Cost-effectiveness of HIV prevention for high-risk groups at scale: an economic evaluation of the Avahan programme in south India

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Summary

Background **Avahan is a large-scale, HIV preventive intervention, targeting high-risk populations in south India. We assessed the cost-effectiveness of Avahan to inform global and national funding institutions who are considering investing in worldwide HIV prevention in concentrated epidemics.**

Methods **We estimated cost effectiveness from a programme perspective in 22 districts in four high-prevalence states. We used the UNAIDS Costing Guidelines for HIV Prevention Strategies as the basis for our costing method, and calculated effect estimates using a dynamic transmission model of HIV and sexually transmitted disease transmission that was parameterised and fitted to locally observed behavioural and prevalence trends. We calculated incremental cost-effective ratios (ICERs), comparing the incremental cost of Avahan per disability-adjusted life-year (DALY) averted versus a no-Avahan counterfactual scenario. We also estimated incremental cost per HIV infection averted and incremental cost per person reached.**

Findings **Avahan reached roughly 150 000 high-risk individuals between 2004 and 2008 in the 22 districts studied, at a mean cost per person reached of US$327 during the 4 years. This reach resulted in an estimated 61 000 HIV infections averted, with roughly 11 000 HIV infections averted in the general population, at a mean incremental cost per HIV infection averted of $785 (SD 166). We estimate that roughly 1 million DALYs were averted across the 22 districts, at a mean incremental cost per DALY averted of $46 (SD 10). Future antiretroviral treatment (ART) cost savings during the lifetime of the cohort exposed to HIV prevention were estimated to be more than $77 million (compared with the slightly more than $50 million spent on Avahan in the 22 districts during the 4 years of the study).**

Interpretation **This study provides evidence that the investment in targeted HIV prevention programmes in south India has been cost effective, and is likely to be cost saving if a commitment is made to provide ART to all that can benefit from it. Policy makers should consider funding and sustaining large-scale targeted HIV prevention programmes in India and beyond.**

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Introduction

More than 2 million people are living with HIV in India.[1] The epidemic is concentrated and predominantly driven by high-risk groups, particularly female sex workers (FSWs) and their clients, men who have sex with men (MSM), and, in some contexts, injecting drug users.[2] The Avahan programme, the Indian AIDS initiative of the Bill & Melinda Gates Foundation, was one of the largest HIV prevention programmes targeted at high-risk groups worldwide. Avahan operated across six Indian states and had a funding commitment of US$258 million between 2004 and 2009.[3] Avahan was implemented through state lead partners, who contracted a plethora of local non-governmental organisations (NGOs) at the district level. From Avahan's inception, rigorous evaluation has been an integral part of the programme,[4] including the assessment of cost-effectiveness.

Avahan has been shown to be effective in the reduction of HIV transmission. In an evaluation that used a combination of detailed biobehavioural surveys and mathematical modelling in a subset of 22 of 83 total districts where it was implemented, medium to strong evidence of effect was reported in most districts modelled, especially those with less condom use in commercial sex at the start of the intervention.[5,6] Avahan averted 42% of all HIV infections during 4 years, corresponding to 68 000 (95% credibility interval 32 000–202 000) cases averted in 22 modelled districts. In 10 years, this number increased to 214 000 (99 000–373 000), representing 57% of HIV infections averted. Geographical extrapolation by use of a statistical regression model to all Avahan districts showed that 202 000 HIV infections were averted in 4 years, increasing to 606 000 HIV infections averted in 10 years.[6]

However, Avahan also incurred substantial costs.[7] Hence, HIV policy makers need to know whether the programme was also cost effective to inform decisions about making sizeable investments in HIV prevention at scale in other similar settings, especially at a time when HIV programmes are facing increasing demands on their scarce resources. So far, few robust studies have investigated the cost-effectiveness of HIV prevention targeted at high-risk groups, with only a handful done in Asia.[8] The most comprehensive estimate so far suggested a potential incremental cost per DALY averted of US$10.[9,7] However, great uncertainty remains around these predictions, with a 30% chance that HIV prevention for FSWs would not be cost effective.[9,7]

Several small project-based studies also suggest that cost-effectiveness could be achieved.[10–12] However, these studies exclude the costs of the substantial effort associated with large-scale implementation.[10] Previous studies also did not have the benefits of extensive target population surveys, did not use dynamic effect estimates, excluded heterogeneity in FSW risk behaviour, and did not fit the effect model to time trends in HIV prevalence.[11,12] In view of this evidence gap and the increasing scarce resources for HIV prevention, we did a large-scale economic evaluation of Avahan to examine whether HIV prevention for high-risk groups could achieve cost-effectiveness in the real world and at scale, and whether it should thus be sustained as a priority investment for global public health.

Methods

Study design

We estimated the cost-effectiveness of Avahan from a provider perspective. Our primary measure is the incremental cost effective ratio (ICER), comparing the incremental cost per DALY averted versus a no-Avahan counterfactual base case. Secondary measures include incremental cost per HIV infection averted and incremental cost per person reached.

We classified HIV prevention as cost effective a priori if the incremental cost per DALY averted was less than the gross domestic product (GDP) per head in 2011 (US$1500).[13] HIV prevention was classified as cost saving if the costs of antiretroviral treatment (ART) during the lifetime of the cohort of individuals exposed to HIV prevention during the first 4 years of the programme outweighed the costs spent in the first 4 years of the programme. Our primary ICER and cost-savings estimates assume that all future costs and DALYS averted are discounted at a 3% rate.

