Occupational Hazards, Public Health Risks

Sex Work and Sexually Transmitted Infections, their
Epidemiological Liaisons and Disease Control Challenges

Richard Steen

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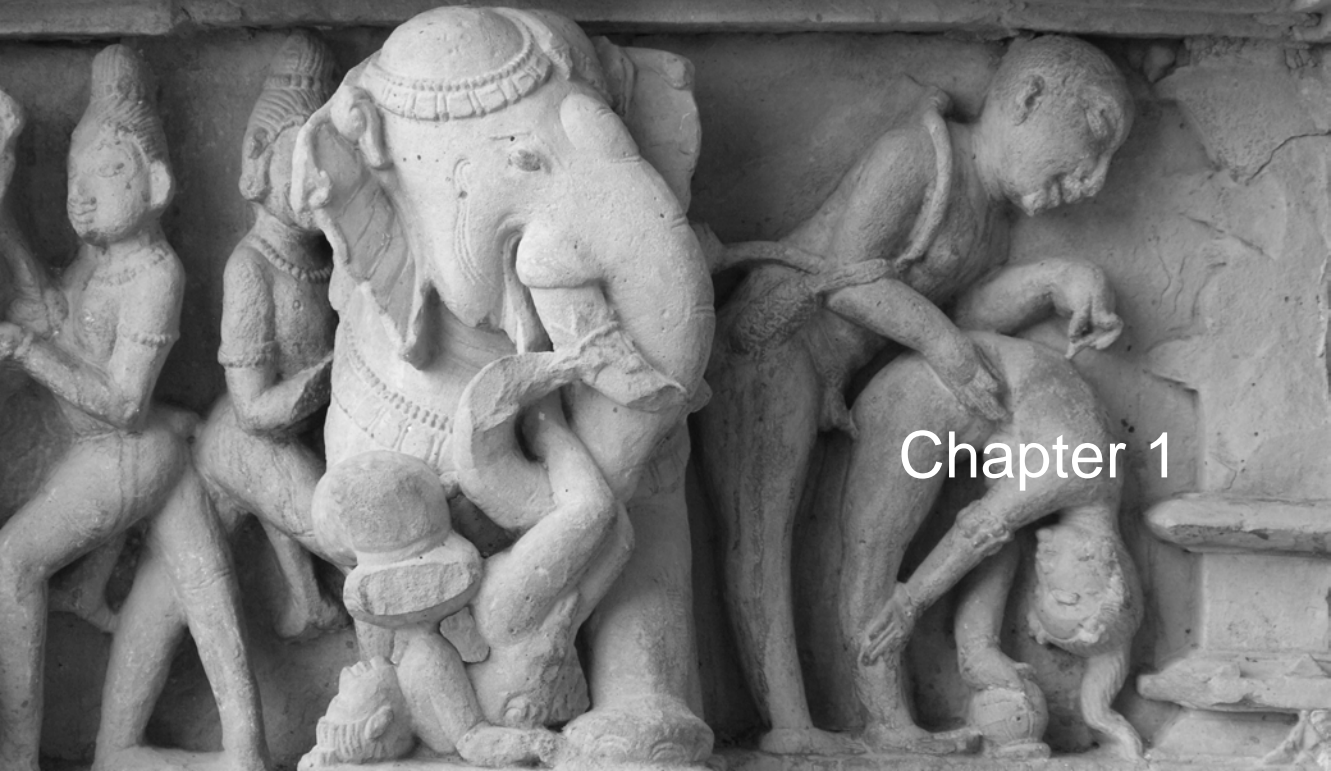Prof.dr. E.C.M. van Gorp
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General introduction

Sex work and STI transmission

Sexually transmitted infections (STIs) represent a large and diverse category within communicable diseases, comprising more than thirty-five pathogens transmissible through sexual contact. [1] Common, curable bacterial and protozoal STIs manifest with ulceration (syphilis, chancroid, LGV) or inflammation and discharge (gonorrhoea, chlamydia, trichomonas) but are often asymptomatic. These are estimated to account for approximately half a billion new infections each year. [2] Incurable viral infections such as herpes simplex virus (HSV), human papilloma virus (HBV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) are several times more prevalent. Common and severe sequelae include pelvic inflammatory disease, infertility, ectopic pregnancy, foetal loss and congenital infections. Both the ulceration and inflammation caused by STIs have been shown to facilitate acquisition and transmission of HIV, raising per-exposure transmission probabilities from an improbable event – less than one per thousand – to as high as two in five exposures. [3–7]

The association between sex work and *venereal disease (VD)*, to use historical terminology, predates modern germ theory by centuries. [8] This understanding was, however, quite limited until very recently. [9] As late as the early nineteenth century, syphilis, chancroid and gonorrhoea were believed to be different manifestations of one disease, yet one intimately linked to sexual promiscuity. With discovery of the microbiological origins and pathogenesis of *venereal disease* and development of diagnostic methods, attention turned increasingly to risks *prostitution* posed to 'unsuspecting' male customers, and by extension, to their families. In this limited and problematic paradigm, sex workers, afflicted with high disease burden, were seen as both 'reservoirs' and 'vectors' to be controlled – by means of public health regulatory measures or criminalisation – in order to protect the public and, above all, the 'innocent victims'.

By the outbreak of the First World War, a more nuanced understanding of the epidemiology of sexually transmitted infections was developing. [8] Moving beyond prevalence differentials, sexual networks came under increased scrutiny. Interventions began to target clients, with special attention to military units whose fighting effectiveness was 'weakened' by *VD-related* hospitalisation. Sex work itself began to be appreciated as an occupation involving considerable vulnerability and risk, for sex worker, client and society. This opened up a more balanced framing of the problem – from blaming victims to understanding sex work as a unique risk network with important interactions at the core of *venereal* epidemiology. These interactions were clarified a generation later for gonorrhoea with development of models of transmission dynamics and 'core' theory. [10,11] The rate of sex partner change – a defining characteristic of sex work – was found to be a key factor driving the reproductive rate. [12-14] Frequent partner change resulted not only in sex workers' disproportionate exposure to STIs but to an important role in transmission as well. The potential of sex work to facilitate if not drive STI epidemics gained traction in the decades immediately preceding emergence of HIV in the 1980s.

Sex work and HIV epidemics

Sex work has received variable attention as a factor in the growth and persistence of HIV epidemics, and as a priority for prevention efforts. Remarkable differences can be seen across regions and over time despite the universal existence of sex work as a social phenomenon.

Intervening in sex work has been credited with halting and reversing several epidemics in Asia, and with freezing others at low levels. In Thailand in the late 1980s, a simple framework of *core transmission* informed a set of structural interventions and targeted condom and STI services that came to be known as the 100% Condom Use Programme (100% CUP). [15] The key structural change was to mandate condom use especially in establishment-based sex work. STI services, including regular screening, were designed to complement and reinforce risk-reduction

in brothels, STI clinic staff implemented the interventions and STI surveillance was used to monitor programme implementation and compliance. This integrated STI/HIV prevention model achieved rapid control of an accelerating and generalizing HIV epidemic and has been successfully replicated in half a dozen Asian countries. [16]

In India, the Sonagachi project developed an approach based on similar analysis of the role of sex work in HIV transmission but implemented as community-based interventions run by sex workers themselves. Intervention elements shared with 100% CUP include attention to structural factors, outreach to sex work venues, targeted condom promotion and STI services. [17] In Sonagachi, condom use rose to high levels, STI rates declined and HIV transmission stabilized early and at a low level across the state of West Bengal. [16] This model has been widely adapted and replicated in South Asia with similar results.

In Africa, however, epidemiological analysis of the role of sex work, and related public health action have been much more limited. While sex workers are acknowledged to have higher prevalence than the population at large, this is discounted in part with arguments about the smaller prevalence differential between sex workers and 'lower-risk' women who can also have very high prevalence. HIV transmission is portrayed as having 'escaped' from core networks which now account for a minority of new infections. Little attention is paid to the potential for onward transmission originating from these relatively small but high-incidence commercial sex networks.

STIs and HIV

The common presence of one or more STIs during commercial sex encounters adds another potent facilitator to HIV transmission dynamics. Poorly controlled STIs were a prominent feature at the onset of explosive HIV epidemics in places like Nairobi in Kenya, Bangkok and Chiang Mai in Thailand, Mumbai and Pune in India. [3, 18–21] In these places, men seen with symptomatic STIs frequently reported recent unprotected sex with a sex worker. Early studies documented strong associations between STIs and HIV acquisition which persisted when controlled for the potential confounding of similar risk behaviours. [22,23] Per-sex-act transmission probabilities were highest among men with ulcerative STIs, were uncircumcised and who reported recent sex with a sex worker, surpassing two-in-five when all three conditions were present. [3]

Early research highlighted the importance of sex work, ulcerative STIs and the male foreskin in exploding African HIV epidemics, and targeted interventions were launched in a number of cities to increase condom use and control STIs among sex workers and their clients. Yet, with a few exceptions, such initiatives remained local and small-scale, limiting impact. Inconclusive

results from several randomised trials undermined support for STI control. [23,24] Unproven theories about HIV transmission in generalising epidemics were advanced to advocate for increasingly non-targeted interventions. [25]

Empirical evidence of intervention impact

In Thailand, the success of 100% CUP became evident within a few years. By the end of the decade, case reports documented STI declines of 95 percent, and chancroid, a major cofactor in HIV transmission, had all but disappeared. [26] HIV prevalence among sex workers steadily declined, followed by general population reductions. By 2005, an estimated 5.7 million HIV infections had been averted. Similar experience has been seen in neighbouring Cambodia and elsewhere in Asia following adaptation of 100% CUP. In China and Mongolia, surveillance reports show that HIV prevalence among sex workers has declined or remained absent. [16] In India and elsewhere in South Asia, declining STI and HIV trends have also been measured following scale-up of targeted interventions based on the Sonagachi model.

Despite differences in regional HIV prevention priorities, interventions with sex workers in a number of African settings have demonstrated similar strategies and outcomes to their Asian counterparts. The early experience of Nairobi – extremely high sex worker HIV prevalence, low condom use, high prevalence of chancroid and other curable STIs – is one example. [27] Within a few years, community-based interventions raised condom use to over 80 percent, curable STIs declined markedly and chancroid disappeared. [28] HIV declines were subsequently reported in Nairobi and nationally following extension of sex worker interventions to other cities. Other sites that have documented positive condom, STI and HIV trends following targeted interventions include Kinshasa, Dakar, Cotonou, Abidjan and South African mining areas. [29-33]

Theory supports practice in explaining the successful control of STI/HIV epidemics in places like Thailand, West Bengal and Nairobi. In the epidemiology of sexually transmitted infections, sex work can be compared to a pump that, by generating new infections at a rapid rate, can inflate epidemics and sustain the pressure needed to drive wider transmission. Rates of partner change orders of magnitude higher than those of the 'casually promiscuous' amplify transmission potential even when the size of core sex work networks is relatively small. When condom use is inconsistent, high prevalence ensures frequent transmission opportunities. Moreover, the high burden of untreated STIs greatly increases HIV transmission probabilities. In the case of HIV, the action of the pump – a product of high prevalence, multiple transmission opportunities and high transmission probabilities – may be over a thousand times

more efficient than the passive diffusion of infection that can occur over time among lower-risk populations.

Given this enormous transmission potential of unprotected sex work and the notable successes of Asian countries in controlling STIs and reversing or stabilising HIV epidemics, it is imperative to ask why sex work has been so neglected in HIV programmes in sub-Saharan Africa. There, with few notable exceptions, prevention efforts are directed at the population at large largely missing sexual networks with the greatest potential for generating new infections.

Research questions

The main question explored in the following chapters concerns the potential importance of targeting sex work in HIV epidemics – *does scaling up basic condom and STI interventions with sex workers and their clients have substantial impact on HIV transmission?* This question is posed in general or universal epidemiological terms, independent of geographic context or stage of HIV epidemics. An important corollary is whether the very large regional differences in actual responses to HIV – in generalised African epidemics compared to concentrated epidemics in Asia – can be justified epidemiologically. This question can be broken down into several smaller ones which will be explored in the following chapters.

1. Is control of curable STIs among sex workers feasible and of benefit to them?

What are targeted interventions with sex workers, can they be implemented and do they make a difference for sex workers themselves? This question is examined drawing on original field research (Chapters 5, 6 and 9), systematic reviews (Chapters 7 and 8) and a policy paper (Chapter 2).

2. Does control of curable STIs among sex workers contribute to STI control in the general population?

Beyond the benefits to sex workers themselves, what public health outcomes – in terms of improvements in STI control – can be expected from targeted interventions? This issue is explored mainly through field research (Chapters 5 and 6) with male clients and migrant workers, and in two reviews (Chapters 3 and 7).

3. Does control of curable STIs among sex workers slow HIV transmission?

Finally, assuming that targeted interventions are able to reduce sex workers' STI burden, which will have an effect on STI transmission among their clients and in the wider population, what effect can these changes be expected to have on HIV epidemics? Chapter 3 reviews the effects of such interventions on STI and HIV epidemics in Asia, while Chapter 4 considers the potential effect of eliminating chancroid, an ulcerative STI strongly associated with both HIV

acquisition and sex work. Relevant modelling work is discussed in Chapters 7 and 8. This work is extended in Chapter 10 using a previously published model of sexual transmission in Kisumu, Kenya. In this model, key assumptions about sex work are reexamined, the model refit and a range of targeted interventions are simulated.

Chapter overview

The content chapters begin with a policy critique of current STI control efforts (Chapter 2) then examine the role of STIs in emergence of Asian HIV epidemics and the role of targeted interventions in controlling them (Chapter 3). The importance of chancroid and other ulcerative STIs in HIV transmission, their link to sex work and potential for control is then explored in a review paper (Chapter 4). Periodic presumptive treatment (PPT) as a component of targeted condom and STI interventions is evaluated in two quasi-experimental studies (Chapters 5 and 6) and two systematic reviews (Chapters 7 and 8), one on efficacy/effectiveness and the other on operational considerations. This is followed by a feasibility paper that describes large scale implementation of such interventions in India (Chapter 9). Finally, the potential contribution of targeted interventions in sex work to HIV prevention in a generalised African epidemic is explored in a modelling paper, with attention to individual intervention components of condom use and STI screening/PPT at different levels of coverage (Chapter 10). A final discussion chapter (Chapter 11) considers the findings in relation to the research questions.

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Control of sexually transmitted infections and prevention of HIV transmission: mending a fractured paradigm

Richard Steen

Teodora Elvira Wi

Anatoli Kamali

Francis Ndowa

Abstract

Control of sexually transmitted infections (STIs) is feasible, leads to improved sexual and reproductive health and contributes to preventing HIV transmission. The most advanced HIV epidemics have developed under conditions of poor STI control, particularly where ulcerative STIs were prevalent. Several countries that have successfully controlled STIs have documented stabilization or reversal of their HIV epidemics.

STI control is a public health outcome measured by reduced incidence and prevalence. The means to achieve this include: (i) targeting and outreach to populations at greatest risk; (ii) promoting and providing condoms and other means of prevention; (iii) effective clinical interventions; (iv) an enabling environment; and (v) reliable data.

Clinical services include STI case management, screening and management of STIs in sex partners. Syndromic case management is effective for most symptomatic curable STIs and screening strategies exist to detect some asymptomatic infections. Presumptive epidemiologic treatment of sex partners and sex workers complement efforts to interrupt transmission and reduce prevalence. Clinical services alone are insufficient for control since many people with STIs do not attend clinics. Outreach and peer education have been effectively used to reach such populations.

STI control requires effective interventions with core populations whose rates of partner change are high enough to sustain transmission. Effective, appropriate targeting is thus necessary and often sufficient to reduce prevalence in the general population. Such efforts are most effective when combined with structural interventions to ensure an enabling environment for prevention. Reliable surveillance and related data are critical for designing and evaluating interventions and for assessing control efforts.

Introduction

In the history of sexually transmitted infection (STI) control, as with other communicable diseases, the pendulum swings between vertical disease-specific and broader horizontal approaches, from a narrow focus on pathogens and their treatment to the wider needs of populations who host and transmit them.

Since the emergence of HIV in the 1980s, STI control efforts have increasingly been defined in relation to HIV programme priorities. [1] Although HIV is itself an STI, efforts to prevent its transmission are largely managed through programmes that are funded, implemented and evaluated independently of other STI control efforts. Such a fractured paradigm has had unfortunate consequences. Too often, neglected STI programmes – the foundation upon which HIV prevention efforts were built – collapse due to reduced funding. As a result, STI clinics and services are understaffed, understocked or disappearing altogether; pregnant women may be offered HIV tests but are no longer screened for syphilis; and STI reporting, an important marker of sexual transmission trends, has largely collapsed. [2,3]

In other areas of communicable disease control, the pendulum is moving in a different direction towards strategies that aim for broad public health benefit while pursuing disease-specific control objectives. Examples include attention to general lung health within the Stop TB partnership and integrated vector management in malaria efforts. The rationale is that sustainable disease control requires coordinated efforts to address common conditions that may facilitate transmission or impede access to prevention, case detection, diagnosis and treatment. [4,5]

This paper describes a unified paradigm of STI control where HIV is an important focus. The approach is analytical and programme-oriented, with attention to public health outcomes and means. We start by reviewing definitions and outlining basic components of STI control, and then examine empirical evidence of the feasibility and benefits of STI control under different conditions. We also consider what happens to HIV under different scenarios and look at the overlap and potential synergies between HIV prevention and STI control efforts.

