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Positive impact of a large-scale HIV prevention programme among female sex workers and clients in South India

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Objective: Estimate the potential impact of Avahan, the India AIDS Initiative, among female sex workers (FSWs) and their clients in five districts of Karnataka state, south India.

Design: Examination of time trends in sexually transmitted infection (STI)/HIV prevalence from serial cross-sectional surveys, combined with mathematical modelling.

Methods: Survey data from each district were used to monitor changes in FSW STI/HIV prevalence during Avahan. A deterministic model, parameterized with district-specific survey data, was used to simulate HIV/HSV-2/syphilis transmission among high-risk groups in each district. Latin hypercube sampling was used to obtain multiple parameter sets that reproduced district-specific HIV prevalence trends. A Bayesian framework tested whether self-reported increases in consistent condom use (CCU) during Avahan were more compatible with FSW HIV prevalence trends than assuming no or slow (preintervention rates) CCU increases, and were used to estimate HIV incidence and infections averted.

Results: Declines in FSW HIV prevalence occurred over 5 years in all districts, and were statistically significant in three. Self-reported increases in CCU were more consistent with observed declines in HIV prevalence in three districts. In all five districts, an estimated 25–64% (32–70%) HIV infections were averted among FSWs (clients) over 5 years. This corresponded to 142–2092 FSW infections averted depending on the district (two-fold to nine-fold more among clients).

Conclusion: Empirical HIV prevalence trends combined with Bayesian modelling have provided plausible evidence that Avahan has reduced HIV transmission among FSWs and their clients. If current CCU levels are sustained, FSW HIV prevalence could decline to low levels by 2015, with many more infections averted.

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Keywords: female sex workers, high-risk groups, HIV/AIDS, impact evaluation, India, large-scale prevention programme, targeted intervention

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Introduction

The HIV epidemic in southern India is highly concentrated among high-risk groups (HRGs), particularly female sex workers (FSWs), their clients and MSM, who contribute disproportionately to HIV transmission compared to the general population [1–3]. Given this epidemiological context, Avahan, the India AIDS Initiative, was developed by the Bill & Melinda Gates Foundation and implemented from December 2003 [2–4]. Avahan's objective was to scale up targeted interventions to at least 80% of HRGs in Karnataka, Andhra Pradesh, Maharashtra and Tamil Nadu states, to reduce HIV transmission among them and subsequently in the general population [1–4]. The common prevention packages included peer-led outreach and education; free condoms; sexually transmitted infection (STI) treatment services; referrals for HIV and tuberculosis testing, and HIV care; empowerment and community mobilization to address local structural barriers; and mass communication programmes. Other services, including condom and STI treatment social marketing and behaviour change communication, were also targeted specifically to clients of FSWs [3–7].

As previously explained [3,8,9], the main Avahan impact evaluation on behavioural and HIV outcomes relies on Integrated Behavioural and Biological Assessments (IBBAs surveys) among targeted HRGs in selected intervention districts, complemented with mathematical modelling.

This paper evaluates the potential impact of Avahan on HIV transmission among FSWs and clients in five districts of Karnataka State – Bangalore urban, Bellary, Belgaum, Mysore and Shimoga, with different epidemiology and history of intervention. Karnataka state has an estimated 76 000 urban FSWs, of whom 60 000 are covered by Avahan in 18 of 27 districts (Supplementary material, Box 1i, http://links.lww.com/QAD/A319) [10,11]. In Mysore and Shimoga, Avahan was and remains the first and only intervention implemented among HRGs [3,10,11]. In Belgaum and Bellary, Avahan was not the first HRG intervention but is now the only one. It is the major HRG intervention but not the only one in Bangalore Urban. Shimoga, Bellary and Bangalore Urban districts have lower FSW HIV prevalences compared to Belgaum and Mysore [6,7]. In these five districts, intervention activities were initiated and scaled up rapidly between January 2004 and June 2005, which prevented true baseline measurements [7,9,12,13]. As no comparable HIV data among FSWs in Karnataka are available for non-Avahan districts, there is no comparable control group [3,7,8,13–15].

The following main analyses are undertaken for each district. First, we determine whether decreases in FSW STI/HIV prevalence have been observed following Avahan implementation. Second, HIV/STI transmission modelling is calibrated (using behavioural and prevalence data) and used within a Bayesian framework to determine whether observed HIV prevalence trends support the evidence of self-reported increases in condom use during Avahan (hypothesis testing) and, if so, to estimate the likely impact of those increases in condom use on HIV prevalence, incidence and infections averted among FSWs and clients. The modelling results and strength of evidence provided by the hypothesis testing are discussed and interpreted in the light of additional evidence on implementation, coverage and intensity of the intervention and relationship between exposure of FSWs to the programme and associated changes in condom use.

Methods

Time trend analysis

HIV/STI trend analysis is based on serial rounds of IBBAs, involving random samples of FSWs, using traditional and time location cluster sampling [6,7]. Three rounds of IBBA have been conducted in all five districts between 2004 and the end of 2011 (Table 1). The first IBBA (R1) was conducted 7–19 months after programme initiation. Round 2 (R2) and Round 3 (R3) follow-up surveys occurred 28–37 and 56–73 months after R1, respectively. Crude and adjusted (for variables that differed significantly between rounds in each district) logistic regression analyses were performed using STATA, version 10.0 (Stata Corp., College Station, Texas, USA) and took into account the sampling weights and cluster sampling design. Logistic regression was used, instead of binomial regression, to avoid convergence issues when controlling for many confounding variables. The study was approved by the institutional review boards of St John's Medical College in Bangalore, India, and the University of Manitoba in Winnipeg, Canada. Additional details on data collection and statistical analyses are provided in Supplementary material (Methods A), http://links.lww.com/QAD/A319 [6,7].

HIV/sexually transmitted infection mathematical model

Model description

A deterministic compartmental model was used to simulate HIV/herpes simplex virus type 2 (HSV-2)/syphilis (Tp) transmission between FSWs and their clients through commercial sex and through longer-term noncommercial partnerships [13]. As chlamydia (R2: 2.8–12.0%) and gonorrhoea (R2: 1.3–3.1%) prevalence was deemed low, urine samples were not collected at R3 and, thus, these infections were not modelled (Table 1). FSWs were stratified by duration of selling sex (overall duration varied between 4 and 14 years across districts), two levels of commercial sexual activity (low and high)

Table 1. Prevalence and odds ratio of HIV and sexually transmitted infection among female sex workers over available rounds of Integrated Behavioural and Biological Assessments in five districts of Karnataka state.