Programme and study setting

We evaluated HIV prevention activities in 22 districts in four of the six Indian states considered to have high HIV prevalence (Andhra Pradesh [0·9%], Karnataka [0·6%], Maharashtra [0·6%], and Tamil Nadu [0·3%] in 2009).[14] With time, HIV prevalence has shown a declining trend in all four states.[14] However, the number of people living with HIV remains high, with Andhra Pradesh having 500 000 people living with HIV followed by Maharashtra (420 000), Karnataka (250 000), and Tamil Nadu (150 000) in 2011.[14]

The Avahan programme contracted grantees at the state level (state lead partners) to work with grass-root NGOs to deliver a package of services to both FSW and MSM populations in these states.[3,15] The standard package implemented by NGOs includes peer-led outreach, education and condom distribution, free treatment of sexually transmitted infections (STIs) through project-operated clinical services or through preferred service providers, free commodity supplies (condoms, STI drugs), and facilitation of community mobilisation. Peer educators promoted condom use and attendance at clinics, and encouraged follow-up and partner treatment. Clinics provided treatment for STIs, referred clients to other clinical services, including HIV and tuberculosis testing, or both, and provided HIV treatment and care. Additional grantees did other activities such as capacity-building, social marketing, trucker programmes, national-level and state-level advocacy, and knowledge-building activities, across each state and nationally.[3,16]

Cost estimation

The UNAIDS Costing Guidelines for HIV Prevention Strategies were taken as the basis for the costing method.[17] Economic costs were estimated for every organisation level: NGO, state lead partners, and the national programme office for every year between 2004 and 2008 in all 22 districts, as part of a larger study into 68 districts across the four Indian states. A full description of methods and the presentation of the cost data used are publicly available.[7] We did not cost the no-Avahan counterfactual because of insufficient data availability at baseline. This approach implicitly assumes that the full cost of Avahan was required to achieve the differences in condom use achieved by Avahan over and above the counterfactual base case. To aid comparability with other studies, our results are presented in two categories: NGO costs (costs incurred at the NGO level only) and programme costs, including costs incurred at the state lead partners and national level (these include activities such as programme management, expertise enhancement [capacity building], and community supply costs).

Total and unit costs were estimated with data for expenditure, resource use, and activity that were obtained from routine reporting, and from staff records and interviews during the period 2004–08. Details of donated goods and services were collected from every district and were valued at market prices. Start-up and training costs were annualised during the lifetime of the project (assumed to be 5 years). The start-up period was defined as project inception until the start of service delivery to the target population. Costs of the evaluation and research activities were excluded.

Personnel costs covered the salaries and expenses of all staff, including peer educators, volunteers, and shared resource personnel. Peer educator time was valued at the honorarium paid, except when not paid. In the latter case, and for other volunteers, time costs were valued using self-reported average earnings or, if unemployed, the payment made to peers in interventions undertaken by the National Aids Control Organisation (NACO), Government of India. Condom costs (where provided to the programme for free) were estimated with the lowest-priced market alternative. The Bill & Melinda Gates Foundation costs were allocated to state lead partners according to the size of the grant during the year of analysis, on the basis of interviews with programme staff. State lead partners' costs were allocated to each of the 22 districts after extensive interviews. The first stage in allocation was to apportion every cost that was reported in expenditure records as being allocated to a specific (or group of) NGOs. On the basis of the interviews, any remainder of costs that could be clearly associated with programme management was allocated to each NGO on an equal basis. All remaining costs (mainly those that related to service provision levels) were allocated according to estimated population size, because this was used by state lead partners to assess and approve budgetary levels for other activities. These state lead partners' costs were combined with NGO expenditures to estimate the costs of different activities based on a combination of interviews, actual use, and for personnel costs on the basis of time sheets.

To estimate potential cost savings, we sourced ART costs from the literature (table 1). Data for the costs of ART in India are insufficient. The costs used do not include the full cost of treatment of opportunistic infections, or costs to maintain adherence with time, and therefore it is highly likely that our estimates of cost savings are conservative.

Unit costs were calculated per number of people reached at least once in a year, measured with data from the programme management information system. The quality of management information system data developed through the time period. Although all NGOs in this studied reported key indicators from start-up in the first year, data quality was not checked by any central authority. Thereafter as the system was computerised, all data were checked, and any inconsistencies were fed back to NGOs for correction. Although this was done retrospectively for the first year data, staff interviewed at the Bill & Melinda Gates Foundation suggested there was some under-reporting in the first year, and thus early unit costs might overestimate the cost per person reached. All data were converted to US$ 2011 prices with the GDP deflator index,[27] and the average exchange rate in the year of data collection.[28] Further details of the costing methods and data (including cost breakdowns between inputs and activities) can be found in a study by Chandrashekar and colleagues.[7]

