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Effectiveness of interventions for the prevention of HIV and other sexually transmitted infections in female sex workers in resource poor setting: a systematic review

Maryam Shahmanesh^{1,2}, Vikram Patel^{2,3}, David Mabey³ and Frances Cowan¹

- 1 Centre for Sexual Health and HIV Research, University College London, London, UK
- 2 Positive People, St Inez, Paniim, Goa, India
- 3 London School of Hygiene and Tropical Medicine, London, UK

Summary

OBJECTIVE To systematically review the evidence for effectiveness of HIV and sexually transmitted infection (STI) prevention interventions in female sex workers in resource poor settings.

METHOD Published and unpublished studies were identified through electronic databases (Cochrane database, Medline, Embase, and Web of Science), hand searching and contacting experts. Randomized-controlled-trials and quasi-experimental studies were included if they were conducted in female sex workers from low and middle income settings; if the exposure was described; if the outcome was externally measurable, it was after the discovery of HIV, and if follow-up was longer than 6 months. *A priori* criteria were used to extract data. Meta-analysis was not performed due to the heterogeneity of studies.

RESULTS Twenty-eight interventions were included. Despite methodological limitations, the evidence suggested that combining sexual risk reduction, condom promotion and improved access to STI treatment reduces HIV and STI acquisition in sex workers receiving the intervention. Strong evidence that regular STI screening or periodic treatment of STIs confers additional protection against HIV was lacking. It appears that structural interventions, policy change or empowerment of sex workers, reduce the prevalence of STIs and HIV.

CONCLUSION Rigorous evaluation of HIV/STI prevention interventions in sex workers is challenging. There is some evidence for the efficacy of multi-component interventions, and/or structural interventions. The effect of these interventions on the wider population has rarely been evaluated.

keywords HIV prevention, female sex workers, evaluation, resource poor settings, sexually transmitted infections, interventions

Introduction

The HIV epidemic continues to spread; 95% of the estimated 33 million people living with HIV reside in resource poor countries (UNAIDS 2007). Several systematic reviews have studied the effectiveness of HIV prevention strategies at both an individual and population level. One concluded that well designed condom promotion interventions targeting core-groups (groups with high rates of partner exchange) are effective (Merson *et al.* 2000). A Cochrane review of sexually transmitted infection (STI) control concluded that, with the exception of the trial of syndromic management of STIs in Mwanza(Grosskurth *et al.* 1995), there is limited evidence from randomized controlled trials (RCT) for STI control as an effective HIV prevention strategy (Sangani *et al.* 2004). A systematic review of STI prevention interventions found that just over

half of 41 interventions identified were effective at reducing STIs (Manhart & Holmes 2005). Authors of a systematic review of structural facilitators and barriers to HIV prevention suggest the need to address macro-social determinants of risk, such as economic policy, migration, gender inequality and sex work legislation (Parker *et al.* 2000).

Mathematical models suggest that targeting core-groups, such as sex workers (SWs), is an effective way to reduce HIV transmission, particularly in the early and accelerated phase of the epidemic (Aral & Blanchard 2002; Boily *et al.* 2002). Given the scale of sex work, with incomes equivalent to 2–14% of Southeast Asia's gross domestic product (Lin 1998), there is an urgent need to identify which interventions are effective in reducing HIV in SWs.

Two important position papers have sought to summarise key strategies for HIV prevention in SWs. One approached HIV as an occupational hazard, advocating

harm reduction strategies such as empowering SWs to use condoms and removing structural barriers to safety (Rekart 2005). The other examined strategies to provide STI treatment for SWs and concluded that, using presumptive periodic treatment (PPT) with single dose antibiotics, followed by regular algorithm-driven screening, was likely to be the most effective strategy (Steen & Dallabetta 2003). The effectiveness of either – harm reduction or STI treatment as an HIV prevention intervention – for SWs has not been systematically assessed. This paper presents the findings of a systematic review of the evidence for the effectiveness of HIV and STI prevention interventions, in female SWs, in resource poor settings.

Materials and methods

Inclusion criteria

Any intervention which intended to prevent HIV and STIs through targeting female SWs in resource poor settings, and which was evaluated in an experimental (RCT) or quasi-experimental (controlled but without randomly assigned control groups, or, time-series) study was eligible for inclusion. Study participants were limited to female SWs, defined as women who exchange sex for money or other gifts and commodities. Studies were only included if they reported at least one outcome measure that could be externally validated (Peterman et al. 2000; Zenilman 2005). This included biological outcomes (HIV incidence and/or STI incidence/prevalence), or measurable health outcome (e.g. condom disposal, health service utilisation). Studies were excluded if they targeted male and transsexual SWs, were conducted prior to the advent of HIV, were based in rich industrial countries, if the focus was harm reduction for injection drug use (IDU), the intervention was not adequately described, or if the duration was less than 6 months.

Search strategy

Databases searched are listed in Table 1. Medline and Embase were searched using the Key Mesh terms and text words (in italics): (Prostitution OR prostitut* OR 'sex work*') AND (HIV OR HIV infection OR HIV seroprevalence OR HIV OR sexually transmitted disease OR 'sexually transmitted infection'). The text words were used to search the other databases. A key non-indexed journal 'Research for Sex Work' (http://www.researchforsexwork.org) and references of review articles and selected studies were hand searched. Web sites of agencies involved in HIV-prevention (UNAIDS, Family Health International and Population Council) and conference abstracts (through Gateway, National Library of Medicine) were searched. First authors and experts in the field were contacted to obtain information on unpublished work, forthcoming manuscripts and research in progress. Unpublished studies and studies published in non-English languages journals were considered for inclusion.

Review methods

Titles and abstracts were entered into Reference Manager Professional Version 10 (ISI ResearchSoft, Philadelphia, USA) and screened in three stages using a ten-item checklist (Figure 1). Data from studies that met the inclusion criteria were extracted using a data collection form. Heterogeneity of interventions precluded a summary statistic of effectiveness. Instead, the qualitative results were summarized in tables categorized by main intervention focus and outcome. The interventions are classified according to the conceptual framework presented in Figure 2. The order in which the studies are reported in the tables reflects methodological vigour.