	Round 1	Round 2	Round 3	Round 2 vs. 1[ref]		Round 3 vs. 1[ref]	
	Prevalence (%)	Prevalence (%)	Prevalence (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)	Crude OR (95% CI)	Adjusted OR[b] (95% CI)
Mysore	$n=429$	$n=425$	$n=425$				
Date of IBBA	August 2004	December 2006	April 2009				
Time since start of Avahan[h]	7 mths	35 mths	63 mths				
Time since R1 IBBA	–	28 mths	56 mths				
HIV	26.1	24.3	10.9	0.91 (0.67–1.22)	0.79 (0.56–1.11)	0.35 (0.23–0.52)	0.31 (0.17–0.57)
Syphilis[g]	24.9	11.4	13.2	0.39 (0.27–0.55)	0.34 (0.23–0.48)	0.46 (0.34–0.63)	0.14 (0.03–0.62)
Chlamydial infection	10.8	4.4	4.6	0.38 (0.23–0.64)	0.44 (0.25–0.76)	0.40 (0.25–0.65)	0.38 (0.19–0.75)
Gonococcal infection	5.4	2.4	0.9	0.43 (0.23–0.83)	0.47 (0.23–0.96)	0.16 (0.05–0.45)	0.22 (0.07–0.71)
					a		c
Shimoga	$n=393$	$n=406$	$n=393$				
Date of IBBA	August 2005	September 2008	September 2011				
Time since start of Avahan[h]	13 mths	50 mths	86 mths				
Time since R1 IBBA	–	37 mths	73 mths				
HIV	9.7	9.0	7.0	0.92 (0.53–1.60)	0.77 (0.41–1.46)	0.70 (0.39–1.27)	0.60 (0.31 –1.16)
Syphilis[g]	4.0	3.8	2.2	0.95 (0.40–2.22)	1.30 (0.44–3.86)	0.53 (0.21–1.30)	0.70 (0.23– 2.12)
Chlamydial infection	5.6	2.8	–	0.48 (0.21–1.10)	0.34 (0.12–0.99)	–	na
Gonococcal infection	1.3	1.3	na	1.00 (0.25–1.15)	0.29 (0.07–1.28)	na	na
					a		d
Belgaum	$n=366$	$n=396$	$n=423$				
Date of IBBA	November 2005	July 2008	September 2010				
Time since start of Avahan[h]	19 mths	51 mths	77 mths				
Time since R1 IBBA	–	32 mths	58 mths				
HIV	33.9	27.3	22.3	0.73 (0.50–1.07)	0.79 (0.53–1.19)	0.56 (0.38–0.82)	0.59 (0.35–0.99)
Syphilis[g]	8.0	12.4	4.9	1.56 (0.73–3.31)	1.52 (0.72–3.21)	0.59 (0.25–1.41)	0.51 (0.18–1.40)
Chlamydial infection	6.5	3.8	na	0.57 (0.26–1.25)	0.34 (0.15–0.74)	na	na
Gonococcal infection	4.7	2.0	na	0.42 (0.13–1.28)	0.24 (0.07–0.83)	na	na
					a		e
Bellary	$n=423$	$n=410$	$n=400$				
Date of IBBA	November 2005	August 2008	November 2010				
Time since start of Avahan[h]	16 mths	49 mths	76 mths				
Time since R1 IBBA	–	33 mths	60 mths				
HIV	15.7	14.1	6.4	0.89 (0.57–1.39)	0.88 (0.49–1.60)	0.37 (0.21–0.63)	0.41 (0.18–0.92)
Syphilis	5.2	7.7	8.0	1.48 (0.73–3.02)	1.08 (0.36–3.23)	1.58 (0.77–3.24)	1.21 (0.48–3.01)
Chlamydial infection	4.1	4.6	na	1.15 (0.50–2.67)	0.77 (0.25–2.34)	na	na
Gonococcal infection	2.7	3.6	na	1.32 (0.53–3.33)	0.31 (0.11–0.89)	na	na
					a		f
Bangalore Urban	$n=673$	$n=741$	$n=718$				
Date of IBBA	July 2006	January 2009	August 2011				
Time since start of Avahan[h]	12 mths	43 mths	61 mths				
Time since R1 IBBA	–	29 mths	50 mths				
HIV	12.7	8.3	9.3	0.60 (0.36–1.01)	0.76 (0.43–1.35)	0.71 (0.43–1.18)	0.86 (0.45–1.65)
Syphilis[g]	12.6	9.5	3.6	0.73 (0.47–1.13)	0.88 (0.58–1.36)	0.26 (0.11–0.64)	0.42 (0.16–1.09)
Chlamydial infection	6.5	12.0	na	1.96 (1.20–3.20)	1.76 (1.04–2.98)	na	na
Gonococcal infection	3.6	3.1	na	0.88 (0.39–1.96)	0.77 (0.33–1.82)	na	na

[ref]IBBA R1 used as the reference group. CI, confidence interval; IBBA, Integrated Behavioural and Biological Assessment; mths, months; 'na', not available: urine specimen not collected; OR, odds ratio. Multivariate models were adjusted for survey rounds as well as the following district-specific characteristics that differed across rounds.
[a]Adjusted for sex work outside place of enumeration in previous 6 months, duration in sex work, place of solicitation (home, brothel/lodge/dabha, public places), proportion of clients who were new.
[b]Adjusted for residence (localite or not), sex work outside place of enumeration previous 6 months, age at sexual debut, age started sex work, amount charged per sex work, proportion of clients who were new, number of regular partners.
[c]Adjusted for age, marital status, residence, place of solicitation, place entertaining the clients (home, brothel/lodge/dabha, public places), amount charged per sex act, monthly income from sex work, proportion of clients who were new, regular partners.
[d]Adjusted for literacy, marital status, residence, ever engaged in sex work in Mumbai, age at sexual debut, age at starting sex work, duration in sex work, place of solicitation, amount charged per sex act, monthly income from sex work, proportion of clients who were new and regular partners.
[e]Adjusted for marital status, residence, age at sexual debut, age starting sex work, place where sex is solicited, charge per sex act and monthly sex work income.
[f]Adjusted for current marital status, sex work outside place of enumeration in previous 6 months, age at starting sex work, duration in sex work, place of solicitation, place of entertainment, proportion of clients who were new, monthly income from sex work.
[g]Syphilis infection was defined as being RPR-positive (rapid plasma regain-positive; any titre) and TPHA-positive (trepanom pallidum particle agglutination assay-positive).
[h]The start of Avahan varied across districts (see Table 2 for dates).