	Model inputs (values or sampling distributions)
Average duration of HIV stages (months)	
Early HIV high viraemia phase	Uniform (2·0, 6·0)[18,19]
Asymptomatic HIV infection	Uniform (70·0, 91·0)[18,19]
Late-stage HIV infection	Uniform (6·0, 18·0)[18,19]
AIDS phase without treatment	Uniform (11·6, 29·4)[18,19]
DALY weight for early and asymptomatic HIV infection	0[20]
DALY weight for late-stage HIV infection	Truncated N (0·22, 0·0018)[20]
DALY weight for AIDS	Truncated N (0·55, 0·0072)[20]
DALY weight on ART	Truncated N (0·053, 0·00013)[20]
Life expectancy without HIV by age group (point estimates*)	
25–29 years	43·8
30–34 years	39·3
35–39 years	34·9
40–44 years	30·7
45–49 years	26·5
50–54 years	22·6
Unit cost per person on ART per year (US$ 2011)	Triangular (200, 400, 600)[21]
Extra life expectancy on ART if HIV positive (years)	Triangular (5·9, 9·5, 26·0)[22–25]
Coverage of ART of eligible individuals (%)	Uniform (21, 40)[26]

Truncated normal distributions truncated at 0 and 1. Triangular distributions specified by minimum, mode, and maximum values. DALY=disability adjusted life-year. ART=antiretroviral treatment. *WHO life expectancy tables, 2009.

Table 1: **Parameters sampled used to estimate infections and DALYs averted with uniform, truncated normal, and triangular distributions**

Effect estimation

A purpose-built dynamic model of HIV/STI transmission was used to calculate HIV infections averted in FSWs, their clients, and MSM, and onward transmission to their long-term non-commercial partners, during the first 4 and 10 years of the Avahan programme.[6] All 22 districts with local biobehavioural surveys were modelled separately with probabilistic sampling methods. These districts were chosen to represent the geography and sociocultural characteristics of key populations across Avahan districts, with the district with the largest known sex worker population in every sociocultural region selected.[29] Within the model, the intervention was assumed to have two effects that directly drive impact: increasing condom use by FSW and enhancing STI treatment in clinics. Other intervention components such as structural interventions and community mobilisation were considered to act indirectly through increasing condom use and access to STI services.

The model used was dynamic (capturing indirect population-level effects not included in cohort models) and was done within a Bayesian framework with detailed district-specific data.[30] This framework produced many parameter sets giving model fits to prevalence data for HIV, herpes simplex virus 2, and syphilis, providing estimates of HIV infections averted with credibility intervals. The appendix provides additional information, and full details of the parameterisation and model and fitting methods used are described elsewhere.[6]

For **WHO life expectancy tables** see http://apps.who.int/gho/data/view.main.60740?lang=en'

See **Online** for appendix

Trends in condom use with time were derived from survey data with a historical cohort method.[31] To estimate incremental effect due to Avahan in the absence of a control group, a simulated counterfactual scenario based on how condom use might have changed without the intervention was considered, for which condom use was also assumed to have continued to increase during the time-period of the intervention, but at the slower preintervention rate.[5,6] This counterfactual scenario represents an extrapolation of what would have happened without Avahan, and allows for continued non-Avahan intervention and behaviour change. It is conservative because it assumes increased condom use even without Avahan. STI treatment was also assumed to continue at preintervention levels. Multiple parameter combinations that were found to be model fits for the previously described intervention scenario were re-run for the counterfactual scenario to estimate the incremental infections averted, providing a range of estimates that were used in the cost-effectiveness analysis.

Cost-effectiveness analysis

We estimated ICERs for every district independently for 4 year (2004–08) and 10-year (2004–14) time periods. The costs for the 10-year period are estimated with the costs per person reached in 2008 multiplied by the numbers of people reached up until 2014. This approach implicitly assumes no major changes in terms of service intervention and commodity prices beyond general price inflation with time. Disability-adjusted life-years (DALYs) averted were estimated from incremental infections averted generated by the effect model, with standard formulae and disability weights for the lifetime of the cohort of people reached during 2004–08 (appendix). Our primary estimates use no age weighting. Table 1 shows the parameters used in the cost effectiveness analysis,[18,19] which correspond with those used in several other HIV prevention cost-effectiveness estimates for India,[12] but not the previous national-level study that estimates DALYs averted during a 20-year time horizon.[9]

We also estimated cost savings from prevention of future ART costs. We assumed no additional preventive effect from ART, because ART coverage in high-risk groups between 2004 and 2008 was extremely low,[26] but focused on the potential cost savings in terms of future ART treatment, assuming different levels of future ART coverage. Table 1 shows survival assumptions and costs of ART. Notably, although ART increases survival time (and therefore reduces the DALYs averted from prevention of HIV intervention) it also substantially increases the costs of that survival. Data for ART costs in India are insufficient, with most studies outdated and very little known about the costs of provision of ART to high-risk groups over a sustained period in different settings. We therefore chose a wide plausible range for cost of first-line treatment.

To estimate mean incremental NGO cost per DALY averted and mean incremental programme cost per DALY averted, we did a probabilistic sensitivity analysis in which we randomly sampled 50 000 combinations of all cost and DALY parameters, as well as model fits, using uniform distributions. We created an acceptability curve to assist policy makers to interpret the uncertainty around cost-effectiveness. Acceptability curves plot the probability that the intervention is cost effective as the willingness-to-pay threshold changes. We also did one-way sensitivity analyses for discount rates used to estimate DALYs averted (values 0%, 3%, and 8%) and future ART coverage (values 21–40% and 80%).

