Trends in HIV-1 in young adults in south India from 2000 to 2004: a prevalence study

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Summary

Background **Major increases in HIV-1 prevalence in India have been predicted. Incident infections need to be tracked to understand the epidemic's course, especially in some southern states of India where the epidemic is more advanced. To estimate incidence, we investigated the prevalence of HIV-1 in young people attending antenatal and sexually transmitted infection (STI) clinics in India.**

Methods **We analysed unlinked, anonymous HIV-1 prevalence data from 294 050 women attending 216 antenatal clinics and 58 790 men attending 132 STI clinics in 2000–04. Southern and northern states were analysed separately.**

Findings **The age-standardised HIV-1 prevalence in women aged 15–24 years in southern states fell from 1·7% to 1·1% in 2000–04 (relative reduction 35%; $p_{trend}<0·0001$, yearly reduction 11%), but did not fall significantly in women aged 25–34 years. Reductions in women aged 15–24 years were seen in key demographic groups and were similar in sites tested continuously or in all sites. Prevalence in the north was about a fifth of that in the south, with no significant decreases (or increases) in 2000–04. Prevalence fell in men aged 20–29 years attending STI clinics in the south ($p_{trend}<0·0001$), including those with ulcerative STIs ($p_{trend}=0·0008$), but reductions were more modest in their northern counterparts.**

Interpretation **A reduction of more than a third in HIV-1 prevalence in 2000–04 in young women in south India seems realistic, and is not easily attributable to bias or to mortality. This fall is probably due to rising condom use by men and female sex workers in south India, and thus reduced transmission to wives. Expansion of peer-based condom and education programmes for sex workers remains a top priority to control HIV-1 in India.**

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Introduction

The National AIDS Control Organisation (NACO) of India has estimated that about 5·1 million people or less than 1% of the adult population (aged 15–49 years) were infected with HIV-1 in 2004.[1] The true prevalence is disputed,[2] because even small changes in prevalence could translate to large absolute numbers of infected individuals. Heterosexual contact is responsible for about 85% of all new HIV-1 infections in India.[1] Several studies suggest that a half to three-quarters of all new HIV-1 infections are due to first or second-generation infections related to male use of female sex work,[3–5] which is common; a 2004 survey in five cities found that 11% of urban adult men often paid for sex, and 29% had ever done so.[6] About 75% of HIV-1 cases reside in the "southern" states of Andhra Pradesh, Karnataka, Maharashtra, and Tamil Nadu, which make up 30% of India's population.[1]

There have been consistent projections of a major increase in people infected with HIV-1,[3,7] but much less evidence on actual growth. India, like most developing countries, uses unlinked, anonymous HIV-1 testing of pregnant women attending antenatal clinics to monitor trends in the general population. Antenatal clinic data provide a large yearly sampling frame, the characteristics of which stay reasonably stable.[8–11] In India, more than 91% of women live with their husbands by the age of 25 years,[12] and should thus represent a reliable group to monitor changes in HIV-1 incidence even though they do not always accurately predict HIV-1 prevalence in the general population: in Tamil Nadu, one study found adult female prevalence in 1998 to be twice (2%) that reported in antenatal clinics (1%),[13] whereas another study found adult female prevalence in urban (1·4%) and rural (0·66%) areas to be similar to antenatal clinic prevalence.[14] The trend in new or incident infections, especially in young people who have recently become sexually active, is the most sensitive marker to track the course of the epidemic. Unfortunately, incidence is hard to measure directly, but prevalence in young women (age 15–24 years) is an indirect but useful proxy.

Here, we estimated the HIV-1 prevalence from 2000 to 2004 in young women attending antenatal clinics and men attending sexually transmitted infection (STI) clinics in southern and northern states in India. We explored whether any of these changes were realistic or whether they could be explained by changes over time in the characteristics of individuals attending these clinics (or where such clinics were established) or (among women) in AIDS mortality.

Methods

Setting

We analysed individual-level data for 1998–2004 from 294 050 women attending antenatal clinics (n=216 in 2004) and 58 790 men attending STI clinics (n=132 in 2004) in India. Tested populations reported here were aged 15–34 years. Clinics do unlinked, anonymous HIV-1 testing every year (as well as STI testing in antenatal clinics) for about 12 consecutive weeks, from public clinics in all 35 states and union territories.[1] Demographic details vary every year, but generally include age, residence, migration status, and education (table 1). Here, we report only data from 2000 onwards, since the number of sites before 2000 was small (antenatal clinics: 17 in 1998, 41 in 1999; STI clinics: 19 in 1998, 34 in 1999). The number of antenatal clinic sites increased from 35 in 2000 to 124 in 2004 in the north, and from 36 to 124 in the south. Standardised and central quality assurance of HIV-1 testing started in late 1999. Some variables, including syphilis (VDRL; Venereal Disease Research Laboratory test) and hepatitis B were recorded only for specific years (table 1). HIV-1 testing follows WHO protocols: two positive HIV-1 enzyme immunoassays results confirm a positive status, and two negative tests confirm a negative status.[15] Indeterminate tests undergo a third immunoassay. These enzyme immunoassay kits have a sensitivity of more than 99% and a specificity of more than 95%,[16] and NACO's central re-testing of all positives and 5% of negatives have shown few false-positive results.[1,15]

States were grouped into the south, consisting of Andhra Pradesh, Karnataka, Maharashtra, and Tamil Nadu (even though Maharashtra is regarded as a western state), and the north, consisting of 14 of the most populous northern states (excluding the northeast states of Nagaland, Manipur, and Mizoram where transmission is dominated by injecting drug use). Southern states are well noted for having about five-fold higher seroprevalence than northern states.[1] Importantly, the two regions seem to have a distinct sexual behaviour pattern (figure 1). A 2001 survey[17] of sexual behaviour in 85 000 adults aged 15–49 years in the general population in 35 states found that 13% of men in the south