Results

Intervention characteristics

Of 6788 articles and 1318 abstracts (including duplicates) identified across databases, 1272 were related to HIV and STIs in female SWs in resource poor settings. Handsearching references and journals, searching websites and conferences and contact with experts identified a further 22 studies. The flow chart (Figure 1) shows that from the

Years Date last search Number of articles
Database searched performed identified

Table I Databases and years searched identified

Database	searched	performed	identined	
Cochrane controlled trial register and Cochrane database of systematic reviews	1998–2006	July 2006	41	
Embase	1980-2006	June 2006	1912	
Medline	1966-2006	June 2006	2175	
Web of Science	1984–2006	July 2006	2660	

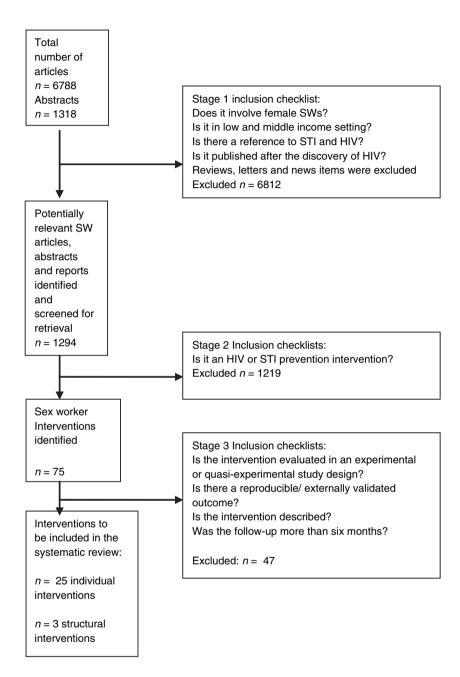


Figure 1 Flow chart: Selection of interventions for the systematic review.

relevant articles located, 26 published and two unpublished studies met the inclusion criteria.

Study populations

Twenty-five studies were conducted with SWs; one with couples (transactional and non-transactional sex partners) visiting a motel; two studied interventions with high-risk

women associated with mines and truck stops. Four studies evaluated the effect on clients.

Study settings

Sixteen (57%) of the studies were in Africa and the remainder were in Asia (n = 8) and Latin America (n = 5). Eleven (39%) were in dedicated SWs clinics; the remainder

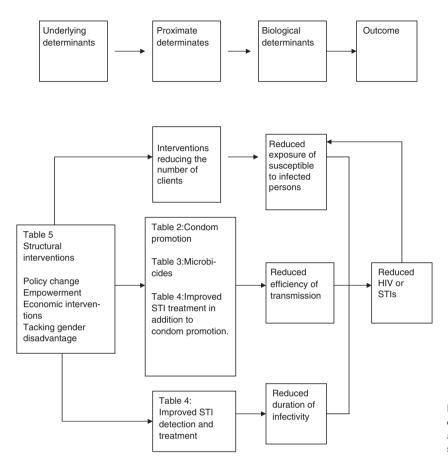


Figure 2 Conceptual framework for examining the interventions to prevent HIV and sexually transmitted infections in settings.

were conducted in brothels (n = 7), communities (n = 7), motels (n = 1) or truck stops (n = 1).

Study design

Eleven studies (39%) were RCTs, three of which were cluster-RCTs. Seventeen (61%) were quasi-experimental including uncontrolled before-and-after studies (n = 11), studies with a non-randomised control arm (n = 3), or a combination of both (n = 3).

Interventions evaluated

Seven studies (25%) evaluated interventions to increase condom use. Four (14%) evaluated the efficacy of the vaginal microbicide nonoxinol-9 (N-9). Fourteen (50%) evaluated a combination of a behavioural intervention and STI treatment, six of which were able to separate out the effectiveness of adding the STI treatment component. Three (11%) structural interventions were multifaceted, with improved STI care and an enabling atmosphere for

risk reduction either through community mobilisation or political/legal sanction.

Outcomes

Twenty-six (93%) studies assessed changes in incident or prevalent HIV or STIs, of which 12 measured HIV incidence. Other outcomes were verifiable measures of condom use such as provision, disposal or use with simulated clients (n = 4), and service utilisation (n = 2).

Summary of findings

There were only two RCTs which examined the effect of behavioural interventions combined with condom promotion (Table 2). In Madagascar, the addition of clinic based risk-reduction counselling to community based peer-counselling reduced incident STIs corresponding to increased self-reported condom use (Feldblum *et al.* 2005). An RCT in Nicaragua found that condoms placed in the rooms or handed to clients were more likely to be used than if made

available at reception. Paradoxically, condoms were less likely to be used in the presence of educational material in the rooms (Egger *et al.* 2000).

Two non-random-cluster-CT looked at the impact of peer education and condom provision in brothel-based SWs in India (Bhave et al. 1995) and Singapore (Archibald et al. 1994; Wong et al. 1998, 2004). They found reductions in incident HIV and STIs (India) and gonorrhoea (Singapore), which corresponded to increased condom use. Another non-random-cluster-CT compared three risk reduction sessions per 6 months to one and found a lower STI risk in the intervention arm that was not sustained over time (Ford et al. 2000a,b, 2002).

As for female controlled methods (Tables 2 and 3), one cluster-RCT with only 25% follow-up in Thailand (Fontanet et al. 1998) and one longitudinal study in Madagascar (Hatzell Hoke et al. 2007) examined the effect of adding female condoms to ongoing programmes. Both found a shift to female condom use, which only corresponded to a decrease in STI prevalence in Madagascar. Four placebo-controlled-RCTs examined different doses of the vaginal microbicide N-9 delivered in a variety of ways (Kreiss et al. 1992; Roddy et al. 1998; Richardson et al. 2001; Van Damme et al. 2002). They showed either no effect or an increased risk of HIV.

Treatment of bacterial sexually transmitted infections combined with behavioural interventions

Three RCTs (Table 4) tested the effectiveness of different STI treatment strategies for SWs, in two of which the primary outcome was incident HIV. The groups in Nairobi (Fonck *et al.* 2000; Kaul *et al.* 2002, 2004) and Benin/Ghana (Labbe *et al.* 2003) looked at the effect of PPT while the group in Cote d'Ivoire (Ghys *et al.* 2001) tested regular screening for STIs. Neither the Cote d'Ivoire nor the Nairobi studies found a difference in HIV incidence between the arms. In Cote d'Ivoire the follow-up was less than 50%. The study of PPT in Nairobi was the only one that reported significant reductions in bacterial STIs in the intervention arm.

A quasi-experimental study of PPT in South Africa found reductions in STIs in SWs after the introduction of the intervention and an inverse relationship between distance from intervention and genital ulcer disease in miners (Steen et al. 2000). Only one of three women were followed-up over the 9 months. An intervention in Nicaragua found that STI treatment vouchers, redeemable at quality approved clinics led to significant drops in STIs in the SWs. This intervention, which in effect provided presumptive treatment to half of the known SWs, showed more substantial reductions in prevalence of STIs if the rounds of voucher

distribution were less than 6 months apart (Borghi *et al.* 2005; Gorter *et al.* 2005; McKay *et al.* 2006). A cluster-RCT of STI delivery systems found that high-risk women at truck-stops preferred dedicated outreach clinics to primary health care centres (Nyamuryekung'e *et al.* 1997).