	NGO cost	Total cost	Total people reached	Mean NGO cost per person reached	Mean programme cost per person reached
Bangalore	2 684 630	5 810 706	23 567	114	247
Belgaum	680 639	1 503 305	8195	83	183
Chitoor	921 677	2 260 456	4315	214	524
E Godavari	120 438	566 278	4982	24	114
Guntur	1 089 054	3 778 974	19 905	55	190
Hyderabad	191 119	735 632	979	195	751
Karimnagar	705 576	1 528 325	6517	108	235
Kolhapur	216 858	780 358	1503	144	519
Madurai	1 057 745	2 774 012	7029	150	395
Parbhani	263 534	1 039 761	2448	108	425
Prakasham	470 766	1 963 486	6552	72	300
Pune	379 093	3 653 650	5617	67	650
Vizag	348 660	1 324 780	4895	71	271
Warangal	394 814	1 288 994	4593	86	281
Yevatmal	250 191	668 949	962	260	695
Mumbai	2 306 908	9 774 029	28 521	81	343
Chennai	1 084 134	2 828 183	6515	166	434
Coimbatore	655 441	1 585 553	4045	162	392
Dharmapuri	566 667	1 450 183	4125	137	352
Mysore	1 199 870	1 850 593	2021	594	916
Bellary	805 949	2 118 616	5030	160	421
Shimoga	511 820	1 248 836	2109	243	592
Total/mean	16 905 581	50 533 660	154 425	109	327

NGO=non-governmental organisation.

Table 2: **NGO and programme cost per district and per person reached 2004–08 (US$ 2011)**

Role of the funding source

The funder of the study had no role in study design, data gathering, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data and final responsibility for the decision to submit for publication.

Results

Table 2 shows the total costs for each of the 22 districts. About a third of the total cost of Avahan in these districts (US$50 533 660) was incurred at the NGO level ($16 905 581) during 4 years. Avahan reached about 154 425 high-risk group members between 2004 and

2008 in the 22 districts, at an NGO cost per person reached of $109 and a programme cost per person reached of $327. The cost per person reached differed substantially between settings, with NGO costs ranging between $24 and $594 per person reached and total costs per person reached ranging between $114 and $916. Notably, some of the sites at the high end of the scale, such as Mysore, were so-called learning sites and had more investment than other districts to allow for the piloting of different intervention approaches.

A programme coverage of 154425 high-risk group members during the 4-year period resulted in 61744 HIV

	HIV infections averted		Incremental cost per HIV infection averted (US$ 2011)			DALYs averted 2004–08	Mean incremental cost per DALY averted (US$ 2011)			
	Total 2004–08	General population only 2004–08	NGO cost only 2004–08	Total cost 2004–08	Total cost 2004–14		NGO cost only 2004–08	Total cost 2004–08	Total cost 2004–14	Total cost 2004–08 (0% discount)
Bangalore	3724 (1250–6197)	600 (104–1096)	721 (247–1195)	1561 (539–2582)	1265 (95–2436)	63229 (21435–105023)	42 (14–71)	92 (31–153)	65 (3–127)	44 (15–73)
Belgaum	2084 (891–3277)	462 (163–761)	327 (131–522)	721 (291–1152)	810 (293–1327)	35332 (15037–55628)	19 (8–31)	43 (17–68)	43 (15–71)	21 (8–33)
