

# Assessment of the population-level effectiveness of the Avahan HIV-prevention programme in South India: a preplanned, causal-pathway-based modelling analysis

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## Summary

**Background** Avahan, the India AIDS initiative of the Bill & Melinda Gates Foundation, was a large-scale, targeted HIV prevention intervention. We aimed to assess its overall effectiveness by estimating the number and proportion of HIV infections averted across Avahan districts, following the causal pathway of the intervention.

**Methods** We created a mathematical model of HIV transmission in high-risk groups and the general population using data from serial cross-sectional surveys (integrated behavioural and biological assessments, IBBA) within a Bayesian framework, which we used to reproduce HIV prevalence trends in female sex workers and their clients, men who have sex with men, and the general population in 24 South Indian districts over the first 4 years (2004–07 or 2005–08 dependent on the district) and the full 10 years (2004–13) of the Avahan programme. We tested whether these prevalence trends were more consistent with self-reported increases in consistent condom use after the implementation of Avahan or with a counterfactual (assuming consistent condom use increased at slower, pre-Avahan rates) using a Bayes factor, which gave a measure of the strength of evidence for the effectiveness estimates. Using regression analysis, we extrapolated the prevention effect in the districts covered by IBBA to all 69 Avahan districts.

**Findings** In 13 of 24 IBBA districts, modelling suggested medium to strong evidence for the large self-reported increase in consistent condom use since Avahan implementation. In the remaining 11 IBBA districts, the evidence was weaker, with consistent condom use generally already high before Avahan began. Roughly 32 700 HIV infections (95% credibility interval 17 900–61 600) were averted over the first 4 years of the programme in the IBBA districts with moderate to strong evidence. Addition of the districts with weaker evidence increased this total to 62 800 (32 000–118 000) averted infections, and extrapolation suggested that 202 000 (98 300–407 000) infections were averted across all 69 Avahan districts in South India, increasing to 606 000 (290 000–1 193 000) over 10 years. Over the first 4 years of the programme 42% of HIV infections were averted, and over 10 years 57% were averted.

**Interpretation** This is the first assessment of Avahan to account for the causal pathway of the intervention, that of changing risk behaviours in female sex workers and high-risk men who have sex with men to avert HIV infections in these groups and the general population. The findings suggest that substantial preventive effects can be achieved by targeted behavioural HIV prevention initiatives.

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## Introduction

In the early 2000s, India was believed to have the highest burden of HIV infections in the world,<sup>1</sup> with prevalence rapidly increasing.<sup>2,3</sup> Therefore, in 2003, the Bill & Melinda Gates Foundation established Avahan, the India AIDS initiative, to target the high-risk groups that the evidence suggested were driving the HIV epidemic in India.<sup>4,5</sup> By reducing the prevalence in these groups, they hoped to interrupt the downstream chain of transmission to the general population. Avahan established a large-scale, targeted HIV preventive intervention, providing services to an estimated 300 000 female sex workers and high-risk men who have sex with men (ie, those who have large numbers of partners, often sell sex, or practice receptive anal sex).<sup>6</sup>

Through state-level providers and local non-governmental organisations (NGOs), Avahan worked in

69 districts in four states of South India (Andhra Pradesh, Karnataka, Maharashtra, and Tamil Nadu). Programme components outside the scope of this assessment were active in other regions, reaching truck drivers and injecting drug users. The standard Avahan care package consisted of peer education and outreach; distribution and social marketing of condoms; treatment of sexually transmitted infections (STIs) for female sex workers and high-risk men who have sex with men; and structural interventions and community mobilisation components to address distal determinants of HIV risk such as violence and stigma.<sup>6</sup> Antiretroviral therapy was not offered as part of this package, but HIV counselling and testing were strongly promoted, with active referral to government antiretroviral therapy centres for individuals who tested positive. Overall, coverage of antiretroviral therapy by government and private clinics reached only

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See Online for appendix

37–45% of the estimated need by 2009,<sup>7,8</sup> although it has since increased.<sup>9</sup>

Rollout of Avahan programme activities began in January, 2004, reaching almost all districts by mid-2005,<sup>10</sup> and with rapid scale-up within each district.<sup>11–13</sup> By December, 2008, more than 75% of the estimated target populations of female sex workers (total population 217 000) and high-risk men who have sex with men (total population 80 000) were being contacted monthly.<sup>10</sup> In 28 districts Avahan was the first and only intervention;<sup>10</sup> in the remaining 41 districts it worked alongside or took over from existing NGO interventions. From an assessment standpoint, this rapid rollout, the presence of other interventions, and ethical considerations mitigated against the use of community-based randomised controlled trials or a stepped-wedge study design.<sup>14–16</sup>

This independent assessment (the CHARME-India project) was planned as an integral part of Avahan.<sup>17</sup> In place of community-based randomised controlled trials, we used mathematical modelling with detailed HIV and STI prevalence and behavioural data to obtain plausible evidence for the effectiveness of the intervention.<sup>17</sup> We first investigated the effect of Avahan in the high-risk groups targeted by the intervention, and then traced the effect on their long-term partners in the general population, reflecting the intended causal pathway of the intervention. We believe that this approach improves on a previous analysis of the population-level effect of Avahan,<sup>18</sup> which did not take into account the high-risk groups on which programme activities focused, but instead used a static approach to model effectiveness through district-level differences in HIV prevalence trends in women attending antenatal care clinics. That analysis was also limited by the fact that antenatal clinic data can be subject to transient biases,<sup>19–21</sup> leading to estimated HIV time trends that are unrepresentative of the general population prevalence.<sup>22</sup>

By means of a Bayesian inference method,<sup>23</sup> we aimed to use hypothesis testing to examine whether observed prevalence trends in high-risk groups were suggestive of evidence for condom use increasing faster during Avahan than beforehand, and to estimate, using the mathematical model, the number and proportion of HIV infections averted by Avahan because of these increases in condom use (ranked by the strength of evidence from the hypothesis testing).