Defining STI control

STI control is a public health outcome, measured as reduced incidence and prevalence, achieved by implementing strategies composed of multiple synergistic interventions. In the literature, the term "STI control" is frequently used interchangeably with "STI treatment", yet these are quite different things. [6,7] Control of any communicable disease is a public health outcome, measured as reduced prevalence (total infections) or incidence (new infections) in a population. Treatment is a biomedical intervention that, unless part of a broader control strategy, usually does not result in lower transmission rates or disease burden.

STI control can be measured in absolute or relative terms, for example, as elimination of chancroid or 50% reduction of the prevalence of gonorrhoea. Monitoring trends of common curable STIs, etiologically or syndromically, can provide evidence of changing incidence. Where STI surveillance is supported and functioning (often it is not), these data also reflect general sexual transmission trends and can be used to assess the adequacy of overall STI/HIV prevention efforts. [8] Since HIV shares many aspects with other STIs – including modes of transmission, behavioural and other cofactors and potential control measures – HIV prevention can logically be situated within the larger, encompassing domain of STI control.

Back to basics

A comprehensive STI control strategy includes targeted community-based interventions, promotion and provision of the means of prevention and effective clinical services within an enabling environment, as well as reliable data to guide the response.

The science and methods of STI control build on several centuries' experience backed by evidence of progressively declining incidence and prevalence, particularly in developed countries. [9] Over the past three decades, these methods have been adapted and are proving valid in some less-developed countries with limited resources. They have also been adapted to better address chronic viral STIs such as herpes simplex virus type 2 and HIV. In many countries, however, such proven control methods have not been implemented consistently or at sufficient scale to have public health impact.

The effectiveness of standard STI control interventions and strategies – from condom promotion to epidemiologic targeting and partner treatment – is supported by extensive empirical evidence. Despite limited data from randomized controlled trials, most have been adapted to form the basis for HIV prevention work. Recent calls for "combination HIV prevention" and "back to basics" approaches to HIV emphasize the use of combinations of feasible and proven interventions. [10,11]

A recent review listed priority STI control interventions to include "STI treatment of high-risk sub-populations, comprehensive case management of symptomatic STIs, antenatal syphilis screening and treatment and ophthalmia neonatorum prophylaxis, condom promotion and risk reduction counselling" with increased emphasis on the role of STI clinics in identifying and counselling HIV-infected persons and in diagnosing and managing their STIs. [12] The review pragmatically provides evidence for the effectiveness of individual intervention components within the fragmented domains of STI control and HIV prevention, while making a case for better alignment of efforts.

What would such aligned control efforts include? Historical experience argues for coordinated effort in five main areas: (i) appropriate epidemiologic targeting; (ii) primary prevention and access to means of prevention; (iii) provision of effective clinical services to shorten the duration of infectivity; (iv) an "enabling environment" for prevention; and (v) reliable data to guide decision-making.

Clinical services

Clinical interventions can be broadly categorized as STI management approaches for symptomatic patients, screening for asymptomatic infections and partner strategies. All should be supported by appropriate efforts to educate, counsel and provide the means, such as condoms, to prevent infection.

STI case management aims to provide rapid and effective treatment to patients presenting with symptoms to break the chain of infection. Shortening the duration of infectivity is an important objective in the control of STI epidemics. There is strong evidence that syndromic case management is an effective approach for patients with urethral discharge and genital ulcers. It has advantages over previous approaches (i.e. etiologic and clinical diagnosis) in most service delivery settings. [12,13] Syndromic case management also performs well for common vaginal infections although it is not designed to detect asymptomatic cervical infections. STI screening and case finding are time-tested approaches for identifying asymptomatic infections. Although feasible, screening to detect cervical infection remains problematic since sensitive tests for detecting gonorrhoea and chlamydial infection remain too expensive for widespread use.

Breaking the chain of infection also involves treating as many sexual partners of people with STIs as can be identified. Several partner treatment strategies have been described with success rates as high as 30–50% (of index patients). [14] Due to frequent uncertainty about STI diagnoses in women and potentially serious social consequences of notification, partner strategies should focus on identifying symptomatic men who should then be offered counselling and assistance with notifying their partners.

Other interventions aim to interrupt transmission through epidemiologic targeting and presumptive treatment. Asking STI patients about the location of recent contacts can help direct prevention efforts to epidemiologically important "hot-spots" where incidence may be high. Presumptive treatment has been used to rapidly reduce STI prevalence among populations at highest risk, such as sex workers. [15]

A relatively new area for STI clinical services is identification and early intervention with people living with HIV, particularly those recently infected. Promising interventions include early HIV testing and counselling of STI patients, detection of acute HIV infection and regular STI screening and treatment to reduce genital viral load. [16] It is important that clinical interventions be seen as an extension of prevention work in the community and, as such, reinforce prevention messages and promote condoms.

STI control cannot be achieved by means of clinical interventions alone. Primary prevention interventions at the clinic and outside, where transmission takes place, are required. Such interventions emphasize the means of prevention, information and referrals to clinical services. [11,17] There is strong evidence that male latex condoms reduce transmission of HIV by at least 80–85%, are effective against most other STIs and reduce the risk of unintended pregnancy. [18] Other barrier methods, such as the female condom, may have advantages over the male condom in some situations, or as backup methods. [19,20]

From the perspective of the STI control programme, the challenge is to make condoms and other means of prevention available and affordable, promote their use and reduce barriers to utilization. Social marketing has proven effective in increasing supply and demand. [21] Maximizing the public health benefit of the condom component of the programme is not simply a question of promotion and distribution in the community at large, however. What matters most is that condoms are used in situations where STIs are most likely to spread. [22]

There is some evidence that other behavioural interventions can be synergistic to targeted condom promotion. In Thailand, explicit messages to men about the risks of STIs from unprotected commercial sex resulted in higher reported condom use, lower reported numbers of sex worker visits and lower infection rates. [22] Behaviour change in the general population, such as delaying sexual debut, may also serve to reduce transmission but there is little evidence to support abstinence or monogamy as stand-alone strategies.

Targeting high-risk populations

Primary prevention and clinical services contribute synergistically to STI control. The success of these efforts depends not on reaching all people but on reaching the right people with effective interventions. If there is a fundamental tenet of STI control, it is that transmission

depends on high rates of sexual partner change. Epidemics are sustained "upstream" in relatively small sub-groups of the population where rates of sexual partner change are sufficient to sustain high incidence (Fig. 1). Secondary or "downstream" transmission accounts for infections among people at lower risk. An important corollary is that prevention efforts that effectively reduce transmission in the high-partner "core" population are necessary, and often sufficient, to reduce transmission in the population at large.

Fig. 1. **Dynamics of STI and HIV transmission**
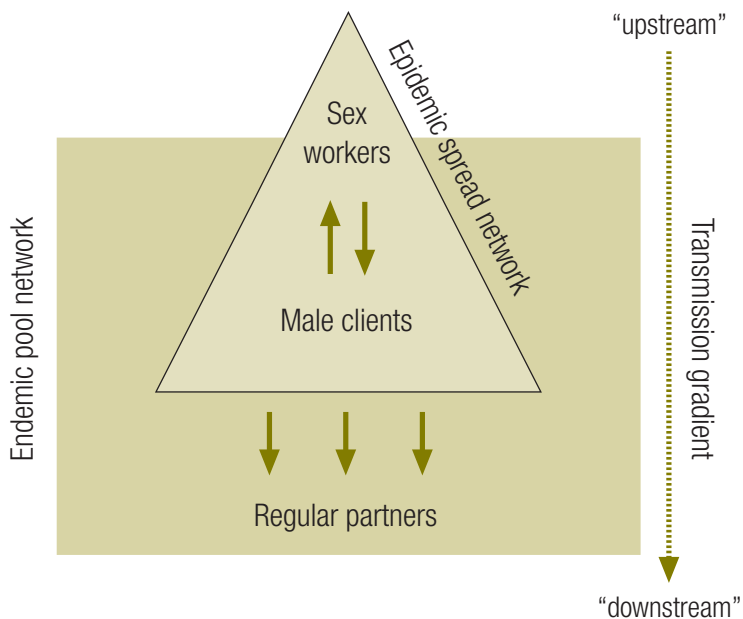
STI, sexually transmitted infection.

This principle is implemented through appropriate targeting of STI control interventions. In Asia, for example, STI control programmes increasingly aim for "saturation coverage" of high-risk populations of sex workers, men who have sex with men, and persons injecting drugs. Other interventions target bridge populations – such as clients and partners of high-risk individuals – through STI clinics or workplace interventions.

Targeting generally builds on two methods – outreach and peer interventions. Programmes begin with mapping to locate and estimate sizes of target populations. [23] Contacts made during this formative stage provide the initial building blocks for peer-based interventions. Peer workers have been shown to be most effective in catalysing change in their communities, from condom use to clinic attendance to structural changes. [24]

Related and important concepts are structural interventions and creating an enabling environment. Structural interventions address root causes of problems, such as the difficulties of individual sex workers to negotiate condom use. By shifting responsibility from the individual to the establishment – in this case by requiring sex work establishments to enforce 100% condom use – better compliance can be achieved and monitored. [22] Other examples of structural interventions include collective action by sex workers to change social conditions that put them at risk. [25]

Such efforts aim to create an enabling environment for prevention. STIs spread most easily among marginalized populations that live with daily risk, have little power to negotiate safer conditions and have poor access to health services. Recent successful examples of STI control have integrated basic prevention components – targeted provision of condoms and STI services – into broader community-based efforts for enabling structural change. [26]

Measuring STI control

STIs are reliable markers of HIV transmission that should be monitored to assess effectiveness of combined prevention efforts. Feasible methods, based on case reporting and periodic surveys, can identify areas where STI control is poor and provide outcome data needed to monitor programme performance. Surveillance should be based on routine STI case reporting, supplemented with special surveys of STI and HIV prevalence, assessment of STI syndrome etiologies, antimicrobial resistance monitoring and risk behaviour prevalence. It is also important to monitor coverage of STI services, particularly for priority population groups.

STI surveillance is a recommended component of second-generation HIV surveillance. Trends of short-duration STIs are more sensitive indicators of high-risk sexual activity than those based on HIV prevalence and can be monitored widely, even in underserved areas where STI control is often poor. Yet few countries maintain systems to collect and use such data. [27]

Empirical evidence

STI control outcomes

STI control has been shown to be feasible in a wide range of countries at different levels of development. STI trends have been on the decline since the early twentieth century in many developed countries and increasingly in resource-constrained countries. For example, China, Cuba and Sri Lanka documented large reductions of STIs in the 1950s and 1960s. STI control is relative and dynamic, however, and sensitive to social and economic change. STI rates surged

in western Europe and North America following introduction of hormonal contraception and in China following economic liberalization. [9,28,29]

More recently, several countries in Asia have documented large reductions in common STIs. Thailand measured a 95% drop in common curable STIs during the 1990s following introduction of the 100% condom use programme implemented by STI clinic staff working with sex work establishments. Chancroid was quickly eliminated, congenital syphilis has become rare and maternal syphilis is stable at about two cases per 1000 pregnant women. [30] Cambodia measured large decreases in both ulcerative and non-ulcerative STIs over five years following a similar intervention. [22,31]

In Africa, STI control efforts have been relatively neglected and STI surveillance is generally inadequate to reliably depict trends. However, several exceptions, where STI control programmes and surveillance have been maintained, provide examples of the feasibility of improving STI control even where resources are limited. Senegal, where sex work is decriminalized and STI services are accessible to sex workers, has reported moderately low and stable STI prevalence. [32,33] In Nairobi, Kenya, targeted interventions with sex workers and improved STI case management in health centres preceded declines in ulcerative and other STIs and local disappearance of chancroid. [34,35]

The scale of decline in STI rates in these examples is noteworthy. Declines of 90% or more in incidence of one or more common curable STIs have been documented in China, Kenya (Nairobi), Sri Lanka and Thailand with rapid elimination of chancroid and congenital syphilis in most settings. [28,30,35] In comparison, intervention trials evaluating STI treatment approaches or limited STI control interventions, have reported much lower STI reductions. [36–38]

HIV prevention outcomes

Evidence supporting the role of STIs as HIV cofactors is extensive and indisputable. Reducing STI prevalence removes cofactors, making HIV transmission less efficient. Countries with poor STI control have been most vulnerable to HIV epidemics, while improvements in STI control parallel or precede declines in HIV incidence and prevalence. There is growing evidence that countries that control STIs are more likely to halt and reverse their HIV epidemics than those that do not. This observation builds on an extensive body of observational and historical evidence which documented: (i) strong associations between several individual STIs and HIV; and (ii) susceptibility of countries with poor STI control to developing sizable HIV epidemics. [1]

More recently, several countries have reported large changes in STI incidence and/or prevalence. Cambodia, Kenya (data from Nairobi) and Thailand show HIV epidemics

stabilizing and reversing in both high-risk and general population groups coincident with or following STI reductions. Sri Lanka had established good STI control before the introduction of HIV and its HIV epidemic has remained low-level for more than two decades. Despite a long-standing civil war and an uncircumcised male population, there is little evidence of transmission within the population and most cases of HIV are found among migrant labourers returning from abroad. The experience of China illustrates how deteriorating STI control since economic liberalization in the 1980s preceded a rapidly increasing HIV epidemic. [28,29]

Implications for programmes

What are the implications for STI control and HIV prevention programmes? If broader STI control is important for HIV prevention, how can this be achieved? What are the conditions where investment in STI control is most likely to contribute to slowing HIV epidemics? Table 1 follows standard epidemiological parameters of disease control to address these questions.

Table 1. **Epidemiologic parameters for control of STIs including HIV**

	Focus	**Methods**	**Notes**
Who?	High coverage of "core" populations of sex workers and men who have sex with men is the first priority. Drug users, also often at high risk through sexual transmission, should also be targeted.	Targeted interventions linked to outreach and clinical services. Several countries have committed to scaling-up targeted interventions to reach saturation coverage of these populations.[39,40]	Targeting is highly efficient. Population-level impact is feasible with interventions directed to core populations who generally comprise less than 5% of the sexually active population.
	Male bridge populations. Efforts should also be made to reach actual or likely clients of sex workers and other bridge populations who disseminate STIs from core networks to the general population.	STI clinic patients are men with recent exposure. Workplace interventions particularly in settings of migrant labour or mobility. Outreach, peer education and STI services in red light districts where transmission potential is high.[40]	Bridge populations may account for 20% or more of the sexually active male population. Interventions likely to reach men at high probability of having STIs and/or acute HIV infection; many report recent sex worker contact.
	STI patients and people living with HIV. A high proportion of STI clinic patients may have acute HIV infection	Provider initiated testing and counselling, STI screening, treatment and counselling for people living with HIV under care.[16,41,42]	Strengthening STI services offers opportunities to treat STIs and offer risk reduction counselling and HIV testing.
What?	Curable ulcerative STIs. Control of curable genital ulcers is highly feasible. Control of these infections correlates well with stabilization of HIV.[43–45]	Effective antibiotic treatment of chancroid and syphilis results in rapid cure. Combined with targeted prevention efforts, control or elimination is feasible.	Data and modelling have established that ulcerative STIs are the most important STI cofactors for HIV transmission.[44]
	Viral ulcerative STIs. HSV-2 being an incurable viral infection requires different control strategies.	Studies have demonstrated the feasibility of suppressing HSV-2 and reducing HSV-2 and HIV concentrations in genital secretions.[46,47]	Ongoing research is exploring optimal regimens for HIV prevention.
	Curable non-ulcerative STIs. Non-ulcerative STIs are prevalent and increase HIV transmission 2–4 times.	Effective antibiotic treatment of gonorrhoea or chlamydial infection reduces HIV viral load to normal levels.[48]	Reductions in gonorrhoea and chlamydial infection have been reported in high and lower risk populations.
Where?	Effective targeting requires a 2-stage process: (i) identifying epidemiologic "hot-spots" where risk is present and/or transmission is believed to be taking place; and (ii) mapping of populations in those areas.	STI surveillance helps identify "hot-spots" in the first stage of mapping. STI case reports from sentinel STI clinics can be used to monitor trends of new male STIs at district levels.	Demonstrated in Thailand and Sri Lanka. Builds on historical experience with contact tracing and STI outbreak control in developed countries.[49,50]
When?	STI control is most effective in preventing HIV transmission: (i) when STIs, particularly ulcers are poorly controlled; and (ii) early in HIV epidemics.	STI surveillance. STI case reports and STI prevalence surveys among high-risk populations can be used to assess impact and monitor trends.	Modelling has shown the potential contribution of STI control to HIV prevention at different phases of STI and HIV epidemics.