Four cohort studies examined the effect of regular STI screening, peer education and condom promotion. In Zaire (Laga *et al.* 1994) and Nairobi (Ngugi *et al.* 1988, 1996) they examined the effect on incident HIV while in Peru (Sanchez *et al.* 2003) and China (Ma *et al.* 2002) the primary outcome was incident STIs. Only the Chinese cohort reported the loss to follow-up, which was 50%. All interventions showed an increase in self reported condom use that corresponded with a reduction in incident HIV and/or STIs.

Four studies from Cote d'Ivoire (Ghys et al. 2002), Benin (Alary et al. 2002), Bolivia (Levine et al. 1998) and South Africa (Williams et al. 2003) compared the situation before and after introducing similar combinations of peer education, condom promotion and regular STI care. In South Africa this was part of a larger intervention that also targeted miners and youth. Only Cote d'Ivoire and Bolivia reported their response rates, which were 90% and 80% respectively. Bacterial STI prevalence dropped in all sites except for South Africa where it paradoxically rose despite increased condom use.

Structural interventions

The best described structural intervention has been the Thai 100% condom programme (Hanenberg et al. 1994; Rojanapithayakorn & Hanenberg 1996; Visrutaratna et al. 1995; Table 5). The countrywide, government led project improved access to affordable STI treatment, and increased condom use through changing social norms and imposing sanctions on dissident sex work establishments. Although there is no control group, various indicators suggest an impact, namely increased condom supply, an 80% reduction in the five major STIs in men (Hanenberg et al. 1994), and a tenfold decrease in STI incidence in new military recruits (Nelson et al. 1996; Celentano et al. 1998). The same magnitude of effect could not be demonstrated in SWs (Kilmarx et al. 1998, 1999).

Another well-described structural intervention was the empowerment of SWs in the Sonagachi red-light area (Table 6). Politicised and empowered SWs created an environment conducive to condom use and improved STI care through collective bargaining with structures of power (police, brokers and brothel-owners). Again without a control arm, the impact of the intervention cannot be quantified; however, HIV prevalence among the SWs of Sonagachi remains in single figures compared with

Place Study design Year Outcome	Study design Outcome	Population Sample	Duration Response rate/follow-up (%)	Intervention	Results*,†
Incident HIV India 1991–1993 (Bhave <i>et al.</i> 1995)	Cluster non-random – CT Incident HIV Syphilis Hep BsAg	N = 2 areas in red-light district $n = 541$ SW & 37 brothel owners	6 months ?/97%	(I) IEC, peer risk reduction counselling, condom promotion (C) No intervention	HIV incidence: (I) 0.05/100 py; (C) 0.16/100 py HIV incidence
Sexually transmitted infection Madagascar 2001 (Feldblum <i>et al.</i> 2005)	on Single blind RCT Incident STIs	N = 1000 SW Stratified by city	6 months ?/90	(I) Clinic-based + community-based peer risk reduction counselling (C) Community-based counselling only	Aggregate STIs OR 0.7 (0.5–0.9) Gonorrhoea OR 0.7 (0.3–1.0) Chlamydia OR 0.7 (0.5–1.0) Trichomonas OR 0.8
India 1991–1993 (Bhave <i>et al.</i> 1995)	Cluster non random – CT Incident HIV Syphilis	N = 2 areas in red-light district n = 541 SW & 37	6 months ?/97%	(I) IEC, peer risk reduction counselling, condom promotion	(0.6–1.2) Syphilis RR 0.36 (p 0.002) Hep B sAg RR 0.27 (0.001)
Singapore 1994–2002 (Archibald <i>et al.</i> 1994; Wong <i>et al.</i> 1998; Wong <i>et al.</i> 2004)	riep bsAg Before and after study Gonorrhoea rates	brothel based $N = 2.737$ old SW and 1986 new SW	8 years 100/60	(C) No mervention (I) Peer risk reduction counselling, condom promotion, IEC material, and deregistration of brothels with high STI rates (C) None (Roch arms mandatory	Gonorrhoea reduced from >30–45/1000 person months to <5/1000 person months Gonorrhoea RR 0.11–0.17
Bali 1997–1998 (Ford <i>et al.</i> 2000a; Ford <i>et al.</i> 2002)	Cluster non-random controlled trial STI incidence	N = 7 $n = 1566 SWs$	24 months ?/50% turn over per 6 months	(Dott) after the state of the sessions in 6 months (C) One risk reduction session in 6 month (Peer counselling and condom promotion in both arms)	Gonorrhoea OR 0.53 (0.33–0.83) Chlamydia OR 0.63 (0.40–0.99) Trichomonas OR 0.91 (0.46–1.81) STIs reduced in both arms and the differences between high and low effort areas declined over

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Table 2 (Continued)

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retrieval OR 1.3 (1.03-1.6) of the final condom use. Presence of IEC material: accounting for 20% To couples: Condom OR 0.7 (0.58-0.86) In rooms: Condom Condom retrieval Aggregate STIs adj Aggregate STI RR 0.76 (0.50-1.16) Female condoms 1.3 (1.09-1.75) Female condoms were used 12% retrieval OR of the time Results*,† and male condom promotion to couple as they registered I.ii) Condoms were handed B. (I) IEC material in room risk reduction counselling C) Condoms available on A. (I.i) Condoms were (I) Addition of female demand at reception condom to ongoing placed in the room Addition of female C) Male condom Intervention rate/follow-up (%) motel 53/48‡ 24 days per 24 weeks ?/26 18 months Duration Response 3/82% n = 6463 couples Research clinic Brothel N = 71N = 19 motels n = 548 SWsPopulation N = 1000**Brothels** Used condoms retrieved Before and after study Cluster RCT with Factorial design Study design from rooms Cluster RCT Incident STI Incident STI Outcome Madagascar 2001-2003 Thailand, 1994-1995 (Fontanet et al. 1998) (Hatzell et al. 2007) (Egger et al. 2000) Nicaragua 1990 Condom disposal Place Year

SW, sex worker; STI, sexually transmitted infection; RCT, randomised controlled trial; IEC, information and education campaign; I, intervention arm; C, control arm; OR, *Where possible RR are calculated from data presented in the papers. Unless otherwise stated RR and OR are quoted for Intervention arm compared with control. odds ratio; adiOR, adjusted odds ratio; RR, risk ratio; adiRR, adjusted risk ratio.