## Methods

### Data sources

The primary data collected as part of the Avahan assessment were the serial cross-sectional integrated behavioural and biological assessment (IBBA) surveys done among female sex workers, their clients, and men who have sex with men in 24 districts, referred to as IBBA districts.<sup>24,25</sup> IBBA districts have about 38% of the female sex workers and 45% of the high-risk men who have sex with men across the 69 Avahan districts in South India. At least two rounds of IBBA for female sex

workers were done in each district, with a median of 37 months between rounds one and two (appendix).

We used IBBA data to obtain behavioural parameter estimates, and HIV and STI prevalence data for model fitting. Additional special behavioural surveys were used to refine the structure of sexual behaviours in the mathematical model (appendix). We also used general population biobehavioural surveys from four IBBA districts,<sup>22,26,27</sup> with concurrent anonymous polling-booth behavioural surveys for examining sensitive behaviours,<sup>28</sup> to derive ranges for behavioural parameters of the general population.

Data collection for the IBBA started 7–24 months after intervention activities began, so no true baseline surveys or pre-Avahan data for condom use exist. Therefore we estimated time trends for consistent condom use before Avahan from IBBA data, as reported previously.<sup>29</sup> After the start of Avahan, consistent condom use was assumed to increase up to the proportions reported in each IBBA survey, because of scale-up in each district, and to remain constant thereafter at the proportion reported in the most recent IBBA. We used these estimated historical trends in consistent condom use to define the intervention condom hypothesis (ie, that consistent condom use increased more rapidly during Avahan than beforehand), used at the hypothesis-testing stage and to estimate effectiveness. Programmatic outputs, such as number of STI clinic visits, were monitored monthly by NGOs from January, 2005,<sup>10</sup> until April, 2011, and were used to estimate syphilis treatment rates (appendix).

Finally, Avahan grantees did mapping exercises to estimate the population sizes of female sex workers and high-risk men who have sex with men. We used the most recent available size estimates for each district. We estimated client population sizes indirectly using a multiplier method that involved balancing the overall frequency of commercial sex reported by female sex workers and their clients (appendix).<sup>30,31</sup> Estimates were validated with data from general population polling-booth surveys<sup>28</sup> where available. Table 1 summarises the main parameters, a full list of which is reported in the appendix.

### Transmission model

A previously reported model of HIV transmission<sup>23</sup> was extended to simulate the HIV epidemic in high-risk groups and between high-risk individuals and their partners in IBBA districts. The model has two components: a deterministic transmission-dynamics model of HIV, herpes simplex virus 2 (HSV2), and syphilis in high-risk groups (high-risk model component); and a linked, individual-based model of HIV and HSV2 transmission to the long-term, non-commercial partners of high-risk men and former high-risk individuals (general-population model component). The individual-based component was chosen to better represent long-term stable relationships.

Both model components incorporated increased transmissibility during acute and late-stage HIV infection

and the cofactor effects of HSV2 on HIV infectivity and susceptibility. The high-risk model component also included the cofactor effect of syphilis on HIV susceptibility. The appendix provides a full description of the model.

### Fitting and hypothesis testing

The two hypotheses we examined were the intervention condom hypothesis, which generally suggests that consistent condom use increased more rapidly during Avahan than beforehand; and the control condom hypothesis, which was defined as consistent condom use increasing at the same rate during Avahan as beforehand—ie, that Avahan had no additional effect on consistent condom use beyond what was already happening. A Bayesian model-fitting algorithm<sup>23,32</sup> was used to test whether each district's observed HIV prevalence trends in high-risk groups were more consistent with one hypothesis or the other. For both hypotheses, consistent condom use remained stable after the final IBBA. The appendix includes the consistent condom use trends for each district.

We defined ranges for each model parameter for each district using data from IBBA and other surveys, as well as the scientific literature for biological parameters (table 1, appendix). We then uniformly sampled these ranges multiple times using Latin hypercube sampling,<sup>33</sup> as described in the appendix. For each parameter set thus created, the model was run twice for both the intervention and control condom hypotheses. Only simulations within the 95% CI of prevalence data for HIV, HSV2, and syphilis from the round one IBBA for different high-risk groups, and within the 95% CI of the adjusted trend in HIV prevalence among female sex workers between round one and later IBBA rounds, were retained as model fits to form the posterior parameter set for that district for the given condom use hypothesis. For hypothesis testing, the Bayes factor, described fully in the appendix and approximated by the ratio of the number of fits to each hypothesis, was used to determine whether there was weak (Bayes factor  $\leq 2$ ), moderate ( $>2$  to 5) or strong ( $>5$ ) evidence<sup>34</sup> for the intervention condom