HSV-2, herpes simplex virus type 2; STI, sexually transmitted infection.

Who?

STI control efforts should focus on core and bridge populations, symptomatic patients and persons living with HIV. High coverage of such key populations as sex workers and men who have sex with men is the first priority. [39,40] Efforts should also be made to reach actual or likely clients of sex workers and other bridge populations who disseminate STIs from core networks to the general population. Clinics providing STI treatment are a good entry point to screen and identify persons living with HIV, and additional effort is required to screen persons living with HIV under care to ensure that any STIs are detected and treated. [16,41,42]

What?

Interventions that reduce STI prevalence will reduce the respective cofactor effect and blunt the efficiency of HIV transmission. Data and modelling have established that ulcerative STIs, particularly chancroid, herpes simplex virus type 2 and syphilis, are the most important STI cofactors for HIV transmission. [43,44] Control of curable genital ulcers – chancroid and syphilis – is highly feasible and correlates well with stabilization of HIV epidemics. [45]

Where?

Identification of high-risk populations generally requires a two-stage process: (i) identification of epidemiologic "hot-spots" where risk is present and/or transmission is believed to be taking place; and (ii) mapping of populations in those areas. The importance of STI surveillance in this first stage of mapping has been demonstrated. [49,50]

When?

Modelling has helped in understanding the potential contribution of STI control to HIV prevention at different phases of STI and HIV epidemics. Two conclusions are apparent, that STI control is most effective in preventing HIV transmission: (i) when STIs, particularly ulcers, are poorly controlled; and (ii) early in HIV epidemics. It thus makes sense to strengthen STI control rapidly when prevalence is found to be high or increasing. However, monitoring STI trends requires reliable surveillance, which is lacking in many countries.

A combination of factors – led by unprotected sex work and ulcerative STIs – create ideal conditions, a "perfect storm", for rapid spread of HIV epidemics. Such conditions are most likely to be found in settings with mobile populations and uncircumcised men. Successful STI control programmes have responded with a combination of interventions, guided by reliable mapping and surveillance, to disrupt those conditions for optimal STI control and HIV prevention outcomes (Fig. 2).

Fig. 2. **Intervention opportunities for STI and HIV transmission**

	Clinical services	STI surveillance data
Sex workers	Targeted intervention clinics	STI prevalence (sex worker syphilis screening)
Male clients	STI clinics workplace clinics	STI incidence (male STI case reports)
Regular partners	Primary care mother and child health clinics	STI prevalence (antenatal syphilis screening)

Targeting intervenes here
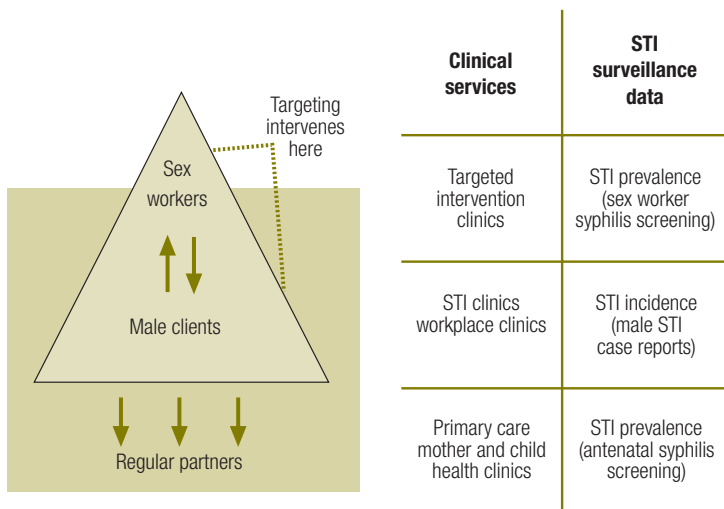
STI, sexually transmitted infection.

Conclusion

In many countries, basic STI services are in disarray as programme resources are determined by decisions relating to a single disease entity. Such a fractured paradigm is as counterproductive for HIV as it is for other STIs. Major HIV epidemics emerged from and spread rapidly under conditions of poor STI control, and further weakening of STI control may well undermine other HIV prevention efforts. Yet experience of countries as diverse as Cambodia, Kenya, Senegal, Sri Lanka and Thailand demonstrate that wider STI control is feasible and that HIV prevention can be strengthened in doing so.

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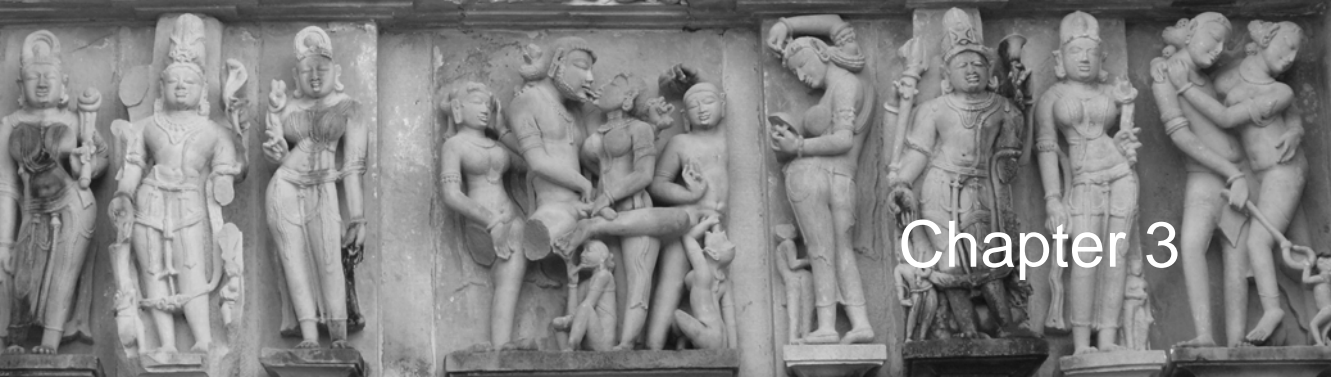
Halting and reversing HIV epidemics in Asia by interrupting transmission in sex work: experience and outcomes from ten countries

Richard Steen

Pengfei Zhao

Teodora Elvira Wi

Neelamanie Punchihewa

Iyanthi Abeyewickreme

Ying-Ru Lo

Abstract

HIV epidemics spread rapidly through Asian sex work networks two decades ago under conditions of high vulnerability, low condom use, intact male foreskins and ulcerative STIs. Experiences implementing interventions to prevent transmission in sex work in ten Asian countries were reviewed. All report increasing condom use trends in sex work. In the seven countries where condom use exceeds 80%, surveillance and other data indicate declining HIV trends or low and stable HIV prevalence with declining STI trends. All four countries with national-level HIV declines among sex workers have also documented significant HIV declines in the general population. While all interventions in sex work included outreach, condom programing and STI services, the largest declines were found in countries that implemented structural interventions on a large scale. Thailand and Cambodia, having controlled transmission early, are closest to providing universal access to HIV care, support and treatment and are exploring HIV elimination strategies.

Background

In Asia as elsewhere, sex work is common and highly diverse. The estimated proportion of adult women (15–49 years) involved in sex work ranges from 0.2 to 2.6%, and the number of regular male clients has been estimated at 75 million. [1,2] Moreover, sex work overlaps considerably with other populations and settings where HIV risk is elevated. More than half of men who have sex with men (MSM) surveyed in four Indian cities reported a commercial sex partner in the past month, [3] In several countries, there is extensive interaction between drug injecting and sex work networks. [4]

HIV epidemics ignited in a handful of urban areas across Asia two decades ago, fuelled by rapid transmission in overlapping sex work and drug injecting networks. Conditions of high vulnerability, low condom use in commercial sex, intact male foreskins and ulcerative STIs stoked high incidence, while migration and population mobility facilitated wider epidemic spread. [5]

Yet a number of Asian countries have succeeded in halting and reversing their HIV epidemics, as estimated by multiple surveillance measures, and in controlling other sexually transmitted infections (STI), largely by focusing efforts on transmission within sex work. [5] In addition, several of these countries have subsequently reached universal access targets for antiretroviral treatment (ART) and related services, under the Millennium Development Goal for HIV (MDG-6). [6]

These experiences pose questions of relevance in and beyond the region.

- What combination of interventions contributed to the observed HIV/STI declines?

- How important to halting and reversing national HIV epidemics is the prevention of transmission in sex work?

- How are control of STI and HIV epidemics related?

- What is the additional role of expanding HIV testing and antiretroviral therapy in reversing HIV epidemics?

- Does preventing transmission in sex work facilitate reaching universal access targets?

This paper explores these questions by relating epidemiological trends and published evidence to the programmatic response. [7]

Methods

Ten Asian countries (limited to the state of West Bengal for India) with low-level, concentrated or generalized HIV epidemics that had implemented interventions to control transmission in sex work were identified for review. The published literature was searched using PubMed for papers addressing sex work and STIs and/or HIV. Papers describing interventions in sex work with outcome data were included for review. Country-level HIV, STI and behavioral surveillance data were triangulated to compare long-term trends among sex workers, high-risk men and the general population and modelling studies were examined for estimates of HIV incidence and additional insights. [8–10] In addition, field work to eight countries was organized to obtain input from key informants – programme managers, sex workers, health workers and NGOs involved in interventions with sex workers. WHO country and regional offices in the Western Pacific and South-East Asia regions coordinated country input and review of the findings.

Early conditions

A number of papers describe early conditions that led to rapid take-off of HIV epidemics. Data from Thailand and India early in their HIV epidemics illustrate how such conditions facilitated widespread HIV transmission.

In Thailand, STI control was not keeping pace with transmission in the mid-1980s when the first AIDS cases were reported among gay men. [11] STI incidence as high as 76.5 new infections per 100 woman-months was reported among Bangkok massage parlor workers. [12] HIV quickly spread among injecting drug users (IDU), and HIV prevalence among sex workers in Chiang Rai Province increased from 1–37%. [13] During 1991–1994, HIV seroprevalence reached 47% for brothel workers and 13% for other sex workers in Chiang Rai; HIV was associated with syphilis, HSV-2 seropositivity and genital ulcer. [14]

By the early 1990s, HIV was spreading widely through male bridging populations. HIV incidence in 1991 was as high as 2.5 per 100 person-years for male military conscripts from northern Thailand. [15] Genital ulceration was strongly associated with seroconversion and prevalence of serologic reactivity to syphilis, chancroid and HSV-2 increased with greater frequency of contact with sex workers. [16] By 1993, 12% of young military recruits based in northern Thailand were found to be HIV positive; HIV seropositivity was associated with commercial sex contact (OR 9.1), STI (OR 6.0) and inconsistent condom use with sex workers (OR 3.1). [17] Incidence of STIs was 17 per 100 person-years, mostly gonorrhea and chancroid. [18]

By 1996, HIV prevalence was as high as 7.1% among pregnant women in Chiang Rai. [19] Among women with no risk factors for HIV other than sex with an HIV-infected partner, 46% were HIV-positive. Women were twice as likely to be HIV positive if their partners had a history of sexually transmitted infection. [20]

Similar patterns and trends were seen in India. In Mumbai, HIV prevalence among STI clinic attendees increased from 1.3% in 1987 to 7% in 1989 and was associated with genital herpes and chancroid. [21] HIV prevalence among sex workers climbed rapidly to 40–50%. [22] Among 215 first-time STI clinic attenders in Bombay in 1995, 31% were HIV seropositive; 74% had genital ulcers of which 52% were chancroid, 25% HSV-2 and 15% syphilis. [23]

In Pune, STI patients with HIV were frequently found to have had contact with a sex worker or were female sex workers themselves; lack of condom use, genital ulcer or discharge and syphilis seroreactivity were significant risk factors. [24] In 1994, among 302 STD clinic attenders with genital ulcers, 23% had chancroid, 26% HSV-2 and 10% syphilis. [25] Between 1993– 1996, among 916 women attending an STI clinic, risk factors for sex workers (HIV prevalence 50%)

were inconsistent condom use and genital ulcer disease or genital warts, while for non-sex workers (HIV prevalence 14%), history of sexual contact with a partner with an STI. [26]

Research from Pune in the mid-1990s provided additional evidence, based on studies of viral shedding, recent seroconverters and prospective cohorts, on how ulcerative and other STIs facilitate both HIV transmission and acquisition. Among 302 patients with genital ulcers (HIV 24%), presence of chancroid, ulcer symptoms for more than 10 days and concurrent diagnosis of cervicitis or urethritis were significantly associated risk factors for HIV ulcer shedding. [27] Among 58 STI clinic attenders who were HIV antibody-negative and p24 antigen positive (recent seroconverters), unprotected sex with a sex worker and a genital ulcer were independent risk factors associated with newly acquired HIV infection. [28] In a cohort of 851 HIV-seronegative persons evaluated prospectively every 3 months for HIV infection, HIV incidence was 26.1 per 100 person-years among sex workers and 8.4 among other women; recurrent genital ulcer disease and urethritis or cervicitis during the follow-up period were independently associated with a seven and threefold increased risk of HIV seroconversion. [29]

Early epidemics in Thailand and India highlight conditions that permitted extremely rapid dissemination of HIV through overlapping sexual and drug injecting networks. These included low condom use in commercial sex and high rates of ulcerative STIs in largely urban settings characterized by high vulnerability, migration and population mobility. High rates of genital ulcers, particularly chancroid, were in turn associated with sex work in areas with low rates of male circumcision, as has been described elsewhere. [30] Such conditions have changed considerably in Thailand and in parts of India, as described below. Elsewhere in Asia, however, conditions still vary greatly. [6]

HIV was spreading to other countries from the late 1980s, with likely cross-border spread between Thailand, Myanmar and Cambodia, from Myanmar to southern China through overlapping drug-use and sex work networks, and from Cambodia to Vietnam facilitated by extensive cross-border and migrant sex work. [31-34] Transmission between India and Nepal, Myanmar and Bangladesh have also been described, as has subsequent cross-border transmission between Vietnam and China. [32] The timing of introduction of HIV, biological and behavioral factors and intervention effects have been posited to explain differential inter-regional growth of HIV epidemics. [5] Modelling projected that adult HIV prevalence could reach 15% prevalence in Thailand and Cambodia in the absence of interventions. [8,35,36]

Types of interventions & scale of the response

In Asia as elsewhere, a range of epidemiological studies confirm that epidemics of sexually transmitted infections including HIV do not spread evenly through populations. [5,37-40]

Rather, epidemiological models of transmission dynamics consistently differentiate high-incidence 'upstream' transmission – between clients and sex workers – from the many secondary infections that result. Infection spreads 'downstream' via male bridging groups that frequently acquire new infections through sex work, then transmit them not only to other sex workers, but also to their regular and casual partners. [40] These transmission dynamics have been extensively described, and epidemiological estimates and projections of transmission by population group increasingly inform strategies to control sexual transmission in the region. [35,36,201]

Most countries in this review have adapted intervention elements from two early experiences that address such transmission dynamics and have proven successful in Asia – the Sonagachi project of community-led structural interventions (CLSI) from India and the 100% condom use programme (100% CUP) from Thailand. [40,41] Both have been described as 'structural interventions' since they address conditions of sex work that influence vulnerability and risk. A third 'service-delivery' model shares many intervention components with the other two but without a strong structural intervention component. More recent interventions have incorporated elements of more than one of these intervention models, for example, the Avahan India AIDS Initiative in India, which has highlighted the importance of a scalable response with a defined 'common minimum program' of intervention components. [42]

As summarized in Table 1, six countries implemented structural interventions to increase condom use in sex work on a national or targeted sub-national scale. Two countries have had strong implementation of community empowerment models at sub-national scale. Other countries have applied a mix of interventions with service strengthening but without major structural intervention components.

Table 1. Categories of national response.			
	CLSI	**100% CUP**	**Non-structural***
National scale		Cambodia China Mongolia Thailand	
Targeted sub-national	India Bangladesh	Myanmar Vietnam	Nepal Indonesia

*Includes neither community empowerment component nor implementation of 100% CUP.
CLSI: Community-led structural interventions; CUP: Condom use programme.

All countries also implement universal access initiatives to scale up ART and related HIV services, which will be discussed later.

Country experience with implementation

Thailand

The 100% CUP was piloted in Rachaburi province in 1989 and then scaled up nationwide between 1991–1992 as an emergency response to a rapidly advancing HIV epidemic. The Thai response leveraged political commitment and public investment to mount a rapid response guided by reliable information and multi-sectoral collaboration. Implemented through a network of public health STI clinics, the 100% CUP achieved early success by saturating coverage of sex establishments where condom use was mandated. [39,43] The responsibility for enforcing condom use was on the establishment, which could be closed if non-compliant (although this was rarely done).

