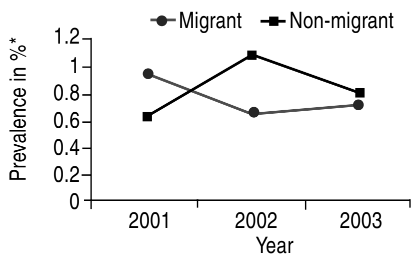

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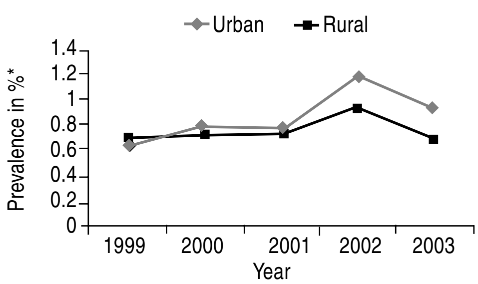
Fig. 4b Variation in HIV-1 prevalence in ANCs by migration status



*Age-standardized to the Indian 2001 Census

Fig. 4c Variation in HIV-1 prevalence in ANCs by residence

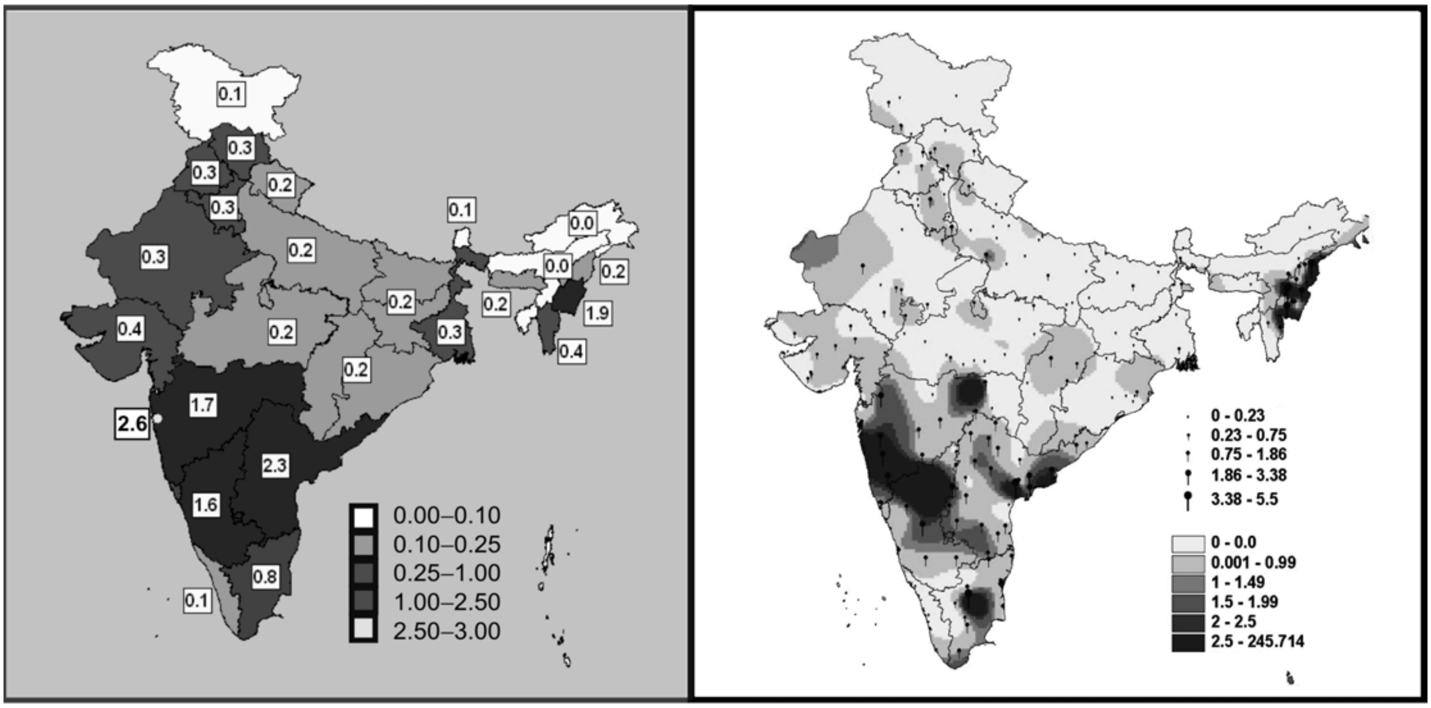


Fig. 5 State-level and focal area HIV-1 prevalence, 2000
Source: Williams *et al.* 2005[38]

- Eastern AP districts, specifically East and West Godavari
- Specific districts of the north-eastarn States of Manipur and Nagaland

The reasons for these particular 'hot spots' are not well understood, and may be a combination of migration patterns. For example, the 1991–2001 Census data trends suggest that a few districts in Karnataka have registered a growth rate lower than that seen for the State overall. The lower growth rate in some districts—Belgaum, Bellary, Bijapur and Raichur, for example—is presumably due to out-migration. (More detailed data are forthcoming from a re-analyses of the Census and Sample Registration System [SRS] data—Sethi *et al.*, forthcoming.) Similarly, some economically prosperous districts in Maharashtra show a higher population growth rate, perhaps suggesting increased in-migration. However, there might well be other factors accounting for such differences, including biological factors, variation in sexual networks in these areas, or better detection (or underdetection in some areas).

Finally, selection biases on who attends ANCs has been voiced as a possible concern, which means that the results of ANCs are unreliable.[18] However, the selection of additional sites has been based largely on the volume of ANC attendees, and as such should not introduce specific biases (as would geographical area-based selection). Moreover, our analyses of HIV-1 negative populations suggest there is little variation in distribution over 1998–2003 of key socioeconomic variables. Overall, about 10% were 15–19 years of age, 45% 20–24 years and 30% 25–29 years. About 30% were illiterate, 25% had primary education and 40% had secondary or higher education. About half were urban and half were rural, and 15% migrant and 85% non-migrant.

Trends and variation of HIV-1 prevalence among STI clinic attendees

These were estimated from among 130,000 adults attending STI clinics from 1998 to 2003. Table 2 provides the overall results from 1998 to 2003 of national STI clinics. The number of sites has increased from 31 in 1998, 52 in 1999, 94 in 2000, 127 in 2001, 159 in 2002 and 163 in 2003. Only 29 sites have been open for more than three years, making projections of trends unreliable before 2000/2001. The overall trends suggest no discernable increase in STI prevalence overall.