	Southern states of India						Northern states of India					
	Age 15–24 years			Age 25–34 years			Age 15–24 years			Age 25–34 years		
	HIV-positive/ tested	ASR % (95% CI)	Odds ratio (95% CI)*	HIV-positive/ tested	ASR % (95% CI)	Odds ratio (95% CI)*	HIV-positive/ tested	ASR % (95% CI)	Odds ratio (95% CI)†	HIV-positive/ tested	ASR % (95% CI)	Odds ratio (95% CI)*
All states	1372/101 592	1·3% (1·2–01·4)	··	821/47 803	1·8% (1·6 to 1·9)	··	243/88 310	0·3% (0·2–0·3)	··	158/56 345	0·3% (0·2–0·3)	··
Age groups												
15–19 years	258/20 105	1·3% (1·1–1·4)	Reference	··	··	··	35/14 311	0·2% (0·2–0·3)	Reference	··	··	··
20–24 years	1114/81 487	1·4% (1·3–1·4)	1·1 (1·0–1·3)	··	··	··	208/73 999	0·3% (0·2–0·3)	1·2 (0·9–1·6)	··	··	··
25–29 years	··	··	··	643/38 458	1·7% (1·5–1·8)	Reference	··	··	··	113/42 358	0·3% (0·2–0·3)	Reference
30–34 years	··	··	··	178/9345	1·9% (1·6–2·2)	1·1 (0·9–1·3)	··	··	··	45/13 987	0·3% (0·2–0·4)	1·2 (1·0–1·6)
Education†												
Literate	774/66 713	1·1% (1·0–1·2)	Reference	395/29 017	1·4% (1·2–1·6)	Reference	130/55 137	0·2% (0·2–0·3)	Reference	85/31 049	0·3% (0·2–0·4)	Reference
Illiterate	417/25 277	1·6% (1·4–1·8)	1·3 (1·2–1·5)	348/14 776	2·4% (2·1–2·7)	1·6 (1·4–1·9)	94/25 153	0·3% (0·2–0·4)	1·7 (1·4– 1·9)	60/20 149	0·3% (0·2–0·4)	1·1 (1·0–1·3)
Residence												
Urban	688/51 051	1·3% (1·2–1·5)	Reference	419/24 767	1·7% (1·5–1·9)	Reference	153/51 366	0·3% (0·2–0·3)	Reference	88/32 445	0·3% (0·2–0·4)	Reference
Rural	684/50 541	1·3% (1·2–1·4)	1·1 (1·0–1·2)	402/23 306	1·8% (1·6–2·1)	1·2 (1·0–1·3)	90/36 944	0·2% (0·2–0·3)	0·8 (0·7–0·9)	70/23 900	0·3% (0·2–0·4)	1·2 (1·0–1·4)
Migrant status†												
Non-migrant	1007/77 762	1·3% (1·2–1·4)	Reference	615/36 786	1·7 (1·6–1·9)	Reference	182/68 403	0·3% (0·2–0·3)	Reference	119/43 755	0·3% (0·2–0·4)	Reference
Migrant	183/13 833	1·2% (1·0–1·5)	1·1 (1·0–1·3)	125/6880	1·9 (1·5–2·3)	1·2 (1·0–1·4)	42/11 490	0·3% (0·2–0·4)	1·4 (1·2–1·7)	26/7128	0·3% (0·2–0·5)	1·5 (1·2–1·9)
Syphilis‡												
Negative	837/74 570	1·1% (1·1–1·2)	Reference	538/35 755	1·6 (1·4–1·7)	Reference	168/61 376	0·3% (0·2–0·3)	Reference	115/38 650	0·3% (0·3–0·4)	Reference
Positive	83/649	15·0% (11·1–18·9)	12·9 (9·7–17·3)	63/342	17·8 (13·2–22·4)	14·8 (11·8–18·6)	201/1382	1·5% (0·6–2·4)	5·4 (3·6–8·0)	13/965	1·4% (0·6–2·3)	4·5 (2·6–7·9)
Yearly change in HIV-1 risk (%)§	··	··	–11 (–16 to –8)	··	··	–6 (–11 to 0·2)	··	··	4 (–4 to 13)	··	··	11 (–3 to 27)

HIV-positive/tested=number of HIV-positive individuals/number of individuals tested. ASR=Age-standardised rate (HIV prevalence standardised to the 2001 census population aged 15–24 or 25–34 years). *Odds ratio from multivariate model adjusting for age, education, residence, migrant status, state, and year; for individuals attending clinics in 2001–04 only. †Not available in 2000. ‡Not available in 2000 and 2001; odds ratios adjusted for age. §Odds ratio for HIV-1 infection per year in 2000–2004 adjusted for age. Adjustment for age, residence, state, and education for 2001–04 yielded similar reductions (ie, in the south for individuals aged 15–24 years, –11 [95% CI –15 to –5]).

Table 1: **HIV-1 prevalence and correlates of infection in women attending antenatal clinics in 2000–04 in the south and north of India**

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reported a non-regular partner in the past year versus 8% of men in the north. Of those men reporting a non-regular partner, about 59% in the south reported more than one partner, whereas in the north, only 45% reported more than one partner. Only about 4% of women in the south reported a non-regular partner in the past year versus 1% in the north; only 30% of these women in both regions reported more than one non-regular partner.