and three levels of consistent condom use (CCU) with occasional clients ('never', 'sometimes' and 'every time'), which varied over time (Supplementary Table S1, http://links.lww.com/QAD/A319). The fraction of sex acts protected by condoms was specified for each CCU level; low and high activity FSWs had specific frequencies of commercial sex, which could be varied across IBBA rounds. An adjustment factor, estimated using complementary data, was also applied to account for over-reporting of FSW condom use (Table 2, Supplementary material, Methods B, http://links.lww.com/QAD/A319) [16]. Condom efficacy was also taken into account [13,17–22]. Occasional clients were stratified by the duration and frequency of commercial sex. Given the lack of sexual mixing data between FSWs and clients, random mixing was assumed according to availability (i.e. proportionately to total number of commercial sex partnerships reported by each risk group).

HIV was modelled with an initial phase of high-infectivity, a long low-infectivity phase and a pre-AIDS phase of increased infectivity [23–26]. Those with AIDS were assumed to cease being sexually active. Cocirculating HSV-2 was modelled dynamically with associated cofactors representing facilitation of HIV and HSV-2 acquisition and transmission [27–29]. Access to antiretroviral treatment (ART) was limited until recently (~8 and 20% of eligible patients with CD4 $<$ 250 by end of 2005 and 2007, respectively); hence, it was not modelled [30,31]. Syphilis was modelled dynamically, including a transient immune stage and disease progression, with background treatment before Avahan, and Avahan-specific treatment and periodic presumptive treatment (PPT) [32–34]. Other than the stage of HIV and HSV-2/Tp cofactors, the force of HIV/STI infection also depended on gender, frequency of sex acts with different partnership types and condom use (details of the model and parameters in Table 2, supplementary material (Methods B), http://links.lww.com/QAD/A319, and supplementary tables S1-S2, http://links.lww.com/QAD/A319). The mathematical model was used to simulate STI/HIV transmission in each district as follows.

Parameter assumptions

Plausible uniform ranges for the prior distributions of biological and district-specific behavioural parameters were specified based on literature reviews and the FSW and client IBBA data, respectively (Table 2, Supplementary tables S1-S2, http://links.lww.com/QAD/A319).

Given the lack of baseline and historical measurements, the model's prior distribution for time trends in CCU (i.e. fraction of FSWs who are 'every time' users) during commercial sex with occasional clients between the start of the epidemic and the start of Avahan was based on estimated CCU trends by Lowndes *et al.* [9] – reconstructed by utilizing two IBBA survey questions that asked FSWs when they started using condoms consistently and when they started commercial sex work [9,13] (Supplementary material, Box1ii, http://links.lww.com/QAD/A319). Following the start of Avahan, CCU with occasional clients in presence of the intervention (i.e. 'estimated CCU trends') was assumed to increase linearly up to levels reported in each IBBA survey and to remain constant after the last round. The validity of these trends is addressed in the discussion. The proportion of FSWs 'sometimes' using condoms after the start of the intervention was assumed to increase linearly from 0% to the estimates from each IBBA round (<10% in each district). The proportion of FSWs 'never' using condoms varied to ensure the sum of proportions always equals 1. In absence of the intervention, as no empirical control groups were available, two plausible control groups (i.e. counterfactuals) were defined for trends in CCU covering the period following Avahan initiation. 'Control 1' assumed no change in CCU (fixed at the CCU level at the start of Avahan), whereas 'Control 2' (more conservative than Control 1) assumed CCU would have continued to increase slowly at the preintervention rate suggested by the 'estimated CCU trends' analysis (Supplementary figure S5, http://links.lww.com/QAD/A319). Based on available data, condom use in noncommercial long-term relationships between HRGs was assumed to be low and constant over time. Syphilis treatment and PPT were parameterized using Avahan's programme monitoring data.

Fitting process and plan of analysis

Latin hypercube sampling was used to randomly select multiple parameter sets from the prior parameter distributions. The model was run with each parameter set between 1987 and 2015. Posterior parameter sets were selected if a set produced modelled FSW and client HIV prevalence projections that lay within the 95% confidence interval (95% CI) of the FSW and client HIV prevalence in all IBBA rounds and prespecified FSW HSV-2/Tp prevalence ranges (for R2 and R3, HIV prevalence figures were adjusted on the R1 distribution of prespecified key confounding variables, excluding those specifically varied over time in the mathematical model) (Supplementary material, Methods C, http://links.lww.com/QAD/A319).

To test whether self-reported increases in condom use during Avahan were consistent with observed HIV prevalence trends (hypothesis testing), the fitting process was repeated for each CCU trend hypothesis (Estimated, Control 1, Control 2). Following previously used methods [13], the 'estimated CCU trend' hypothesis was deemed most likely only if it achieved a higher frequency of fits (proportion of prior parameter sets that produced model fits) than the two alternative control CCU trend hypotheses. The hypothesis testing stages were undertaken to validate the CCU trends as they were retrospectively estimated from self-reported CCU data.