Figures 6a and 6b provide the STI HIV-1 prevalence trends by high-prevalence States, the north-eastern States and the rest of India, as well as within the high-prevalenc States. HIV-1 prevalence among STI attendees are almost 6–8-fold higher in the high-prevalence States, and about

Table 2. Trends in HIV-1 prevalence among STI clinic attendees from 1998 to 2003

Year	Number positive/number tested	Prevalence %*	95% CI
1998	329/5,439	5.60	4.94–6.26
1999	654/10,364	5.85	5.37–6.33
2000	1203/17,203	6.55	6.15–6.95
2001	1495/27,044	5.18	4.90–5.47
2002	1838/33,734	5.02	4.77–5.27
2003	2033/35,739	5.22	4.97–5.47
All	7552/129,523		

STI: sexually transmitted infection
*Age-standardized to the Indian 2001 Census

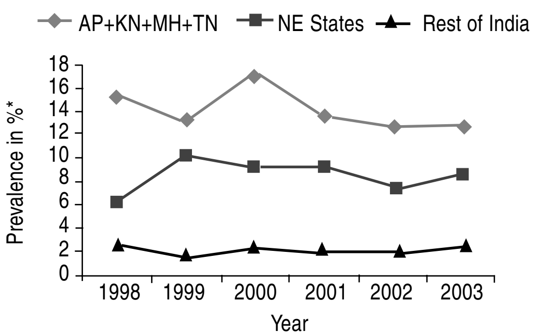
50% higher than in the north-eastern States. Among individual States, it is notable that levels of HIV-1 are much higher in AP than in other States.

As among the ANC populations, it was seen that lower education groups attending STI clinics have a higher HIV-1 prevalence with little change over time, and little differences by residence or migration status (data not shown).

Determinants of HIV-1 infection: Available literature

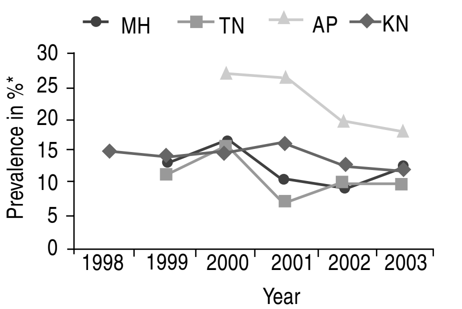
We analysed the following risk factors: risky behaviour (paid sex, no condom use and history of STI), GUD, lack of male circumcision, and alcohol use. Paid sex contacts were associated with an odds ratio (OR) of 4.7 (95% confidence interval [CI] 2.7–8.2). The OR for presence of GUD was 3.6 (CI 2.5–5.0), and that for lack of male circumcision was 2.1 (CI 1.3–3.5).

The potential for a reduction in the outcome of disease if a risk factor is removed is known as the attributable fraction. Attributable fractions in these populations for paid sex, history of and/or existing genital ulcers, lack of male circumcision, and alcohol use were 71%, 48%, 47%, 25%, respectively. Note that because there are several ways to avoid infection, the individual attributable fractions can add up to more than 100%. In addition, these attributable fractions are not population-based because of the selected nature of the population. The prevalence of each of these variables in the HIV-1 negative group was quite high, being 66%, 39%, 80%, 37% for paid sex contacts, history of and/or existing genital ulcers, lack of male circumcision,



*Age-standardized to the Indian 2001 Census

Fig. 6a Variation in STI clinic HIV-1 prevalence for major regions



*Age-standardized to the Indian 2001 Census

Fig. 6b Variation in STI clinic HIV-1 prevalence for selected States

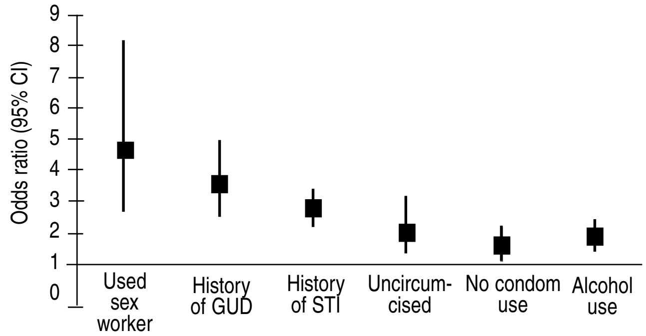


Fig. 7 Meta-analysis of risk factors for HIV-1 among high-risk groups

GUD: genital ulcer disease; STI: sexually transmitted infection

Source: Chen *et al.* (in preparation)

and alcohol use, respectively. This suggests that the control groups in these sites are also vulnerable populations, and that the true contribution of these risk factors may be much more substantial than shown in the meta-analysis here. Figure 7 summarizes these results.

Indirect evidence that differences in male sexual behaviour, most commonly from use of sex work, can be found in the national BSS. Data from this survey is presented in Table 3. It indicates the percentage of 85,000 adults aged 15–49 years who report having a non-regular partner in the past 12 months by region. Overall, the high-prevalence States have markedly greater proportions reporting non-regular partners. This is particularly evident among males.

The major differences are even more evident when the numbers of reported sex partners are stratified by gender and region (Figs 8a and 8b). A much greater proportion of males in the high-prevalence States report having had 2 or more partners as compared to either the north-eastern States or the rest of India. Among females, differences between regions are much less evident. These findings are compatible with the idea that variation in patterns of sexual networks, particularly the use of sex work by males, are a major factor affecting State-level variation in HIV prevalence (especially in the south). Moreover, the wider dispersion of numbers of sexual partners among males (and, to a lesser extent, among females) in the high-prevalence States suggests that HIV-1 would be more likely to spread rapidly in these States (given that growth of HIV-1 is a function of the dispersion of sexual contacts).[2]

There are no direct estimates of what proportion of infections are due to sex work. Indirect estimates, based on assumptions derived from our previous work (of condom use, number of contacts, infectivity and overall HIV-1

Table 3. Prevalence of self-reported non-regular partner in the past 12 months, by gender and region, 2001

Gender	AP+KN+MH+TN	NE States	Rest of India
Male	12.9	2.6	7.9
Female	4.4	0.5	1.1

Source: Salil *et al.* (forthcoming)