Study population

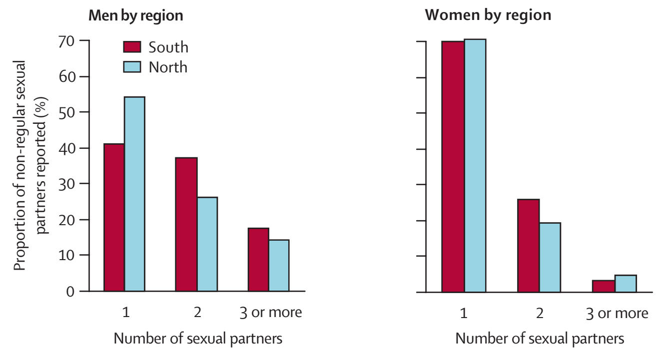
For reasons already discussed, we focused on women aged 15–24 years.[8–11] We focused on trends in STI clinics attended by men, because these individuals represent an important bridge for transmission from sex workers to low-risk partners.[3–6] Men with a syndromic diagnosis of ulcerative STIs were included as a subgroup analysis of those who would have probably engaged in recent high-risk sexual activity (including use of sex work). These men are at especially high risk of HIV-1, because ulcerative STIs are a cofactor in HIV-1 infection.[18] Female STI data are more complicated to interpret than male STI data, because the syndromic diagnosis of STIs is misclassified more often in women than in men.[19] Additionally, we could not interpret which individuals attending STI clinics were female sex workers. We focus on men aged 20–29 years attending STI clinics, to capture the average 5-year gap between men and women at marriage,[12] and because STIs in young men are more likely to represent recent infection than STIs in older men.

Statistical analysis

We used the 2001 Indian census for direct standardisation for age of yearly HIV-1 prevalence estimates in individuals attending antenatal and STI clinics, each with 95% binomial confidence limits. Multivariate logistic regression was used to estimate yearly changes in risk for HIV-1 as a test for trend.[20] As recommended previously,[9] analyses were grouped according to ages 15–24 and 25–34 years. However, trends for every 5-year stratum were generally similar to grouped results, with the exception of a slight increase at age 15–19 years compared with age 20–24 years in those who attended antenatal clinics in the north (data not shown). Because site codes varied from year to year, we could only adjust estimates of HIV-1 risk by state, but not by individual site. The most important effect of this could be a small overestimation of the SE of the effect of year. Analyses of age-specific antenatal clinic trends for the four southern states separately yielded results that were generally consistent with results for all southern states combined (webfigure 1). We used SAS version 8.2 for logistic regression of the odds ratio of infection with HIV-1 for the following variables: 5-year age group, residence, education, migrant status, state, year, and VDRL.

Role of the funding source

Funding sources or NACO had no role in study design, data analysis, data interpretation, or writing of the report.



		None	Any	1	2	3 or more	None	Any	1	2	3 or more
South	n	6686	991	407	370	174	7322	340	238	88	11
	%	87·1%	12·9%	41·1%	37·3%	17·6%	95·6%	4·4%	70·0%	25·9%	3·2%
North	n	29487	2534	1374	665	364	32609	365	259	71	18
	%	92·1%	7·9%	54·2%	26·2%	14·4%	98·9%	1·1%	71·0%	19·5%	4·9%

Figure 1: **Number of non-regular sexual partners reported by general population in past 12 months**
Of individuals who reported a non-regular partner, the proportion not specifying a number were: men, south 40 (4·0%), north 131 (5·2%); women, south 3 (0·9%), north 17 (4·7%).

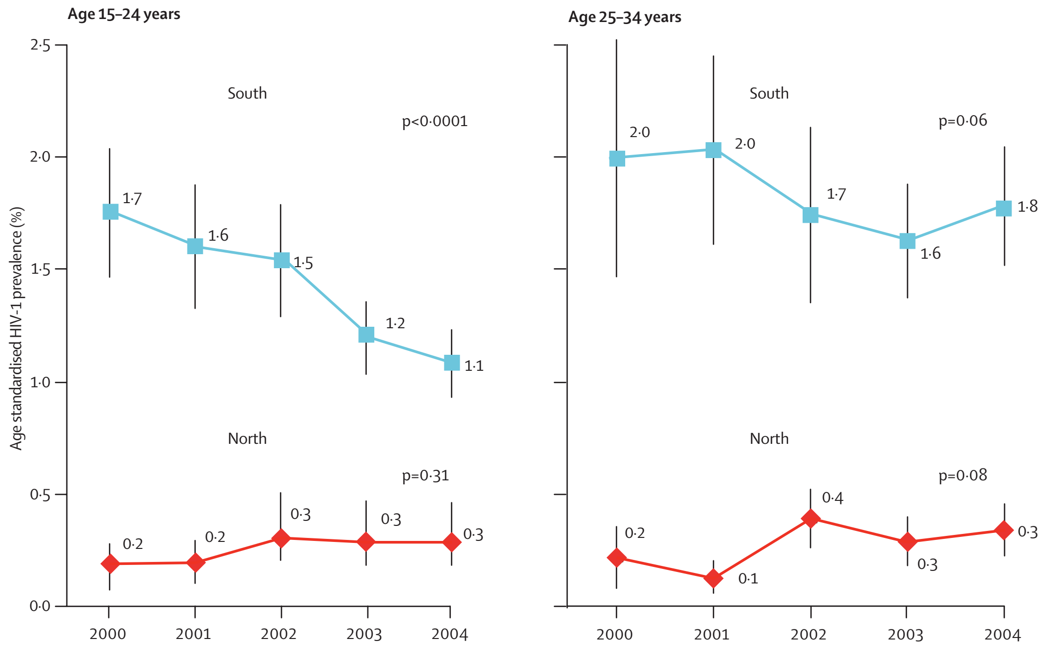
The lead author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The mean age of women attending antenatal clinics was 23 years (34416 [11%] aged 15–19 years, 155486 [52%] 20–24 years, 80816 [27%] 25–29 years, and 23332 [8%] 30–34 years); only 6957 (2%) were older than 35 years. The mean age of men attending STI clinics was 29 years (4626 [8%] aged 15–19 years, 12711 [22%] 20–24 years, 14140 [24%] 25–29 years, 11293 [19%] 30–34 years, and 7717 [13%] 35–39 years); only 8303 (14%) were older than 40 years. The overall age-standardised HIV-1 prevalence among people who attended antenatal clinics aged 15–49 years was 1·6% (95% CI 1·4–1·8) in the south and 0·3% (0·2–0·5) in the North in 2000–04. In both regions, we recorded differences in prevalence by education, residence, and migration (table 1).