OR 0.89 (0.84-0.94)

C) No IEC in room

†Numbers in brackets following OR and RR are the 95% confidence intervals.

Percentage of all the motels approached who agreed to participate/percentage of condoms distributed that was retrieved.

Table 3 Vaginal microbicides

Place Year	Study design Outcome	Population Sample	Duration Response rate/ follow up (%)	Intervention	Results
Incident HIV Benin, Cote d'Ivoire, South Africa & Thailand 1996–2000		STI clinics and truck stops $N = 765 \text{ SW}$	48 weeks 76/68	(I) 52.5 mg: nonoxinol-9 vaginal gel	HIV incidence adiRR 1.5 (1.0–2.2) HIV incidence (>3.5 applications per day)
(van Danme et al. 2002) Cameroon 1994–1996 (Roddy et al. 1998)	Genital testons Double blind RCT Incident HIV Incident STI	N = 1170 SWs	21 months 65/73	(I) 70 mg nonoxinol-9 film (C) Identical placebo	TRR 5.3 (2.1–5.0) HIV incidence RR 1.0 (0.7–1.5)
Kenya 1987–1990 (Kreiss <i>et al.</i> 1992)		Research clinic N = 138 SWs	14–17 months 100/84	(I) 1000 mg nonoxinol-9 vaginal sponge (C) non-identical placeho	HIV incidence ^{adj} RR 1.6 (0.8–2.8) Genital lesions RR 3.3 (<i>P</i> < 0.001).
Kenya 1996–1998 (Richardson <i>et al.</i> 2001)	Double blind RCT Incident HIV Incident STIs	Research cohort $N = 278$	19 months ?/69	(I) 52.5 mg nonoxinol-9 gel (C) Placebo	HIV incidence RR 0.75 (0.37-1.53)
Sexually transmitted infection Benin, Cote d'Ivoire, South Africa & Thailand 1996–2000	Triple Blind RCT Incident HIV Incident STI Geniral Jesions	STI clinics and truck stops $N = 765 \text{ SW}$	48 weeks 76/68	(I) 52.5 mg: nonoxinol-9 vaginal gel (C) Identical placebo	Gonorrhoea ^{adi} RR 1.2 (0.9–1.6) Chlamydia ^{adi} RR 1.2 (0.8–1.6)
Cameroon 1994–1996 (Roddy et al. 1998)		N = 1170 SWs	21 months 65/73	(I) 70 mg nonoxinol-9 film (C) Identical placebo	Gonorrhoea RR 1.1 (0.8–1.4) Chlamydia RR 0.9 (0.7–1.3)
Kenya 1987–1990 (Kreiss <i>et al.</i> 1992)	Un-blinded RCT Incident HIV	Research clinic N = 138 SWs	14–17 months 100/84	(I) 1000 mg nonoxinol-9 vaginal sponge	Gonorrhoea $^{\text{adj}}$ RR 0.4 ($P < 0.001$)
Kenya 1996–1998 (Richardson <i>et al.</i> 2001)	Double blind RCT Incident HIV Incident STIs	Research cohort $N = 278$	19 months ?/69	(I) 52.5 mg nonoxinol-9 gel	Gonorrhoea RR 1.8 (1.0–3.1) Chlamydia RR 1.4 (0.6–3.1) Trichomonas RR 0.8 (0.5–1.3)

SW, sex worker; STI, sexually transmitted infection; RCT, randomised controlled trial; IEC, information and education campaign; I, intervention arm; C, control arm; OR, odds ratio; ^{adj}OR, adjusted odds ratio; RR, risk ratio; adjusted risk ratio.

Place Year	Study design Outcome	Population Setting	Duration Response rate/follow-up (%) Intervention	Intervention	Results
Incident HIV Cote d'Ivoire 1994–1997 (Ghys et al. 2001)	RCT Incident HIV Incident STI	SW clinic $N = 542$	42 months 45/42	(I) Monthly genital examination, microscopy & treatment (C) Examination and treatment only when symptomatic (Peer education & condom promotion both arms)	HIV incidence (I) 5.3/100 py (C) 8.5/100 py (P = 0.5) HIV incidence RR 0.62 (0.5) HIV reductions in BOTH arms ^{adj} RR 0.42 (0.18–0.96). Women attending 80% of scheduled clinic visits less likely
Kenya 1998–2002 (Fonck <i>et al.</i> 2000; Kaul <i>et al.</i> 2002, 2004)	Double blind placebo controlled RCT Incident HIV Incident STI	N = 466 SWs	969 person years 89/73	(c) Monthly presumptive treatment with 1 g azithromycin (c) Placebo (Peer education & condom promotion hoth arme)	To seroconvert T = 0.04 HV incidence (I) 4/100 py & (C) 3.2/100 py HIV incidence RR 1.2 (0.6–2.5)
Zaire 1988–1991 (Laga <i>et al</i> . 1994)	Longitudinal cohort Incident HIV Incident STI	Dedicated SW clinic $N = 531$	36 months ?/?	Promotion com arms) Monthly STD screen & treat 3 monthly voluntary counselling and HIV testing & risk reduction counselling Peer education & condom promotion	HIV incidence rates dropped from 11.7/100 py to 4.4/100 py HIV incidence RR 0.4 (<i>P</i> 0.003) HIV incidence in irregular compared with regular clinic attendes RR 6.3
Kenya 1985–1986 Longitudinal coh (Ngugi et al. 1988, 1996) Non-random CT Incident HIV Incident STI	Longitudinal cohort & Non-random CT Incident HIV Incident STI	Cohort (1985) $N = 595$: (I.1) $N = 91$ SW (I.2) $N = 67$ SW (C)New recruits (1986) $N = 205$	1–23 months ?/?	(1.1) Peer education, condom promotion, 6 monthly group risk reduction counselling, and individual counselling. (1.2) As above without individual counselling (C) Recent recruits before any intervention groups also received periodic STI screening	Reported condom use was associated with reduced incident HIV OR 0.34 (0.13–0.92) Condom use (I.1) 78%, (I.2) 64% and (C) 52%
Sexually transmitted infection Cote d'Ivoire 1994–1997 (Ghys <i>et al.</i> 2001)	RCT Incident HIV Incident STI	SW clinic $N = 542$	42 months 45/42	or treatment when symptomatic) (I) Monthly genital examination, microscopy & treatment only when symptomatic [Peer education & condom promotion both arms]	No significant difference between STI incidence