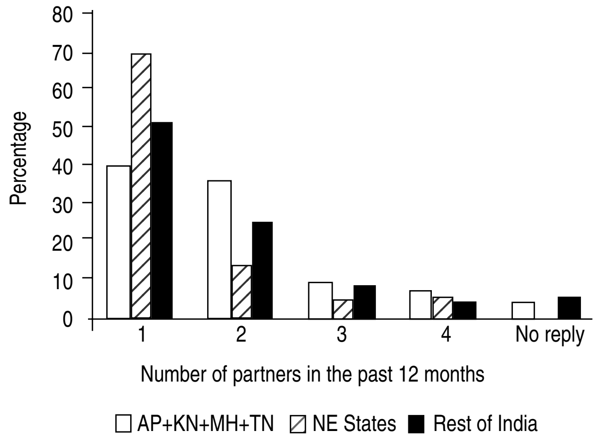


Fig. 8a Number of reported sexual partners in the past year, India, 2001 by region—Males

Source: Salil *et al.* (forthcoming)

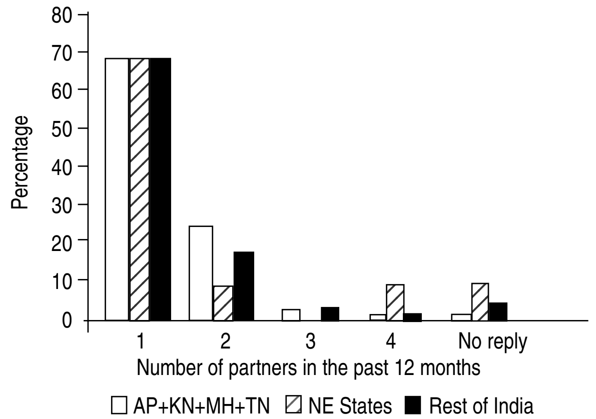


Fig. 8b Number of reported sexual partners in the past year, India, 2001 by region—Females

Source: Salil *et al.* (forthcoming)

infections) are presented in Table 4. This analysis also supports the hypothesis that most new infections in the high-prevalence States of the south are due to first- or second-generation spread through female sex workers and their male clients.

Future growth of HIV-1 infection and potential impact of interventions

Future growth of HIV-1 in India is, by its nature, difficult to predict. Various projection models have been done[21,22]

Table 4. Indirect estimates of the proportion of new infections due to sex work in the high-prevalence States

Prevalence of HIV-1 in female sex workers (%)	No. of female sex workers (in thousand)		Percentage of all infections due to female sex work	
	Low	High	Low	High
40	97	116	63	75
50	121	145	79	94
60	146	174	95	99

Source: Jha *et al.* (unpublished)

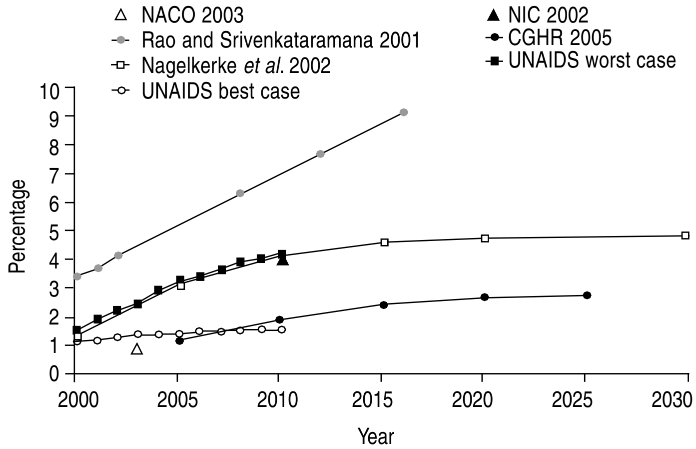


Fig. 9 Projections of HIV among adults in India. (NIC 2002,[21] Nagelkerke *et al.*[22] Rao and Srivenkataramana,[35] UNAIDS best-case and worst-case scenarios,[36] CGHR 2005[37])

and these are summarized in Fig. 9. The extremely rapid growth predicted some years ago does not appear to be occurring in India, based on the observed trends in ANC populations (*see below*).

A reasonable project model might involve the comparison of two scenarios: a worst-case and a best-case scenario. The worst-case scenario produced by UNAIDS in 1999 suggested growth to about 4% adult prevalence by 2010. More detailed work by Nagelkerke *et al.*[22] suggested this rate of increase would continue to about a 5% equilibrium prevalence by 2020.

The Centre for Global Health Research (CGHR) updated modelling uses the Nagelkerke scenarios and updates these using more up-to-date Indian data, and a slightly different projection model. These are less optimistic than the UNAIDS best-case scenario of 1999, and suggest that a little below 3% of the adult Indian population will be HIV-1 positive by 2025.

For the remainder of this report, we will refer to projections using the CGHR conservative model, and assess the impact of interventions with both the Nagelkerke 2002 and CGHR 2005 models.

Even with the modest growth scenario of about 3% equilibrium prevalence, about 500 lakh additional Indians will become HIV-1 infected over the next two decades (Fig. 10). This means that about 150–180 lakh Indians will be HIV-1 positive by 2015, making India the country with the largest absolute burden of HIV-1 infections in the world. Aside from China, no other population is likely to show such large absolute growth.

The CGHR models have not yet been adapted for specific regions of India and, with marked migration across States, such models are less robust than is the overall growth model. It can already be seen that the incidence of new infections will be 40% higher in 2015 than in 2005 (Fig. 11). Women have about a two-fold higher incidence than men in 2005, due to female sex work, as well as a higher biological susceptibility of high- and low-risk women to HIV-1

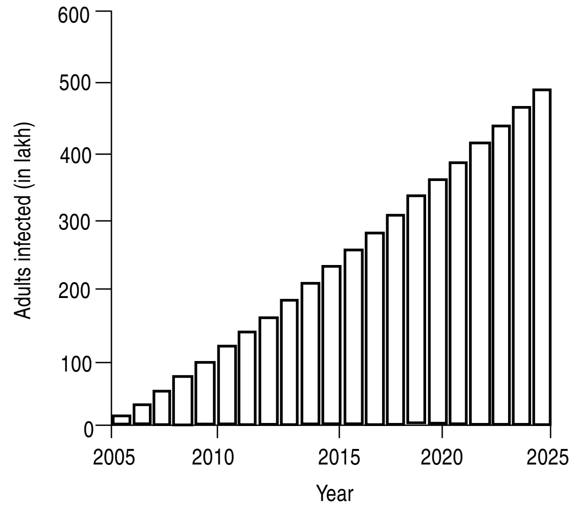


Fig. 10 Cumulative HIV-1 infections from 2005 to 2025 in India (in lakh)