The age-standardised HIV-1 prevalence in women aged 15–24 years in the south fell significantly from 1·7% to 1·1% in 2000–04 (absolute reduction 0·6%; relative reduction 35%; figure 2). The yearly reduction was 11% (95% CI 8–16) when adjusted for age, with very similar reductions seen when adjusted for age, education, residence, and state, in 2001–04. By contrast, we did not record a significant reduction at ages 25–34 years (2·0% to 1·8%; absolute reduction 0·2%; relative reduction 10%; figure 2). Prevalence in women aged 15–24 years in the north were about a fifth of that in the south, but no significant change in 2000–04 was seen; nor was there a significant change at ages 25–34 years (figure 2). In view of our aim to estimate trends in incident infections, most of our remaining analyses focused on women aged 15–24 years.

See **Online** for webfigure 1



Year	2000	2001	2002	2003	2004	2000	2001	2002	2003	2004
South										
Number of sites	36	48	54	119	124	36	48	54	119	124
HIV-positive/tested	181/9599	205/12 641	230/15 030	377/31 751	379/32 571	78/4010	125/6238	109/6271	244/15 077	265/16 207
Difference between 2000 and 2004					Z=4·09, p<0·0001					Z=0·70, p=0·48
North										
Number of sites	35	77	86	93	92	35	77	86	93	92
HIV-positive/tested	19/8006	35/17 219	69/19 972	64/21 752	56/21 361	13/5144	17/11 385	47/12 539	38/13 639	43/13 638
Difference between 2000 and 2004					Z=1·00, p=0·32					Z=1·35, p=0·18

***Figure 2:* Age-standardised HIV-1 prevalence in women attending antenatal clinics in 2000–04 in the south and north of India**
HIV-positive/tested=number of HIV-positive individuals/number of individuals tested. Boxes and diamonds (lines) are prevalence (95% CI).

The reductions in the age-standardised prevalence in women aged 15–24 years in the south were consistent in subgroup analyses, including comparisons between urban and rural residency, educated and illiterate status, and migrant and non-migrant status (figure 3). In the north, no significant change in HIV-1 prevalence was seen among subgroups, apart from modest but non-significant increases in migrant women.

It is already known that women are less likely to visit an antenatal clinic if: they are older, have high parity, are illiterate, or are poor.[8–11] Our multivariate analyses (table 1) found that some of these factors, specifically education, residence, and migration (in the north) were important correlates of HIV-1 infection in women aged 15–49 years who attended antenatal clinics. These results were adjusted for age, state, and year.

Table 2 shows that the age structure and migrant status of individuals attending antenatal clinics aged 15–35 years was mostly consistent over time in the south and north. We recorded a non-significant decrease in the proportion of VDRL-positive people who attended antenatal clinics in the north, although data for VDRL status were available only from 2002 to 2004 (table 2). There was a steady increase in the proportion of the total tested women from rural areas, indicating the expanded coverage of testing to rural populations. Among southern women, a small (5%) but significant absolute decrease in the percentage of illiterate individuals attending was also recorded. The apparent paradox of expanded rural sites but fewer illiterate people could be explained because even the rural sites attract a substantial proportion of urban (and probably educated) women in those areas.[8–11] Additional data (not shown) for 2003–04 from 101 antenatal clinic sites in rural areas[1] in the south showed little difference in overall age-standardised prevalence with our data; also, the correlates of infection were similar to those in table 1.

Trends at ages 15–24 years were generally consistent when the 28 antenatal clinic sites in the south open continuously from 2000 to 2004 were compared with all sites (figure 4). A significantly decreasing trend was seen in sites that were open continuously and all sites. Trends were also similar in the 24 continuously open sites compared with all sites in north India in 2000–04 (year 2000, 15 HIV-positive individuals of 5394 individuals tested; 2001, 16 of 5343; 2002, 16 of 5557; 2003, 14 of 5349; 2004, 23 of 5668; p_{trend}=0·22). There was no significant trend in HIV-positive individuals attending antenatal clinics in the north from all sites in 2000–04 (p_{trend}=0·31). Trend slopes between attendances at all sites compared with attendances at continuously open sites did not differ