Table 4 (Continued)					
Place Year	Study design Outcome	Population Setting	Duration Response rate/follow-up (%)	Intervention	Results
Kenya 1998–2002 (Fonck <i>et al.</i> 2000; Kaul <i>et al.</i> 2002, 2004)	Double blind placebo controlled RCT Incident HIV Incident STI	N = 466 SWs	969 person years 89/73	(I) Monthly presumptive treatment with 1 g azithromycin (C) Placebo (Peer education & condom promotion both arms)	Gonorrhoea RR 0.46 (0.31–0.68) Chlamydia RR 0.38 (0.26 to 0.57) Trichomonas RR 0.56 (0.40–0.78) No significant reductions in the incidence of Sentilia
Benin and Ghana 2001–2002 (Labbe <i>et al</i> . 2003)	Double blind placebo controlled cluster RCT Incident STI	18 clusters $N = 384$ SW, $N = 706$ clients $N = 252$ SW, $N = 1073$ clients Individual randomisation $N = 181$ SW	9 months ?/80	(I) Presumptive periodic treatment azithromycin 1 g first month and Ciprofloxacin 500 mg given second and third month. Cycle repeated (C) placebo (Peer education & condom promotion both amen.	In the includence of syphinis Gonorrhoea RR 0.78 ($P = 0.37$) Chlamydia RR 1.9; ($P = 0.77$) No significant difference in STI incidence in clients There was a drop in generrhoea in both groups often analyzant
South Africa 1996–1997 (Steen et al. 2000)	Before and after study of SWs and miners Non-random control group distant from intervention Prevalence of STIs	Mobile SW clinic $N = 407 \text{ SWs}$ $N = 608 \text{ & } N = 928$ miners	9 months ?/32	promotion both arms) (I) Monthly presumptive periodic treatment 1 g azithromycin to SWs (Condom promotion & IEC)	FSWs Gonorrhoea & chlamydia RR 0.24 (P < 0.001) Genital ulcer disease RR 0.17 (P < 0.001) Miners Gonorrhoea & chlamydia RR 0.6 (P < 0.001) Genital ulcer disease RR 0.22 (P < 0.001) Inverse relation between attending mine clinic with a genital ulcer and distance to intervention (p
Nicaragua 1995-2004 (Borghi <i>et al.</i> 2005; Gorter <i>et al.</i> 2005; McKay <i>et al.</i> 2006)	Observational study of time trends repeat cross sectional studies Service utilisation STI prevalence	Community based N = 1500 SW	9 years 50% vouchers utilised/na	distributed for free STI treatment at designated clinics. The package consists of presumptive treatment with azithromycin 1 g, screening for syphilis, trichomonas, candid, bacterial vaginosis and cervical cytology	tor trend 0.002). Aggregate STIs RR 0.5 Annual drop: Gonorrhoea (8%), Trichomonas (9%), & syphilis (16%) Optimal gap for voucher distribution <6 months

Table 4 (Continued)					
Place Year	Study design Outcome	Population Setting	Duration Response rate/follow-up (%)	Intervention	Results
Zaire 1988–1991 (Laga <i>et al.</i> 1994)	Longitudinal cohort Incident HIV Incident STI	Dedicated SW clinic $N = 531$	36 months ?/?	Monthly STD screen & treat 3 monthly voluntary counselling and HIV testing & risk reduction counselling	Incidence of all STDs except chlamydia decreased over 3 years (<i>P</i> < 0.01)
Kenya 1985–1986 (Ngugi <i>et al.</i> 1988, 1996)	Longitudinal cohort & Non-random CT Incident HIV Incident STI	Cohort (1985) N = 595: (I.1) N = 91 SW (I.2) N = 67 SW (C) New recruits (1986) N = 205	1–23 months ?/?	(I.1) Peer education, condom promotion, 6 monthly group risk reduction counselling, and individual counselling (I.2) As above without individual counselling (C) Recent recruits before any intervention (Intervention groups also received periodic STI screening or treatment	Annual gonorrhoea rate woman RR 0.23 (<i>P</i> < 0.001) Decline in men attending STI clinic in intervention site compared to non-intervention site (<i>P</i> < 0.001)
Peru 1994–1995 (Sanchez <i>et al.</i> 2003)	Longitudinal cohort Incident STI	N = 917 SW	22 months 95/?	when symptomatic) Risk reduction counselling, condom promotion and monthly STI screen and treat	Chlamydia ^{adi} OR 0.47 (0.28– 0.79.) Gonorrhoea ^{adi} OR 1.16 (0.61–2.3) Trichomonas ^{adi} OR 0.19
China 1998–1999 (Ma <i>et al.</i> 2002)	Longitudinal cohort Incident STI	N = 966	6 months ?/53	Risk reduction counselling 2 monthly STI screen and treat	(0.09-0.37) Gonorrhoea RR 0.3 (0.11-0.75) Trichomonas RR 0.14 (0.04-0.45) Chlamydia RR 0.24 (0.14-
Cote d' Ivoire 1991–1997 (Ghys <i>et al.</i> 2002) Benin 1993–1999 (Alary <i>et al.</i> 2002)	Before & after repeat cross-sections HIV Prevalence STI Prevalence Before & after repeat cross-sections HIV Prevalence STI Prevalence	Community based $N = 5218$ $N = 374$ $N = 365$ $N = 591$	6 years 90/na 6 years ?/na	Peer education & IEC & condom promotion Voluntary counselling and HIV testing & STI care Peer education & IEC & condom promotion Monthly STI screen & treat	Gonorrhoea RR 0.3 (P < 0.001) Syphilis RR 0.1 (P < 0.001) Syphilis adiOR 0.24 (0.09– 0.56) Gonorrhoea adiOR 0.47 (0.39–0.65)