Direct services included promotion and distribution of condoms and STI checkups. STI clinics were expanded and staff conducted regular outreach to sex establishments to promote prevention and STI screening. Importantly, systematic collection of basic data was carried out to inform the program. This included annual mapping of sex establishments and enumeration of sex workers, behavioral monitoring (focusing on condom use and number of clients) and STI screening. Monitoring activities are largely built into the day-to-day activities of the STI clinics, requiring few special surveys. As sex work changed to more indirect forms (massage, karaoke and bar-based), interventions were adapted to include more outreach and to increase involvement of sex workers.

The initial results in Thailand were dramatic and led to adaptation and replication in several other countries. Sex workers were enabled to demand condom use and access STI care, which rapidly slowed transmission. [40,43] The program also had large-scale public heath impact. Rates of curable STIs fell by over 95% nationwide during the 1990s and HIV prevalence declined in most population groups. [11,15,44,45] By 2002, an estimated 5.7 million HIV infections had been averted; this includes sex workers and their clients but also – including averted secondary infections – far larger numbers of people at lower-risk. [35] As Thailand's epidemic began to come under control, implementation of 100% CUP broadened in several ways – interventions were expanded from establishment-based sex work to others venues, NGOs and CBOs became more involved, especially in non-establishment settings and clinical services were strengthened. [43] Early control of transmission enabled Thailand to become one of the first Asian countries to achieve universal access to HIV care, support and treatment. Yet, despite the early success of prevention and treatment programs, transmission may be increasing among men who have sex with men, in particular among young MSM and male sex workers. [46]

West Bengal, India

The Sonagachi experience began in a large red-light area of Kolkata, with a small team of peer educators and health workers committed to promoting condoms and providing STI services. These are now part of a broader effort to improve living and working conditions for members of the community. [41] Beginning with peer interventions and STI clinics, a community empowerment model progressively developed to take on a range of health and social harms faced by sex workers. [47,48] Sex workers participate actively in all aspects of both community interventions and clinic-based services.

Confronting conditions of high vulnerability and vested interest, the initial STI/HIV Intervention Project established outreach to brothels, condom promotion and STI services. These initial successes in addressing HIV and STIs increased community participation and confidence to take on other problems that contributed to their high vulnerability. Within a few years, Sonagachi sex workers had formed a community-based organization, Durbar Mahila Samanwaya Committee (DMSC), with democratic, collective decision-making processes. Over 60,000 sex workers participate throughout the state of West Bengal, savings and credit schemes have reduced dependency on sex work and self-regulatory boards effectively address a range of abuses from trafficking to child prostitution. DMSC's community development process or community-led structural intervention (CLSI), its developmental stages, facilitating and inhibiting factors have been well described. [49-58] One community intervention trial showed that condom use was significantly increased among sex workers participating in the intervention compared to the control group. [59]

By the late 1990s, DMSC was replicating interventions across the state of West Bengal which grew to cover an estimated 85% of sex workers. This experience has informed development of community-based interventions in Mysore district (Ashodaya Samithi) in South India and elsewhere, as well as national policy and scale-up in high-prevalence states. [60] India has progressively scaled up interventions based on a CLSI model beginning in the late 1990s. Subsequently, Avahan targeted six high-prevalence states, extending community-based models and reporting consistent outcomes of high condom use, declining STIs and stabilization of HIV epidemics. [61] Avahan supports NGOs to organize outreach, community mobilization and dedicated clinics for sex workers, developing methods – such as capacity building systems, common minimum programs and micro-planning – to facilitate implementation at scale. [42,62,63] DMSC, Ashodaya, Avahan and others conduct advocacy to promote enabling conditions for prevention work and actively support transition of targeted intervention models to the national program. [64]

Today, HIV prevalence among sex workers in Kolkata remains low (5%), compared to rates higher than 50% reported from red-light districts of Mumbai, Pune and Goa [47]. Syphilis prevalence has declined from 25% in 1992 to below 1% in 2008 [48].

Cambodia

Cambodia confronted HIV under extremely vulnerable conditions in the early 1990s as the country emerged from instability. Rapid growth of HIV, which by the mid-1990s had become the largest in Asia, was fuelled by unprotected sex work and high prevalence of other STIs. A 1996 study showed high rates of chancroid and other ulcerative STIs, cofactors which facilitated rapid HIV transmission in neighboring Thailand. [65] Early NGO interventions were strengthened by the 100% CUP, which was piloted in Sihanoukville in 1998 and extended nationwide in 2000–2001. [66] Condom use in sex work increased from <40% in 1996 to consistently over 90% since 2001. HIV prevalence among direct (brothel-based) sex workers (DSW) decreased from 42% in 1996 to 14% by 2006. STIs declined by more than half between 1996 and 2001 among both sex workers and high-risk male groups. National HIV prevalence has been declining from a peak of 2% in 1998 to 0.6% in 2011. Modelled estimates of HIV incidence among female sex workers decreased from 10.2% in 1999 to 1.6% in 2006. [67] These are similar to findings from an IgG BED-CEIA study of HSS samples from 1999–2002: HIV incidence declined from 13.9–6.5% among direct sex workers (DSW); from 5.1–2.9% among in direct sex workers (IDSW); from 1.7–0.3% among police; and from 0.7–0.6% among pregnant women. [68]

Despite early evidence of increasing condom use and decreasing HIV/STI rates in sex work, Cambodia's MoH closely monitored intervention coverage and outcomes, strengthening its program in several ways over time – reaching non-brothel-based 'entertainment workers', providing more comprehensive HIV and reproductive health services. An early study described the potential extension of HIV from urban to rural areas as older sex workers were found to move to less competitive areas. [69] Other intervention linked studies describe attempts to improve and extend services – an evaluation of STI services in border areas and introduction of the female condom, tried by 16% of sex workers. [70-72] Continuing and new challenges including high STI incidence and amphetamine-type stimulant use and attempts to address them were reported. [73,74]

However, forced closure of brothels in 2008 – by Ministry of Interior implementing an anti-trafficking law – disrupted programs and increased the vulnerability of sex workers. [66,76,77] The National AIDS Authority and MoH have subsequently taken steps to rebuild programs and promote a more enabling environment in sex work settings (unpublished reports), maintaining

high rates of condom use in sex work settings. As in Thailand, early control of transmission has enabled Cambodia to provide universal access to care and treatment, reaching MDG targets early. HIV testing and treatment coverage is estimated to be above 80%, contributing to further decreases in HIV transmission. The number of new infections, estimated between fifteen and twenty thousand annually in the early 1990s, had been reduced to about 2,100 by 2009 when about 93% of those eligible for anti-retroviral treatment were being treated, and is estimated at 1000 in 2011. [67,78,202]

China

China experienced a sharp rise in both sex work and STIs following the Open Door Policy in the late 1970s. [79] The HIV epidemic started among IDUs and plasma donors but the major mode of transmission has shifted to sexual contact. A surplus of men and a large migrant workforce are important factors and transmission among MSM is growing. [80,81] An estimated 2.8–4.5 million female sex workers (18–37 million clients) in China are highly mobile working in direct and indirect sex venues as well as freelance sex work. [82] Estimates of the number of male sex workers range from 4.9% to 24% of 7 million MSM, most of whom live in cities and have both male and female clients. [82]

During 2001–2003, the 100% CUP was piloted in four provinces: Hubei, Jiangsu, Hunan and Hainan. Results showed increasing condom use and declining STI rates among sex workers, prompting nationwide implementation in 2004 with dissemination of high-level decrees and related technical guidelines. [83] Local multi-sectoral steering committees were organized with participation of local authorities, establishment owners, health department and police. The Chinese Center for Disease Control and Prevention (CDC) were responsible for organizing outreach work, testing and referrals for clinical services.

A number of intervention-linked studies and reviews were carried out to inform strategy development in China. [84-90] Venue-level factors, such as condom availability and managerial and social support of HIV prevention in commercial sex venues, were shown to be as important as interpersonal factors in ensuring condom use in sex work. [87] A five-city trial conducted in 2000–2001 showed that outreach to sex establishments with condom promotion and STI services increased condom use from 55–68% and reduced STIs by up to 85%. [88] An intervention trial in Guangxi Autonomous Region demonstrated the efficacy of cultural adaptation of a brief VCT intervention among FSWs in China showing increases in consistent condom use with clients and decreases in STIs over 6 months. [89] The prevalence of gonorrhea fell from 26% at baseline to 4% after intervention, and chlamydia from about 41–26%.

National policy and program support for targeted interventions were established between 2004 and 2006. China estimated intervention program coverage for female sex workers at 74% in 2009. [82] Reported condom use by female sex workers has increased rapidly in identified sex work areas. HIV remains low among female sex workers (0.4% in 2010) in sentinel surveillance having declined from 1.2% in 2002. Yet there is concern that other sex workers may be missed by current outreach efforts, particularly in a criminalized environment with periodic police crack-downs and detentions. Low-level sex workers working outside known sex work venues in some areas report lower condom use and have higher syphilis rates than the national surveillance sample. Interventions with male sex workers and with sex workers who use drugs raise separate challenges. [82] HIV transmission is rapidly increasing among urban men who have sex with men. Injecting drug use was found to be the single greatest risk factor for HIV infection among female sex workers in one study from Yunnan Province. [90]

Indonesia

Adult HIV prevalence is estimated to be 0.2% for Indonesia, yet is steadily increasing and has surpassed 2% in Tanah Papua. Sexual transmission has surpassed drug injecting as the major mode of transmission. In 2006, an estimated 221,000 women worked in the sex industry serving 4 million clients per year. [91] HIV prevalence among sex workers has increased progressively to 9.4% with high variability by sentinel site, and condom use remains low. [91] Although a 100% condom use policy was adopted as part of the 2003–2007 national strategy, implementation has been limited and uneven. [91] This has been attributed partly to health sector decentralization, partly to cultural attitudes toward sex work and condoms. Higher condom use and lower STIs have been reported from sites with strong implementation. [92]

Several studies report intervention-linked outcomes. In Bali, an early peer education program experienced frequent turnover due to high mobility. [93] Clusters where peer educators continued to work had higher levels of condom use (82 vs 73%, p=0.15) and lower gonorrhea prevalence (39 vs 55%, p=0.05). Three recent studies analyze IBBS data to assess strengthened STI services. Increasing condom use and decreases in gonorrhea and chlamydia of up to 80% were reported from two sites following condom promotion/supply and provision of effective STI drugs and periodic presumptive treatment (PPT) for STIs. [92] In adjusted cross-sectional analysis, attending clinic checkups and having received PPT were associated with lower prevalence of gonorrhea, chlamydia and syphilis. [94,95] In a study of female sex workers, HIV incidence by BED assay was found to be higher in direct brothel settings (p<0.001) and among those reporting genital ulcers in the past year (p<0.001), those with active syphilis (p=0.017), and those not receiving PPT during the previous 6 months (p=0.045). [96]

Since 2009, national strategies emphasize prevention of sexual transmission through multi-stakeholder mobilization and support for enabling environments. Interventions aim to empower sex workers to increase condom use and access health services, and are supported by improved condom supply and more comprehensive clinical services. The program also seeks to increase demand for condom use in sex work among high-risk men through workplace and other programs, and is addressing MSM and waria (transgender) with an emphasis on those who sell or buy sex.

No intervention-linked research studies were identified for Mongolia, Myanmar, Nepal or Bangladesh and only one was found for Vietnam. Nevertheless, program data and interviews provide a partial picture of their epidemics and national responses.

Mongolia

Mongolia has, according to WHO and national sources, maintained a very low HIV epidemic with fewer than 100 persons identified with HIV as of 2011. Yet other STIs accounted for 40% of all reported infectious diseases in 2009. Prevention in sex work was almost non-existent before 2002 when a study reported that 88% of sex workers never used condoms. A 100% condom use programme (CUP) piloted in Darkhan-Uul, a city with high reported STIs, showed an increase in condom use to over 90% and reductions of syphilis. The program was scaled up with high-level political support between 2003 and 2007 to cover all provinces. The main focus of the work was on increasing condom use in sex work and on creating an enabling environment for prevention work. During this period, reported condom use by sex workers (with last client) increased rapidly in all identified sex work areas, to above 90% in three second-generation surveillance (SGS) surveys from 2005. No HIV has been detected among sex workers by SGS and declining syphilis trends were seen for most populations surveyed. However, high mobility of sex workers and their informal and changing work settings complicate outreach and follow-up. To address this, local AIDS committees were established in 2009 at provincial level to reinforce implementation, STI cabinets expanded services and drop-in centers were introduced in several hotspot areas. Nevertheless, continued high syphilis prevalence (27.5% in 2011 SGS) among female sex workers and low coverage of HIV services suggest program gaps and ongoing potential for STI and HIV transmission.

Myanmar

After 100% Targeted Condom Promotion pilots in four townships demonstrated an increase in condom use among sex workers (from 61% in 2001 to 91% in 2002) and halving of syphilis prevalence, Myanmar expanded coverage to 11 additional townships in 2002, and 43 in 2003. [40,97] Program expansion was supported by UN agencies, NGOs and donors. By the end of 2004, the program was reaching 110 townships and by 2006, 152 of all 324 townships in the country. A WHO external review of the TCP in 2005 documented both progress and weaknesses including uneven implementation in some townships during the rapid expansion. Over the period of implementation, reported condom use has risen to high levels (96% in Mandalay and Yangon) and syphilis trends are declining in most sites. [98] HIV prevalence among young sex workers, a proxy for incidence, has declined from >40% before 2005 to <10% in 2009 [6]. HIV prevalence among women attending antenatal clinics has declined from >2.5% in 2001 and to <1% in 2009. [6]

Nepal

In Nepal, interventions with sex workers started slowly from the mid-1990s with education and condom promotion in Kathmandu and a few other towns following description of risks related to sex work. [99] A 2001 survey of 500 Kathmandu Valley sex workers measured 15.7% HIV and 14.3% active syphilis prevalence among street-based sex workers (2.5% and 3.5% among establishment-based). HIV prevalence was highest among street-based sex workers who regularly injected drugs (80%) and among those who had worked as sex workers in India (>40%) or Mumbai (>70%). From the mid-1990s, NGOs began peer interventions, opened drop-in centers and provided condoms and STI services to sex workers. Meanwhile, targeted interventions with sex workers in Mumbai and other Indian migrant destination areas were beginning to slow transmission in distal high-risk networks of Nepali migrant workers. Studies among sex workers during the 1990s were mostly done in Kathmandu – where HIV prevalence reached 17% among selected sex worker samples – but did not reflect regional differences. The first integrated bio-behavioral surveys (IBBS), conducted in 2003–2004 after several years of interventions, found HIV prevalence to be 2% among sex workers in the highways districts, in Kathmandu and Pokhara Valleys. Importantly, these studies established that condom use, although variable, had already risen significantly from the low levels in the 1990s. More recent IBBS data support apparent stabilization of HIV among sex workers at around 2% in the same regions as reported condom use has risen and syphilis continues to decline. Large reductions in gonorrhea prevalence among sex workers provide additional evidence of declining sexual transmission in sex work.

Bangladesh

Bangladesh was influenced by the response to HIV in neighboring West Bengal and began early to improve conditions before HIV began spreading among sex workers and clients. Technical support from Sonagachi informed early interventions – to mobilise sex workers, raise awareness, promote condom use and provide STI services – in brothels and among street-based sex workers [100]. These early efforts were reportedly disrupted and sex worker vulnerability increased following forced closure of two large brothels [101]. In 1998 HIV surveillance revealed no HIV among Dhaka street-based female sex workers, 0% and 1.5% at two large brothels. Syphilis prevalence, however, was 57% among the street-based sex workers and 46% at one brothel [102,103]. Gradually, brothel sex work has shifted to hotels and other informal venues. Street-based sex work continues to be highly vulnerable. More recent data suggest that transmission risk also remains high among hotel-based sex workers.

Vietnam

In Vietnam, sexual transmission of HIV was increasing in southern provinces bordering Cambodia, reaching 9.5% among sex workers in An Giang in 1996. [104] A 100% condom use programme was piloted in 2000 in Halong city, Quang Ninh and Can Tho provinces, was expanded to 42 provinces beginning in 2004 and included as a part of the 2006 HIV Law which emphasized harm reduction approaches. Yet, continued criminalization of sex work and drug use underlines conflicting public health and 'public security' agendas, increasing sex worker vulnerability and detentions, disrupting peer interventions and reducing access to services.

Sentinel surveillance covering 40 provinces showed HIV prevalence declines among female sex workers from 5.9% in 2002 to 3.2% in 2009. [6] The IBBS in 2009 found that HIV prevalence among FSWs in 10 provinces was 8.5%, ranging from 0.3% (in Danang) to 23% (among street-based FSWs in Hai Phong), with higher HIV rates in cities where a high proportion of sex workers inject drugs. A community intervention trial provided user-friendly STI services – including regular checkups with screening or PPT – for female sex workers in five border provinces through mobile teams to multiple sites chosen by the sex workers. Lower HIV prevalence and significant reductions in gonorrhea and chlamydia but not syphilis were reported. [105]

Outcomes from intervention studies, reviews & surveillance data

Intervention research in the peer-reviewed literature presents an uneven picture with >90% of papers focusing on five countries (including the state of West Bengal). However, all countries have published detailed surveillance reports with trends of condom use, HIV and STIs. These sources of data are summarized in Table 2.