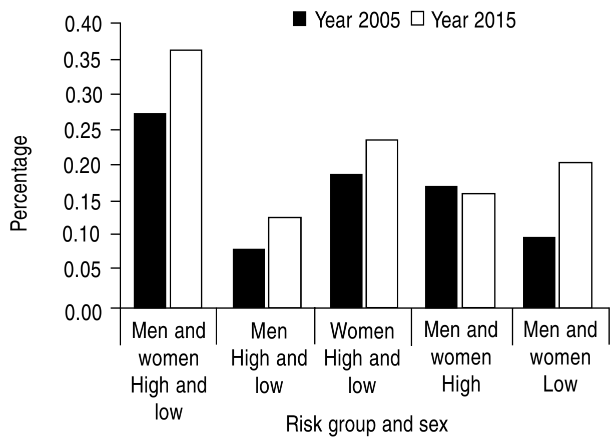


Fig. 11 HIV-1 incidence by gender and risk group in India, 2005 and 2015

infection.[23] The higher incidence among women is likely to be maintained to 2015, and more of the women infected will be low-risk women (chiefly wives of men who visit sex workers sometimes or often).

The CGHR and Nagelkerke models examine interventions to reduce HIV-1 growth (Table 5). These are the following:

Table 5. New HIV-1 infections that can be avoided in India with various interventions over the next two or three decades

Interventions	Nagelkerke *et al.*[22] 2001/02 (%)	CGHR 2005[37] (%)
Preventive interventions		
75% consistent condom use by FSW	–83	–38
30% reduction in the transmission of STIs	–48	–39
50% reduction in mother-to-child transmission	–6	—
40% reduction in commercial sex work by 15-year-olds entering the adult population	—	–39
Hypothetical: no commercial sex work	—	–90
Hypothetical HIV-1 vaccine with 50% effectiveness, 95% coverage of		
General population with no adverse behaviour change	–57	—
FSW with no adverse behaviour change	–61	—
General population with full adverse behaviour change	+13	—
FSW with full adverse behaviour change	+27	—
Treatment: Antiretrovirals with 50% coverage in the general population and no adverse behaviour change	–19	

FSW: female sex worker; STI: sexually transmitted infection; CGHR: Centre for Global Health Research

Preventive interventions

1. Increases in consistent condom use by female sex workers from an estimated 25% to 40% to 75%.[3] Such reductions have been noted in numerous studies and most notably in places such as Sonagachi, Kolkata; Kibari and Pumwani, Kenya, Thailand and Cambodia.[24–28] The key intervention is peer-based outreach programmes (usually led by NGOs or CBOs) that reach female sex workers (FSWs), provide education, condoms, negotiating skills and access to basic health services. No specific new technologies are required. Sex workers are identified using participatory mapping efforts.
2. Reductions in HIV-1 transmission by about 30% due to community-based STI management using syndromic management and existing antibiotics. There continues to be controversy about the role of STI treatment in HIV-1 transmission, but a careful examination of all evidence to date suggests that STI treatment, especially for populations where HIV-1 is still dependent on sex work-based transmission, is effective.[29] We have used a modest 30% reduction in transmission parameters for this intervention.
3. Use of antiretrovirals to prevent mother-to-child HIV-1 transmission results in a transmission reduction of at least 50%. This includes provision of breast milk substitutes for transmission after delivery.
4. A 'Uganda' type intervention which results from mass change in behaviour of general populations leading to a 40% reduction in the uptake rate of commercial sex by 15-year-olds (both males paying for sex and females entering paid sex). Such an intervention is difficult, however, to reproduce outside of Uganda. In that setting, there was such a high level of infection (about one-fifth of adults), and deaths were so commonly reported that mass behaviour change followed.[30] Indirect analyses suggest that this change in behaviour was due to informal communication networks rather than the result of any specific information campaign. Nonetheless, to outline the potential impact of such an intervention, we have included this.
5. The hypothetical scenario of no commercial sex whatsoever. This is akin to the 'AB' or abstinence and be faithful components of the 'ABC' strategy proposed by the US administration as a possibly effective strategy. There is no clear way to tell if such an intervention is possible, but it is included nonetheless.
6. Hypothetical HIV-1 vaccines. For these, we assume 50% vaccine efficacy—that the vaccine reduces lifetime trans-

mission by 50% among susceptible populations (this is not the same as 100% efficacy among half of all people vaccinated). The 50% efficacy estimate is arbitrary, but consistent with recent discussions of a feasible vaccine.[31] We assume vaccines can reach either 95% of the sexually active adult population, or 95% of sex workers, both within 7 years from start-up. With these, two other scenarios follow. The first is that there is no change in the proportion of commercial sex workers that uses condoms (that is, no 'adverse behaviour change'). The second is that those immunized stop using condoms during commercial sex, believing that they are protected from infection. There is already existing evidence of such 'treatment optimism' from the antiretroviral literature in western and developing populations,[32] and condom use among men who premedicate with antibiotics prior to sex work is much lower than those who do not take antibiotics.[33] Thus, adverse behaviour change is not an implausible scenario.

7. Antiretrovirals used among all eligible AIDS patients (i.e. late-stage ARV treatment) covering some 50% of the adult population. Here too, we assume that those who get treated receive additional advice and counselling and do not have adverse behaviour change.

The summary of the results for these interventions, using the relative reductions in new infections between 2000 and 2033 (for the Nagelkerke model) or 2005–2025 (for the CHGR model) are shown in Table 5, and selected interventions for the CGHR model are shown in Fig. 12.

The most effective strategy would be, of course, to have no commercial sex work at all. This would avoid 90% of future HIV-1 infections. However, increases in consistent condom use can achieve between 40% and 80% reduction in HIV-1 growth over the next few decades. Such strategies are widely practicable, and indeed form the basis for the Gates Foundation 'Avahan' programme.