Place Year	Study design Outcome	Population Setting	Duration Response rate/follow-up (%)	Intervention	Results
Bolivia, 1992–1995 (Levine <i>et al.</i> 1998)	Before & after Repeat cross-sections STI prevalence	Brothel based $N = 508$	3 years 80/na	Periodic STI screen & treat Condom promotion Clinic based individual counselling	Gonorrhoea RR 0.6 (P < 0.001) Syphilis RR 0.4 (0.02) Genital ulcer disease RR 0.8 (P < 0.006)
South Africa 1998–2000 (Williams <i>et al.</i> 2003)	Before & after cross-sections STI prevalence	SW $N = 121 \& N = 93$ Stratified random sample of men, women & miners $N = 899$ & $N = 769$	2 years ?/na	Community level intervention: Peers educators from SW, Mine workers & youth. Condom promotion Train health care workers in syndromic STI management Monthly presumptive treatment with azithromycin	Miners Chlamydia adiOR 4.23 (<i>P</i> < 0.001), Gonorrhoea 2.61 (<i>P</i> < 0.001), Syphilis (RPR) 1.57 (<i>P</i> = 0.02) Men Chlamydia adi OR 3.54 (<i>P</i> < 0.001) Women Chlamydia adi OR 1.88 (<i>P</i> < 0.001) Syphilis adiOR 2.06 (<i>P</i> < 0.001)
Service uptake Tanzania 1993–1994 (Nyamuryekung'e et al. 1997)	Cluster RCT Service utilisation	N = 7 truck stops $n = 330$ high risk women	12 months ?/na	Different STI treatment delivery: (I.1) Primary Health Care worker led outreach clinic twice per week (I.2) Primary Health Clinic with STI drugs (I.3) Doctor led outreach clinic every 3 months (C) Primary Health clinic without STI drugs (Standard of care)	Intervention (1) 1.43 visits/woman Intervention (2) 1 visit/woman Intervention (3): 1.23 visits/woman Control: 0.4 visits/woman

SW, sex worker; STI, sexually transmitted infection; RCT, randomised controlled trial; IEC, information and education campaign; I, intervention arm; C, control arm; OR, odds ratio; **adjOR*, adjusted odds ratio; **RR, risk ratio; **adjusted risk ratio;

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Table 4 (Continued)

Table 5 Structural interventions (Thailand)

Country, Year	Primary intervention	Study population	Study design Outcome variables	Results
Thailand (Hanenberg et al. 1994; Rojanapithayakorn & Hanenberg 1996) 1989–1994	100% condom program: Government led supply of condoms to SW establishments Sanctions for brothels fail to adhere to 100% condom Large scale media campaign targeting male clients to use condoms with SWs Increased number of STI clinics Free weekly STI tests for SW	Country wide	HIV surveillance data from blood donors, pregnant women, SWs, male STI clinic attendees, 21-year-old army conscripts Statistics on the SW establishments from male STI clinic attendees and annual field surveys STI clinic attendees and annual field surveys and hospital out patient departments. Condoms procured by the government and distributed Condoms sold to retailers	Condom use in commercial sex establishment increased from 14 to 94% Government supplied condoms for 70% of SW and private sector for 50% (1992) Five major STDs decreased by 79% in men
Thailand (Visrutaratna et al. 1995) 1989–1992	Pilot for 100% condom program Superstar peer-educators Condom promotion Model brothel Encourage peer pressure amongst brothel owners Supply free condoms Cost benefit for brothel owners	500 brothel based sex workers in Chiang Mai	Before and after X-section Participation in intervention Before and after behaviour data Refusal of simulated client w/o condom	Participation up to 100% of identified female SWs No decline in clients or net income Before intervention 40% refused sex without condom After 90% refused simulated client after 2 months and around 80% after one year
Thailand (Nelson <i>et al.</i> 1996; Celentano <i>et al.</i> 1998) 1991–1995	100% condom programme STD treatment at baseline Incident STDs treated	2417 and 1669 military conscripts in the north of Thailand (random 19–23 year olds as selected by lottery) 90% contribute person time to the analysis. 70% followed up 24 months	Comparing two Cohorts Six monthly surveys HIV incidence STD incidence Sexual behaviour	10 fold decrease in STD incidence between 1991 cohort and 1993 cohort from 17/100 py to 1.8/100 py (<i>P</i> < 0.0001) HIV incidence from 2.48/100 py to 0.55/100 py RR 0.22 (<i>P</i> < 0.0001) Brothel visits down from half to 1/3 Inconsistent condom use with SWs down from 14% to 2.5% (<i>P</i> < 0.0001)
Thailand (Kilmarx <i>et al.</i> 1998, 1999) 1991–1994	100% condom use program:	Brothel based female sex workers over 16 and Thai nationals $N = 500$ 16% loss to FU	Cohort study – before and after intervention HIV incidence STD incidence	adjRR for incident HIV brothel based c.f. non-brothel based 7.3 CI 2.5 to 21.9 (p 0.05) Brothel based higher HIV incidence throughout

SW, sex worker; adjusted risk ratio; STI, sexually transmitted infection.

 Table 6
 Structural interventions (Sonagachi)

Country, Year:	Primary intervention	Study population	Study design Outcome variables	Results
India, Calcutta (Chakraborty et al. 1994; Das et al. 1994; Jana et al. 1994, 1998, 2004; Pal et al. 1994; Jana & Singh 1995) 1991–now	Sonagachi (red-light area wide) project: (i) Empowerment: through self organisation of SWs (ii) Defining and tackling needs, legal advice, child immunisation, literacy and HIV prevention (iii) Collective bargaining with prolice, harders and broads.	Women living in Sonagachi	Cross sectional surveys Surveillance data for STIs and HIV	Collective represents 60 000 SWs HIV prevalence in SWs has remained at <10% which is three to tenfold less than SWs elsewhere in India, e.g. Mumbai. Since 1992 drop in Trepanoma Pallidum hemagglutination assay (TPHA) from 63 5% to 17%
Sonagachi vs. NACO (Gangopadhyay et al. 2005) 2003	owners in HIV prevention (iv) Condom promotion (v) Improved STI treatment (I) As above (C) Condom promotion & IEC & peer education	(I) Stratified random sample of 200 brothel based SW in Sonagachi N = 173 (87% response rate) (C) All SW from neighbouring area N = 169 (65% response rate)	Non-random CT Outcome measures Behaviour and a combined clinical and laboratory diagnosis of STIs	Significant baseline differences between intervention and control arms Sonagachi women had significantly better health seeking behaviour and optimism scores No difference in bacterial STIs.

SW, sex worker; STI, sexually transmitted infection; RCT, randomised controlled trial; IEC, information and education campaign; I, intervention arm; C, control arm; OR, odds ratio; **adjOR*, adjusted odds ratio; **RR, risk ratio; **adjusted ratio

prevalences of over 50% reported from similar settings elsewhere in India. A three- to fivefold reduction in prevalent STIs was documented (Chakraborty *et al.* 1994; Das *et al.* 1994; Jana *et al.* 1994, 1998, 2004; Pal *et al.* 1994; Jana & Singh 1995). There has been one quasi-experimental study comparing Sonagachi with neighbouring brothels; but marked baseline differences, particularly higher client numbers in Sonagachi, limit interpretation of the finding of no difference in STI prevalence (Gangopadhyay *et al.* 2005).