Table 2. Summary of intervention research and surveillance data.			
Country	**Intervention research (from literature review)**	**Reviews and (reports)**	**Surveillance**
Bangladesh	Jenkins 2002	Azim 2008 (UNAIDS 2000) (PPT report)	HSS: 2011
Cambodia	Heng 2003, Phal 2009, Busza 2004, Heng 2008, 2008, Couture 2011	(Data Hub HIV & sex work report)	HSS: 1997–2000, 2003, 2006 BSS: 1997–2001, 2003, 2010 STI: 2001, 2005; IBBS: 2012
China	Yang 2005, Li 2006, Rou 2007, Lau 2008, Zhongdan 2008	Hong 2008, Wang 2007 (Data Hub HIV & sex work report)	HIV and condom use survey data: 1995–2010
Indonesia	Ford 2000, Bollen 2010, Magnani 2010, Majid 2010, Morineau 2011	(Data Hub HIV & sex work report)	IBBS: 2002, 2011?
Mongolia	None found		SGS (HIV, condom use, syphilis): 2002, 2005, 2007, 2009, 2011
Myanmar	None found	(Data Hub HIV & sex work report)	HSS 2000-2011
Nepal	None found		IBBS: 2003, 2004, 2006, 2008, 2009, 2011
Thailand	Hanenberg 1994, Celentano 2000	(Data Hub HIV & sex work report)	HIV: Routine STI case report data: 1982–2010
Vietnam	Thuong 2007	Nguyen 2010	HSS: 2000-2009 Syphilis case reports 2006–2010
West Bengal, India	Basu 2004, Evans 2008, 2008, 2010, Ghose 2008, 2011, Cornish 2007, 2010, Swendenman 2009		Integrated surveillance (HIV, condom use, syphilis): 1992, 1993, 1995, 1998, 2001, 2005, 2008

IBBS: Integrated bio-behavioral surveys; SGS: Second-generation surveillance; STI: Sexually transmitted infections.

Surveillance is a primary source of behavioral and biological data, which are often triangulated for high and lower-risk populations to monitor outcomes and estimate trends. [106] Based on these, HIV incidence in Asia is estimated to have declined overall by an estimated 20% between 2001 and 2009, falling by >25% in Cambodia, India, Nepal and Thailand. [6] Prevalence of HIV and other STIs among sex workers varies greatly across Asia. Data from 281 sentinel surveillance sites in nine countries for 2007–2009, showed that HIV prevalence among female sex workers was below 1% in 33% of sites, between 5–15% in 39% and 20–55% in 25% of sites. In Thailand, it was below 5% in all except four of 51 sites while in Sri Lanka, HIV was undetected among female sex workers in all eight sites. Available trend data from seven countries indicate significant decreases in HIV prevalence among young FSWs in Cambodia, India, Myanmar and Thailand. [6] Table 3 (see original paper) summarizes key condom use, HIV and STI trends from national surveillance data and related modelling estimates.

Select trends of key indicators related to sex work from these surveillance data are depicted below. Figure 1 shows that countries where higher levels of condom use are reported by sex workers also report greater reductions in sex worker HIV prevalence.

Figure 1. Reported. (A) Condom use in sex work and **(B)** sex worker HIV prevalence trends.
Source: see TABLE 2.
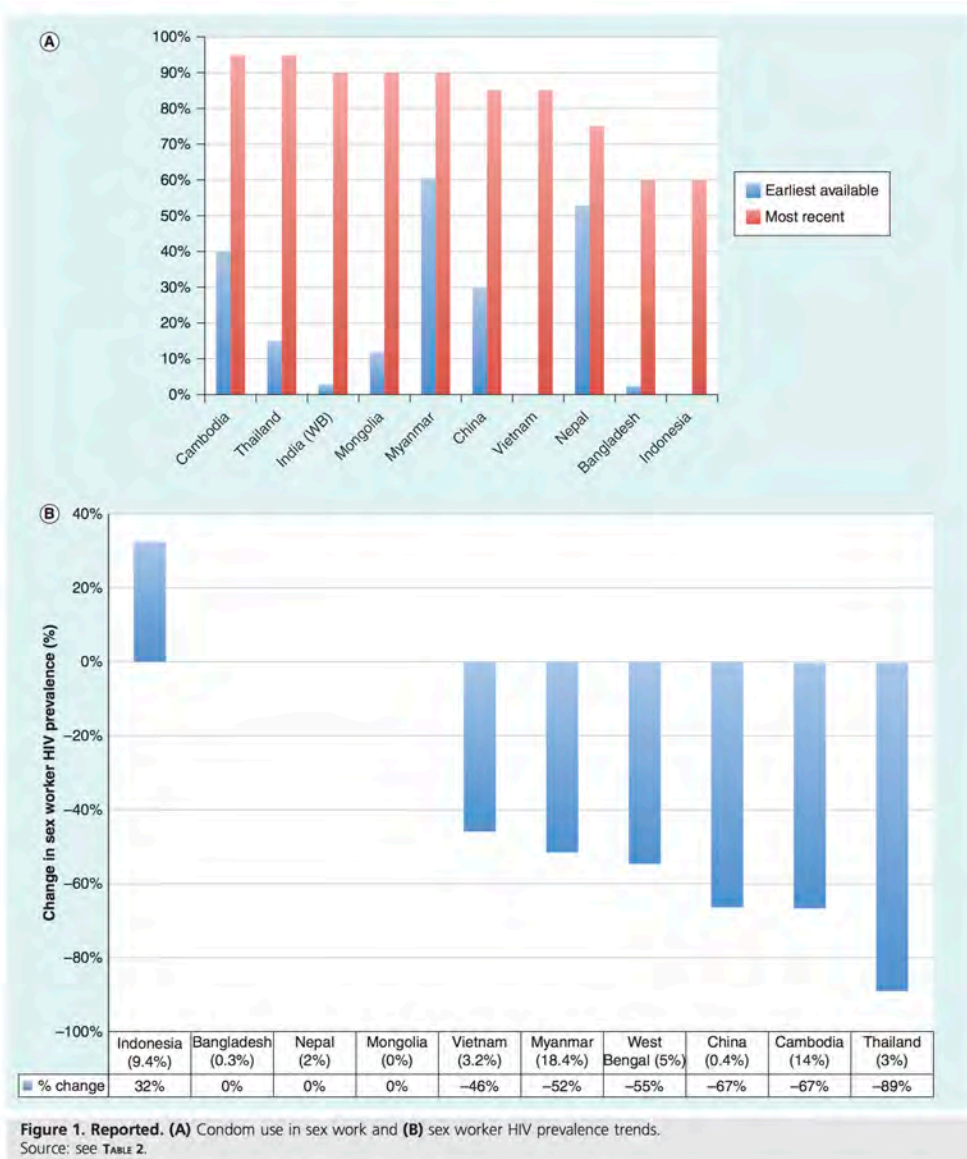
Figure 2 compares HIV prevalence trends among sex workers with those for all adults – declining in both groups for Cambodia, Myanmar and Thailand and rising in Indonesia. Comparable data are not available for West Bengal.

(A)	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Cambodia (direct)			9	24	39	38	40.9	39.3	42.6	33.2	31.1	28.95	26.8	23.4	20.5	17.6	14.7			
Indonesia													1	2.7	6.4	11	8.1	14.6	10.2	
Myanmar												33.5	32.3	31.4	27.5	32	33.5	15.6	18.4	
Thailand (direct)	9.3	15.2	23	28	27.6	27.9	28.2	26.1	21.1	16	18	16.6	12.3	10.6	7.4	6.8	4.6	5.3	4.05	2.8

(B)	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Cambodia						1.2	1.7	1.9	2	1.9	1.6	1.5	1.4	1.2	1.1	1	0.9	0.9	0.8	0.7
Indonesia	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.2	0.2
Myanmar	0.2	0.3	0.4	0.4	0.5	0.6	0.6	0.7	0.7	0.7	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6
Thailand	1	1.5	1.8	2	2.1	2.1	2.1	2	2	1.9	1.8	1.7	1.6	1.5	1.5	1.5	1.4	1.4	1.3	1.3

Figure 2. (A) HIV prevalence trends among sex workers. **(B)** Adult HIV prevalence trends, in concentrated and generalized epidemics. Source: see TABLE 2.

Figure 3 shows HIV prevalence trends among sex workers in countries with lower-level epidemics.

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
China	0	0	0.2	0.2	0.4	1.1	1	1.2	0.9	0.9	0.4	0.5	0.4	0.2	0.6	0.4
Mongolia								0			0		0		0	
Vietnam						3.53	4.66	5.9	3.76	4.42	3.48	4.2	3.86	3.12	3.17	

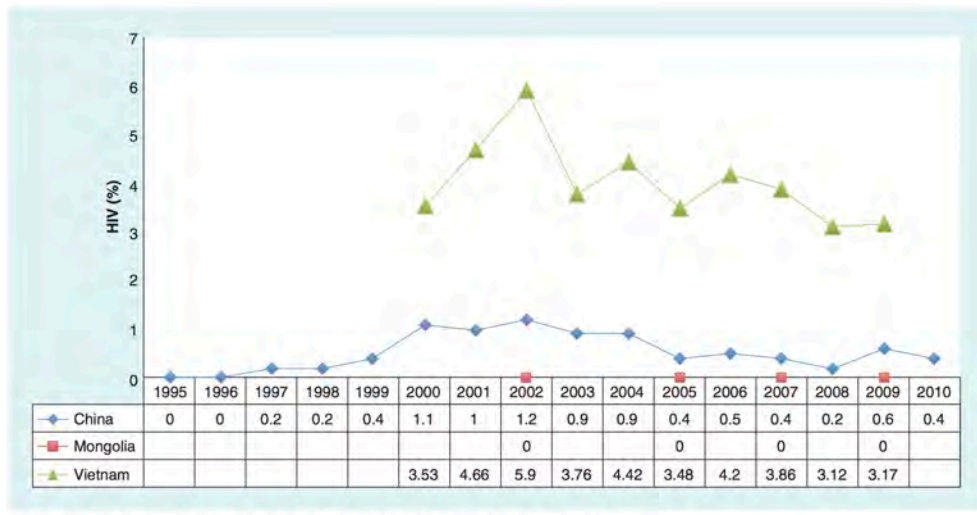**Figure 3. HIV prevalence trends among sex workers in lower-level epidemics.**
Source: see TABLE 2.

Syphilis trends among sex workers and antenatal clinic attenders are reported by several countries using different methods. With the exception of Mongolia and Indonesia, recent syphilis prevalence among sex workers is well below 10%, compared to 10–30% before 2000 (Figure 4) and is declining among both sex workers and pregnant women in Cambodia, Thailand and Myanmar. Fewer countries report trends of other STIs. Thailand has the most complete STI surveillance, based on monthly case reports from all districts. Using these data, Thailand documented reductions of 80% and 95% in curable STIs within 5 and 10 years of implementing 100% CUP. Ulcerative STIs have declined dramatically to 0.2% for syphilis and no cases of chancroid or LGV during the last 5 years. Cambodia measured large decreases in gonorrhea, chlamydia and genital ulcers between 1996 and 2001 among sex workers and high-risk male groups.
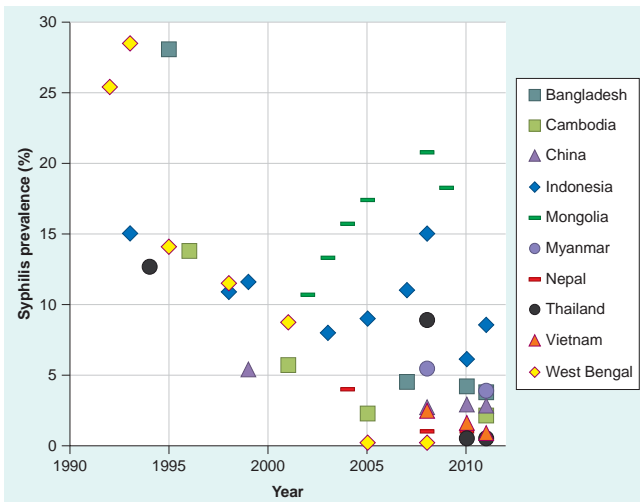
Figure 4. Reported syphilis prevalence among female sex workers.
Source: see TABLE 2, [115].

Expert commentary

Nearly a quarter century ago, HIV epidemics erupted in several Asian cities, facilitated by common conditions of vulnerability, risk and population mobility, subsequently seeding epidemics widely throughout the region. Unprotected sex work and ulcerative STIs (related to male circumcision status) were important proximal risk factors in early epidemics. We reviewed the public health literature and national sources of surveillance and program data to describe interventions in sex work and behavioral and biological outcomes over time. For almost half the countries reviewed, however, peer-reviewed studies reporting interventions and outcomes, were either rare or absent.

Despite these limitations, differences in the scale and evolution of STI/HIV epidemics across Asia, and of country responses to those epidemics are increasingly apparent in surveillance trends. Interventions to raise condom use and improve STI treatment in sex work networks have led to substantial declines in STI and HIV transmission in several countries, while stabilizing or increasing in others. Countries that reduced new HIV infections early have subsequently had the most success in scaling up ART, which in turn has likely contributed to further slowing of HIV transmission in recent years.

There are limitations to be considered in interpretation of prevalence trends, which may be influenced by mobility or other changes in populations. Sex workers in Asia in particular are often highly mobile, both geographically and across types of sex work. Sizeable shifts, for example, from direct, brothel-based sex work to more indirect forms, have been described in

several countries. Nevertheless, the magnitude of prevalence declines in several countries is substantial and consistent across types of sex work, and mirrored in similar declines among other populations, such as bridging groups of high risk men. Confidence in declining trends is also boosted when STI trends move in the same direction, as in Thailand, Cambodia, West Bengal, also on a national scale in China and Mongolia and sub-nationally in several other countries. Available incidence trends – and prevalence trends in cohorts of young sex workers (Cambodia, Myanmar) and likely clients (Thailand) – also reinforce credibility of changes.

These experiences demonstrate that rapid control of sexually transmitted epidemics is feasible under different conditions, from settings with highly organized, establishment-based sex work to places where sex work is less structured and/or street-based. Moreover, the interventions used appear to be highly efficient, producing population-level impact by reaching a relatively small proportion of the population. Successful interventions share several common components – peer outreach, condom programing and STI services – and are driven by sound public health principles.

Structural interventions can greatly enhance the effect of direct condom and STI interventions by changing fundamental conditions of sex work. The most dramatic results – large decreases in curable STIs, elimination of chancroid and reversal of HIV epidemics – have occurred where effective structural interventions have been implemented on a large scale. Condom use rose and epidemics responded rapidly in at least four Asian countries following national implementation of 100% condom use programmes (CUPs). In areas where community-led structural interventions are a strong component, sex workers have gone beyond HIV risk to address a broader range of conditions such as trafficking and violence that affect their lives.

Effective STI/HIV control must reach adequate levels of coverage in order to have impact, and be sustained over time. Relaxation of control measures can lead to rapid rebound transmission of STIs, and increased spread of HIV. It is also clear from Asian experience that success and sustainability of interventions with sex workers and other vulnerable and marginalized populations require 'enabling environments' that facilitate outreach and access to services. Criminalization of sex work, misguided anti-trafficking measures and other law enforcement efforts that increase vulnerability and drive sex workers underground may have unrecognized negative public health effects. Experience from nearly all countries covered in this review argues for decriminalization of sex work to advance public health objectives.

Asian experience also highlights interactions and synergies between STI and HIV epidemics, and the importance of comprehensive STI control efforts. The fastest growing HIV epidemics initially took off in areas with poor control of other STIs. Ulcerative STIs including chancroid

and syphilis were strongly associated with HIV transmission and rapid control of these infections preceded HIV declines. Where effective STI control efforts have been implemented at sufficient scale, HIV trends followed declines of other STIs. Where prevalence of STIs was low to begin with, as in Sri Lanka for example, HIV epidemics have not taken off. [6,107]

Patterns of STI epidemics are certainly different in countries with and without male circumcision, and these patterns are important for HIV. [108] Chancroid specifically is uncommon in populations where men are circumcised and, as has been documented, its presence, closely linked to sex work, greatly amplifies HIV transmission. [109] Yet chancroid and other STIs have been easily controlled in a number of Asian countries despite low rates of male circumcision, and this control appears to be important for slowing HIV epidemic progression. [5,11,40]

Finally, while more difficult to assess, wider availability of ART has likely contributed to declining HIV trends in recent years. Early ART may reduce HIV transmission by 96%, and reduced HIV transmission has been reported in ecological studies with high ART coverage. [110] Modelling in China and Vietnam suggest that the addition of periodic HIV testing and counseling, and ART will contribute to further decreases in HIV incidence. [111,112] Yet, ART provision on a large scale is a relatively recent opportunity, and was clearly not a factor in the early epidemic declines described above. Still, the contribution of ART can be expected to increase as eligibility criteria for ART are revised, admitting more people into treatment earlier. There is thus a high potential for complementarity between targeted primary prevention efforts in sex work and HIV testing and treatment. Offering earlier ART to sex workers – whether through pre- or post-exposure prophylaxis, treatment as prevention, or other strategy – may result in further reductions of HIV transmission. Yet, there is little information on access to treatment or coverage for marginalized populations at highest risk. These are important areas for further research.