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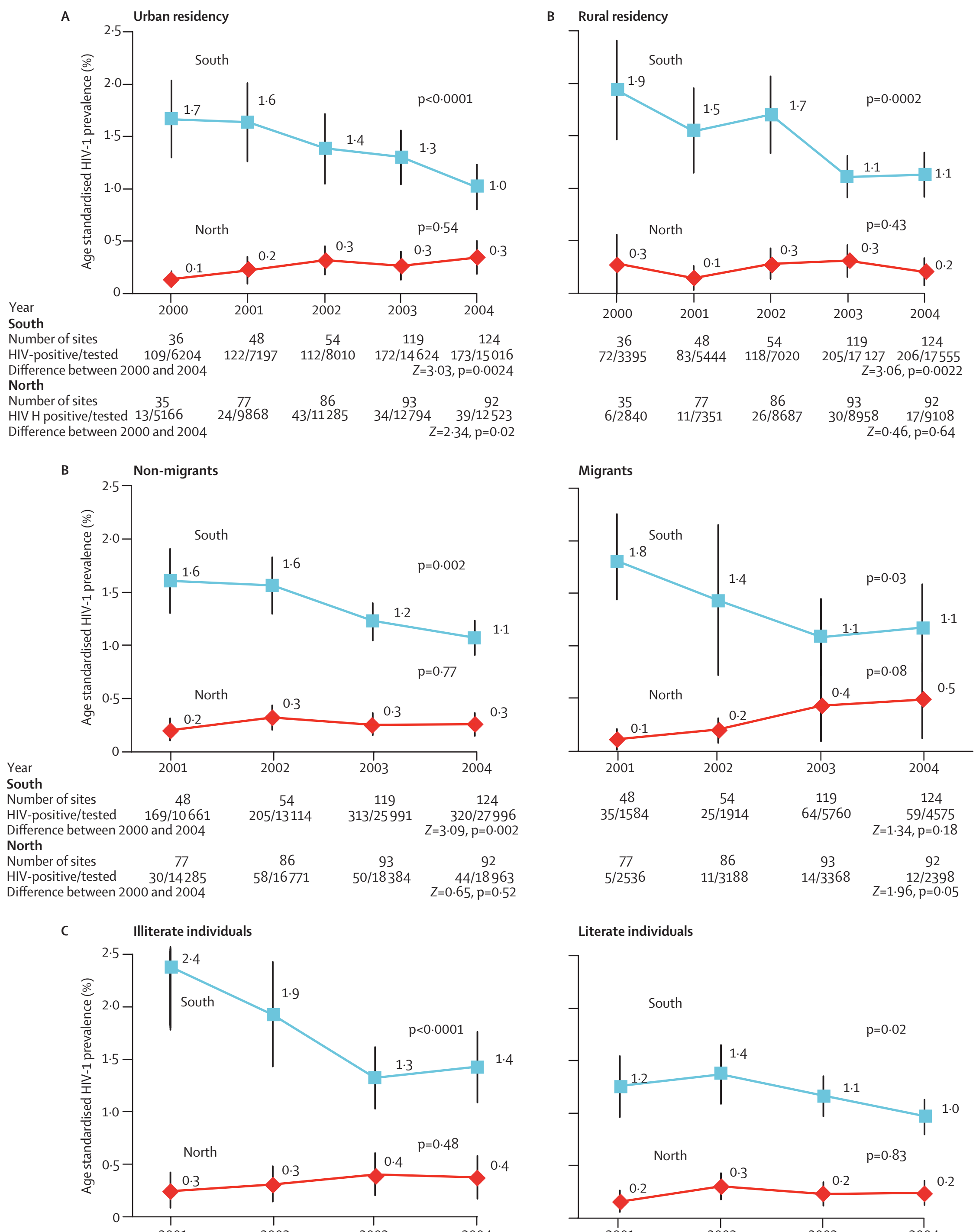

A Urban residency

Year	2000	2001	2002	2003	2004
South					
Number of sites	36	48	54	119	124
HIV-positive/tested	109/6204	122/7197	112/8010	172/14 624	173/15 016
Difference between 2000 and 2004					Z=3·03, p=0·0024
North					
Number of sites	35	77	86	93	92
HIV H positive/tested	13/5166	24/9868	43/11 285	34/12 794	39/12 523
Difference between 2000 and 2004					Z=2·34, p=0·02

B Rural residency

Year	2000	2001	2002	2003	2004
South					
Number of sites	36	48	54	119	124
HIV-positive/tested	72/3395	83/5444	118/7020	205/17 127	206/17 555
Difference between 2000 and 2004					Z=3·06, p=0·0022
North					
Number of sites	35	77	86	93	92
HIV-positive/tested	6/2840	11/7351	26/8687	30/8958	17/9108
Difference between 2000 and 2004					Z=0·46, p=0·64

B Non-migrants

Year	2001	2002	2003	2004
South				
Number of sites	48	54	119	124
HIV-positive/tested	169/10 661	205/13 114	313/25 991	320/27 996
Difference between 2000 and 2004				Z=3·09, p=0·002
North				
Number of sites	77	86	93	92
HIV-positive/tested	30/14 285	58/16 771	50/18 384	44/18 963
Difference between 2000 and 2004				Z=0·65, p=0·52

Migrants

Year	2001	2002	2003	2004
South				
Number of sites	48	54	119	124
HIV-positive/tested	35/1584	25/1914	64/5760	59/4575
Difference between 2000 and 2004				Z=1·34, p=0·18
North				
Number of sites	77	86	93	92
HIV-positive/tested	5/2536	11/3188	14/3368	12/2398
Difference between 2000 and 2004				Z=1·96, p=0·05

C Illiterate individuals

Year	2001	2002	2003	2004
South				
Number of sites	48	54	119	124
HIV-positive/tested	88/3815	83/4502	125/8719	121/8241
Difference between 2000 and 2004				Z=2·73, p=0·0063
North				
Number of sites	77	86	93	92
HIV-positive/tested	15/5245	25/6257	30/6818	24/6833
Difference between 2000 and 2004				Z=0·92, p=0·36

Literate individuals

Year	2001	2002	2003	2004
South				
Number of sites	48	54	119	124
HIV-positive/tested	117/8826	147/10 525	252/23 032	258/24 330
Difference between 2000 and 2004				Z=1·70, p=0·09
North				
Number of sites	77	86	93	92
HIV-positive/tested	20/11 974	44/13 701	34/14 934	32/14 528
Difference between 2000 and 2004				Z=0·98, p=0·32

***Figure 3:* Age-standardised HIV-1 prevalence in women aged 15–24 years attending antenatal clinics in 2000–04 in the south and north of India by (A) residence, (B) migrant status, and (C) literacy**
HIV-positive/tested=number of HIV-positive individuals/ number of individuals tested. Boxes and diamonds (lines) are prevalence (95% CI).