Chitoor	5977 (448–11505)	1032 (0–2207)	154 (0–359)	378 (0–882)	208 (0–430)	104616 7984–201249)	9 (0–20)	22 (0–50)	10 (0–21)	10 (0–24)
E Godavari	1761 (1082–2440)	311 (142–480)	68 (41–96)	322 (195–448)	363 (200–527)	30741 (18715–42768)	4 (2–6)	18 (11–26)	19 (10–27)	9 (5–12)
Guntur	8216 (4541–11892)	1775 (942–2608)	133 (66–199)	460 (228–692)	556 (202–910)	138362 (76221–200502)	8 (4–12)	27 (13–41)	30 (10–50)	13 (6–20)
Hyderabad	89 (0–286)	25 (0–75)	2139 (0–14725)	8232 (0–56754)	7736 (0–96264)	1561 (0–4997)	122 (0–848)	471 (0–3269)	397 (0–5319)	221 (0–1540)
Karimnagar	4734 (2151–7316)	908 (260–1557)	149 (49–249)	323 (107–539)	291 (78–504)	82831 (37762–127899)	9 (3–14)	18 (6–31)	15 (4–26)	9 (3–14)
Kolhapur	312 (0–952)	71 (0–222)	696 (NaN–NaN)	2501 (NaN–NaN)	3298 (0–113140)	5454 (0–16678)	40 (NaN–NaN)	143 (NaN–NaN)	171 (0–5935)	67 (NaN–NaN)
Madurai	10025 (2748–17302)	2053 (351–3755)	106 (5–206)	277 (14–540)	199 (56–342)	167898 (44226–291570)	6 (0–12)	17 (1–32)	10 (3–18)	8 (0–16)
Parbhani	594 (0–1347)	101 (0–241)	444 (0–3773)	1752 (0–14882)	1801 (0–29466)	10555 (0–23973)	25 (0–213)	99 (0–841)	90 (0–1606)	45 (0–391)
Prakasham	1739 (509–2968)	266 (45–487)	271 (52–489)	1129 (220–2039)	684 (142–1225)	30475 (8820–52129)	15 (3–28)	64 (12–117)	34 (7–61)	30 (6–55)
Pune	520 (0–1130)	104 (0–247)	729 (0–4475)	7026 (0–43092)	13453 (0–63311)	9199 (0–20102)	41 (0–250)	397 (0–2406)	722 (0–3344)	185 (0–1111)
Vizag	1492 (968–2017)	222 (84–360)	234 (151–316)	888 (580–1195)	1200 (721–1679)	27004 (17195–36814)	13 (8–18)	49 (31–67)	60 (35–85)	22 (14–30)
Warangal	1330 (370–2290)	159 (22–296)	297 (69–524)	969 (227–1711)	1044 (0–2117)	23098 (6535–39661)	17 (4–30)	56 (13–98)	54 (0–110)	26 (6–47)
Yevatmal	1291 (244–2338)	280 (47–514)	194 (0–427)	518 (0–1141)	1300 (0–3229)	22724 (4309–41140)	11 (0–24)	29 (0–65)	71 (0–179)	14 (0–30)
Mumbai	1534 (0–3151)	328 (0–691)	1504 (0–4407)	6371 (0–18685)	12954 (0–32693)	27169 (0–55770)	85 (0–249)	360 (0–1056)	702 (0–1749)	168 (0–482)
Chennai	1850 (434–3265)	258 (0–553)	586 (0–1197)	1529 (0–3118)	907 (0–2620)	32244 (7591–56898)	34 (0–69)	88 (0–181)	45 (0–136)	41 (0–84)
Coimbatore	3020 (0–6279)	456 (0–1069)	217 (0–489)	525 (0–1181)	318 (0–649)	52426 (0–109050)	13 (0–28)	30 (0–68)	16 (0–32)	14 (0–33)
Dharmapuri	4838 (272–9403)	891 (0–1999)	117 (0–255)	300 (0–651)	336 (0–748)	84343 (4707–163979)	7 (0–15)	17 (0–38)	18 (0–40)	8 (0–18)
Mysore	1694 (980–2409)	337 (134–541)	708 (407–1009)	1092 (628–1556)	949 (527–1370)	28886 (16676–41097)	42 (24–59)	64 (36–92)	49 (27–72)	31 (17–44)
Bellary	4079 (1063–7096)	910 (179–1640)	198 (32–363)	519 (88–950)	495 (41–950)	68990 (18208–119773)	12 (2–21)	31 (5–56)	26 (2–51)	15 (2–27)
Shimoga	862 (293–1431)	209 (54–364)	594 (137–1051)	1449 (336–2562)	911 (175–1646)	14549 (4979–24118)	35 (8–62)	86 (19–152)	47 (9–85)	41 (9–74)
Total	61744 (48908–74580)	11755 (8847–14663)	263 (207–318)	785 (619–951)	692 (541–842)	1061255 (840416–1282094)	15 (12–19)	46 (36–55)	36 (28–43)	22 (17–26)