There has been one controlled study of a structural intervention combining elements from both the group empowerment model of Sonagachi and the political sanctions of Thailand (Table 7). The study, conducted in 68 brothels in two cities in the Dominican Republic, compared the addition of regional policy change, which penalised the brothel management for failing to enforce 100% condom use, against an intervention that combined SW solidarity, environmental cues for condom use, improved STI care, and self-regulation of the brothels. There were greater reductions in STI prevalence and a corresponding increase in likelihood of rejecting unsafe sex in the city where, the 100% condom use policy was in force. Condom use increased in individual SWs and was associated with reduced incident STIs in both arms of the study. However, the likelihood of a brothel adhering to the 100% condom use programme was 10% greater in the policy change area (Kerrigan et al. 2003, 2006).

Discussion

To the best of our knowledge, this is the first systematic review of HIV and STI prevention interventions in female SWs in resource poor countries. Although there were a considerable number of descriptive studies of sex work in resource poor settings, we only identified 28 that evaluated interventions with externally measurable outcomes. Less than half of these were RCTs, the robustness of which was compromised by very high attrition rates. We identified four broad categories of intervention: behavioural interventions with condom promotion, addition of vaginal microbicide, addition of STI treatment, and structural interventions. The small number of methodologically rigorous studies reflects the considerable challenges of studying this group. The diversity in type of intervention, study design, and outcome measures made calculation of a summary measure of effectiveness inappropriate.

What interventions worked?

Risk reduction counselling coupled with condom promotion reduced HIV or STI risk or increased condom use in all the five studies that tested this hypothesis (Bhave et al. 1995; Egger et al. 2000; Ford et al. 2003; Wong et al. 2004; Feldblum et al. 2005). Additional support for the effectiveness of condom promotion comes from observed reductions in HIV incidence in both arms of STI treatment RCTs (Ghys et al. 2001; Kaul et al. 2004) and the relationship between increases in self reported condom use and reductions in infections in two of the cohorts (Ngugi et al. 1988; Laga et al. 1994). Despite the methodological limitations of these studies, the consistency of the direction of change, the dose response, the association between participation in the intervention, self-reported condom use and reduced infection rates, and biological plausibility suggest that this is an effective strategy.

Two studies assessed female condom promotion and showed an increase in female condom uptake (Fontanet et al. 1998; Hatzell Hoke et al. 2007). There is only weak evidence from the before and after study of related reductions in STI incidence (Hatzell Hoke et al. 2007). N-9 did not reduce HIV incidence and a meta-analysis of all N-9 studies found a relative risk for HIV of 1.12; CI 0.88–1.42 (Wilkinson et al. 2002). Trials of other microbicides are under way.

The two RCTs of PPT and regular screening of STIs were unable to prove the hypothesis that STI treatment in SWs will reduce HIV acquisition (Ghys *et al.* 2001; Kaul *et al.* 2004). The failure of two of the RCTs to show an effect of presumptive treatment or regular screening on STI rates may be explained by a type 2 error (loss of power from sizable reductions in STI rates in the control as well as intervention arms) (Ghys *et al.* 2001; Labbe *et al.* 2003). The RCT that did show an effect of presumptive treatment on STI rates detected this sample size problem and lengthened the enrolment period accordingly (Kaul *et al.* 2002, 2004).

One quasi-experimental study suggests that increasing the interval between rounds of PPT may lessen its impact on STI prevalence (Gorter *et al.* 2005). Other studies also suggest that the effect of presumptive treatment is short lived (Behets *et al.* 2005; Cowan *et al.* 2005a). The effectiveness of the Nicaraguan voucher system in enabling nearly half of the SWs countrywide to access STI health services (Gorter *et al.* 2005) and the preference for outreach services in truck-stops (Nyamuryekung'e *et al.* 1997) suggests that innovative outreach services may improve the coverage of dispersed and clandestine SWs.

100% condom use programme was a countrywide multicomponent intervention that sought to increase condom use, reduce the number of commercial sexual encounters and improve provision for STI treatment. It is impossible to disentangle the relative importance of the different components of the intervention from each other, or secular

Table 7 Structural interventions (Dominican Republic)

Country Year	Primary intervention	Study population	Study design Outcome variables	Results
Dominican Republic (Kerrigan et al. 2006) 1999–2000	(C) Brothel-based intervention: (1) Solidarity through regular meetings between SWs & management (2) Environmental cues for condoms (3) Improved clinical care through liaison & training for the government's mandatory monthly STI screens (4) Monitoring and reporting the performance of the brothels (1) In addition to 1–4 above: Policy and regulation: regional policy made condom use between clients and SWs mandatory & implementation the brothel owners and management's responsibility. This policy was enforced through a mixture of support and sanctions.	(C) Santa Dominga (34 brothels) (I) Puerto Plata (34 brothels) Participatory observations at all brothels Cross-sectional survey before and after intervention <i>n</i> = 200 SWs per city (recruited from the mandatory government STI clinics-every third SW on a designated day) Response rate 95%.	Before and after X-sectional studies Non-random comparison: STI Condom use Rejection of unsafe sex Number of establishments without STIs per month Exposure to intervention	Decrease in STIs was only significant in intervention arm (1) adj OR 0.50; CI 0.32 to 0.78 (C) adj OR 0.60; CI 0.32 to 1.03 (I) Increased proportion of brothels with no new STIs OR 1.20; CI 1.0 to 1.31 (I) Increased rejection of unsafe sex adj OR 3.86; CI 1.96 to 7.58 Observed adherence to the intervention was significantly associated with reduced STIs adj OR 0.52; CI 0.35 to 0.78 Adherence increased at an individual level in both arms (P < 0.001) Adherence at an establishment level only increased in intervention arm adj OR 2.50 (I) 1.35 (I) 1.2; CI 1.11 to 1.3

SW, sex worker; STI, sexually transmitted infection; RCT, randomised controlled trial; IEC, information and education campaign; I, intervention arm; C, control arm; OR, odds ratio; **adjOR*, adjusted odds ratio; **RA, risk ratio; **adjusted risk ratio;

trends. The observational data from the Sonagachi Project suggest that empowering SWs may reduce their HIV and STI risk. However, the reproducibility of this approach remains unproven (Basu *et al.* 2004). The Dominican Republic attempt to disentangle the relative effects of policy and empowerment suggests that while pressure to create 'model brothels' through self-regulation resulted in a decrease in STIs, there was a greater effect in the city where the 'model brothel' was enforced through policy (Kerrigan *et al.* 2003).

Potential biases of the review process

Given the heterogeneity of the study designs, a funnel plot for publication bias was not done; however there is likely to be publication bias. While some RCTs were unable to show an effect, almost all quasi-experimental studies reported statistically significant findings in favour of the intervention being tested.