Table 2. Ranges for district-specific model parameters (prior distribution) for condom use and syphilis treatment before and after Avahan implementation sampled from during the model fitting stage.[d]

Definition of model input	Mysore	Belgaum	Bellary	Shimoga	Bangalore
Condom use between FSWs and clients for each condom use time trends hypothesis before and after the start of Avahan (Supplementary figure S5, http://links.lww.com/QAD/A319)					
'Estimated CCU trends' (in presence of intervention)					
Annual rate of increase in condom use prior to intervention	0.016–0.038	0.033–0.057	0.039–0.065	0.027–0.060	0–0.044
Proportion who are consistent condom users					
Start of the intervention	0.13–0.24	0.42–0.55	0.30–0.48	0.21–0.39	0.39–0.54
IBBA R1	0.31–0.40	0.87–0.95	0.67–0.79	0.49–0.62	0.74–0.82
IBBA R2	0.62–0.73	0.86–0.93	0.85–0.93	0.79–0.89	0.83–0.89
IBBA R3	0.88–0.94	0.95–0.99	0.83–0.92	na	na
Control group 1					
Annual rate of increase in condom use prior to intervention	0.016–0.038	0.033–0.057	0.039–0.065	0.027–0.060	0–0.436
Proportion who are consistent condom users from the start of the intervention onwards	0.13–0.24	0.42–0.55	0.30–0.48	0.21–0.39	0.39–0.54
Control group 2					
Annual rate of increase in condom use prior to intervention until the latest IBBA (R3 except in Shimoga and Bangalore)	0.016–0.038	0.033–0.057	0.039–0.065	0.027–0.060	0–0.436
Proportion who are consistent condom users at the start of the intervention	0.13–0.24	0.42–0.55	0.30–0.48	0.21–0.39	0.39–0.54
For all condom assumptions (CCU, Control 1 and 2)					
Proportion of FSW who report 'sometimes/often' using condoms with occasional clients					
IBBA R2	0.25–0.37	0.07–0.14	0.06–0.13	0.07–0.17	0.09–0.15
IBBA R3	0.06–0.12	0.01–0.05	0.05–0.11	na	na
Proportion of sex acts with occasional clients when a condom is used by					
FSW 'Always' using condoms	0.82–0.93	0.92–0.97	0.91–0.97	0.83–0.94	0.91–0.97
FSW 'Often/sometimes' using condoms	0.54–0.67	0.34–0.84	0.44–0.77	0.53–0.74	0.56–0.74
FSW 'Never' using condoms	0.07–0.38	0.0–0.63	0.34–0.77	0.18–0.46	0.02–0.32
Adjustment factor for overreporting of condom use – 'relative reduction in the fraction of commercial sex acts protected by condoms[b]	0.00–0.25	0.00–0.25	0.00–0.25	0.00–0.25	0.00–0.25
Fraction (%) of sex acts protected in main partnerships between married or cohabiting partners before and after 2004	2.0–13.9	4.7–13.3	3.0–9.4	2.0–6.4	8.6–16.6
Condom efficacy per sex act for HIV (%) [17,18]	80–95	80–95	80–95	80–95	80–95
Condom efficacy per sex act for HSV-2 and syphilis (%) [13,29,30]	40–70	40–70	40–70	40–70	40–70
Syphilis treatment					
Fraction (%) of FSW receiving antibiotics in absence of Avahan (i.e. background treatment)	9.8–27.8	9.8–27.8	9.8–27.8	9.8–27.8	9.8–27.8
Fraction (%) of clients symptomatic for syphilis[c]	21–50	21–50	21–50	21–50	21–50
Fraction (%) of clients seeking background treatment when symptomatic	0–100	0–100	0–100	0–100	0–100
Fraction (%) of FSWs seeking Avahan treatment for syphilis[a]	10.0–30.0	10.0–30.0	10.0–30.0	10.0–30.0	10.0–30.0
Number of FSWs receiving presumptive positive treatment (PPT)[a,e]					
From start of Avahan to Jan 2007 (number receiving PPT every 3 months)	132–175	282–431	979–1501	80–163	281–810
After Jan 2007 (number receiving PPT every 6 months)	435–633	595–646	117–1021	13-89	1000–1656
Mean duration of infection of FSW seeking Avahan treatment for syphilis (months)	0.26–0.40	0.46–0.71	0.58–0.81	0.40–0.65	0.36–0.54
Assumptions for impact assessment					
Start of Avahan	January 2004	April 2004	July 2004	July 2004	June 2005
Consistent condom use in presence of intervention	Based on district-specific 'estimated CCU trends'				
Condom use trends (counterfactual) in simulated control group after 2004 in absence of intervention	Control 1 or 2				
Syphilis treatment in control group	No Avahan PPT after 2004, 0% seeking Avahan Tp treatment				

Additional model parameters and fitting data shown in Supplementary tables S1–S3, http://links.lww.com/QAD/A319. 'na', not available at the time of the modelling analysis – R3 data were only used in trends analysis (Table 1), which are quicker to carry. CCU, consistent condom use; FSW, female sex worker; IBBA, Integrated Behavioural and Biological Assessment.
[a]Avahan programme monitoring (MIS) data; and calculation as in [21].
[b]The adjustment factor is based on the ratio of condom use reported by clients vs. female sex workers in IBBA [16].
[c]Lower limit based on IBBA data across districts, upper limit based on Orroth *et al.* [22].
[d]Ranges are generally based on 95% confidence intervals derived from the IBBA surveys.
[e]Reynold Washington personal communication.

Our hypothesis testing method was validated on simulated data and showed good discriminating power (Supplementary material: Methods D, http://links.lww.com/QAD/A319). The posterior parameter sets from the 'estimated CCU trends' fitting results were then used to simulate the trends in HIV prevalence and incidence in presence of intervention, and in its absence by substituting the Control 1 or 2 CCU trends (all other parameters remaining the same). The number and prevented fraction of HIV infections since the start of Avahan were estimated from these simulated incidence trends with multiple posterior parameter sets being used to reflect the uncertainty in the model projections, using 95% credibility intervals (95% CrIs). The impact estimates using Control 2 are more conservative than those using Control 1 because Control 2 assumes CCU increases in the absence of an intervention. With either control group, no additional syphilis treatment by Avahan was assumed.

Results

Data analysis of time trends

HIV prevalence declines occurred across rounds in all districts but were only statistically significant over 5 years (R1 to R3) in Mysore, Belgaum and Bellary in the adjusted analysis (Table 1). Chlamydia, gonorrhoea and syphilis prevalence also declined significantly between R1 and R2 or R3 in Mysore. Adjusted STI trends, between R1 and R2, were more variable in other districts. Declines in chlamydia prevalence were significant in Shimoga and Belgaum, nonsignificant in Bellary, but increased in Bangalore. Gonorrhoea declined significantly in Belgaum and Bellary but not significantly in Shimoga or Bangalore. No significant trends in syphilis prevalence occurred except in Mysore.