Data are mean (SD 1·96). DALY=disability-adjusted life-year. NGO=non-governmental organisation. NaN=undefined.

Table 3: **Effect and cost effectiveness by district (unadjusted for future antiretroviral treatment costs)**

infections averted in total, with 11755 HIV infections averted in the general population alone. The mean NGO cost per HIV infection averted was $263 and the mean programme cost per HIV infection averted was $785 (table 3). When costs and effect were extended for 10 years, the mean programme cost per HIV infection averted fell to $692. Conversio of HIV infections averted into DALYs, we estimated that 1061255 DALYs were averted across the 22 districts, at a mean incremental NGO cost per DALY averted of US$15, and a mean incremental programme cost per DALY averted of $46 at a 3% discount rate without including ART cost savings.

	DALYs averted 2004–08	Number of people on ART averted	Total cohort lifetime ART savings (US$ 2011)	Mean incremental cost per DALY averted (US$ 2011)			
				NGO cost 2004–08	Total cost 2004–08	Total cost 2004–14	Total cost 2004–08 (sensitivity analysis 80% ART coverage)
Bangalore	54 040 (17 721 to 90 359)	1135 (273 to 1997)	4 829 494 (−122 900 to 9 781 889)	Dom (Dom to 41)	Dom (Dom to 116)	Dom (Dom to 92)	Dom (Dom to 129)
Belgaum	30 130 (12 489 to 47 771)	636 (201 to 1071)	2 711 433 (66 035 to 5 356 830)	Dom (Dom to 12)	Dom (Dom to 41)	Dom (Dom to 45)	Dom (Dom to 69)
Chitoor	89 715 (6357 to 173 073)	1822 (0 to 3647)	7 792 459 (−2 092 675 to 17 677 592)	Dom (Dom to 1)	Dom (Dom to 20)	Dom (Dom to 4)	Dom (Dom to 31)
E Godavari	26 364 (15 688 to 37 039)	537 (253 to 822)	2 289 596 (304 361 to 4 274 831)	Dom	Dom (Dom to 10)	Dom (Dom,12)	Dom (Dom to 29)
Guntur	117 984 (63 190 to 172 779)	2503 (1082 to 3925)	10 679 678 (1 084 848 to 20 274 509)	Dom	Dom (Dom to 21)	Dom (Dom to 26)	Dom (Dom to 50)
Hyderabad	1339 (0 to 4295)	27 (0 to 88)	116 214 (−169 528 to 401 956)	Dom (Dom to 906)	463 (Dom to 3740)	385 (Dom to 6149)	441 (Dom to 5110)
Karimnagar	71 079 (31 601 to 110 557)	1444 (492 to 2396)	6 151 329 (236 447 to 12 066 211)	Dom (Dom to 0)	Dom (Dom to 11)	Dom (Dom to 8)	Dom (Dom to 29)
Kolhapur	4668 (0 to 14 288)	96 (0 to 299)	407 737 (−539 623 to 1 355 098)	Dom (NaN to NaN)	80 (NaN to NaN)	121 (Dom to 6869)	Dom (NaN to NaN)
Madurai	143 169 (36 395 to 249 943)	3059 (555 to 5562)	13 056 142 (−1 275 073 to 27 387 356)	Dom	Dom (Dom to 10)	Dom (Dom to 3)	Dom (Dom to 37)
Parbhani	9079 (0 to 20 649)	182 (0 to 427)	773 278 (−458 898 to 2 005 454)	Dom (Dom to 174)	29 (Dom to 903)	29 (Dom to 1801)	Dom (Dom to 1086)
Prakasham	26 143 (7366 to 44 920)	530 (105 to 956)	2 264 163 (−188 251 to 4 716 577)	Dom (Dom to 8)	Dom (Dom to 81)	Dom (Dom to 34)	Dom (Dom to 88)
Pune	7905 (0 to 17 317)	159 (0 to 357)	673 993 (−312 244 to 1 660 230)	Dom (Dom to 215)	377 (Dom to 2728)	759 (Dom to 3830)	325 (Dom to 3640)
Vizag	23 285 (14 494 to 32 075)	455 (226 to 684)	1 941 814 (272 408 to 3 611 220)	Dom (Dom to 4)	Dom (Dom to 45)	Dom (Dom to 61)	Dom (Dom to 55)
Warangal	19 776 (5457 to 34 095)	405 (75 to 736)	1 728 117 (−148 578 to 3 604 812)	Dom (Dom to 10)	Dom (Dom to 64)	Dom (Dom to 75)	Dom (Dom to 79)
Yevatmal	19 524 (3558 to 35 491)	394 (41 to 746)	1 678 688 (−260 446 to 3 617 822)	Dom (Dom to 3)	Dom (Dom to 31)	0 (Dom to 140)	Dom (Dom to 42)
Mumbai	23 335 (0 to 47 972)	468 (0 to 996)	1 995 413 (−735 688 to 4 726 513)	Dom (Dom to 216)	333 (Dom to 1145)	735 (Dom to 1956)	266 (Dom to 1397)
Chennai	27 656 (6259 to 49 052)	563 (87 to 1040)	2 406 104 (−282 164 to 5 094 371)	Dom (Dom to 37)	15 (Dom to 143)	Dom (Dom to 98)	Dom (Dom to 143)
Coimbatore	44 879 (0 to 93 673)	921 (0 to 1985)	3 917 035 (−1 426 947 to 9 261 016)	Dom (Dom to 6)	Dom (Dom to 34)	Dom (Dom to 11)	Dom (Dom to 49)
Dharmapuri	72 298 (3482 to 141 115)	1477 (0 to 2986)	6 290 088 (−1 618 884 to 14 199 061)	Dom	Dom (Dom to 11)	Dom (Dom to 14)	Dom (Dom to 27)
Mysore	24 668 (13 910 to 35 426)	517 (228 to 806)	2 207 376 (239 689 to 4 175 064)	Dom (Dom to 37)	Dom (Dom to 65)	Dom (Dom to 49)	Dom (Dom to 89)
Bellary	58 844 (15 034 to 102 654)	1244 (217 to 2271)	5 307 096 (−541 201 to 11 155 392)	Dom (Dom to 4)	Dom (Dom to 28)	Dom (Dom to 25)	Dom (Dom to 53)
Shimoga	12 403 (4134 to 20 672)	263 (62 to 465)	1 122 213 (−49 722 to 2 294 147)	Dom (Dom to 34)	Dom (Dom to 115)	Dom (Dom to 55)	Dom (Dom to 128)
Total	907 888 (716 689 to 1 099 086)	18 833 (14 435 to 23 232)	77 004 792 (52 809 309 to 101 200 276)	Dom	Dom	Dom	Dom

Data are mean (SD 1·96). Dom=dominated (the intervention dominates the counterfactual where the intervention is on average less costly and more effective than the counterfactual. Where there is no SD reported then the intervention dominates for all estimates within SD 1·96 of the mean.

Table 4: **Effect and cost effectiveness, adjusted for future antiretroviral treatment cost**

The mean cost per DALY averted varied substantially by district, ranging between a mean incremental NGO cost per DALY averted of $4 and $122, and a mean incremental programme cost per DALY averted of $17 and $471. In one district (Kolhapur) where condom use was high and increasing rapidly before Avahan, the uncertainty range in the cost per DALY averted was undefined. In this district, condom use in the counterfactual scenario could be the same as in the intervention scenario, meaning that the number of infections averted would be zero, and hence the cost per DALY averted could be infinite.