Interventions not published in peer reviewed journals are under-represented (Hopewell *et al.* 2007). Even within the grey literature there is potential for selection bias, as interventions funded or sanctioned by the larger donors are more likely to be accessed through UNAIDS, FHI or Population Council reports and best practice publications. As in all systematic reviews, despite extensive hand searching, there is still the possibility of indexing bias (Hopewell *et al.* 2002).

The review was restricted to evaluated interventions that had externally validatable outcome measures of effectiveness. This may have excluded less rigorously evaluated but nevertheless important and potentially effective interventions (Wilson *et al.* 1990; Chipfakacha 1993; Asamoah-Adu *et al.* 1994; Nairne 1999; Ganasinghe 2000; Campbell & Mzaidume 2001). However, self reported measures of, for example, condom use are unreliable and were therefore excluded from this review (Peterman *et al.* 2000; Zenilman 2005).

A limitation of this systematic review is that only interventions that involved women who exchange sex for gifts or money could be included. This means that potentially effective interventions with high risk women such as bar workers, who were not explicit about the transactional nature of their sexual behaviour, were excluded (Riedner *et al.* 2006).

Potential biases of the studies and other methodological issues

Properly conducted RCTs are the best way of assessing the effectiveness of health care interventions. In this review, fewer than half of the studies were RCTs and only just over

half had any controls. The effect size of the quasiexperimental studies is greater than the RCTs, and several RCTs showed no effect.

Studies primarily targeted professional SWs working in brothels or red-light districts. In reality much sex work takes place in less organised settings, which would affect the broader applicability of the findings. Forty percent of the studies recruited participants from an STI clinic that had been specifically established for SWs. Participants in a disease prevention intervention may not be representative of all SWs; they may be more adherent, more visible and more likely to have received HIV prevention information. This may lead to participation bias. Analysis of the Kenyan cohort as an open cohort found a drop in incidence of HIV over time, which the investigators attribute to secular trends and the cohort attracting lower risk SWs with the passage of time (Baeten et al. 2000). In addition, half of new HIV infections occurred within the first 6 months of joining the cohort, and 75% occurred within the first year (Baeten et al. 2000), which may reflect the selection of higher risk individuals early in the cohort's life (Beyrer et al. 1996). These are alternative explanations for the drop in HIV incidence, detected in two of the cohorts, after introducing the interventions (Ngugi et al. 1988; Laga et al. 1994).

Sex workers are highly mobile. Over half of the studies that followed SWs reported attrition rates as high as 75%. This compromises the validity of the resultant outcome (Beyrer *et al.* 1996; Beyrer & Nelson 1997). In one cohort, if all the women lost to follow-up were non-compliant, the 50% increase in condom use reported would be a more modest 10% (Ma *et al.* 2002).

To minimise recall and social desirability bias, only studies with reproducible outcomes were included (Peterman *et al.* 2000; Zenilman 2005). However, for a study to be powered to detect change subsequent to an intervention there needs to be a low baseline prevalence and high incidence of the outcome of choice. In at least three RCTs, the lower than expected infection rates after enrolment may have resulted in a type 2 error contributing to the lack of effect found (Ghys *et al.* 2001; Labbe *et al.* 2003; Kaul *et al.* 2004).

The HIV prevention in SWs is a core group intervention, STIs are a communicable disease and any intervention to reduce STIs may have a herd effect. Thus, any evaluation of STI and HIV prevention should also consider impact at a population level. None of these studies looked at HIV incidence in the bridge or general population, and only one out of the four studies that measured the effect of the intervention on STIs in clients found an effect.

Sex workers are a heterogeneous group. Factors such as relative number of the SWs in relation to the bridge and

general population, as well as the structure of the sexual networks and stage of the epidemic influence the extent to which they behave as a 'core' group (Lowndes *et al.* 2002; Cowan *et al.* 2005b; Nagot *et al.* 2005) Given the small number of effective studies, we were unable to explore the relationship between phase of the epidemic and effectiveness of the intervention.

Given the complexity and multifaceted nature of these interventions, indicators of exposure to the intervention would have assisted interpretation. Unfortunately the indicators to measure exposure commonly reported, e.g. number of clinic visits or educational events attended, are also measures of adherence. In the absence of controls, finding an association between these measures of exposure and outcomes may be confounded by other factors associated with being an 'adherent' participant in disease prevention. Data collection methods can behave as interventions, e.g. behavioural questionnaires could reinforce the behaviour message or social desirability bias. Equally, legally imposed 'model brothels' may encourage management to implement additional, undocumented, interventions.

Few of the cluster-controlled trials accounted for intercluster correlation in either the power calculation or in the analysis stage. This could result in a greater measure of effect than if clustering had been considered (Hayes *et al.* 2000). In three studies, only two areas were compared, so we cannot exclude residual confounding or chance (Bhave *et al.* 1995; Wong *et al.* 1998; Kerrigan *et al.* 2006).

Conclusions

The methodological challenges to conducting studies in such a clandestine and mobile group suggest that caution should be exercised when interpreting the results. None of the RCTs showed an impact on HIV incidence. However, the observational data suggests that there is some evidence for the effectiveness of risk reduction counselling and condom promotion.

There is evidence that condom promotion and regular access to improved STI management reduces STI burden in SWs. There's no unequivocal evidence that intensive STI management in SWs has any additional benefit in HIV prevention. Innovative STI delivery methods, such as vouchers, may improve coverage.

There is some evidence that policy support for SW interventions as well as strategies that empower the women improve coverage, acceptability and adherence to the intervention. There is still uncertainty around the efficacy of STI treatment in HIV prevention for SWs, what is the best STI treatment strategy, what components of structural interventions work, and what the potential negative

ramifications of targeting SWs are (e.g. stigma, violence, and driving sex work underground or into areas less identified with 'professional' sex work, such as bars and dance halls). In addition, there is limited data available on the wider public health benefits of targeting SWs. There is a need to explore the effectiveness of comprehensive HIV care packages for SWs, new microbicides, HSV-2 prophylaxis and pre-exposure prophylaxis. Evaluations of interventions that reach community-based SWs who work outside brothel-based settings and red-lights districts are required.

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Corresponding Author Maryam Shahmanesh, Centre for Sexual Health and HIV Research, Royal Free and University College School of Medicine, 3rd floor, Mortimer Market Centre, off Capper Street, London, UK. Tel.: +44 7776 185 572; Fax: +44 207 530 5044; E-mail: bamaryjoon@yahoo.co.uk