Mathematical modelling

Hypothesis testing of trends in condom use

The 'estimated CCU trends' was most likely for Bellary, Shimoga, Mysore and Bangalore, with only Bangalore not receiving over 2.5 times more fits for these CCU trends than the two control CCU trends. However, Belgaum received less fits to the 'estimated CCU trends' than the 'Control CCU trends' (Table 3). These results suggest that large increases in CCU most probably occurred during Avahan in all districts other than Belgaum and possibly Bangalore.

Predicted female sex worker and client HIV prevalence trends over time

Model projections based on the 'estimated CCU trends' suggest that FSW HIV prevalence has been decreasing in all districts since 2004–2005. Indeed, the FSW HIV prevalence may decline to low levels by 2015 (<2–10% depending on district) without the need for any additional interventions (Fig. 1). However, prevalence peaked earlier in districts where Avahan was not the first intervention (Belgaum, Bellary) because condom use increased earlier than in other districts, and the Belgaum HIV epidemic was more mature at the start of Avahan than elsewhere (Supplementary figure S5, http://links.lww.com/QAD/A319). Without condom use increasing after 2004 (Control 1 CCU trend), the FSW and client's HIV prevalence may have remained fairly stable or increased slightly for a few years in Mysore, Bellary and Bangalore; decreased in Belgaum; and increased in Shimoga (Fig. 1, Supplementary figure S6, http://links.lww.com/QAD/A319).

HIV incidence and infections averted

At the R1 IBBA, the modelled FSW HIV incidence was lowest in Shimoga (2.6 per 100 person-years) and highest in Mysore (11.7 per 100 person-years), and reduced to 1.1 and 3.3 per 100 person-years at R2/R3, respectively (Supplementary table S4, http://links.lww.com/QAD/A319). Table 4 shows the predicted prevented fraction and number of HIV infections averted among FSWs and clients for each district over different time periods, estimated by assuming either counterfactual (control groups 1 or 2). Using Control 2, the median prevented fraction among FSWs (among clients) increased from 16–20% (17–23%) in year 1 to more than 43% (>49%) over 5 years across all districts except Belgaum (Table 4B). The increase in condom use following Avahan is estimated to have prevented 36.7% (95% CrI 27.0–43.7%, Belgaum) to 55.4% (95% CrI 39.1–68.1%, Shimoga) of new HIV infections among FSWs from the start of Avahan to 2011, and between 46.0% (95% CrI 34.2–54.0, Belgaum) and 59.0% (95% CrI 47.3–72.8, Bangalore) among clients (Table 4B). Due to differences in population sizes across districts, this translates to between 220 (95% CrI 120–406, Shimoga) and 1255 (95% CrI 660–2530, Bangalore) new HIV infections being averted among FSWs by 2011. Two-fold to nine-fold more infections are averted in clients than FSWs (Table 4) in each district due to their larger population size. Lastly, syphilis treatment alone is estimated to prevent on average a maximum of 6% of new HIV infections over 10 years (Table 4C).

Discussion

This is the first evaluation of the Avahan intervention among high-risk populations in Karnataka state using a preplanned evaluation framework [8]. Our results suggest Avahan has been effective, particularly in Bellary, Shimoga and Mysore. FSW HIV prevalence declined in all districts, with statistical significance in three districts. The decline in HIV prevalence may have been facilitated by the fast turnover of sex workers. STI trends were less consistent than HIV trends potentially reflecting variation in programme effectiveness, degree of implementation (e.g. syphilis screening took off in 2008, except for Mysore where it started earlier), and different and faster transmission dynamics or a lack of statistical power. However, delays in conducting the first IBBA mean that the prevalence of curable STIs (especially those with short duration such as chlamydia or gonorrhoea) may have already decreased appreciably before the R1 IBBA [21,22,35]. Thus, the observed reduction in STI may underestimate the true decrease following programme implementation. Interestingly, Mysore, which had the earliest R1 IBBA, noted the largest declines in all STIs between R1 and R2. Lastly, a recent analysis combining the five Karnataka districts showed significant declines in HIV and all STIs between R1 and R2 IBBA [7].

Our Bayesian modelling analysis strongly suggests that the observed declines in FSW HIV prevalence in Shimoga,

Table 3. Testing the likelihood of each Avahan condom use trend based on target fitting.

District	Condom use trend	Number of parameter sets sampled to find model fits (N)	Total number of model fits obtained (n^a) to the available IBBA HIV data for each district: (i) 3 data points used for fitting: R1 & R2 FSW IBBA and R1 client IBBA data	(ii) 4 data points used for fitting: R1, R2 & R3[b] FSW IBBA and R1 client IBBA data	(iii) Ratio of fits 'estimated CCU trends' vs. Control 1[c1] or Control 2[c2]
Mysore	Control 1	200 000	121[s1,**]	2[s1,**]	65.5[c1]
	Control 2	200 000	215[s,**]	52[s,**]	2.5[c2]
	Estimated CCU trends^	200 000	131	131	–
Shimoga	Control 1	200 000	105[s1,**]	na	3.6[c1]
	Control 2	200 000	130[s,**]	na	2.9[c2]
	Estimated CCU trends^	200 000	374	na	–
Belgaum	Control 1	1 000 000	2188[s1,**]	2188[s1,**]	0.3[c1]
	Control 2	1 000 000	2910[s,**]	2575[s,**]	0.3[c2]
	Estimated CCU trends^	1 000 000	11056	74	–
Bellary	Control 1	100 000	56[s1,**]	0[s1,**]	∞[c1]
	Control 2	100 000	105[s,**]	7[s,**]	44[c2]
	Estimated CCU trends^	100 000	318	310	–
Bangalore Urban	Control 1	500 000	75[s1,**]	na	1.4[c1]
	Control 2	500 000	83[s,*]	na	1.3[c2]
	Estimated CCU trends^	500 000	108	na	–

CCU, consistent condom use; FSW, female sex worker; IBBA, Integrated Behavioural and Biological Assessment. **Indicate a P value less than 0.02 and *a P value = 0.07 for the χ^2 test comparing the frequency of model fits between the two following CCU trends hypothesis: [s1]Control 1 with the 'estimated CCU trends' or [s]Control 2 with the 'estimated CCU trends'; ^ 'estimated CCU trends' as shown in Supplementary material figure S5, http://links.lww.com/QAD/A319; Control 1: Same CCU trends as the 'estimated CCU trends' before the start of Avahan and constant thereafter; Control 2: Same CCU trends as the 'estimated CCU trends' before the start of Avahan and then increases at preintervention rate until the last IBBA (R3 in Mysore, Bellary and Belgaum and R2 in Shimoga and Bangalore Urban) and constant thereafter. na: not available; [a] 'n' parameter sets out of the N parameters sets sampled agreed with the available prevalence data at the different rounds. [b]R3 IBBA data were only used at the fitting stage for Mysore, Bellary and Belgaum as it was not available at the time of the modelling analysis in Shimoga and Bangalore .[c1]Ratio of the number of adequate model fits using the estimated CCU trends compared to the number of adequate model fits when using control 1; [c2] as [c1] but using control 2.