	HIV prevalence in female sex workers, round one IBBA (%)	HIV prevalence ratio* in female sex workers	Consistent condom use at start of Avahan (%)	Consistent condom use at final IBBA round (%)	Number of clients per female sex worker per week, round 1 IBBA	Female sex worker population size (n)
<b>Andhra Pradesh</b>						
Karimnagar	21.1	0.30	8.3	75.0	8.9	2885
Warangal	10.8	0.39	12.2	76.1	9.4	1982
Vizag	14.2	0.74	15.2	85.1	14.3	1312
Prakasham	11.1	0.79	4.1	95.6	13.1	3226
Chittoor	8.0	1.21	6.6	84.3	11.1	7040
Guntur	21.3	0.67	10.1	82.9	15.5	6380
East Godavari	26.3	0.89	29.9	97.2	12.9	1392
Hyderabad	14.3	0.83	39.5	70.0	6.3	885
<b>Karnataka</b>						
Bellary	15.6	0.44	38.8	87.4	11.3	4286
Mysore	26.1	0.58	18.3	91.2	7.8	2278
Shimoga	9.7	0.88	29.9	83.8	6.2	1882
Belgaum	33.9	0.75	48.5	96.6	13.7	2000
Bangalore	12.7	0.86	46.7	85.7	8.2	12 438
<b>Maharashtra</b>						
Mumbai	16.2	0.87	72.3	86.1	9.3	10 599
Parbhani	15.9	0.63	56.0	98.1	10.1	1535
Kolhapur	33.0	0.87	80.3	99.5	17.4	833
Yavatmal	37.3	0.58	55.2	98.7	24.4	969
Pune	38.1	0.71	85.9	96.7	13.7	5948
Thane	10.0	1.38	88.1	86.7	11.5	11 889
<b>Tamil Nadu</b>						
Dharmapuri	12.4	0.58	9.7	73.7	12.4	2786
Coimbatore	6.3	1.16	3.9	95.9	6.8	2000
Chennai	2.2	0.63	31.1	94.5	6.5	4000
Madurai	4.3	1.55	18.0	99.8	7.2	7887
Salem	12.6	1.05	19.8	94.7	7.5	3353

IBBA=integrated behavioural and biological assessment. \*Ratio of final IBBA round to IBBA round one.

**Table 1: Mean HIV data used in fitting and mean prior values for key parameters in the model, by district**

hypothesis compared with the control hypothesis in that district. This method is similar to techniques used in previous analyses.<sup>23,32,35,36</sup>

### Effectiveness analysis

For each modelled district, we obtained between 30 and 266 fitted runs for the intervention condom hypothesis, capturing the uncertainty from biological and behavioural parameters in the model projections. These runs generated district-level estimates of HIV prevalence and incidence over time, as well as the number of HIV infections among high-risk individuals and linked infections to long-term partners of present and former high-risk individuals. To estimate effectiveness in each district, we produced a matched counterfactual for each model fit of the intervention condom hypothesis, using the same posterior parameter set, but instead assuming that consistent condom use increased in accordance with the control condom hypothesis and that syphilis treatment remained at the assumed background rate. We calculated HIV infections averted for each model fit relative to this matched counterfactual, and combined these fits to give a 95% credibility interval (CrI) for the number and proportion of infections averted in each district using likelihood weights,<sup>23</sup> as described in the appendix. Effectiveness was calculated over 4 and 10 years because these time periods corresponded to the first phase of the Avahan programme (2004–07 or 2005–08 dependent on the district, during which time it reached scale<sup>10</sup>) and entirety of the programme (2004–13), respectively. The programme has now largely been handed over to the Indian Government.

We estimated infections averted among female sex workers; clients of female sex workers; men who have sex with men; and long-term, non-commercial partners of clients and men who have sex with men. We derived five alternative overall effectiveness estimates across all

Avahan districts with increasing uncertainty, representing the hypothesis-testing results and the fact that not all IBBA districts had done surveys among men who have sex with men and the general population. Table 2 and the appendix fully describe these estimates and the sources of uncertainty. The first estimate included only IBBA districts in which the evidence for the intervention condom hypothesis was moderate to strong (ie, Bayes factor >2), and estimates of infections averted among men who have sex with men and the general population were included only for districts with data available for these populations. Effectiveness among men who have sex with men and the general population in districts with moderate to strong evidence were added successively to produce the subsequent estimates. For the fourth estimate, districts with weak evidence (Bayes factor ≤2) were included. Finally, because IBBA were only done in about a third of all Avahan districts, we extrapolated our estimates to all non-IBBA districts. We used linear regression for the estimates of HIV infections averted in modelled IBBA districts to extrapolate to non-IBBA districts using data, such as the sizes of high-risk populations, available across all Avahan districts. This estimate produced the overall number of HIV infections averted over the first 4 and all 10 years of Avahan in South India, but with the highest degree of uncertainty.