The mean incremental programme cost per DALY averted declined to $36 when the time period was extended to 10 years, fell to $22 per DALY averted when DALYs were not discounted (table 3), and rose to $129 at an 8% discount rate (data not shown). Inclusion of ART costs resulted in an ART cost saving (for the lifetimes of the high-risk cohort of 154425) of $77004792 (compared with the $50533660 spent on Avahan) in the 22 districts (table 4). Mean savings across the 22 districts that increased substantially as our assumptions about ART coverage increased (table 4). The figure shows acceptability curves to represent the uncertainty in our estimates. Figure A shows the acceptability curves across all 22 districts when ICERS in each district are assumed to have no correlation across districts. Figure B shows the acceptability curve when perfect correlation is assumed. Both results show that our estimates of cost-effectiveness are robust, with 100% of sampled ICERS remaining well below the willingness-to-pay threshold.

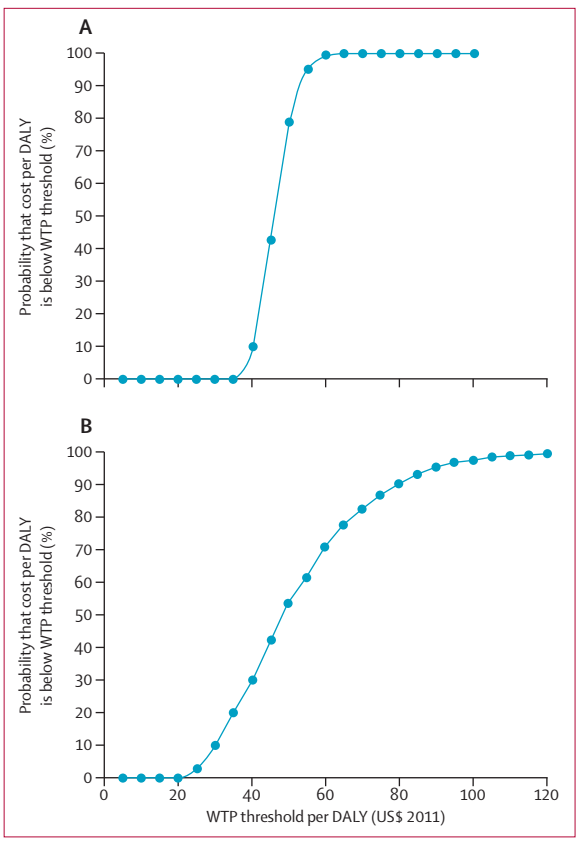

Figure: **Probability that incremental programme cost per disability-adjusted life-year (DALY) averted is below willingness-to-pay (WTP) threshold for all 22 districts (unadjusted for antiretroviral treatment [ART] costs)**
(A) Assumes no correlation of mean ICERs across districts. (B) Assumes perfect correlation of mean ICERs across districts.

Discussion

Our results confirm previous evidence from national models and pilot studies[9,10] suggesting that HIV prevention programmes targeted at high-risk groups at scale are cost effective (panel). Our estimates of incremental cost per DALY averted are substantially below the willingness-to-pay threshold and within the ranges achieved by other HIV preventive interventions.[8,22] Our findings therefore suggest that HIV prevention interventions focused on high-risk groups are good value for money in India and similar settings.

Our estimates of incremental cost per DALY averted are higher than those previously estimated for India.[11] This difference is, to a large extent, due to the fact that we measured costs incurred above the NGO level in our analysis.[7] These costs are important to consider because they are incremental and are likely to be a substantial component of the effort to scale up HIV prevention rapidly, especially in any setting where NGO capacity is weak. We also found higher numbers of clients per FSW and more baseline condom use than in previous studies,[10] and a slower rate of increase in condom use, possibly reflecting the longer start-up period of larger scale programmes.[5] Finally, we also chose a more conservative counterfactual than in previous studies.

Although our estimates of the incremental cost per DALY averted are higher than previous studies, the greater precision surrounding our estimates (primarily due to our extensive cost data collection, the fitting of the model, and use of in-depth local data from high-quality surveys designed to parameterise the model), allows us to be more certain that targeted HIV prevention in India has been cost effective. The remaining uncertainty we noted is largely due to the wide credibility interval we noted around the effect estimates. This stems from the challenges of accurately mapping high-risk populations; the absence of baseline data for both condom use and HIV prevalence, which might be unavoidable in real-life evaluation of marginalised populations[32] and which meant that condom trends were derived with additional uncertainty; and the relatively wide range of epidemic trajectories that could fit prevalence data at two or three timepoints.

We also noted a substantial variation in costs, effect, and cost-effectiveness by district. Although the few study sites means that statistical exploration of the drivers of this variation is challenging, complementary analyses of the costs from all Avahan districts show that both

programme scope and scale are key drivers of cost variation between districts.[7] Specifically, ongoing analysis suggests that the way in which programmes contract out STI services, the involvement of the community, and the type of FSW reached might explain the variation of costs between districts. We also note substantial economies of scale (with no diseconomies observed at high levels of coverage). HIV prevention programmes therefore have to carefully consider the size of the NGO contracted, weighing the benefits of small community NGOs against the lower costs of larger NGOs that can benefit from economies of scale. Moreover, in our modelling work, we have identified several contextual factors that are likely to drive differences in impact at the district level, such as the baseline level of condom use, the presence of other targeted HIV interventions and the size of the sex worker population.[6] The effect of these contextual factors means that care should also be taken before generalisation of our findings to other settings; these explanatory factors are also likely to vary by the stage of HIV epidemic and setting.