The second most practicable strategy would be to accelerate increase in STI treatment, especially for GUD in India. Bacterial STIs are easily treatable. Trends in bacterial GUD or ulcerative herpes simplex virus (HSV)-2 in India are not well understood. Some African data suggest, for example, that a high prevalence of HSV-2 might account for a substantial proportion of HIV-1 infection.[4]

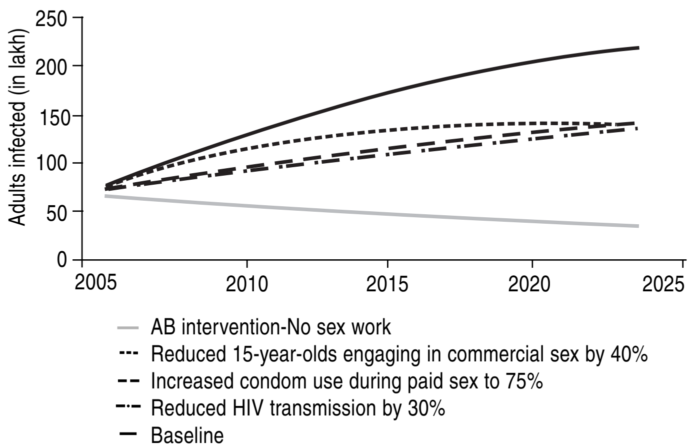


Fig. 12 Comparison of preventive interventions for HIV-1 in India

A 'Uganda' type intervention that changes young people's sexual behaviour is unlikely to be achieved through education alone. Careful reviews have concluded that intensive education programmes tend to raise awareness but not change behaviour among youth.[34] Moreover, such a strategy may be applicable only in advanced AIDS epidemics where many people are dying from AIDS, and this provides an important information signal to the uninfected. Such a strategy would be as effective as an STI strategy in our model.

Antiretrovirals are effective at reducing mother-to-child transmission, but the overall reduction in HIV-1 levels is only modest as the infected children do not pass the infection to others. Antiretrovirals for adult populations have a dramatic short-term impact on mortality, but as resistance appears, their overall effectiveness is limited (about 19% reduction in HIV-1 growth). Moreover, the assumption in the model that there is no adverse behaviour change due to the use of antiretrovirals is an optimistic one.

Similarly, even with a hypothetical HIV-1 vaccine, it can be seen that targeting such a vaccine to female sex work might be as effective as to the general population (in both about 60% of the HIV-1 growth is avoided). However, widespread use of a vaccine leading to behavioural disinhibition and a reduction in male condom use with FSWs could offset the potential benefits of a vaccine and the epidemic could worsen by 13% to 27%. Thus, even with an HIV-1 vaccine programme, strategies to reach CSWs and intervene using peer-based education programmes will be needed.

Figure 12 shows these results in graphic form, using the CGHR model for 2005–2025 and in terms of the annual prevalence of HIV-1 infections.

Further details of the model, including the results of sensitivity analyses will be published shortly.

Implications for HIV-1 and STI control and surveillance

The chief implications of these analyses are as follows:

1. Existing evidence suggests a modestly growing, but highly variable, HIV-1 epidemic in India. Currently, about 50–60 lakh people are infected, with the largest burden in a handful of States: AP, Karnataka and Maharashtra in particular, but also TN, Nagaland and Manipur.
2. Even with modest growth scenarios, perhaps some 500 lakh more Indians will become HIV-1 infected over the next two decades. This growth is very likely to affect specific hot-spot areas at much higher levels than the overall growth would suggest.

3. The chief determinant of the epidemic appears to be transmission from sex work networks, involving use by mobile males of FSWs and secondary infection of regular partners of such males.
4. The most effective and widely practicable strategies to reduce the growth of HIV-1 infection in India are to ensure high rates of consistent condom use among FSWs and their clients, and to increase access to syndromic management of STIs for the general population. These two strategies should be the cornerstone of any response to control AIDS in India.
5. Effective monitoring through routine, robust, reliable, low-cost and long-term epidemiological studies, and surveillance of risk behaviours for HIV-1 and STI are required in India. We endorse here the recommendations of a group of epidemiological experts (Kumar *et al.* forthcoming) which called for greatly expanded quality and coverage of routine ANC and STI surveillance, carefully designed general population studies, and specific integrated biological and behavioural surveys (*see* Appendix 1 for the full list of recommendations).

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Appendix 1

Improving the monitoring of HIV/AIDS in India in the high-risk and general population Ad Hoc Review by Epidemiological Experts*

Summary

An expert group of epidemiological experts provides ten specific recommendations on how to improve the monitoring of HIV-1 infection and its determinants among high-risk and low-risk populations in India. Monitoring the evolution of HIV-1 in India is central to establishing if control programmes are working (or not). The major recommendations of this report include:

- Re-analyses of the considerable number of existing behavioural and other data at district or subdistrict levels;
- Ensuring that integrated biological and behavioural surveillance is done in a way to ensure that target populations are reliably sampled, and that biases in reporting condom use are recorded;
- A pilot programme of 40 districts for enhanced ANC testing for HIV-1 and STIs among the general population, with quality control, re-sampling and creation of central repositories;
- Ensuring than future population-based behavioural or biological surveys are done with adequate methodological attention so that they provide meaningful data representative of the population and with adequate sample size; and
- Ensuring that the surveillance efforts are integrated into overall capacity building and sustainable monitoring strategies to monitor what is clearly a very heterogeneous epidemic.

Background

Several epidemiologists from India and around the world met in Ahmedabad on 6 January 2005 and in Bangalore from 11 to15 January 2005 to review the epidemiology of HIV-1 in India, and the best options to improve the monitoring of incidence, prevalence and mortality from HIV-1 infection. The Bangalore meeting was held concurrently with the Monitoring and Evaluation (M&E) meeting of the Bill and Melinda Gates Foundation (BMGF) Avahan programme.

The Avahan programme is a US$ 200 million five-year control programme focusing on 71 high-prevalence districts

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(a combined population of 1450 lakh). The primary target groups will be approximately 300,000 FSWs and their clients. Specific changes in HIV-1 prevalence will be monitored through integrated behavioural and biological surveys (IBBS) among 100,000 people (over years 1, 3 and 5), detailed studies in general populations and special surveys in high-risk populations. Mathematical models will be used to evaluate 'counter-factual' scenarios, and cost-effectiveness of interventions. Much of the IBBS work will be implemented by Indian Council of Medical Research (ICMR) institutions in various States of India, led by the National AIDS Research Institute (NARI).