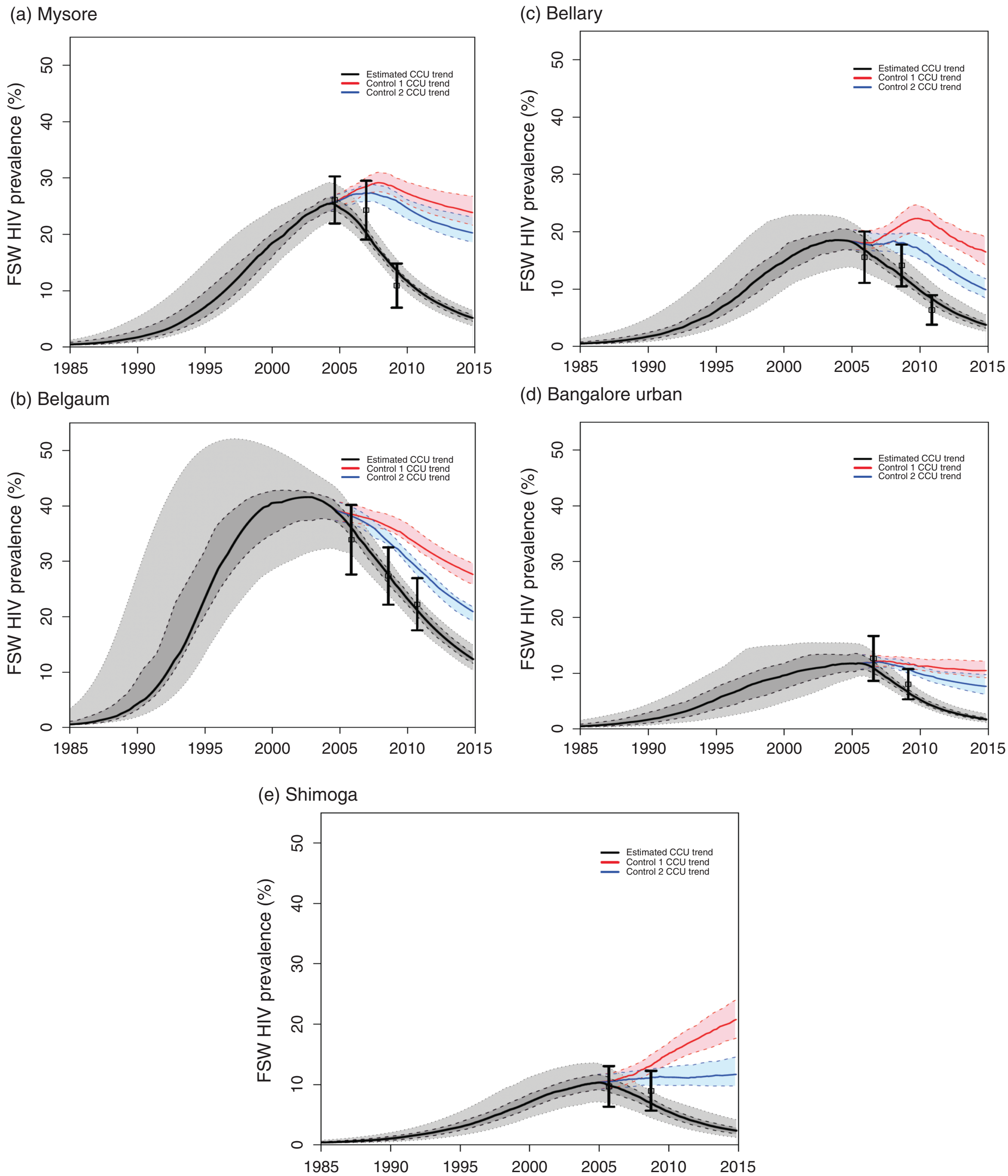

Fig. 1. Female sex worker HIV prevalence over time simulated under the three different condom hypothesis trends. Predicted female sex worker HIV prevalence over time simulated under the 'estimated consistent condom use (CCU) trends' in presence of the intervention and the two alternative CCU trends (Control 1 and Control 2 CCU trends) to simulate HIV prevalence in absence of the intervention in (a) Mysore, (b) Belgaum, (c) Bellary, (d) Bangalore Urban and (e) Shimoga districts. Shown on the graphs are the mean (dark lines black, blue and red) and the 75% credibility interval (CrI; shaded area) for each hypothesis. The paler grey area represents the 95% CrI. Also shown is the available Integrated Behavioural and Biological Assessment (IBBA) survey prevalence data (mean and 95% confidence intervals, CIs). As the model was fitted to the adjusted HIV prevalence in R2 and/or R3, the HIV prediction may not fall exactly within the 95% CI of the HIV prevalence data. The transient increase in prevalence with Control 1 and 2 CCU trends in (a) and (c) are due to the increase in number of clients of FSWs after R1.