Five year view

Asian experience argues that control of STI/HIV epidemics is feasible with existing prevention methods. The next 5 years may see a slowing and even reversal of HIV epidemics in the few Asian countries where this has not yet occurred. In addition, where epidemic control has been achieved, new targets – including elimination of HIV transmission – are under active consideration.

Thailand and Cambodia offer examples of such possibilities. Having reduced estimated HIV incidence by more than 80–90% from more than 140,000 cases annually during the early 1990s

to an estimated 12,800 in 2008 in Thailand, and from fifteen to twenty thousand in the mid-1990s to about one thousand in 2011 in Cambodia, current strategies aim to reduce incidence further. [67] Thailand and China, for example, have set new targets for 50% incidence reductions, while Cambodia is aiming for elimination of new HIV infections by 2020. [113,114] These are ambitious tasks requiring extension of comprehensive prevention and treatment interventions – first of all, to cover gaps among populations at highest risk. Several countries – including China, Indonesia, Mongolia and Thailand – have recently reported rapid HIV and STI increases among men who have sex with men and transgender women. [2] Different sexual networks, often overlapping with sex work, are involved. Experience gained in interrupting transmission with female sex workers – including supportive policy, strong program implementation and quality service delivery – may need to be adapted to work effectively with male and transgender sex workers, their clients and partners, to reduce transmission in these overlapping sexual networks.

To eliminate new HIV infections, appropriate services must also reach much larger populations at intermediate or low risk. Yet considerable progress has already been made – scale-up of HIV treatment, with high case detection, uptake and retention along the cascade of interventions from HIV testing to care and treatment, likely reduces HIV incidence further while bringing needed services to those affected by the epidemic. [6,113,114] It is important to emphasize the complementarity of these new programs with interventions that reduce transmission in sex work. Without large numbers of new infections from sex work, provision of treatment and related HIV services becomes more feasible and resulting viral suppression can contribute to further reductions in transmission. Cambodia and Thailand were able to effectively broaden their response partly because they succeeded in reducing transmission in high-incidence sexual networks. This stands in contrast to many countries that struggle to meet increasing demand for treatment in expanding HIV epidemics. Sex workers should also have access to HIV testing and ART contributing to further reduction of transmission to their clients, regular partners and children. Yet few countries monitor data on ART coverage and uptake by risk population.

Changing patterns of sex work, emerging epidemics among men who have sex with men and cross-border transmission are among current challenges in the region. Meeting these, while maintaining past achievements, will require sustained efforts and more enabling conditions for prevention. Nevertheless, the prospect of eliminating new HIV infections by extending appropriate public health interventions appears credible for the first time, precisely in those countries that first demonstrated how epidemics could be reversed. The next 5 years should show how feasible such aspirations are.

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Eradicating chancroid

Richard Steen

Abstract

Genital ulcers are important cofactors of HIV transmission in the countries most severely affected by HIV/AIDS. Chancroid is a common cause of genital ulcer in all 18 countries where adult HIV prevalence surpasses 8% and is rare in countries with low-level HIV epidemics.

Haemophilus ducreyi, the causative organism of chancroid, is biologically vulnerable and occupies a precarious epidemiological niche. Both simple, topical hygiene and male circumcision greatly reduce risk of infection and several classes of antibiotics — some of which can be administered in single-dose treatment regimens — provide rapid cure. *H. ducreyi* depends on sexual networks with high rates of partner change for its survival, thriving in environments characterized by male mobility and intensive commercial sex activity. Elimination of *H. ducreyi* infection from vulnerable groups results in disappearance of chancroid from the larger community.

Once endemic in Europe and North America, chancroid began a steady decline early in the twentieth century, well before the discovery of antibiotics. Social changes — resulting in changing patterns of commercial sex — probably disrupted the conditions needed to sustain chancroid as an endemic disease. Sporadic outbreaks are now easily controlled when effective curative and preventive services are made available to sex workers and their clients. More recently, chancroid prevalence has declined markedly in countries such as the Philippines, Senegal, and Thailand, a development that may contribute to stabilization of the HIV epidemics in these countries. Eradication of chancroid is a feasible public health objective. Protecting sex workers and their clients from exposure to sexually transmitted diseases (STDs) and improving curative services for STDs are among the proven strategies that could be employed.

Introduction

Chancroid has evaded scrutiny as an important sexually transmitted disease (STD), even though an estimated 7 million cases of chancroid occur yearly. [1] Chancroid is the soft chancre of *Haemophilus ducreyi* and is common in many of the world's poorest regions with the weakest public health infrastructure, such as areas of Africa, Asia, and the Caribbean. Where chancroid is endemic, genital ulcers are common, sometimes surpassing discharges as the most common STD syndrome. [2-4] These regions also have some of the highest rates of human immunodeficiency virus (HIV) infection in the world and chancroid is common in all 18 countries where adult HIV prevalence surpasses 8%. This confluence of high rates of chancroid, genital ulcers, and HIV points to a cofactor that may account for a large proportion of new HIV infections acquired heterosexually in the most severely affected countries of the world.

Chancroid was endemic in most parts of the world well into the 20th century. Several decades before the discovery of sulfa drugs and penicillin, however, chancroid began a steady decline in Europe and North America, and disappeared as a major STD even before it could be recognized as such. Similar declines have been seen in other countries, including China, the Philippines, Senegal, and Thailand. A review of this epidemiological transition could suggest ways of eliminating chancroid from other regions.

This paper considers the feasibility and potential benefits of chancroid eradication. Evidence from the literature on the biological and epidemiological aspects of *H. ducreyi* infection and the role of chancroid in facilitating HIV transmission is summarized. The historical evidence for the global decline in chancroid is presented, together with a discussion of the social and public health conditions that appear to maintain chancroid in a tenuous biological niche.

Biological and epidemiological features of chancroid

Etiological agent

Chancroid is caused by the Gram-negative bacillus *H. ducreyi* and results in superficial ulcerations, often with suppurant regional lymphadenopathy. Its biology and pathogenesis have been well described; [5,6] in its classic form, it is differentiated from syphilis by the soft, irregular borders of the ulcerations (soft chancres) that are painful. Most infections are clinically apparent, although there is some controversy over the extent and importance of asymptomatic disease in women. [7,8] However, clinical differentiation from other types of genital ulcers is not reliable [9-10] and *H. ducreyi* is also hard to culture [11], factors which pose a problem for control strategies based on etiological identification. For these reasons, current international

standards recommend syndromic co-treatment of chancroid and syphilis for effective case management of patients with genital ulcers. [12,13]

Treatment

Chancroid can be treated with macrolides, quinolones, and some third-generation cephalosporins. [14-16] Single doses of certain antibiotics, such as ciprofloxacin and azithromycin, are highly effective [14,17] although longer treatments may be more effective in uncircumcised males and patients with HIV infection. [4,18,19] Antibiotics may also provide some protection from reinfection: one study estimated that the prophylactic effect of a single dose of azithromycin against new *H. ducreyi* infection lasted as long as two months after treatment. [20]

Protection against infection

Topical hygiene is also effective in reducing *H. ducreyi* transmission. During the First World War, simple washing with soap and water within a few hours of sexual exposure was effective in reducing risk of chancroid. [21,22] Male circumcision is highly protective against both *H. ducreyi* [6] and HIV infection [23-26], and the interaction of chancroid and HIV infection accounts for at least part of the HIV-protective effect of circumcision.

Spread of the disease

Chancroid is closely associated with prostitution. [27-30] Data from chancroid-endemic regions have documented that most cases of chancroid occur in people who had direct exposure with a commercial sex worker or whose partner had direct exposure, and outbreaks typically show high male to female ratios. [7,27] This pattern is a sign of the relative vulnerability of *H. ducreyi* compared to other common bacterial pathogens that cause STDs: *H. ducreyi* has a short duration of infectivity and requires frequent contacts to spread within a population. *H. ducreyi* can survive (i.e. maintain a reproductive rate greater than one) only in sub-groups of the population with a sufficient turnover of sex partners. Based on reproductive rate calculations, minimal rates of partner change are estimated to be 15–20 sex partners per year. [6,31] Chancroid is thus not a sustainable infection in sexual networks with low rates of partner change. In theory, control measures that eliminate infection from subgroups with the highest rates of partner change would eradicate chancroid from the larger community. Importantly for disease control, *H. ducreyi* has no non-human reservoir.

Cofactors in HIV transmission

Genital ulcer disease is a recognized risk factor for HIV infection. Strong associations between HIV seropositivity and genital ulcer disease [23,32] have been reported and the odds and risk ratios are higher than for non-ulcerative STDs. [33] Cross-sectional and prospective population studies do not accurately measure the increased risk of HIV infection, however, and underestimate the importance of genital ulcer disease as a cofactor in HIV transmission. Data from Kenya and Thailand, for example, suggest that genital ulcers may increase the risk of HIV infection as much as 50–300 times per unprotected act of vaginal intercourse [34-36] and facilitate a large proportion of new HIV infections in countries where genital ulcers are common.

In many countries with high HIV-infection rates chancroid is the most common cause of genital ulcer disease, and there are strong associations between chancroid and HIV seropositivity. [37-39] The incidence and prevalence of chancroid varies greatly by country and region, however, for reasons that are poorly understood. [1] Indeed, the global epidemiology of chancroid is so poorly documented that it is not included in WHO estimates of the global incidence of curable STDs. [40] However, there is a close geographical association between chancroid and HIV infection (Table 1). In countries of eastern and southern Africa, where chancroid is endemic, the HIV-infection rates are the highest in the world. [41,58] In Asia, the four countries with generalized HIV epidemics all had endemic levels of chancroid when their HIV epidemics started (Thailand subsequently reduced chancroid to non-endemic levels). In contrast, chancroid is rare in countries with low HIV-infection rates.

The disappearance of chancroid from Europe and North America

Prevalence

Although distinctions between venereal diseases were blurred during the 1800s, available evidence suggests that chancroid was commonplace in Europe and North America during the 19th and early 20th centuries. Conditions favourable to transmission certainly existed [59]: 19th-century economic expansion fuelled migration and unprecedented numbers of men were drawn to urban areas, which stimulated demand for commercial sex. As late as 1913, a British commission estimated that 10% of the urban population had syphilis and an even greater proportion had gonorrhoea. [60] Such conditions and STD rates are comparable to those in many developing countries today.

Table 1. Chancroid prevalence in African and Asian countries with the highest rates of HIV-1 prevalence[a]

Country	Adult HIV prevalence rate as a %	Chancroid prevalence rate as a %	n	Sample (method of determination)	Reference
Africa					
Botswana	36	26	108	Symptomatic ulcers (C)[d]	42
				Mineworkers from Botswana (C)	43
Swaziland	25	44	–	Symptomatic ulcers (C)	44
Zimbabwe	25	46	–	Symptomatic ulcers (C)	3
Lesotho	24	56	100	Symptomatic ulcers (P)[e]	45
Namibia	20	–	–	–	No published data
South Africa	20	70	210	Symptomatic ulcers (C)	46
		22	100		47
Zambia	20	47 (male)	139	Symptomatic ulcers (CD)[f]	48
		30 (female)	98		
Malawi	16	26	778	Symptomatic ulcers (P)	4
Central African Republic	14	Most common GUD[b] etiology	–	Symptomatic ulcers (CD)[f]	49
Kenya	14	62	97	Symptomatic ulcers (C)	50
		35	168		51
Mozambique	13	–	–	–	No published data
Djibouti	12	–	–	–	No published data
Burundi	11	–	–	–	No published data
Côte d'Ivoire	11	47	–	Symptomatic sex workers (P)	52
Ethiopia	11	19	–	Sex workers (S)[g]	53
Rwanda	11	18	109	Symptomatic ulcers (C)	54
		29	395		55
Uganda	8	9.8 (male)	–	Rural adult cohort (S)	39
		7.3 (female)	–		
United Republic of Tanzania	8	–	–	–	No published data
Asia					
Cambodia	4	21.5	17	High- and low-risk men and women (P)	56
Myanmar	2	–	–	–	No published data
Thailand	2	95% decline in incidence 1989–93	–	National surveillance	57
India	1	26% (of all reported STDs[c])	–	National STD reporting, Ministry of Health	1

[a] Source of HIV prevalence data: ref. *41*. Dates of HIV data do not correspond with dates of cited chancroid studies.

[b] GUD = genital ulcer disease.

[c] STD = sexually transmitted disease.

[d] C = culture.

[e] P = polymerase chain reaction.

[f] CD = clinical diagnosis.

[g] S = serology.

Bassereau and Ricord distinguished the soft from the indurated (syphilitic) chancre in 1852 and Ducrey identified the causative organism of chancroid in 1889. [6,61] In 19th-century debates over how to reliably differentiate syphilitic sores likely to "affect the constitution" from the "simple sore" of shorter duration that did not, the latter was said to occur "four times as frequently as the true syphilitic sore". [62] Puche in 1858 noted that over 80% of 10 000 ulcers in a series of French patients were classified as being of the soft type. [61] Sullivan, writing in 1939, noted that "the disease occurs endemically in Italy and Northern Africa where indigent prostitutes more or less consistently harbor the bacillus... and the number of chancroidal infections exceeds that of syphilitic infections". [5]

Another picture of the social conditions that favoured transmission of STDs in general, and of chancroid specifically, can be constructed from descriptions of 19th-century urban America and its thriving tenderloin areas with overt street- and brothel-based prostitution. [63] According to Gilfoyle, "many women chose or felt compelled at some point to engage in prostitution in numbers unmatched in New York's history, either before or since". [64] Walt Whitman noted in the late 1850s "that 19 out of 20 of the mass of American young men, who live in or visit the great cities, are more or less familiar with houses of prostitution and are customers to them". [64] Available statistics certainly reveal a high incidence of STDs at that time [65] and venereal rates among prostitutes were estimated to be 75–90%. [21]

A disease on the decline

Despite the evidence that chancroid was prevalent in the 19th and early 20th centuries, there were signs that the disease was declining. In England, for example, Hall reported that chancroid was prevalent until the early 20th century. [60] Sullivan, in 1939, noted: "very likely it is less common now than it was in the last century". [5] Data from military sources support this idea [66,67]: in the United States Army in 1908, chancroid was more prevalent than syphilis, but declined more rapidly than syphilis between 1908 and 1930 (Fig. 1). Hall also pointed out that sulfonamides, introduced in 1937, were "also effective against chancroid, the incidence of which was already declining remarkably for reasons which are obscure". [60]

Fig. 1. **Comparison of chancroid and syphilis incidence rates, United States Army, 1908–30**
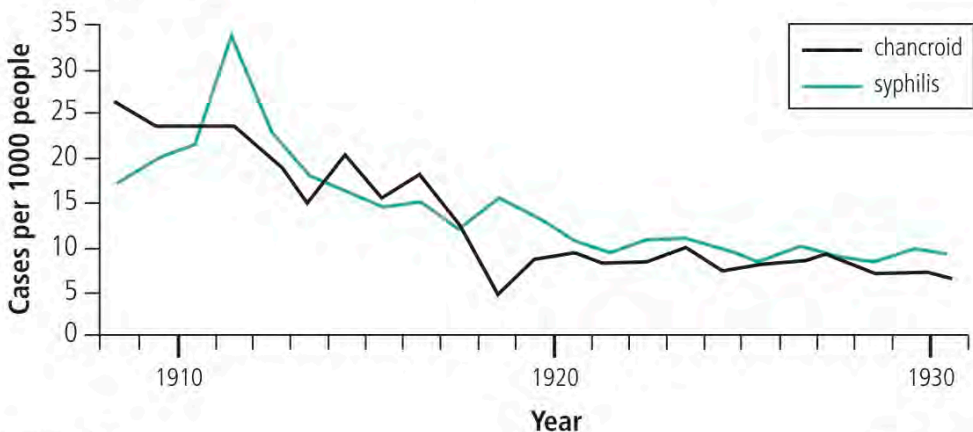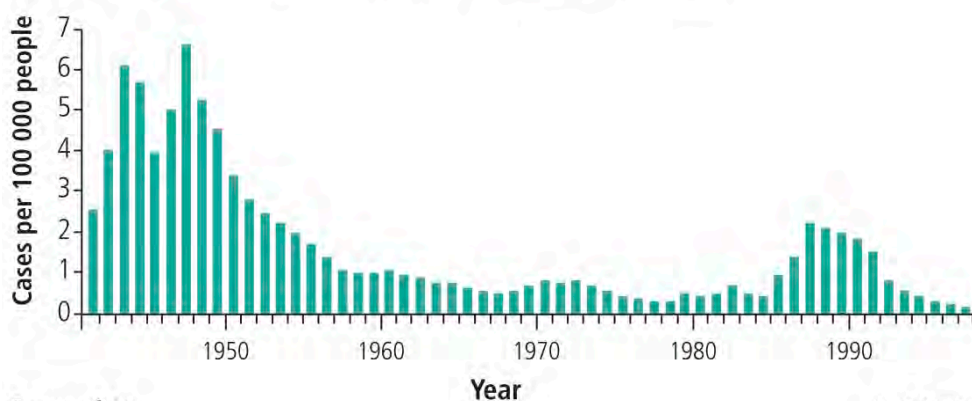
Source: ref. 5.