Concurrently, the National AIDS Control Programme (NACO) has made a decision to focus its communication and NGO-led peer-based education components of the Second National AIDS Control Project (US$ 200 million/5 years, expiring 2005) on improving coverage for FSWs and clients. India is also a core country for WHO's '3 by 5' programme for antiretroviral access, with the goal of placing 300,000 people on ARVs by the end of 2005. NACO has also begun to discuss a Third IDA credit with the World Bank for HIV/AIDS control. Importantly, NACO has also set an ambitious goal 'Zero by Seven', assumed to mean there will be no new increases in the HIV-1 infection prevalence rate above the levels of 2006.

Thus, for a variety of stakeholders, there is a fresh need to examine the methods to expand and strengthen the epidemiology of HIV-1 in India to monitor the evolution of what is already clearly a heterogeneous epidemic, to inform the success of control programmes and new interventions (such as the introduction of antiretrovirals), and to identify research questions that are central to new interventions (such as HIV-1 vaccines).

The epidemiological group focused on the following items in its discussion and made specific recommendations on each:

- The existing evidence on HIV-1 growth in India, including variation and the implication for the variation for control programmes;
- Methodological strengths and areas requiring further attention for monitoring HIV-1 among general and high-risk populations;
- Links of the current monitoring efforts to longer-term capacity building for epidemiological studies in India.

Existing evidence on HIV-1 epidemiology in India

The known epidemiology of HIV-1 growth in India will be highlighted in detail in a forthcoming report by the National Commission on Macroeconomics and Health. Salient highlights include the following:

- HIV-1 prevalence is estimated to be about 1% of the adult population (15–49 years), but this is highly variable. The States of Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu are estimated to contain most of the prevalent infections (but gaps in routine surveillance in north India are substantial).
- Geographical and demographic 'hot spots' have been identified. 'Hot spots' of HIV-1 from sexual transmission are most notable in the Maharashtra/Mumbai–northern Karnataka corridor, in/around the Nagpur area in Maharashtra, coastal districts of Andhra Pradesh, in Namakakkal in Tamil Nadu. 'Hot spots' from injecting drug use are notable in Manipur and Nagaland.
- As of now, the demographics of these hot spots (age, sex and occupational risk-groups at a minimum) have not been described. Moreover, given the migratory nature of the populations at high risk, and gaps in routine surveillance in several States, caution is needed to state that only selected areas are 'hot spots'.
- The overall growth of HIV-1 from 1998 to 2003 has been modest but steady. Future growth is uncertain, and will be informed by the 2004 ANC data.
- Model-based projections of growth of HIV-1 suggest that at a minimum, 500 lakh *new* infections can be expected over the next two decades in India overall. However, the major increase is likely to occur in selected areas of certain States.
- Control of these hot spots remains critical to curbing overall HIV-1 growth in India.
- State-level prevalence averages rely on political/administrative units and are likely meaningless.

Monitoring HIV-1 prevalence and incidence, and risk factors among high-risk populations

High-risk, vulnerable populations such as sex workers (SW) and their clients are central to the growth of HIV-1 in India. Indirect estimates suggest that most new infections in the heterosexual population arise from the male use of FSWs. However, these data are debated, and more direct epidemiological confirmation is needed.

Over the past few years, major surveillance efforts for these populations have focused on STI clinics (about 250 consecutive males and females tested anonymously and in an unlinked fashion twice a year in about 163 sentinel sites at public facilities), mapping of these populations in several districts/States, and on behavioural surveys in several districts/States. Voluntary counselling and testing centres (VCTCs) are available in almost each district in the southern States, and a growing number of northern States. Both these clinics have substantial selection biases from the populations that attend them. However, they can still be useful in tracking information on selected risk factors in self-selected, high-risk populations.

The Avahan programme's planned expansion to include biological samples (blood for HIV-1, HSV-2 and syphilis; urine for *C. trachomatis* and *N. gonorrhoeae*) from a 100,000 strong high-risk population over 5 years (2005, 2007 and 2009) should provide a substantial amount of new and important information on these otherwise hard-to-reach populations. Similarly, Avahan plans to implement BSS (questions only) annually in each of the 71 Avahan districts, which should provide substantial new evidence on such populations.

The group identified the key gaps in this approach:

- Caution in trying to design questions to measure intimate and complex sexual behaviour. Ultimately, many of these behaviours are not observable with even detailed survey instruments. Results from a few participants are not readily applicable to other populations.
- The sample frame designed may not be the one implemented due to the very mobile nature of sex work. The Frontiers project IBBS among 6500 FSWs and 6500 MSM in over a dozen districts of Andhra Pradesh found that actual sampling frames could not always be actually implemented due to changes in mobile populations between mapping/sampling and survey.
- There is too great a complexity in the IBBS, such as including genital examination on a subset of women and too long a questionnaire. The IBBS should retain as its core focus a simple, widely practicable questionnaire that can be reproduced in subsequent years. Specific needs for the mathematical model should not lead to too many questions (some of which are not answerable).
- Only 27 of the 71 Avahan districts are covered under the IBBS, and the selection of these districts is based on programme coverage and other criteria. This risks introducing subtle biases where intervention programmes focus more sharply on the IBBS districts to show good performance/quality.
- The wide variation in sex work practices even within a district site implies that IBBS results may be hard to generalize for that district. For example, the Frontiers project experience showed nearly three-fold differences in condom use among FSWs in the same districts.
- There is likely overreporting of condom use by FSWs in existing surveys. This implies that the IBBS design may not have optimal power to detect changes in condom use. Moreover, as the Avahan programme expands, and community participation increases, more plausible, but lower levels of condom use might be reported. This may lead to the false conclusion that the interventions *lowered* condom use.
- To avoid erroneous conclusions, some simple validation/re-survey methods focusing on condom use need to be introduced throughout the IBBS to understand under- or overreporting. These 'correction factors' cannot be extrapolated safely to other geographical areas or to other specific subpopulations (such as street-based or brothel-based FSWs). Thus, considerable caution will be required in interpreting the results.
- Reported STI levels may be lower than anticipated, so that the IBBS may not have adequate power for detecting changes in STI outcomes of interest for each district. Detailed power calculations using lower STI levels would help evaluate at what level the changes in STI outcomes could be detected with the planned sample size, e.g. for groups of districts or at the State level.
- There is limited coverage of the IBSS or BSS in the northern areas of India, particularly in cities with more than 10 lakh population and, presumably, having large migration levels.

Recommendations

1. An expert group assemble, re-analyse and synthesize all of the existing BSS and IBBS data, mapping studies, and other information using as disaggregated levels as possible (district at a minimum). The expert group should identify which districts/cities that are not covered by existing BSS/mapping or other related surveys require such surveys.