Table 4. Predicted number (No) and cumulative fraction (prevented fraction)[a] (95% credibility interval) of new HIV infections averted due to the increase in condom use and the improved syphilis treatment since the start of Avahan comparing model predictions with the 'estimated consistent condom use trends' and Control group 1 or 2.[d,e]

A. Using control group 1[b]		Over 1st year	Over 3 years	Over 5 years	To end of 2011	To end of 2014
Mysore –FSW	PF (%)	17.1 (11.7–24.3)	35.9 (30.2–41.3)	47.4 (41.5–54.3)	54.1 (47.7–61.2)	61.1 (54.4–68.2)
Shimoga –FSW	PF (%)	18.6 (12.3–27.4)	40.7 (29.6–53.2)	59.1 (47.5–69.0)	66.9 (56.0–75.6)	76.8 (67.7–84.0)
Belgaum –FSW	PF (%)	19.9 (15.1–24.1)	36.4 (28.6–42.1)	43.9 (36.4–49.1)	47.8 (40.9–52.8)	53.5 (46.7–58.0)
Bellary –FSW	PF (%)	22.9 (14.4–29.2)	46.1 (31.9–56.5)	60.9 (48.0–71.1)	65.4 (52.4–75.3)	71.4 (59.3–80.5)
Bangalore Urban –FSW	PF (%)	21.2 (15.0–27.9)	42.2 (32.2–52.7)	54.2 (43.6–64.4)	57.4 (46.4–67.2)	67.3 (56.5–76.4)
B. Using control group 2[b]		**Over 1st year**	**Over 3 years**	**Over 5 years**	**To end of 2011**	**To end of Avahan (end of 2014)**
Mysore –FSW	PF (%)	15.6 (10.4–22.5)	31.7 (26.4–39.1)	42.6 (36.5–50.8)	49.2 (42.4–57.6)	56.2 (48.7–65.0)
	No	30 (19–47)	187 (126–272)	411 (273–592)	633 (409–926)	1004 (616–1476)
Clients	PF (%)	17.0 (11.1–24.3)	36.3 (30.4–46.2)	49.0 (42.3–57.8)	55.5 (48.1–64.3)	62.2 (54.1–70.9)
	No	70 (34–133)	475 (236–769)	1033 (502–1644)	1512 (706–2511)	2221 (994–3851)
Shimoga –FSW	PF (%)	15.8 (9.2–25.5)	33.7 (21.7–46.4)	48.3 (33.6–61.1)	55.4 (39.1–68.1)	65.7 (48.0–77.8)
	No	9 (5–18)	60 (32–99)	148 (80–257)	220 (120–406)	400 (218–769)
Clients	PF (%)	17.0 (10.4–26.6)	35.8 (23.3–47.9)	51.6 (36.9–63.5)	58.9 (43.6–71.0)	68.9 (53.2–80.6)
	No	58 (25–110)	356 (158–671)	835 (405–1566)	1228 (594–2506)	2189 (1004–4619)
Belgaum –FSW	PF (%)	17.8 (12.4–21.3)	29.8 (22.1–36.2)	34.1 (25.1–40.6)%	36.7 (27.0–43.7)	40.5 (29.4–48.3)
	No	23 (17–32)	115 (86–156)	206 (142–273)	276 (183–365)	393 (248–524)
Clients	PF (%)	21.5 (15.9–27.2)	38.9 (29.3–47.9)	43.4 (32.4–52.1)	46.0 (34.2–54.0)	49.4 (36.1–57.1)
	No	209 (138–352)	1047 (710–1697)	1791 (1129–2863)	2326 (1444–3678)	3216 (1989–4986)
Bellary –FSW	PF (%)	19.5 (11.8–26.7)	38.1 (24.1–49.1)	49.0 (32.8–62.1)	52.7 (35.6–66.4)	57.9 (39.3–72.2)
	No	27 (13–51)	161 (75–285)	343 (167–615)	444 (214–800)	633 (288–1098)
Clients	PF (%)	21.7 (12.9–28.4)	42.7 (27.7–52.3)	54.5 (38.5–66.4)	58.6 (41.4–70.9)	63.8 (44.6–76.1)
	No	257 (115–532)	1490 (605–3170)	3152 (1387–7465)	4106 (1748–9405)	5497 (2255–11 710)
Bangalore Urban –FSW	PF (%)	19.5 (13.6–27.8)	37.5 (27.6–52.5)	47.9 (37.5–63.5)	50.6 (40.1–66.2)	60.1 (47.2–75.1)
	No	93 (55–158)	536 (311–948)	1055 (574–2092)	1255 (660–2530)	2220 (1024–4822)
Clients	PF (%)	23.2 (16.3–31.7)	44.6 (32.9–59.1)	56.1 (44.5–70.3)	59.0 (47.3–72.8)	68.0 (56.8–81.0)
	No	295 (139–558)	1744 (722–3465)	3476 (1325–7506)	4104 (1517–8985)	6750 (2314–16 660)
C. Tp treatment only[c]		**Over 1st year**	**Over 3 years**	**Over 5 years**	**To end of 2011**	**To end of Avahan (end of 2014)**
Mysore –FSW	PF (%)	3.1 (1.0–7.5)	2.3 (–0.2–7.5)	2.4 (–0.2–8.2)	2.6 (–0.3–8.6)	2.7 (–0.5–9.4)
Shimoga –FSW	PF (%)	3.7 (0.3–7.8)	4.8 (0.3–10.1)	5.2 (0.3–11.4)%	5.3 (0.3–12.3)%	5.6 (0.3–13.6)
Belgaum –FSW	PF (%)	3.0 (1.0–6.3)	2.8 (0.4–6.4)	2.7 (0.1–7.2)	2.8 (0.0–7.8)	3.1 (–0.1–8.8)
Bellary –FSW	PF (%)	5.0 (2.1–9.1)	5.6 (1.8–12.0)	5.3 (1.4–13.2)	5.4 (1.3–13.4)	5.4 (1.4–13.2)
Bangalore Urban –FSW	PF (%)	3.5 (0.9–6.8)	3.9 (0.4–7.7)	4.0 (0.3–8.6)	4.0 (0.2–8.9)	4.3 (0.1–10.0)

CCU, consistent condom use; FSW, female sex worker; PF, prevented fraction.
[a]Prevented fraction, [number of new infections occurring between the start of Avahan (T1) and time T2 in absence of the intervention (I_1) minus the number of new infections between T1-T2 in presence of the intervention (I_0)] divided by I_1.
[b]Reflects the Impact of Syphilis (Tp) treatment and condom use.
[c]Reflects the Impact of Syphilis (Tp) treatment only – assumes same condom use as the 'estimated CCU trends' but no increase in Tp treatment due to Avahan – note that negative PF values are possible because in some instances, the more rapid syphilis treatment makes the latent people susceptible again that can increase syphilis incidence and prevalence over time and increase HIV incidence through the cofactor effect for HIV.
[d]All these projections assume constant condom use after the last round of Integrated Behavioural and Biological Assessment (IBBA) surveys (R2 in Shimoga and Bangalore, R3 in Mysore, Belgaum and Bellary).
[e]Impact estimates and 95% credibility intervals (95% CrI) were generated by using the projections from each posterior parameter set weighted by the likelihood of the model projection as explained in methods and supplementary material, Methods C, http://links.lww.com/QAD/A319.