WHO 01.168

Following the introduction of sulfa drugs and penicillin, chancroid became a rarity in Europe, with occasional outbreaks linked to imported cases. [68] In 1995, fewer than four ulcers per 1000 people seen at genitourinary clinics in Great Britain were classified as chancroid, lyphogranuloma venereum, or donovanosis. [2] Reliable statistics for North America became available following the Second World War, when antibiotic treatment drove a new approach to STD control. Reported rates of chancroid in the United States civilian population decreased by more than 80-fold between 1947 and 1997 (Fig. 2) and chancroid had essentially disappeared as an endemic disease by the late 1950s. Subsequent outbreaks, including a sustained increase in the late 1980s, were usually linked to imported cases and limited to commercial sex networks, and were rapidly controlled though focused case finding and presumptive treatment of genital ulcers. [70-73]

Fig.2. **Chancroid incidence rates in the USA, 1941–98**

Source: ref 69.

WHO 01.169

Several factors probably contributed to the disappearance of chancroid as an endemic disease in developed western societies. The introduction of antibiotics clearly played an important role. It is likely, though, that the decline of chancroid began earlier with significant social changes and shifting patterns of prostitution. Commercial sex dynamics changed radically with reduced migration and improved economic options for women. [21] The demise of the brothel and transformation of sex work to less overt forms with fewer partners probably reduced the size of the core group and limited opportunities for transmission. In Europe, 19th-century regulation of prostitution with periodic health examinations may also have contributed to lower rates of transmission by reducing contact between symptomatic sex workers and clients.

Epidemiological transition in developing countries

Today, the social and public health conditions in many developing countries are similar to those of western industrialized societies at the turn of the 20th century. Rapidly growing urban areas offer elusive alternatives to rural poverty and opportunities for women lag behind those for men. Urban migration is often disproportionately male, which drives demand for commercial sex services. Migrant labour and civil unrest further destabilize community and family life. Even though these conditions favour STD transmission, chancroid has declined in some areas where it once was common.

In Africa

In southern and eastern parts of Africa, where rates of circumcision are low and HIV prevalence is high, chancroid is endemic. It is much less common in West Africa, however, where importation of chancroid from other regions may be important in maintaining transmission. [38] In Kenya, where the importance of chancroid in HIV transmission was first described in the late 1980s [6,74], interventions targeting sex workers and STD patients were implemented. Reported condom use by sex workers has since increased to over 80% in project areas and the incidence of genital ulcers has declined. Chancroid, once the most common ulcer etiology, now accounts for fewer than 10% of genital ulcers seen in clinics in Nairobi, Kenya. [75]

In Senegal, HIV prevalence among pregnant women has been below 1% for more than a decade. A strong multisectoral response, an effective STD control programme and early legalization of prostitution have been credited for this low level. [76] Special clinical services, for example, offer regular examination and treatment for registered sex workers. Not only has there been a significant decline in STD rates among sex workers and pregnant women between 1991 and 1996, but genital ulcers are also no longer common [77] and chancroid is reportedly rare. [78]

In South Africa, migrant labour is employed on a large scale in mining and other industries, creating favourable conditions for transmitting *H. ducreyi*, HIV, and other STD pathogens. Recently, interventions providing curative and preventive services, including monthly presumptive antibiotic treatment to women at risk, have been implemented in several gold-mining communities. One community reported large reductions in curable STDs among the women using the services. [79] At the start of the intervention, chancroid was the main cause of genital ulcers among the women attending, but after the third month of the intervention it was no longer seen, even among new clinic attendees. [80] In miners living in the area, the

prevalence of genital ulcers declined by 78% within nine months and ongoing surveillance shows a sustained reduction relative to the prevalence in other mining areas. [81]

In Asia

Chancroid is rare in Asian countries with stable, low-level HIV epidemics. In the Philippines, for example, treatment for chancroid is not included in the national guidelines for treatment of genital ulcers, although chancroid once was common there. [82] Genital ulcers are reportedly rare and HIV rates have remained at or below 1%, even among registered and freelance sex workers, who have much higher rates of other bacterial STDs. [83] Low rates of chancroid and genital ulcers are also seen in other countries in the region with low-level HIV epidemics. [84]

Among the four Asian countries with generalized HIV epidemics, chancroid is also prevalent, or was so when HIV was introduced in the 1980s. Thailand, however, succeeded in controlling the common curable STDs in the 1990s [85] and managed to significantly slow HIV transmission. [86] Within five years of introducing the 100% condom policy in commercial sex establishments in 1989, the incidence of bacterial STDs fell by over 80%. [57,87] Chancroid led the decline with a 95% decrease (Fig. 3).

Fig. 3. **Reductions in incidence of syphilis, gonorrhoea, and chancroid in Thailand, relative to 1987 levels**

Source: ref. 57.

WHO 01.170
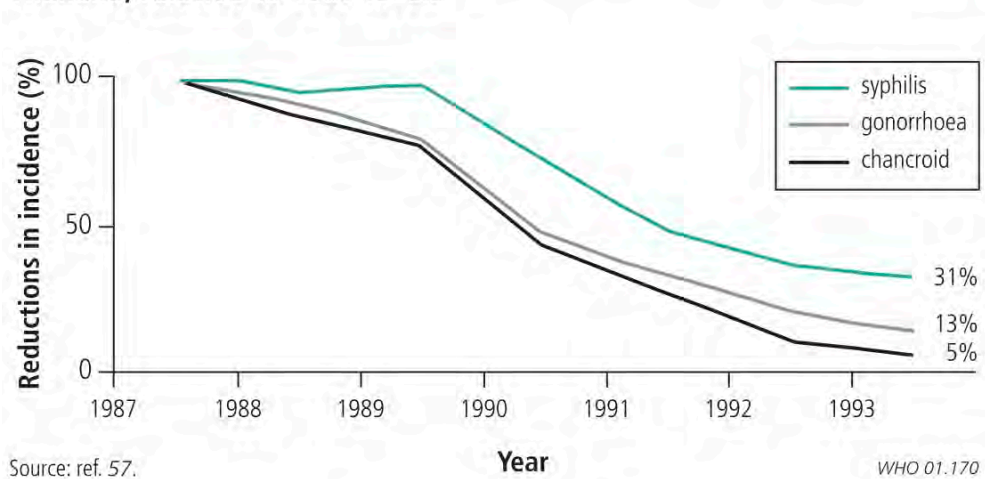
While the condom policy targeting sex workers and their clients was probably the most important factor, it was not the only one. Both chancroid and gonorrhoea rates had started to decline several years earlier, probably in response to the widespread availability of quinolone antibiotics after 1986. [15] Also during this period, a focused effort to eliminate chancroid was carried out in 23 sex establishments in Bangkok. From 1990 to 1991, over 2000 lower-class female sex workers were offered presumptive treatment with ciprofloxacin (500 mg every 3

months). Chancroid among their male clients reportedly fell 46%, despite no change in condom use and limited coverage of sex establishments. [88] Today, chancroid is rarely seen in Thailand, despite an active commercial sex industry and low rates of male circumcision.

Discussion

H. ducreyi has demonstrated its extreme vulnerability in settings as diverse as Bangkok (Thailand), Nairobi (Kenya), New York (USA), and Paris (France). Without conscious effort or control programmes, chancroid has moved from endemicity to a sporadic epidemiological curiosity in many countries. Recent examples of elimination or control in endemic areas of Asia and Africa suggest that chancroid eradication may be a feasible objective.

Based on an examination of the decline in chancroid rates over the last century, interventions in three areas appear to undermine endemic chancroid. First, the organization and patterns of commercial sex appear to be primary determinants of chancroid transmission, and these are influenced by social factors such as migration and opportunities for women. Second, preventive measures, such as widespread condom use by commercial sex workers, can break the chancroid transmission cycle, even when conditions favour the spread of chancroid. Third, effective antibiotic treatment of the highest-risk populations can reduce chancroid transmission in the short term and lead to a rapid decline in chancroid prevalence.

Interventions in these three areas reduce the *H. ducreyi* reproductive rate (R_0), according to the equation $R_0 = \beta cD$, by lowering the rate of partner change (c), the transmission efficiency (β), and the duration of infectivity (D) in vulnerable sexual networks. By acting through separate mechanisms, the interventions are synergistic. In Thailand, for example, despite emphasis on the 100% condom policy [87], all three factors (β, c, and D) probably played a role: STD transmission rates fell as fewer men sought commercial sex; the rates of partner change dropped; more commercial sex acts were protected by condoms; and effective STD treatment became widely available.

Feasibility of chancroid eradication

Biological and epidemiological factors determine whether infectious diseases are suitable for eradication, elimination, or enhanced control, and chancroid meets three important criteria required for eradication. [89] First, it is identifiable, both syndromically and etiologically, which assists treatment and enables more accurate surveillance. Second, the infection is easily cured: there are several effective, single-dosed antimicrobial treatments, one of which provides extensive post-treatment prophylaxis. Third, *H. ducreyi* has no non-human reservoir and is not

sustainable outside the most active human sexual networks. A highly focused effort to eliminate infection from those networks could therefore plausibly eradicate chancroid in endemic areas.

Experience of controlling chancroid outbreaks in non-endemic areas can provide insight into ways of eliminating chancroid infection and preventing its reoccurrence. Successful interventions include: targeted preventive and curative services for sex workers, since regular screening and presumptive treatment can rapidly reduce prevalence; effective syndromic management of genital ulcers, to sustain control; and peer interventions, to maintain high levels of preventive behaviour. Other interventions could also be investigated, such as post-exposure male hygiene or more affordable, accurate diagnostics. Research needs would be largely operational and should focus on adapting strategies to local conditions. As with other disease control efforts [86], interventions should ideally be implemented in a manner that strengthens existing services and forms links with other STD control objectives (such as syphilis elimination). For example, improved surveillance would benefit both chancroid and general STD control efforts. Syndromic surveillance of genital ulcers with periodic etiological confirmation would provide relevant indicators as well as facilitate the study of the role of genital ulcers in HIV transmission.

In summary, the continued existence of chancroid reflects a correctable imbalance. Conditions that appear to be necessary to sustain chancroid in a population include a commercial sex environment intensive enough to expose sufficient numbers of women to high numbers of sexual partners and the absence of basic preventive and curative control measures to blunt that exposure. In this sense, chancroid can be seen as a sentinel disease whose continued presence indicates that existing STD control efforts are wholly inadequate relative to sexual transmission dynamics. As STD control is a progressive and relative goal, controlling chancroid arguably represents an early step in the process. With the majority of new HIV infections occurring in remaining regions of high chancroid prevalence, it may be an opportune time to consider chancroid eradication as a priority for preventing HIV infection as well as for general STD control.

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Chapter 5

Evidence of declining STD prevalence in a South African mining community following a core-group intervention

Richard Steen

Bea Vuylsteke

Tony DeCoito

Stori Ralepeli

Glenda Fehler

Jacci Conley

Liesbeth Bruckers

Gina Dallabetta

Ron Ballard

Abstract

Objectives

To reduce the prevalence of curable sexually transmitted diseases (STDs) in a South African mining community through provision of STD treatment services, including periodic presumptive treatment and prevention education to a core group of high-risk women living in areas around the mines.

Methods

Women at high risk for STDs attended a mobile clinic monthly for examination and counseling, and were treated presumptively for bacterial STDs with a directly observed 1G dose of azithromycin. Gonococcal and chlamydial infection rates were measured by urine ligase chain reaction, and genital ulcers were assessed by clinical examination. Changes in STD prevalence among local miners were assessed through comparison of prevalence in two cross-sectional samples of miners taken 9 months apart, and through routine disease surveillance at mine health facilities.

Results

During the first 9 months of the intervention, 407 women used the services. Baseline prevalence of *Neisseria gonorrhoeae* and/or *Chlamydia trachomatis* in women was 24.9%; 9.7% of these women had clinical evidence of genital ulcer disease (GUD). The proportion of women with incident gonococcal or chlamydial infections at the first monthly return visit (69% follow-up rate) was 12.3%, and genital ulcers were found in 4.4% of these women. In the miner population, the prevalence of *N. gonorrhoeae* and/or *C. trachomatis* was 10.9% at baseline and 6.2% at the 9-month follow-up examination (P<0.001). The prevalence of GUD by clinical examination was 5.8% at baseline and 1.3% at follow-up examination (P<0.001). Rates of symptomatic STDs seen at mine health facilities decreased among miners in the intervention area compared with miners living farther from the site and with less exposure to the project.

Discussion

Provision of STD treatment services to a core group of high-risk women may significantly reduce their burden of disease, and may contribute to a reduction in community STD prevalence. In the absence of sensitive and affordable screening tests for STDs in women, periodic presumptive treatment coupled with prevention education is a feasible approach to providing STD services in this population.

Epidemiologic [1-3] and biological [4-7] evidence support the role of conventional sexually transmitted diseases (STDs) in increasing HlV susceptibility and infectiousness, and the effect of STD treatment in reducing genital viral excretion. [8-9] This evidence has been applied in a community-based randomized trial conducted in Mwanza, Tanzania, where improving STD case management in health facilities resulted in a 40% reduction in HIV transmission. [10]

Public health interventions that reduce community STD prevalence could potentially have a larger impact on HlV transmission. [11] Strategies that have been used to rapidly lower STD prevalence include 1) treatment of general population groups, [12,13] and 2) more selective presumptive treatment of core groups with high rates of both STDs and sexual partner change. [14] For reports on gonorrhea, the effect of one-time mass treatment bas been transient, with prevalence returning to previous levels in the absence of other control measures. [13,14] There are few studies reporting the use of periodic presumptive treatment in core-group populations to reduce community STD prevalence. [15] If such an approach were effective, it would arguably be more acceptable and cost-effective than population-based mass treatment.

Factors that lead to the disruption of communities or the separation of couples are known to enhance the spread of STDs. [16-17] Commercial sex flourishes under conditions of migrancy [18]; studies conducted early in the African HIV epidemic revealed an association between high urban adult male/female ratios, which is indicative of male migration, commercial sex activity, and high rates of STDs and HIV. [19] The more recent extension of the HIV epidemic to rural areas in many African countries may be fueled by the movement of migrant laborers to and from their home communities.

Commercial sex is a prominent feature around many South African mines where thousands of male migrant workers live in single-sex hostels, and is regarded to be one of the key factors in the maintenance of high STD rates in mining communities. [20-21] Previous efforts to control STD in these mining communities have had minimal success (personal communication, Ron Ballard, 1999). Historically, mining companies have concentrated their attention exclusively on their employees, and little effort has been made to reach the sexual contacts of the miners.

To complement services provided by the mine clinics, we designed an intervention to provide acceptable and effective STD treatment and preventive services to women living around the mines. The objective of this study was to assess the impact of STD treatment and prevention services for high-risk women on these women and the male migrant community in the intervention area. Specific objectives were to 1) measure STD incidence and preventive

behavior among the women during the intervention; and 2) to assess STD prevalence and clinic attendance rates for STD treatment in male mine workers before and after implementation.

Methods

Study Design

This intervention-linked research used a longitudinal study design with repeated measurements of STD infection among women participants. High-risk women were referred by peer outreach workers to a mobile clinic where monthly examination and presumptive treatment, prevention education, and condoms were provided. Syndromic STD management was offered to women with symptomatic STDs. The prevalence of STDs and behavioral indicators were determined at monthly intervals for the women participants. The prevalence of STDs among miners was measured in two separate cross-sectional samples at baseline and 9 months later. Outpatient records at mine health facilities were examined to monitor rates of symptomatic STD among miners in the area.

Intervention Site

The intervention was conducted from October 1996 to June 1997 in a Free State mining town in South Africa with an estimated population of 80,000 persons, including approximately 13,000 miners. Ninety percent of these miners live in single-sex hostels near the mine shafts where they work. A mobile clinic service for high-risk women was established near a commercial area surrounded by 3 mine hostels (H2, H3, H4) with a miner population of approximately 3,700. Two other hostels (V1, V2) were located at an intermediate distance (2-4km), and two hostels (Ml, M3) were located more than 5 km from the project area. Community mapping was carried out to identify taverns, shebeens (unlicensed liquor outlets), and other meeting places where miners relaxed after work. Previous ethnographic research conducted in the area had shown that many women frequenting these establishments provide sexual services to the miners in exchange for some material benefit.