	South, n (%)						North, n (%)					
	2000	2001	2002	2003	2004	p	2000	2001	2002	2003	2004	p
Women aged 15–34 years attending antenatal clinics												
Number of sites	36	48	54	119	124	..	35	77	86	93	92	..
Number tested	13 609	18 879	21 301	46 828	48 778	..	13 150	28 604	32 511	35 391	34 999	..
Age groups												
15–24 years	9599 (70%)	12 641 (67%)	15 030 (71%)	31 751 (68%)	32 571 (67%)	0·25	8006 (61%)	17 219 (60%)	19 972 (61%)	21 752 (62%)	21 361 (61%)	0·41
25–34 years	4010 (30%)	6238 (33%)	6271 (29%)	15 077 (32%)	16 207 (33%)	0·25	5144 (39%)	11 385 (40%)	12 539 (39%)	13 639 (38%)	13 638 (39%)	0·41
Residence												
Rural	4776 (35%)	7925 (42%)	9647 (45%)	25 020 (53%)	26 209 (54%)	0·01	4631 (35%)	12 446 (44%)	14 125 (43%)	14 813 (42%)	14 829 (42%)	0·52
Urban	8833 (65%)	10 954 (58%)	11 654 (55%)	21 808 (47%)	22 569 (46%)	0·01	8519 (65%)	16 158 (56%)	18 386 (57%)	20 578 (58%)	20 170 (58%)	0·52
Migration												
Non-migrant	n/a	15 853 (86%)	18 444 (87%)	38 217 (82%)	42 034 (86%)	0·80	n/a	23 747 (85%)	27 434 (84%)	29 836 (84%)	31 141 (89%)	0·11
Migrant	n/a	2503 (14%)	2855 (13%)	8611 (18%)	6744 (14%)	0·85	n/a	4142 (15%)	5063 (16%)	5555 (16%)	3858 (11%)	0·33
Education												
Illiterate	n/a	6185 (33%)	6826 (32%)	13 753 (29%)	13 289 (27%)	0·01	n/a	9675 (34%)	11 315 (35%)	12 120 (34%)	12 192 (35%)	0·36
Literate	n/a	12 694 (67%)	14 472 (68%)	33 075 (71%)	35 489 (73%)	0·01	n/a	18 929 (66%)	21 179 (65%)	23 271 (66%)	22 807 (65%)	0·39
VDRL status												
Negative	n/a	n/a	15 607 (99%)	46 348 (99%)	48 370 (99%)	0·94	n/a	n/a	30 977 (97%)	34 701 (98%)	34 348 (98%)	0·29
Positive	n/a	n/a	106 (1%)	477 (1%)	408 (1%)	0·94	n/a	n/a	1024 (3%)	688 (2%)	635 (2%)	0·29
Men aged 15–34 years attending STI clinics												
Number of sites	20	28	38	38	41	..	44	73	84	88	91	..
Number tested	1805	2005	3307	3152	3510	..	3155	5180	6253	7035	7368	..
Age groups												
15–24 years	636 (35%)	721 (36%)	1115 (34%)	1123 (36%)	1234 (35%)	0·99	1424 (45%)	2270 (44%)	2670 (43%)	2916 (41%)	3228 (44%)	0·50
25–34 years	1169 (65%)	1284 (64%)	2192 (66%)	2029 (64%)	2276 (65%)	0·99	1731 (55%)	2910 (56%)	3583 (57%)	4119 (59%)	4140 (56%)	0·50
Residence												
Rural	686 (38%)	743 (37%)	1425 (43%)	1302 (41%)	1302 (43%)	0·12	934 (30%)	1979 (38%)	2681 (43%)	2929 (42%)	2957 (40%)	0·23
Urban	1119 (62%)	1262 (63%)	1882 (57%)	1850 (59%)	1992 (57%)	0·12	2223 (70%)	3201 (62%)	3572 (57%)	4106 (58%)	4411 (60%)	0·23
Migration												
Non-migrant	n/a	1685 (84%)	2678 (81%)	2558 (81%)	2970 (85%)	0·68	n/a	4043 (81%)	5169 (83%)	6043 (86%)	5862 (80%)	0·82
Migrant	n/a	319 (16%)	626 (19%)	594 (19%)	540 (15%)	0·70	n/a	971 (19%)	1070 (17%)	992 (14%)	1506 (20%)	0·89
Education												
Illiterate	n/a	403 (20%)	559 (17%)	608 (19%)	593 (17%)	0·53	n/a	695 (13%)	888 (14%)	925 (13%)	1124 (15%)	0·42
Literate	n/a	1602 (80%)	2748 (83%)	2544 (81%)	2917 (83%)	0·56	n/a	4485 (87%)	5363 (86%)	6110 (87%)	6244 (85%)	0·42
VDRL status												
Negative	n/a	n/a	2519 (96%)	3027 (96%)	3327 (95%)	0·54	n/a	n/a	5943 (96%)	6651 (95%)	7054 (96%)	0·94
Positive	n/a	n/a	116 (4%)	124 (4%)	183 (5%)	0·54	n/a	n/a	246 (4%)	383 (5%)	309 (4%)	0·94

n/a=not available.

Table 2: **Selected characteristics of individuals who attended antenatal and STI clinics in 2000–04 in the south and north of India**

significantly (south, p for differences=0·49; north, p for differences=0·63).

We recorded a fall in age-standardised HIV-1 prevalence in men aged 20–29 years attending STI clinics in the south in 2000–04 (absolute reduction 7·6%; relative reduction 36%; figure 5). Similar decreases in prevalence were seen for the subset of men reporting ulcerative STIs (absolute reduction 6·7%; relative reduction 32%; figure 5). As with antenatal clinics, prevalence in the north was lower than in the south: the north showed a non-significant reduction in men attending STI clinics (absolute reduction 0·4%; relative reduction 15%; figure 5). Similar trends were seen for the subgroup of men reporting ulcerative STIs. Trends were similar between the 19 STI clinics in the south and the 37 sites in the north that were open continuously in 2000–04 compared with all the sites in their respective regions (data not shown).