### Role of the funding source

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

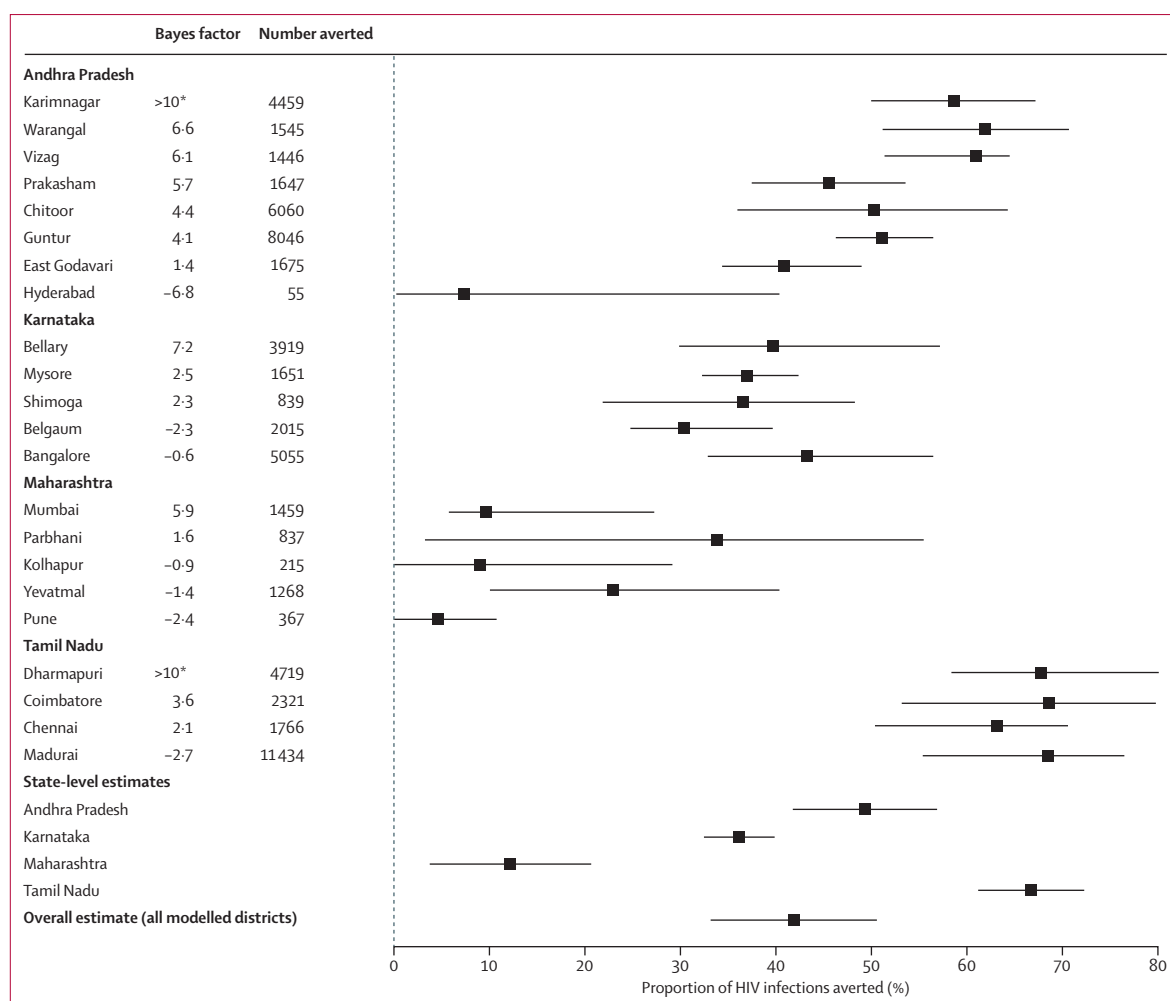
### Results

Figure 1 provides a summary of the results of the hypothesis-testing analysis. Two of the 24 IBBA districts

	Including effect in men who have sex with men	Including effect in general population	Which districts included?	Median HIV infections averted (95% CrI)	
				First 4 years (2004–07 or 2005–08)	10 years (2004–13)
13 IBBA districts	Only in eight districts with IBBAs for men who have sex with men	Only in four districts with general population surveys	Only IBBA districts with medium or strong evidence	32 700 (17 900–61 600)	105 000 (53 100–195 000)
13 IBBA districts	All 13 districts	Only in four districts with general population surveys	Only IBBA districts with medium or strong evidence	35 300 (18 800–64 600)	116 000 (52 500–200 000)
13 IBBA districts	All 13 districts	All 13 districts	Only IBBA districts with medium or strong evidence	39 900 (20 800–76 300)	140 000 (61 500–246 000)
All 22 IBBA districts	All 22 districts	All 22 districts	All 22 districts	62 800 (32 000–118 000)	214 000 (99 000–373 000)
All 69 Avahan districts	All districts	All districts	All districts	202 000 (98 300–407 000)	606 000* (290 000–1 193 000)

CrI=credibility interval. IBBA=integrated behavioural and biological assessment. \*The estimate for the number of HIV infections averted over 10 years in all 69 Avahan districts has the highest degree of uncertainty.

**Table 2: Estimates of the number of HIV infections averted over the first 4 years and all 10 years of Avahan, with decreasing certainty**



**Figure 1: Proportions and total numbers of HIV infections averted over first 4 years of Avahan in each modelled IBBA district, including estimates from men who have sex with men and the general population**