   The re-analyses should also review the age, sex, socioeconomic background of the respondents and compile any available data on non-response so as to better understand who participates in these surveys, and why. The re-analyses should also aim to document the variation in reported condom use by specific sites or types of sex workers.

   NACO and the owners of these primary data should work to make the primary and raw data from these completed surveys (most of which were publicly funded) available to the study team. (Indeed, the full anonymous and unlinked results should be freely available on the website of NACO—akin to the easy access to the raw data files of the NFHS-2.)
2. The selection of the Avahan districts for inclusion in the first IBBS should be done by an independent statistical panel, who can also advise on related options for future surveys (such as rolling sample frame with partial overlap). This is the procedure used for the Registrar General's Sample Registration System and other major surveys.
3. The early pilot results of the Avahan IBBS should be reviewed critically for compliance rates, feasibility and other aspects so as to help simplify the IBBS implementation in the first and second rounds. Avahan should keep open the possibility of simplifying procedures so that more districts with a larger sample size are included in subsequent rounds (especially if the power calculations show that condom use and STI prevalence are not as predicted).
4. HIV-1 incidence testing through 'detuned' methods may well be very useful in monitoring changes between the 2005, 2007 and 2009 surveys. Here again, caution is needed to ensure that the enrolled populations (which will certainly differ over the years) are comparable.
5. Despite considerable selection biases among STI and VCTC attendees, this population has a high HIV-1

positivity rate and is therefore useful to study high-risk populations. Specific, case–control studies among these populations should be designed, focusing on risk factors for HIV-1 infection, including sex work contact, age at first sexual exposure, male circumcision status, STI of various types, consistency of condom use and use of HIV-1 preventive or treatment services. These studies can also help validate if surrogate questions such as time away from home are a useful proxy for unprotected sex contact with a non-regular partner.

Monitoring HIV-1 prevalence, incidence and risk factors among general populations

The ultimate success of control programmes and the mitigation of the social and economic costs of HIV/AIDS can only be determined by prevalence, incidence and mortality among general populations. The chief source of epidemiological information are female ANC attendees, and proposed general population surveys. Each is reviewed in turn.

ANC surveillance

ANC sites have expanded from 38 in 1998 to 266 as of 2003. These rely on semi-annual anonymous, unlinked testing of about 400 consecutive women attending ANC sites at public institutions. Only half of the sites have been open for more than three years. Overall, only about 65% of women used public facilities for antenatal care, but this proportion is much higher in the southern States and Maharashtra, where HIV-1 levels appear higher.

The ANC data have been able to demonstrate, despite weakness shown below, that the HIV-1 epidemic is concentrated in certain areas in States where it is measured (*see* the section on 'Background' above). The ANC data have also been able to provide reasonable, but by no means fully certain, evidence that in some urban settings like Delhi, Chandigarh and Gujarat, HIV-1 levels in the general population have not increased dramatically (staying well below 0.5% for several years).

The biases among women attending ANCs have not been well studied in India. However, preliminary re-analyses by NACO suggest that there was little variation in age, education, residence and migration patterns between 1998 and 2003 among HIV-1 negative women.

Additional analyses are required to confirm if these groups are representative of local levels of the enrolment area's ever-married women (forthcoming analyses). Similarly, the amount of information that is possible to collect (including limited questions on sexual behaviour, risk-taking) is limited.

The chief weaknesses of the ANC data are two: first, they do not capture information on males. Second, they are more useful for detecting trends, and have not been well validated for measurement of HIV-1 incidence or prevalence in the general community. Results from the Tamil Nadu Community Prevalence Survey suggest that ANC prevalence is two-fold lower than the overall State level, but the Bagalkot Community Survey suggests that the two are comparable (*see below* for caveats of general population surveys). Similarly, there are reports of inconsistent quality in testing (including adherence to ELISA testing procedures), sampling frame (including recruiting non-representative populations), and overall supervision.

Because the ANC data represent the best existing and reasonably low-cost method for tracking changes in the general population, these represent the most cost-effective and practicable base from which to expand. Already, ANC has expanded to all districts in the high-prevalence States for 2004.

Recommendations

1. Considerable efforts be made to improve the quality and completeness of ANC data testing from all parts of India. These would include:

- Test in at least one public facility and ideally one private/ NGO facility in all districts of India.
- Add focused questions on sexual behaviour (including knowledge of paid sex, husband's time away from home plus wife's time away from home during pregnancy when the husband is alone in the house, religion and male circumcision status, HIV-1 testing, use of antiretrovirals, condom use, access to HIV-1 interventions).
- Add questions on tobacco and alcohol use by husband.
- Add routine measurement for other viral and bacterial STIs, specifically HSV-2, syphilis, and possible *C. trachomatis* antibodies (as a marker of sexual risk).
- Add incidence testing ('detuned') in some areas.
- Create a central long-term biorepository of a random percentage of tested samples for future biological testing (the last three to be done in a phased manner after adequate pilots).

2. A network of academic institutions, working with NARI, NACO and others conduct a pilot quality control study covering some 40 districts (including identified 'hot spot districts' as given in the section on 'Existing evidence on HIV-1 epidemiology in India').

   The pilot would aim to provide training and standardization to ANC staff in proper epidemiological questions, and in specimen collection. The network would introduce innovation such as use of a rolling sample (not simply twice a year), training of ANC staff in interview methods and good quality HIV-1 and STI testing, use of a 10% re-sample, central archiving of all positive samples, a random percentage of negatives for specialized testing (including detuned assays) and quality control. The central samples could be used for focused biological research (for example, on variation in viral and host factors that may explain the remarkable heterogeneity of HIV-1 in India).

3. Based on the pilot, ICMR/NACO consider expansion and quality control of ANC sites as the central pillar of the proposed third World Bank IDA credit.

General population surveys, including the planned NFHS-3

Major completed activities for general population surveys include a National Behavioural Survey in General Population (NBS) covering 85,000 adults in major States of India completed in 2001, a forthcoming National Community Prevalence Study (the results of which are not yet available), and a planned National Family Health Survey-3 (NHFS-3), which would include HIV-1 testing in about 125,000 adults in high-prevalence States.