Selection biases among men using STI clinics were expected to be greater than women attending antenatal clinics, and sampling of STI populations was not as consistent as sampling for antenatal clinic populations in India.[1]

Discussion

We show evidence of a reduction of more than a third in HIV-1 incidence in 2000–04 in young women attending

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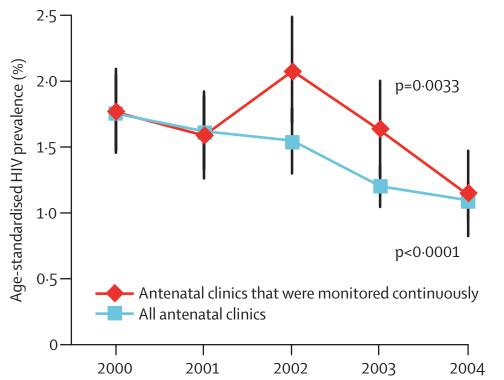


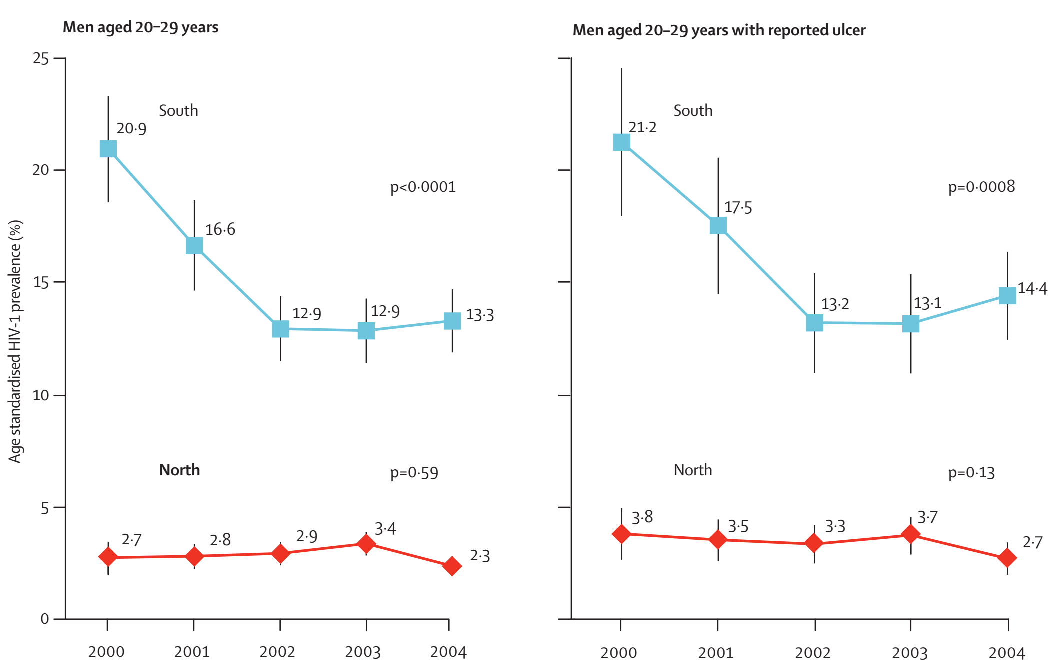
Year	2000	2001	2002	2003	2004
South					
Number of sites	36	48	54	119	124
HIV-positve/tested	181/9599	205/12 641	230/15 030	377/31 751	379/32 571
South Continuous					
Number of sites	28	28	28	28	28
HIV-positve/tested	142/7591	133/7552	159/8016	120/7401	93/8142

Figure 4: **Age-standardised HIV prevalence in women aged 15–24 years attending antenatal clinics monitored continuously and all sites in 2000–04 in the south and north of India**

p_{trend} adjusted for age and residence. HIV-positive/tested=number of HIV-positive individuals/number of individuals tested. Boxes and diamonds (lines) are prevalence (95% CI).

antenatal clinics in the four southern states of India while there was no change in the northern states. Unlike previous analyses,[1,2] ours had the advantage of examination of individual-level data, classification of variables in their epidemiological context, and proper age-adjustment. Two key questions arise: are such trends true or due to biases, and if true, what might account for the falling incidence in the south?

The reduction in HIV-1 among young women in the south seems to be real. Decreases were consistent across subgroups of residence, migration, and education. Antenatal clinic sites have existed for 2–3 years in nearly all the 115 districts in the south, and a large number of women were tested. Moreover, use of public antenatal clinics by women in the general population is high—approaching 80%, as measured by receipt of two doses of tetanus toxoid in their last pregnancy.[12] Selection biases do not provide plausible alternative explanations: there has been only modest change in the demographics of women attending these clinics (table 2). Subtle selection biases, such as changes in sexual behaviour, cannot be excluded. In particular, mathematical models from African antenatal clinic data[9] predict age-based HIV-1 prevalence might drop spuriously if the age at sexual debut changes rapidly.



Year	2000	2001	2002	2003	2004	2000	2001	2002	2003	2004
South										
Number of sites	20	28	38	38	41	20	28	38	38	41
HIV-positive/tested	244/1132	220/1253	278/2068	269/1983	304/2198	130/592	108/582	122/885	118/856	180/1192
Difference between 2000 and 2004					Z=5·39, p<0·0001					Z=3·46, p=0·0002
North										
Number of sites	44	73	84	88	91	44	73	84	88	91
HIV-positive/tested	56/2013	90/3209	118/3978	152/4440	108/4577	40/1047	53/1490	57/1686	75/1989	54/1984
Difference between 2000 and 2004					Z=0·94, p=0·34					Z=1·59, p=0·11

Figure 5: **Age-standardised HIV-1 prevalence in men aged 20–29 years attending STI clinics in 2000–04, and in those with genital ulcers in the south and north of India**

HIV-positive/tested=number of HIV-positive individuals/number of individuals tested. Boxes and diamonds (lines) are prevalence (95% CI).

However, such models need validation in the Indian context of a much lower HIV-1 prevalence than that seen in Africa and the specific pattern of non-regular sexual partnerships seen in India.[3] Reported data on mean age of female marriage from 1971 to 1999[12] show only modest changes (yearly % change from 1971 to 1999: 0·4 each in Andhra Pradesh, Karnataka, and Maharashtra; 0·2 in Tamil Nadu; and 0·5 in India overall), although some groups such as women in urban areas in Maharashtra show greater changes. To the extent that selection biases correlate with education, residency, and migration, they would probably cause only modest shifts over time and have been partly adjusted in our multivariate results. Finally, trends were similar for sites that are open continuously and for all sites. Notably, NACO's chief criterion for selecting new sites was the volume of individuals going to antenatal clinics, which should not be biased by HIV-1 status.