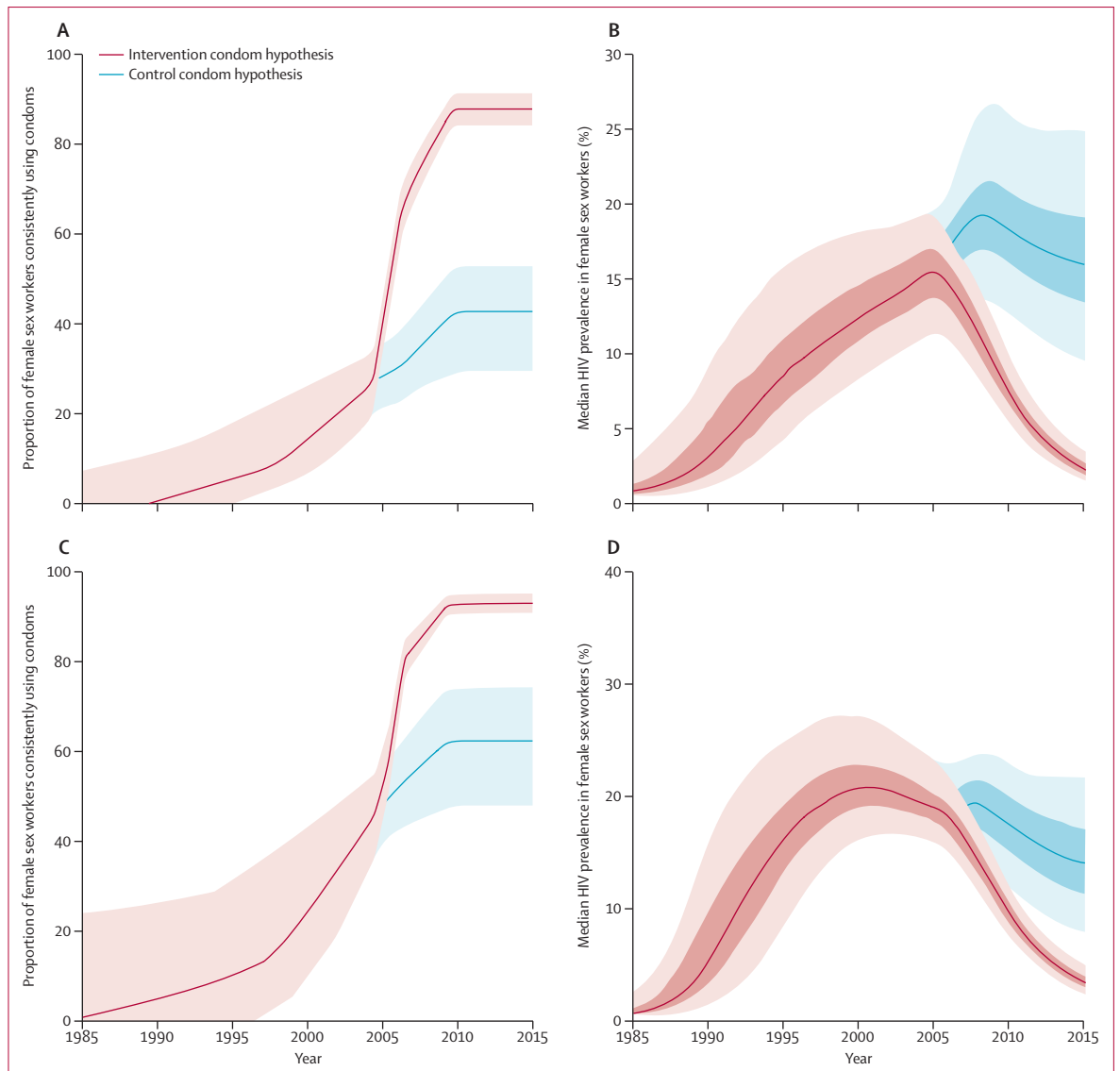
The Bayes factor describes the strength of evidence for the effectiveness estimate in each district (strong evidence=Bayes factor >5; moderate evidence=Bayes factor >2 to 5; and weak evidence=Bayes factor ≤2). IBBA=integrated behavioural and biological assessment. \*No fits to the control condom hypothesis.

(Salem and Thane) could not be analysed because they had no fits with either the intervention or the control condom hypothesis, due to conflicting trends in HIV prevalence data between different risk groups.

Seven of the remaining 22 districts had strong evidence (Bayes factor >5) and six had moderate evidence (Bayes factor >2 to 5) that consistent condom use by female sex workers increased during Avahan. Nine districts had weak evidence (Bayes factor ≤2). In districts with weak evidence, the overall difference in consistent condom use between the intervention and control condom hypotheses in 2010 was generally smaller (16%) than for districts with moderate or strong evidence (57%;  $p=0.01$  [Mann-Whitney test of the medians]; figure 2). This result was partly caused by the estimated baseline consistent condom use being higher (48%) in the districts with weak evidence than in the districts with moderate to strong evidence (12%). In four of the five modelled

districts in which Avahan was the first intervention targeted at female sex workers, there was moderate or strong evidence for the intervention condom hypothesis; the exception was Yevatmal, where there was weak evidence, probably because its small IBBA sample size of female sex workers resulted in less informative estimates of condom use and HIV prevalence.

Figure 1 also shows the overall district-specific median proportions and numbers of infections averted in all population groups (including the general population) over the first 4 years of Avahan. New HIV infections decreased substantially in most IBBA districts, with 42% (95% CrI 33–51) of infections averted across the modelled districts. Generally, a larger proportion of infections was averted in districts with moderate to strong evidence than in those with weak evidence (median 51% vs 30%). Intervention effectiveness varied across states, largely because of differences in baseline consistent condom use,



**Figure 2: Trends in consistent condom use and HIV prevalence among female sex workers**

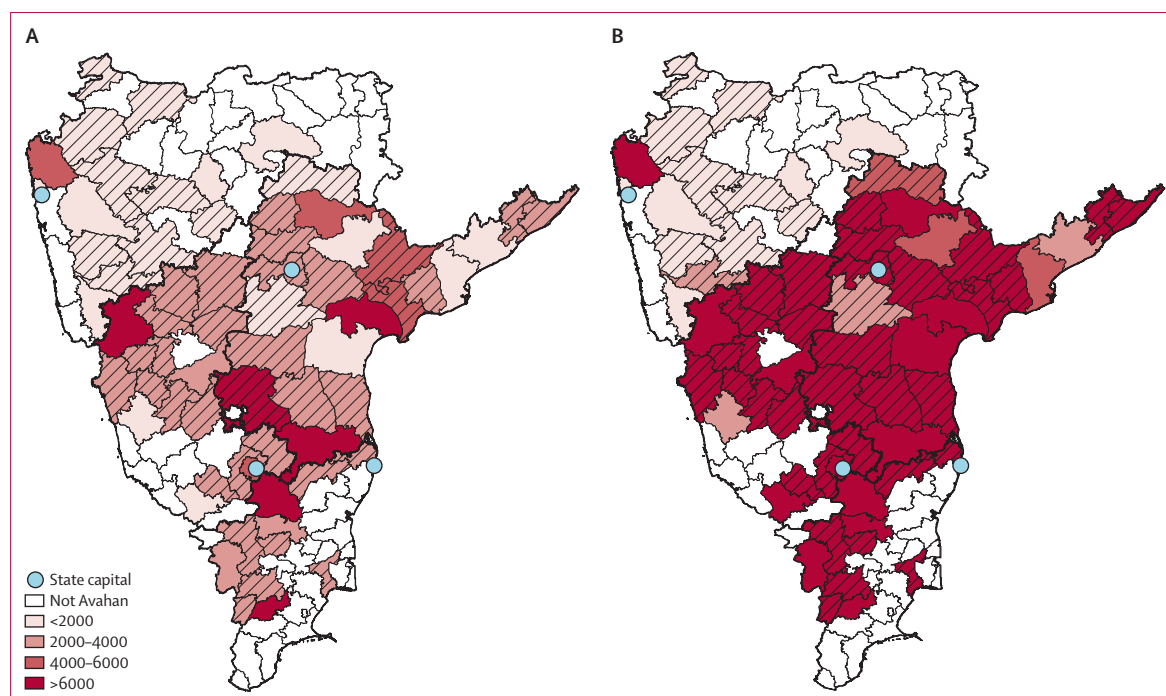
(A) Consistent condom use in districts with moderate to strong evidence. (B) HIV prevalence in districts with moderate to strong evidence. (C) Consistent condom use in districts with weak evidence. (D) HIV prevalence in districts with weak evidence. District-level estimates were weighted by the relative population size of female sex workers. Data are median values, with dark shaded areas representing 50% credibility intervals (CrIs) and light shaded areas representing 95% CrIs.