Mysore and Bellary are consistent with large self-reported increases in condom use during Avahan ('estimated CCU trends'). The evidence was moderate for Bangalore and weaker for Belgaum. Thus, CCU increases following Avahan are likely responsible for most of the decline in FSW HIV prevalence in all districts, except Belgaum. In Belgaum, HIV prevalence may have declined without condom use increasing during Avahan, partly due to the natural dynamics of the epidemic and pre-Avahan increases in condom use because Avahan was not the first intervention. This highlights how models can help interpret HIV time trends more cautiously when evaluating an intervention's impact.

Our modelling analysis highlights the time required to substantially avert infections among HRGs. Across the four districts with stronger evidence (excludes Belgaum) for increasing condom use during Avahan and using a conservative counterfactual (Control 2), we estimated that 36–68% of new HIV infections were prevented among FSWs over 7 years (until 2011) compared to 9–28% and 22–53 over 1 and 3 years, respectively. Interestingly, up to 20% larger fraction of infections were averted among clients.

Given the 'real life' evaluation challenges faced (no randomized control groups, delayed baseline measurements), our results have limitations, which have been partly circumvented through our analytic approach. First, our 'estimated CCU trends' in presence of intervention were based on reconstructed CCU trends from self-reported behavioural data, which were liable to recall and social desirability biases [9]. However, our Bayesian modelling analysis showed that these 'estimated CCU trends' are generally more consistent with HIV prevalence trends than assuming no or slow increases in CCU, suggesting that these trends have some basis. Despite the modelling analysis suggesting that these increases in condom use partially caused the observed decline in HIV prevalence, it cannot directly attribute the CCU changes to Avahan without additional information (Supplementary material, Background section, http://links.lww.com/QAD/A319). Complementary process monitoring data collected as part of Avahan indicate that the intervention has been rapidly implemented and scaled up in Karnataka (Supplementary material, Box 1i, http://links.lww.com/QAD/A319) [10,11]. Consistent with our 'estimated CCU trends', additional evidence suggests that Avahan may have accounted for 88% of the abrupt increase in condom availability following the start of Avahan in these Karnataka districts (Supplementary material, Box 1ii, http://links.lww.com/QAD/A319) [36]. Importantly, analyses of R1 and R2 FSW behavioural data from Karnataka found a dose–response relationship between intervention exposure and self-reported condom use in commercial partnerships (Supplementary figure S4, http://links.lww.com/QAD/A319) [37]. In this dose–response analysis, the levels of CCU with occasional clients reported by those not in contact with the Avahan intervention were compatible with the CCU levels obtained from the average 'estimated CCU trends' around the time that Avahan started (Supplementary figure S3-S4, http://links.lww.com/QAD/A319). Together, these results suggest that much of the CCU increases can be attributed to Avahan, especially in districts where Avahan has remained the only HRG programme (Mysore, Shimoga).

To minimize model misspecification, the model structure was carefully developed to reflect important sources of observed behavioural heterogeneity, based on analyses of the key determinants of HIV infection in the IBBA surveys. Nevertheless, as with any modelling analysis, simplifying assumptions were made. As no data on sexual mixing were available for commercial sex work partnerships, we assumed random mixing between clients and FSWs. Although sexual mixing influences the spread of infection, its effect on intervention impact projections is more modest when models of high-risk populations are fitted to detailed HIV prevalence data [38]. In the absence of HIV incidence data, we fitted the model to FSW HIV prevalence data, and estimated infections averted using modelling. The modelled HIV incidence at the time of the first IBBA ranged between 2 and 12 per 100 person-years across districts, reflecting different intervention histories and condom use levels prior to Avahan, which is not directly comparable but is consistent with the only available HIV incidence estimate from Pune between 1993 and 2007 [39]. Our Bayesian framework allows to reflect parameter uncertainty in our impact estimates – using only one parameter set could have produced overly optimistic or pessimistic estimates. Finally, in validation experiments, our hypothesis testing methods showed good discriminating power to identify or reject increasing CCU trends when it is true or false, respectively, especially for districts with four IBBA rounds or where the ratio of fits exceeds one appreciably (Supplementary table S5, http://links.lww.com/QAD/A319).

Unfortunately, comparable data on HIV/STI prevalence and behaviour among FSWs over time were only available from intervention districts [3,8,14,15]. Given the lack of control group to indicate how condom use would have evolved without Avahan, we based our impact estimates on a conservative counterfactual, which assumed condom use would have increased at preintervention rates without Avahan. This is more conservative than assuming a stable condom use counterfactual as typically done. Despite the use of mapping and cluster random sampling, changes in the composition of the FSW population may have influenced the decline in HIV prevalence. However, we accounted for potential differences in two ways: by allowing the parameters for the frequency of commercial sex acts to change over time in the modelling analysis, and by accounting for other changes in key confounding factors by using adjusted HIV prevalence at the fitting stage. There was no evidence for a large reduction in FSW duration across IBBA rounds. We did not model ART because coverage was low during Avahan and unlikely to have influenced results.

Our analysis has several implications for future evaluations of HIV intervention programmes. Here, the Bayesian modelling approach was crucial for the success of the evaluation. Otherwise, the evaluation would have relied on trends in risk behaviour and HIV/STI prevalence from delayed IBBA surveys only. Our modelling analysis helped interpret trends and estimate impact while accounting for the natural dynamics of infection, past history of interventions, district-specific epidemiological contexts and uncertainty in the 'estimated CCU trends'. The use of models for hypothesis testing provided a mechanism to grade the strength of evidence for intervention impact.

Our results have important policy implications. The empirical and modelling results provide plausible evidence that condom use during commercial sex has increased during Avahan, and contributed to reducing HIV transmission between FSWs and clients in Karnataka. These assertions are strengthened by strong evidence for the successful implementation of the Avahan programme, and that increases in condom use among FSWs are associated with programme exposure. Our study supports the notion that HIV prevention programmes targeted at HRGs are feasible and can have considerable impact.

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Conflicts of interest

All authors report no conflicts of interest.

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