As women become HIV-1 infected, they are less likely to attend antenatal clinics because of reduced fertility and higher mortality. These biases are more common for older women.[11] Indeed, the absence of a major increase in HIV-1 in women aged 25–34 years in the south could be due to a downward attenuation of fertility in HIV-1 positive women at these ages. Finally, a median of 50% of all women aged 20–49 years report sterilisation in the south, which is much higher than the proportion in the north. The age of sterilisation is usually older than age 25 years (after childbearing), and sterilisation might thus reduce HIV-1 detection at older ages in antenatal clinics. However, the median age of sterilisation has been reported to be stable for the past decade or so before 1999.[12] Importantly, antenatal clinic data cannot record primary HIV-1 transmission from infected but unmarried men. Our own estimates suggest that unmarried men represent a substantial proportion of all sex worker users, but the proportion has probably not changed in the past 5 years or so.

Rapid increases in mortality would remove HIV-1 infected women from antenatal clinic testing. The estimated mean time from infection to death has been estimated at 7–9 years in India.[21] If mortality were the major cause of recorded reductions, we would expect prevalence to fall at older ages, with offsetting increases at younger ages—a pattern recently described in Uganda.[22] In fact, we recorded the opposite findings, suggesting that incidence is falling at young ages. In the general population, all-cause mortality rates in women aged 15–34 years in the south have been low and generally falling (webfigure 2). At young ages, all-cause mortality should be reasonably sensitive to increases in AIDS mortality, since the major competing causes (maternal deaths and injuries) vary little over the past 5 years. Direct evidence on the level of AIDS mortality should be available next year.[23]

See **Online** for webfigure 2

Since HIV-1 prevalence in the north is only about a fifth of that seen in the south, and the north had a lower coverage of sites than the south (most of the 478 districts in the north did not have antenatal or STI clinics),[1] our available data had adequate power only to exclude major increases or decreases in HIV-1 incidence in young people. Moreover, only 50% of pregnant women reported using public antenatal clinics in the north.[13] Indeed, age-standardised VDRL prevalence was higher in northern women aged 15–24 years than in southern women (data not shown). This difference could indicate reduced STI treatment rates in the north, evidence of an earlier stage of the HIV-1 epidemic or other variables.[3,9] However, major changes in education, migration, and residency, and selection biases at ages 15–34 years (table 2), or in antenatal clinic testing site can be reasonably excluded as explanations for the flat trends in HIV-1 prevalence among young women in the north.

Observed reductions are best understood in the context of what is known about sexual networks and transmission patterns in south India.[3–6] Men reporting non-regular partners report more of these partners than men in the north (figure 1). Although men could over-report—and women under-report—the number of sexual partners, the most plausible explanation for such differences is male use of female sex workers.[3–6] Networks of men having sex with other men need further study, but reported prevalence is probably too low to account for the very large reported differences in the number of non-regular partners between men and women in both regions or the smaller reported differences between men in the south and those in the north: one survey[24] of five (mostly northern) states reported that 4% of adult men had sex with a man in the past year, and a similar survey in Chennai,[25] Tamil Nadu, reported 6% of adult men ever had sex with a man.

What could account for the reduction of HIV-1 prevalence in the South? Mathematical models of sex-work-based networks find that the prevalence is very sensitive to increases in abstinence from sex work or in condom use with sex work.[3] Use of condoms between married couples is probably not relevant to the reductions seen in the south; it is well below 3% in the south and has changed little from 1992 to 1999.[12] HIV-1 trends in young men attending STI clinics provide an imperfect snapshot of high-risk men, including those who have recently visited sex workers. The fall in the south could be explained by increased condom use or increased abstinence, and is probably not due to STI antibiotic treatment, since reductions also occurred in men with ulcerative, and presumably viral, STIs. In 2004, about 70–80% of female sex workers in Maharashtra[26] and Tamil Nadu[27] reported condom use with their last client, with lower percentages for all recent partners, and lower percentages still with regular non-paying partners. Data for male abstinence from sex workers are not well reported: indirect evidence from surveys of female sex workers in Tamil Nadu in 1996–2004 has shown increases in condom use, but no change in the number of clients per day.[27] Reports of rising condom use accord with major increases in HIV-1 control programmes funded by the World Bank and various external agencies from 1999 onward aimed at

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female sex workers. Furthermore, early reductions are apparent in Tamil Nadu (webfigure 1), where control programmes began earlier than in other states.

Our study has two key implications. First, strategies that focus on high coverage and quality of peer interventions—not only for female sex-workers specifically, but also for men who have sex with men—with condoms, education, and negotiation skills offer the best hope to attenuate overall growth of HIV-1 in India.[28] Such strategies are partly in place in the south, but must be extended to high coverage in each southern district (especially in Andhra Pradesh and Karnataka where coverage lags behind). Equally important, sex-worker interventions should be replicated in the north, especially in urban and rural hot-spots.[29,30] Second, enhanced routine surveillance, including further investigation of risk factors, parity, and additional STI testing via antenatal clinics and other sites, is a powerful and cost-effective way[30] to monitor the growth of India's large and heterogeneous HIV-1 epidemic.

Contributors

The National Institute of Health and Family Welfare is responsible for the overall analyses of antenatal and STI clinic data. R Kumar, P Jha, N Dhingra, P Bhatia, P Mony, P Millson, and M Bhattacharya are among the principal investigators of the International Studies of HIV/AIDS Consortium. The paper was conceived by R Kumar, P Jha, P Arora and N Nagelkerke. Statistical analyses were done by R Kumar, P Arora, N Nagelkerke, and P Jha. All the authors participated in data interpretation and in the writing of the manuscript.

Conflict of interest statement

We declare that we have no conflict of interest.

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