with 67% of infections averted in Tamil Nadu, 49% in Andhra Pradesh, 36% in Karnataka, and 12% in Maharashtra. Over 10 years, effectiveness increased in all districts, with 57% (46–68%) of HIV infections averted across the modelled districts.

The median number of HIV infections averted per district over the first 4 years of the programme varied from 55 to more than 11400. Six districts (four with moderate to strong evidence) contributed 63% of all infections averted, whereas the bottom six by contribution (five with weak evidence) contributed only 6%. The total number of infections averted each year increased from 5000 in year 1 to 14000 in year 2, 20000 in year 3, and 23800 in year 4.

Over the first 4 years, most HIV infections were averted among clients of female sex workers (51% of all infections averted), who formed the largest high-risk subpopulation, followed by the general population (19%), men who have sex with men (17%), and female sex workers (13%).

The district-specific estimates of effectiveness (figure 1) include infections averted in all population subgroups over the first 4 years, even for districts without surveys of men who have sex with men and the general population, and the state-level and overall proportion of infections averted across all modelled districts. Table 2 shows the overall infections averted over 4 and 10 years, by increasing degree of uncertainty.



**Figure 3:** Distribution of the number of HIV infections averted over first 4 years (A) and all 10 years (B) across all Avahan districts in southern India. Districts that were not modelled are shaded with diagonal stripes.

In 18 IBBA districts, the modelled HIV prevalence among female sex workers fell during the first 4 years under the intervention condom hypothesis by 11% to 52% dependent on the district, whereas it increased in four districts. Over 10 years, the projected median HIV prevalence fell in all districts to less than 14% among female sex workers, with only six districts having a median prevalence higher than 5% in this subpopulation (district-level prevalence-trend graphs are provided in the appendix). By comparison, under the control condom hypothesis HIV prevalence among female sex workers remained high, with seven districts having a prevalence higher than 20% after 10 years. Figure 2 shows the mean prevalence trends weighted by the size of the female sex worker population, grouped by strength of evidence. After the first 4 years, the HIV incidence ratio between the intervention and matched counterfactual varied by between 0.08 and 0.92 (median 0.30) across modelled districts. For the intervention condom hypothesis, incidence in low-risk women fell during the first 4 years in 19 districts, and after 10 years it had fallen by at least 70% in all districts, with larger reductions in incidence among female sex workers (appendix).

When only the subset of variables available across all Avahan districts was used, 62% of the variability in the number of HIV infections averted over the first 4 years across IBBA districts, as measured by the  $R^2$  value of the linear regression model, was accounted for by: the number of female sex workers in a district (positively associated, accounted for 24% of the variability);

whether Avahan was the main intervention provider for female sex workers in the first year in that district (positively associated, 26%); and being a district in Maharashtra state (negatively associated, 12%). When this regression model, described in the appendix, was used to extrapolate effectiveness estimates to all non-IBBA districts, the overall effectiveness of Avahan for all 69 districts was estimated to be 202 000 HIV infections averted over the first 4 years (table 2), with 37% of infections averted in Andhra Pradesh, 30% in Karnataka, 8% in Maharashtra, and 25% in Tamil Nadu. Over 10 years, the number of infections averted increased to 606 000 across all districts. The two regression models for effectiveness over 4 and 10 years had the same independent variables, although they were built independently. Figure 3 shows how the number of infections averted varied geographically across all Avahan districts.

### Discussion

Our results provide evidence for a large-scale increase in consistent condom use in high-risk groups since the start of the Avahan programme. Hypothesis-testing results show HIV prevalence trends are consistent with self-reported trends in consistent condom use by female sex workers and men who have sex with men in most districts, and that consistent condom use increased faster after the introduction of Avahan than before. Across the 22 modelled districts, the increases in consistent condom use that occurred during the first 4 years of Avahan are

estimated to have averted 42% of HIV infections, increasing to 57% over 10 years of the programme. This increase translates to 32700–39900 HIV infections averted over the first 4 years in districts with moderate to strong evidence, or 62800 across all modelled districts. Extrapolating to all 69 Avahan districts, we estimate that 202000 HIV infections could have been averted over the first 4 years of Avahan, increasing to 606000 over 10 years. Both prevalence and incidence fell steeply in most districts, across all risk groups.