The group concluded that there were considerable methodological challenges in general population surveys. The central goal of such surveys is to generate prevalence rates and risk profiles representative of the general population, but it is precisely in this area that weaknesses are most notable. Consider the following:

- It is well known that those who refuse to join such surveys are different from those who participate. This may be due to three factors: non-response; non-availability of economically and physically active young males during surveys; and the limited ability to capture migrant populations, hence possible underrepresentation of these in general population surveys. Thus, higher-risk, more mobile females or males may often not be captured in the house listing procedures used. The Male Sexual Behaviour General Population Survey (GPS) in Vellore showed a response rate of 87% and that non-respondents were more likely to be older (35–40 years of age), married, and having white-collar jobs or affluent private businesses. Surrogates of risk-taking (smoking or alcohol use) were not different between responders and non-responders). No other large-scale BSS or IBBS that we reviewed has reported on the characteristics of the non-respondents (including age, sex, marital status, occupation, education, time away from home) and surrogates of risk-taking (such as smoking or alcohol use). The NBS does not provide any table that compares the interviewed population to the Census characteristics.
- The experience from the General Population Survey conducted in the Bagalkot district of Karnataka is telling. The original study design aimed for 7000 adults, based on a census-based house listing. Only about 4600 agreed to participate and, of these, only about 3500 provided blood samples. Thus, with the HIV-1 status available in only about half of the target population, the study cannot be representative.
- Experience from various studies suggests that while behavioural data, or blood or urine samples may be obtained (including from the NHFS-2), obtaining both creates numerous problems with community participation. This implies that any survey which attempts to do both needs to be designed with considerable care, and only after use of extensive pilots. Similarly, while past NFHS surveys have had high participation rates among those selected, the planned introduction of HIV-1 testing in NHFS-3 may well lower overall response rates, and thus make difficult or impossible the comparison of fertility and other indicators to earlier NHFS rounds.

Adequate sample sizes are needed for general population surveys, given that the estimated prevalence of HIV-1 among adults is still quite low (2% as an upper level in most settings). The specific objectives of general population surveys need to be taken into account in sample size estimates. For example, generating a State-level average for HIV-1 prevalence is of limited use, given that it is already evident that HIV-1 epidemics are remarkably heterogeneous within a State (or even a district). Consider the following:

- The NHFS-3 proposal calls for testing some 125,000 adults in high-prevalence States or, on an average, about 6400 men and 6400 women in each of the high-prevalence States. However, this would generate only about 60 positive cases among women and men each, or only 2–3 positives among women in each district for an average State. This number of positives is too small to validate local ANC results.
- Similarly, the design effect is likely underestimated as the marked heterogeneity in HIV-1 levels within a State mean that sampling errors could lead to underestimation, and inability to reproduce the findings in future surveys.
- The absolute number of HIV-1 positive persons is too small to do any meaningful bivariate analyses except at the national level.

The design document for the NHFS-3 is not clear in the efficiency of testing strategies. A very large number of samples (125,000) will need to be tested to generate only a few positive results (some 1000–2500). Methods to increase the use of pooled samples and their relevance to blood spots are not clear. Similarly, the NHFS-3 proposes, quite wrongly, to destroy the samples after testing.

A better sample frame for large HIV-1 prevalence surveys is likely to be the Sample Registration System (SRS). The SRS covers about 10–11 units per district on an average, each with about 1000–1500 people (of which about 40% would be 15–49 years of age). The SRS is representative of the population. Because house lists are known, they can provide meaningful information on the non-response characteristics of those surveyed. Moreover, the new SRS sample frame will be followed to 2014, thus enabling prospective follow-up.

Table A1.1 NHFS-3 sample size estimates for each of the high-prevalence States

Group	Assumed HIV prevalence rate (%)	Assumed design effect*	Proposed minimum sample size	Confidence interval		Absolute number of positives	
				Lower (%)	Upper (%)	Lower bound	Upper bound
Women and men separately	1.50	1.25	6,400	1.1	1.9	70	122
	1.25	1.25	6,400	0.9	1.6	58	102
	0.75	1.25	6,400	0.5	1.0	32	64
Both women and men together	1.50	1.25	12,800	1.2	1.8	154	230
	1.25	1.25	12,800	1.0	1.5	128	192
	0.75	1.25	12,800	0.6	0.9	77	115

*Note that the design effect used is optimistic—it may well be two-fold or higher

Recommendations

1. A NACO/Avahan expert group should review the results of all existing community prevalence studies, including appropriate information on non-respondents, sample size estimates, validation of results of sexual behaviour, and other aspects.
2. The utility of general population surveys of HIV-1 and STIs in conjunction with other biological tests be first evaluated in well-designed pilot studies in about 3–4 States. These pilots would pay attention to the following options:

- Surveys focused only on blood-based household health surveys (comprising blood pressure and other physical measurements, along with a blood spot on filter paper), with limited sexual behavioural questions (but with likely high compliance rates).
- Validation of indirect questions on sexual behaviour (for example, use of surrogate markers such as time away from home for use of sex work).
- Use of biological markers to define sexual behaviour risk (for example, *C. trachomatis* or HSV-2 antibodies correlate with lifetime number of sexual partners in western settings).
- Alternative sampling strategies, such as sampling only men, or sampling men and women in alternative households.
- Careful attention to methods for collection, processing and long-term biorepository of collected samples, including choice of samples (lowering the costs of testing with pooling methods), cheaper indigenous assays and other aspects of laboratory quality control.
- Careful attention to methods for the use of large survey datasets within the SRS to create anonymous, unlinked subsamples for population-based, age, sex, and region or hot spot-specific HIV-1 and STI prevalence.

Monitoring AIDS mortality

Especially due to expanding access to antiretrovirals, studying mortality from AIDS will be required. The forthcoming Registrar General of India (RGI)–Centre for Global Health Research (CGHR) prospective study of 60 lakh Indians, capturing some 150,000 deaths from 2001 to 2003 and an additional 75,000 deaths from 2004 to 2005 should provide robust and direct estimates of AIDS mortality, and the socioeconomic and limited behavioural correlates of such mortality.

Capacity-building for monitoring HIV-1 and sustainability of efforts

The expert group strongly endorsed the view that standalone monitoring and evaluation efforts, while required for project monitoring and donor accountability, need to be integrated into an overall nationally led strategy. Such a strategy would build capacity for routine, robust, low-cost, and long-term monitoring of a remarkably heterogeneous HIV-1 epidemic. The expert group believes that the above set of efforts, with close coordination between NACO, ICMR, Avahan and others can be a model for developing countries to build sustainable monitoring systems.