Although this study confirms that HIV prevention at scale can be highly cost effective and potentially cost saving, several unresolved questions remain regarding the most affordable model of scale-up. The costs shown here represent 22 districts, but are part of a wider costing study that has collected costs from 64 districts in India. From this broader costing study, we estimate that the annual cost of sustaining Avahan across four states is around $35 million.[7] This is a sizeable sum, but remains a small proportion of the national health budget of around $5 billion per year.[7] However, in view of recent budget cuts and the substantial disease burden in India, questions are being raised as to whether the Avahan HIV prevention model, with a high level of intensity support and community involvement, is the most cost-effective way forward; and whether it is possible to achieve the same effect with a lower scale or reduced scope of services. Further work is ongoing with the dataset we present to explore these questions, in particular to examine the effect of increased investment in community mobilisation on HIV prevention programme cost-effectiveness, and threshold levels of coverage required to achieve a satisfactory effect.

Finally, important limitations should be noted that affect both our economic evaluation and those of most previous studies. First, our study excluded any economic welfare benefit to the recipients of HIV programmes by exclusion of other health and economic benefits, such as DALY gains from reductions in violence, reductions in the number of cases of other STIs, reduced orphanhood from HIV, and other welfare gains for the increased empowerment of high-risk group members. Second, we excluded the costs incurred by the high-risk group members themselves, such as the opportunity cost of time spent with peer educators. Although the exclusion of costs incurred by high-risk group members could mean that we have overestimated cost-effectiveness, these costs are likely to be small in view of the outreach nature of the Avahan programme. Third, compared with other Avahan districts, the 22 districts included in this study were more likely to have a pre-existing intervention and thus effect and cost-effectiveness might be lower than in other districts. Finally, our estimates of ART cost only included first-line treatment, so are likely to underestimate the true future resource requirements of ART.

This study provides evidence, with local data from a programme delivered to scale, that the large investment in targeted HIV prevention programmes made in India during the past decade has not only had an effect, but has been cost effective. To our knowledge, our findings are the best evidence so far to suggest that those responsible for HIV prevention programme development should consider sustaining and expanding investment in such programmes in India and beyond as a priority strategy for combating HIV.

Panel: Research in context

Systematic review

In 2009, a systematic review by Galarraga and colleagues[8] identified that few robust studies have assessed the cost effectiveness of HIV prevention, with only a handful done in Asia, and that more than 25 years into the AIDS epidemic and billions of dollars of spending later, much work is still to be done both on costs and effectiveness to adequately inform HIV prevention planning. Since then empirical research on the cost-effectiveness for HIV prevention for high-risk groups has primarily either been further studies at a small scale, or has used national level data and models, requiring a large number of assumptions to be made.

Interpretation

Our work uses extensive primary data collection on costs and behavioural change in 22 districts in India, combined with a mathematical model of how this change affects HIV transmission, to estimate the cost-effectiveness of HIV prevention focused on high-risk groups at scale. It thus presents depth of empirically based estimates of cost effectiveness without parallel globally. Our estimates of costs per disability-adjust life-year (DALY) averted are higher than those of previous studies of targeted HIV prevention,[10] mainly because we included programme costs incurred above the service level, and noted higher numbers of clients per female sex workers, more baseline condom use, and a slower rate of increase in condom use than in previous studies.[10] However, the greater precision surrounding our estimates allows us to confirm these previous estimates, with a robust empirical basis, and conclude that the large investment in targeted HIV prevention in India has been cost effective in reducing HIV infection and is highly likely to be cost saving in the long run. Individuals working in HIV programmes in concentrated epidemic settings should therefore continue to invest (or expand investment) in HIV prevention for high-risk groups.

Contributors

All authors were involved in aspects of study design, data collection, and/or analysis of data used in the report. AV, MP, SC, and LG wrote the first draft of the report. All authors contributed to subsequent drafts of the report and reviewed the final version before submission.

Declaration of interests

MC-B reports grants and personal fees from the Bill & Melinda Gates Foundation both during the conduct of the study and outside of the submitted work. AV declares no competing interests. SM reports grants and personal fees from the Bill & Melinda Gates Foundation during the conduct of the study, grants and personal fees from Bill & Melinda Gates Foundation, and grants from Canadian Institutes of Health Research, outside the submitted work. SC reports grants from the Bill & Melinda Gates Foundation, grants from International Development Research Centre, and a scholarship amount for an International Masters Degree in Health and Pharmacoeconomics from HIV Research Trust UK during the conduct of the study. MA reports grants from the Bill & Melinda Gates Foundation during the conduct of the study; and grants from the Bill & Melinda Gates Foundation, Canadian Institutes of Health Research, Canadian Foundation for AIDS Research, and International Development Research Centre outside the submitted work. MP declares no competing interests. LG reports grants from London School of Hygiene & Tropical Medicine during the conduct of the study; grants from the European Developing Countries Trial Programme, from the Australian Department for Foreign Affairs and Trade, from the Department for International Development, UK, from the National Institute for Health Research, England outside the submitted work; has a grant pending from University of New South Wales; and has previously published work on the costs of government funded HIV prevention for vulnerable groups in India, funded by the Wellcome Trust. JB received a grant and personal fees from the Bill & Melinda Gates Foundation during the conduct of the study. PV and CML declare no competing interests. GS reports grants from Bill & Melinda Gates Foundation during the conduct of the study.

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