For districts in which hypothesis testing did not show evidence of increased consistent condom use due to Avahan, this finding was probably because consistent condom use was generally quite high before Avahan (figure 2). Our attribution of effectiveness to Avahan is supported by other analyses. First, research by Bradley and colleagues<sup>37</sup> showed that condom distribution increased substantially in Karnataka after 2004, mainly because of Avahan, and suggested that the proportion of sex acts between female sex workers and their clients that were protected by a condom increased from 16–24% in 2004 to 81–89% in 2008. Second, statistical analysis of the reconstructed trend data for consistent condom use by female sex workers suggests that use increased faster after the beginning of Avahan than before in ten of 18 districts.<sup>29</sup> Finally, survey data suggest a dose-response relation between condom use between female sex workers and their clients and both time since first contact with Avahan staff and the number of condom demonstrations seen.<sup>38</sup>

The effectiveness of the intervention varied across districts, with the proportion of infections averted inversely related to pre-intervention consistent condom use (appendix). Understandably, for districts in which previous interventions had already led to high consistent condom use among high-risk groups before Avahan, only small, incremental effects could be achieved. Districts with low HIV prevalence and low consistent condom use at baseline, such as those in Tamil Nadu, had more infections averted than other districts, because the epidemic had more potential to grow.

Our results differ in several important ways from those of the previous assessment of Avahan by Ng and colleagues,<sup>18</sup> which estimated that 100200 HIV infections were averted by Avahan between 2004 and 2008. The earlier analysis compared HIV prevalence trends in women attending antenatal care clinics between Avahan and non-Avahan districts, with the assumption that intervention coverage was higher in Avahan districts. By contrast, our method compared the HIV epidemic trends in each district with what might have occurred in the absence of Avahan or any other intense, core-group intervention. Ng and colleagues' analysis probably underestimated the effectiveness of Avahan, since the Indian Government, through the National AIDS Control Organisation (NACO), implemented high-coverage, targeted interventions in many non-Avahan districts,<sup>9</sup> so

non-Avahan districts have been exposed to interventions and cannot always be used as a valid counterfactual.

For example, in Tamil Nadu, Ng and colleagues<sup>18</sup> reported no evidence for the effectiveness of Avahan, probably because of the long history of interventions in many of the non-Avahan districts in that state. By contrast, because Avahan was usually the first and only intervention in the districts of Tamil Nadu in which it operated, our analysis estimated that 25% of HIV infections averted across all Avahan districts were in that state. Although Banandur and colleagues<sup>39</sup> used a similar method to Ng and colleagues,<sup>18</sup> their estimate of 87000 HIV infections averted in Karnataka state between 2004 and 2008 is fairly close to our estimate of 60300 over 4 years (data not shown).

The two approaches to the assessment of Avahan differ in other ways. The previous analyses took into account only the eventual effect on the general population, without investigating the causal pathway through which the intervention achieved its effects.<sup>16</sup> By contrast, our analysis first assessed effectiveness in the high-risk groups that were the focus of the Avahan programme, and then projected how this effect propagated to the general population, thereby taking into account the targeted nature of the intervention. It thus addresses some of the issues related to causation (panel).

Assessment of the effectiveness of HIV preventive interventions is crucial for determining which strategies should be prioritised.<sup>46</sup> This study sought to determine whether there is evidence that Avahan reduced the transmission of HIV among high-risk groups and the general population. It represents the first preplanned, integrated use of mathematical modelling and data collection for assessment of a real-life, large-scale HIV intervention programme,<sup>17</sup> and its success suggests that our assessment design could be a viable alternative to randomised controlled trials.<sup>40,43</sup>

The mathematical model used was developed specifically to assess Avahan, with a structure reflecting important sources of heterogeneity in IBBA data. The model was refined in consultation with epidemiologists and other expert non-modellers, and through exploratory modelling work.<sup>4,20,23</sup> The IBBA surveys used a detailed sampling frame derived from careful mapping of venues, and were designed for this assessment, providing previously unavailable information on HIV prevalence and risk behaviour of high-risk individuals across a large number of districts. Combined with systematically gathered programme data and size-mapping estimates, these survey data allowed for detailed and robust mathematical modelling projections of the effectiveness of Avahan in many different settings, while accounting for uncertainty in estimates. We used an assessment design established<sup>17</sup> at the beginning of the study to minimise assessor biases. The effectiveness estimates were deliberately chosen to be conservative, with the assumption of the counterfactual scenario that condom



use would have continued increasing at pre-Avahan rates in the absence of Avahan. Although the results for all 69 districts are based on an extrapolation from a linear regression model of IBBA districts, and therefore have more uncertainty, we present results with different degrees of strength of evidence to quantify how uncertain our results are.

The approach used, of estimating effectiveness relative to a matched counterfactual, can be regarded as an attempt to reach the ideal estimation of relative risk, namely the comparison of a population to itself with the exposure removed.<sup>47</sup> However, it is not possible to know exactly what would have happened if Avahan had not intervened, and the absence of true empirical baseline data increases uncertainty. In some districts pre-existing interventions were present, which might have led to increased condom use in the absence of Avahan. Although our conservative counterfactual makes allowances for this, the absence of data from districts without any Avahan intervention makes the attribution of effectiveness to the programme with absolute certainty difficult. Additionally, limitations arise from the use of reconstructed condom trends based on self-reported condom use, and although we tried to allow for social desirability biases within the modelling, as well as cross-validating with non-survey methods,<sup>37</sup> it is not possible to know if this issue has been fully accounted for, although the use of Bayesian hypothesis testing provides further evidence that these trends are credible in these settings.

Effectiveness estimates are dependent on the sizes of the high-risk populations, and although mapping studies were specifically done in Avahan districts, the accurate mapping of hidden populations is challenging.<sup>48</sup> Migration from non-Avahan districts could reduce estimated effectiveness. Antiretroviral therapy could also be changing the epidemic, leading to higher HIV prevalence as survival improves. However, although long-term projections could be affected by increasing access to antiretroviral therapy, coverage remained low until after 2008, by which time IBBA surveys in most districts had been completed.<sup>49</sup> Moreover, modelling work suggests that the increase in HIV infections averted by antiretroviral therapy on top of the effect of Avahan is small (unpublished). Finally, although the IBBA districts comprise almost a third of all Avahan districts, they were not chosen randomly, so might not be representative.<sup>50</sup>

However, these data limitations, such as the absence of baseline data, are neither intrinsic nor unique to our approach, and reflect the realities of programme implementation and real-life assessment.<sup>15</sup> Our use of a simulated matched counterfactual for each district means that non-random district selection is less problematic than for approaches in which Avahan and non-Avahan districts are compared, such as in the study by Ng and colleagues,<sup>18</sup> or community-based randomised controlled trials, for which it might not be possible to

### Panel: Research in context

#### Systematic review

Avahan was a large-scale, complex HIV preventive intervention. Uniquely for such a large programme, assessment was based on a preplanned combination of serial cross-sectional data and mathematical modelling.<sup>17</sup> The use of mathematical modelling for assessment of health programmes was reviewed by Garnett and colleagues,<sup>40</sup> with the present assessment used as an example. Some effectiveness assessments of interventions targeted at female sex workers were done before Avahan,<sup>41,42</sup> including one study<sup>42</sup> that examined the effect on the general population. In 2011, Ng and colleagues<sup>18</sup> reported an assessment of Avahan in which they compared trends in HIV prevalence in women attending antenatal care clinics between Avahan and non-Avahan districts within the same Indian states. They used level of intervention effort measured in terms of programme spending to take into account the fact that, in many districts, a mix of Avahan and non-Avahan interventions were targeting the same high-risk populations. The investigators estimated that from 2004 to 2008, Avahan had averted about 100 000 HIV cases. Their approach, however, did not take into account the causal pathway that could have led to a reduced HIV incidence.<sup>16</sup> Using a similar method, Banandur and colleagues<sup>39</sup> estimated that 87 000 HIV infections were averted by Avahan in Karnataka state alone over the same period.

#### Interpretation

Our study constitutes probably the most rigorous use of mathematical modelling for the assessment of a public health programme so far reported. We show that this approach is feasible and provides an alternative to community-based randomised controlled trials, which might not be the ideal approach to assess large, complex interventions.<sup>43</sup> In particular, a randomised trial would not have allowed for the context-specific, community-led response that was an integral part of Avahan.<sup>44</sup> Model projections of HIV prevalence were fitted to multiple rounds of data from different risk groups, and a Bayesian framework was used to assess the strength of evidence for effectiveness. Additionally, we explicitly modelled the causal pathway of the intervention. Our study also incorporated different degrees of uncertainty dependent on the amount of data available for each district. Our results generally support those of Ng and colleagues,<sup>18</sup> showing that Avahan has prevented a large number of HIV cases in India. However, our estimate of 202 000 HIV cases averted over the first 4 years of the programme is about double that estimated by Ng and colleagues.<sup>18</sup> This difference was probably due to the differences in the methods used. Whereas the previous assessment compared Avahan with other interventions, our assessment used a modelled counterfactual, in which exposure to Avahan was removed from the intervention population. Our assessment meets the criteria for plausibility in the Habicht and colleagues' framework,<sup>45</sup> and can be replicated for assessment of other large-scale, complex interventions.

find comparable control districts, leading to imbalance.<sup>51</sup> A further issue for these alternative assessment designs, which rely on non-Avahan control districts, is the scaling-up of targeted interventions by NACO in non-Avahan districts since 2007,<sup>9</sup> meaning that such analyses are effectively comparing Avahan with NACO interventions. Finally, although a step-wedge design can be useful for assessing intermediate outcomes, the present combined approach might be more suitable for assessing HIV interventions in populations, since changes in HIV prevalence and incidence might not be measurable for a long time.<sup>51</sup>

In summary, using mathematical modelling to quantitatively synthesise HIV and STI prevalence data with key setting-specific behavioural indicators, we have shown strong and plausible evidence for a large

intervention effect of Avahan, which increased over time, based on Habicht and colleagues<sup>45</sup> scale for assessing the strength of evidence for effectiveness of public health interventions. This effect occurred through increased condom use, brought about by removing barriers to use via intervention components including distribution and social marketing of condoms, peer outreach, STI treatment, structural intervention, and community mobilisation. In an era focused on antiretroviral therapy as prevention, these results show that behaviour-focused, core-group-targeted HIV preventive interventions can be rapidly and successfully implemented at scale. The low coverage of such programmes in many regions of the world should be addressed, since with high coverage these programmes have the potential to substantially reduce concentrated HIV epidemics.<sup>52,53</sup>

#### Contributors

M-CB, PV, CML, SM, JFB, BMR, RW, and MA designed the study. MP, PV, and M-CB developed the model structure and the model analysis plan. KND and MP did the data analysis for the development and parameterisation of the model. MP developed the model and undertook all the model analyses. MP, PV, MCB, and MA interpreted model results. MA, SM, CML, JFB, JB, BMR, RW, RA, MM, and RSP had major roles in collecting the data used by the model. MP, M-CB, PV, and MA wrote the first draft of the report. All authors contributed to subsequent drafts of the report and reviewed the final version before submission.

#### Conflicts of interest

MA received funding from the Bill & Melinda Gates Foundation for this study. SM and JFB received a dual-purpose grant from the Bill & Melinda Gates Foundation to implement and assess the intervention in Karnataka state, and RA and RSP received a grant from the Bill & Melinda Gates Foundation to assess the intervention outside Karnataka. All other authors declare that they have no conflicts of interest.

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