Recruitment of Women

Project staff conducted focus-group discussions with women contacted at identified meeting places to discuss the intervention and pretest data collection instruments. Peer educators were then selected and trained to provide information to women about sexual risk reduction, condom use, and the advantages of using the clinical services. After training, peer educators distributed clinic referral cards to high-risk women, and encouraged them to attend the mobile

clinic monthly. No incentives other than the services themselves were used to encourage clinic attendance.

Intervention

Sexually transmitted disease services for high-risk women were provided at a mobile clinic staffed by a professional nurse who was trained in the study protocol. All women referred to the clinic received an initial assessment and treatment or referral; those women who met the risk-based inclusion criteria (i.e., reporting commercial sex work or having at least three regular or non-regular partners) were enrolled and advised to return for monthly clinic visits.

Upon enrollment, each woman was administered a standardized questionnaire to obtain information regarding demographics, obstetrics, sexual history, and current symptoms. A genital examination, which included speculum, was performed and a urine sample was collected. Venipuncture was performed to obtain serum for serologic testing for syphilis. Urine specimens were stored in a cold box in the mobile clinic and transported daily to the laboratory in Johannesburg, where the specimens were aliquoted and frozen at -20ºC. Specimen were analyzed for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* using ligase chain reaction (LCR) (LCx, Abbott, Chicago, IL). Serum was tested for quantitative rapid plasma reagin assay (Immutrep, Omega Diagnostics, Alloa, Scotland).

All participants were given presumptive treatment with one 1G dose of azithromycin under direct observation. Azithromycin was chosen for its activity against *C trachomatis*, *N gonorrhoeae*, and *Haemophilus ducreyi*, which are common pathogens in the community. [22-25] It was emphasized that the medication was effective for only a few STDs, and that taking the medication was not a substitute for other preventive measures such as partner reduction and condom use. In addition, women with genital ulcerations that were noted on examination were administered a single intramuscular injection of 2.4 million units benzathine penicillin to provide coverage for primary syphilis; women found to have vaginal discharge on examination were given one 2G dose of metronidazole to cover *Trichomonas vaginalis* infection and bacterial vaginosis, and 200 mg clotrimazole vaginal suppositories for 3 days for yeast infection in addition to their azithromycin therapy. At the first follow-up visit, all women with reactive syphilis serology were treated with a single injection of 2.4 million units benzathine penicillin.

At monthly follow-up visits, risk behavior was assessed using a brief questionnaire to determine symptoms, number and types of sexual partners, and condom use. The physical examination was repeated, and urine was collected for LCR testing. All women were given azithromycin, and specific signs and symptoms of STDs were treated as described above. The importance of

consistent condom use was stressed by the nurse at each clinic visit and by peer educators in the field.

To evaluate the impact of the intervention on community STD prevalence, miners living in hostels in the intervention area were examined. Two separate samples of consecutive miners presenting for annual pre-leave physical examinations were screened for signs and symptoms of STDs at baseline and 9 months later. Discharge and ulcers were noted, and a first-catch urine sample was collected for LCR testing for *N gonorrhoeae* and *C trachomatis*, as described above. Results were returned within 2 weeks, and free treatment was provided to miners with positive test results.

Mine hospital records of outpatient visits were available for the period of December 1995 to June 1997. Average attendance rates for STD were computed for each mine hostel during the periods of December 1995 to June 1996 and December 1996 to June 1997; these rates were compared with the total number of outpatient visits for those periods. Rates from hostels in the intervention area were compared with those from more distant hostels.

Analysis

Data analysis was performed using Epilnfo (Centers for Disease Control and Prevention, Atlanta, GA) and SAS (SAS Institute, Cary, NC) statistical packages. The chi-square test was used to compare proportions, and the generalized estimating equation (GEE) [26-27] was used to analyze repeat measures of STD infection in women. Temporal explanatory variables including time enrolled in the study, time between visits, and calendar time were modelled to predict infection with the primary STD response variables. In modelling explanatory variables, discriminant analysis was used to determine breakpoints for transforming continuous variables to categorical variables.

Results

Women Using the Services

During the initial 9 months of the intervention, 407 women were seen at the project clinic at least once, and 710 follow-up visits were registered. Follow-up rates were 69%, 48%, and 32% respectively for visits 2, 3 and 4. The median interval between visits was 29 days (range 17-195 days).

The mean age of women attending was 32.9 years at baseline; 70% of these women were South African, and 29% were from neighboring Lesotho. The median length of stay in the area was 3 years, 22% of the women had arrived within the past 1 year. Whereas less than 1% of women

were married, 30% reported living with a man, and more than 80% of women reported having one or more regular partners who provided some monetary or in-kind support. Baseline risk profiles and preventive behavior for all women, for women who attended the clinic at least three times, and for women who dropped out before the third visit are summarized in Table 1. Women who returned to the clinic at least three times were slightly older than but had similar risk profiles to women who attended only once or twice.

Table 1. Baseline risk profile and preventive behavior among women using STD services

	All women	Women who did not return	Women with at least 1 follow-up	P value
Number	407	147	260	
Mean age	32.9	31.8	33.4	0.04
Report clients	25.9%	27.4%	25.1%	0.6
median # casual clients	2	2	2	0.5
condom use sometimes	25.5%	12.8%	33.3%	0.02
% condom use last work day	2.9%	0.0%	3.2%	0.2
Report regular partners	82.8%	82.3%	83.1%	0.8
median # regular partners	2	2	2	0.8
ever condom use	23.9%	22.9%	24.4%	0.8
Past history of STD	66.1%	68.7%	64.6%	0.4
received no treatment	43.5%	46.5%	41.7%	0.4

At the initial visit, 17.3% of women tested positive for *N gonorrhoeae*, and 14.3% of women tested positive for *C trachomatis*. One in four women (24.9%) had a gonococcal or chlamydial infection or both. Genital ulcers were noted during examination in 9.7% of women. A total of 33.8% women had a reactive syphilis serology, and 49.4% of the women had evidence of one or more of the previously described infections. There was no significant difference in the prevalence of any STD measured at the first visit when comparing women who attended the clinic at least three times with women who attended less than three times (data not shown).

After treatment, rates for all STDs measured at follow-up visits were significantly lower than at baseline. Table 2 shows the prevalence of gonorrhea, chlamydial infection, and GUD at the first four visits; rates are also shown for the subgroup of women who returned for at least three visits. Post-treatment prevalence is an approximation of the incidence rate of new infection, and suggests high levels of STD exposure (Figure 1).

Table 2. STD prevalence rates in women at baseline and follow-up visits

	n	Gonorrhea (GC)	Chlamydia (CT)	GC &/or CT	Genital ulcer	Symptomatic ulcer*
All enrolled women						
first visit	407	17.3%	14.3%	24.9%	9.7%	6.4%
second visit	260	8.3%	4.0%	12.3%	4.4%	1.5%
third visit	172	7.6%	2.9%	10.6%	3.3%	1.2%
fourth visit	108	4.7%	0.9%	5.7%	5.7%	0.9%
Women with at least 3 visits						
first visit	172	14.6%	13.5%	22.8%	10.0%	7.6%
second visit	172	9.6%	5.4%	15.0%	3.2%	0.6%
third visit	172	7.6%	2.9%	10.6%	3.3%	1.2%

*operational definition: women complaining of genital ulcers which were confirmed on examination (asymptomatic women were not routinely examined for ulcers at follow-up visits).

Figure 1. Sexually transmitted disease prevalence and reported condom use in women at baseline and follow-up visits (from Table 2)
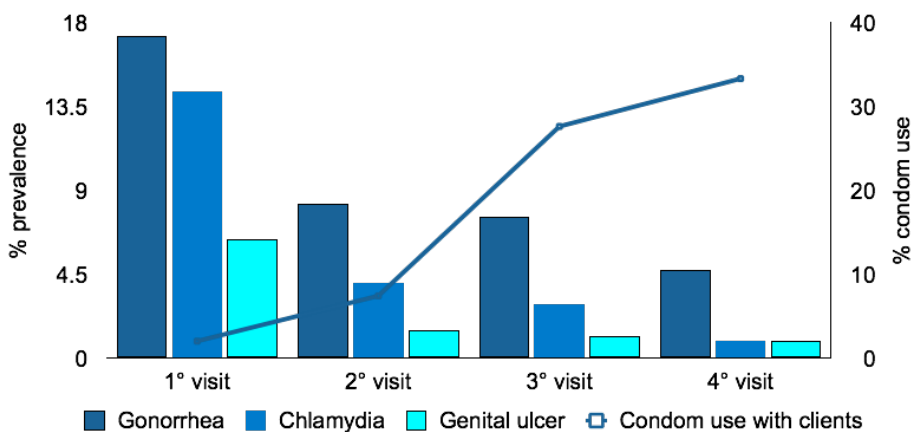
Repeated measurement analysis was used to compare STD prevalence rates at follow-up visits to rates measured at baseline. Several time covariates (i.e., time between visits, time in the study, and calendar time) were included in the model. Prevalence of all infections were significantly lower than at baseline when the interval between visits was less than 1.3 months (P=0.003, chlamydia; P=0.002, gonorrhea; P=0.02, symptomatic GUD). The prevalence of gonorrhea among women seen around the Easter holiday was significantly higher than that measured at baseline (P=0.01). In the presence of these other time covariates, overall time in the study was not a significant factor in explaining the probability of infection compared with the baseline.

Reported condom use with all clients during the woman's last working day increased significantly from 2.0% at the first visit to 7.4%, 27.6%, and 33.3% at the second, third, and fourth visits, respectively (chi-square for trend, P<0.00001), although only a minority of women admitted to having casual clients. No significant change was noted in condom use with regular partners.

Sexually Transmitted Disease Prevalence Among Miners

Prevalence rates of *N gonorrhoeae*, *C trachomatis*, and GUD in miners from the intervention area presenting for routine pre-leave examinations before the intervention (n=608) and 9 months later (n=928) are presented in Table 3 (Figure 2). The prevalence of gonorrhea and/or chlamydia decreased from 10.9% to 6.2% (P<0.001), and the prevalence of GUD decreased from 5.8% to 1.3% (P<0.001).

Table 3. STD prevalence in miners before and 9 months after start of intervention

	Before	After	*P* value
Gonorrhea (GC)	5.2%	3.4%	0.075
Chlamydia (CT)	6.6%	3.5%	0.005
GC &/or CT	10.9%	6.2%	<0.001
Genital ulcer	5.8%	1.3%	<0.001

Figure 2. Sexually transmitted disease prevalence in miners before and 9 months after start of intervention (from Table 3)
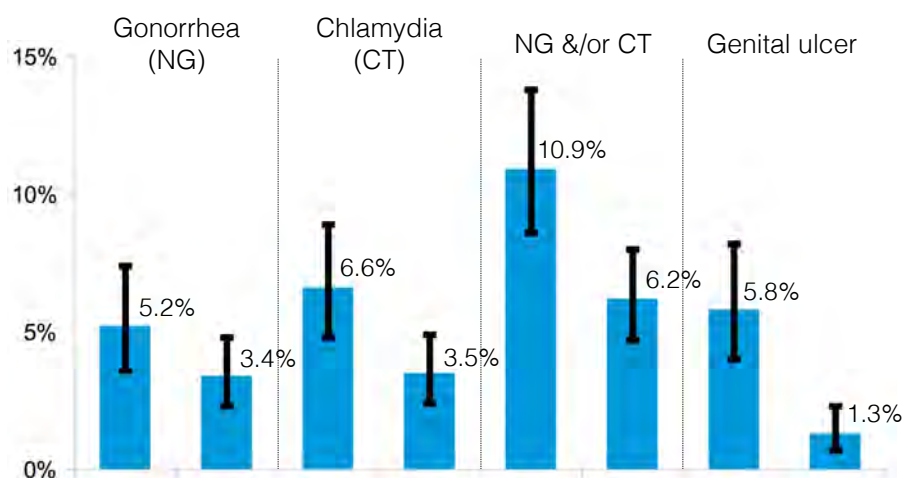
Mine hospital outpatient records were monitored for changes in rates of visits for new STD episodes. In the year preceding the intervention, 1,130 STD visits were recorded for a miner population of 10,559 (10.7 visits per 100 miners). Table 4 presents mean monthly rates of STD visits by mine hostel group for the periods of December 1995 to June 1996 and December 1996 to June 1997. During the post-intervention period, STD attendance rates decreased for miners at the Harmony mines (H2/H3/H3) closest to the intervention area; for more distant hostels, the difference was inversely related to distance from the intervention. This pattern was most evident with GUD (Figure 3). The ratio of STD visits to all outpatient visits also decreased for hostels closest to the intervention when compared with more distant hostel.

Table 4. Mean monthly rates of outpatient STD visits by mine hostel group

	H2/H3/H4 (intervention)	V1/V2 (intermediate)	M1/M3 (distant)	Chi-square for trend (p)
Distance from intervention	1-2km	2-4km	>5km	
Average miner population	3665	3634	3184	
All STD / miner population				
Dec. 95 - Jun. 96	1.18%	1.16%	0.64%	
Dec. 96 - Jun 97	0.92%	1.05%	0.85%	
percent change	**-22.4%**	**-9.4%**	**33.6%**	**0.004**
Genital ulcer / miner population				
Dec. 95 - Jun. 96	0.64%	0.61%	0.33%	
Dec. 96 - Jun 97	0.34%	0.46%	0.41%	
percent change	**-46.8%**	**-24.4%**	**26.3%**	**0.002**
STD visits / All OPD visits				
Dec. 95 - Jun. 96	2.82%	2.92%	1.37%	
Dec. 96 - Jun 97	1.81%	2.09%	1.71%	
percent change	**-35.9%**	**-28.4%**	**25.2%**	**0.04**

Figure 3. Mean monthly rates of outpatient GUD visits by distance from intervention
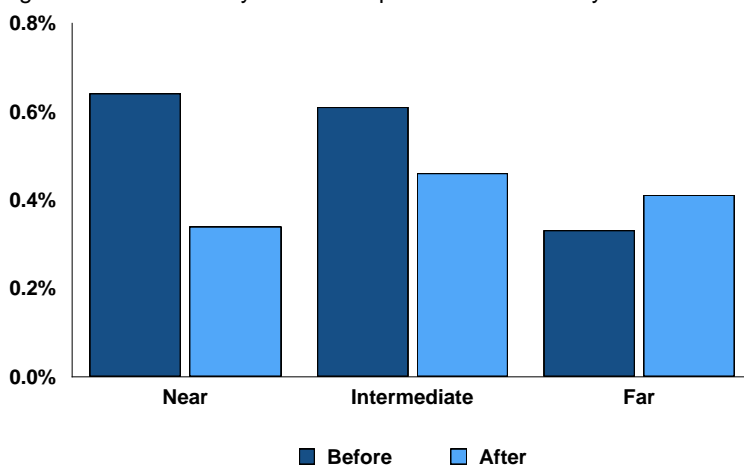
Discussion

The results of this intervention research suggest that provision of effective curative and preventive services to high-risk women may have a significant impact on STD rates in these women and on community STD prevalence. Despite its short duration, the study reported here offers evidence of the utility of a core-group approach to STD control, and information on what may constitute feasible and effective STD services for high-risk women.

Epidemiologic treatment has been advocated as a strategy for reducing STD prevalence in areas of high endemicity. [28-29] One such approach, general-population mass treatment, has an advantage over clinic-based care because people with asymptomatic or minimally symptomatic infections are reached. A randomized community-controlled trial of mass treatment of all consenting adults 15-59 years was recently conducted in the rural Rakai district of Uganda. [12] This approach had a significant impact on community prevalence of some STDs; however, concerns have been raised about the logistics and costs of such an intervention and its replicability outside of a research setting. [30] In addition, intermittent mass treatment may have little effect on underlying STD transmission dynamics and resultant incidence of new infections.

Interventions focusing on core groups (e.g., commercial sex workers and their clients) are potentially more effective and cost-effective in reducing community prevalence of STD than general population efforts. [11,31] Focal outbreaks of syphilis and chancroid in North America have been contained through interventions with commercial sex workers and their clients. [l5,32] and evidence from Nairobi and Zimbabwe [33] suggests that targeted peer intervention

with commercial sex workers have contributed to lower community STD prevalence. Thailand's 100% Condom Program [34] provides perhaps the best example of the potential of a core-group intervention; applied on a national scale, promotion and enforcement of condom use in commercial sex establishments led to reductions of more than 80% in STD incidence and an apparent decline in HIV incidence. [35,36]

Other approaches to reducing STD prevalence in core groups may be possible. Commercial sex workers and their partners have significantly higher rates of STD than the general population, [37-39] yet health-care services are often not available, accessible, or acceptable to these high-risk populations. In the few demonstration projects where quality STD services have been made available to commercial sex workers, decreases in STD and increases in prevention behavior have been documented. [37-41] A major limitation faced by providers of such services is the expense and low sensitivity of screening tests. [42-43] The high proportion of asymptomatic infections in women makes identification of persons who need STD treatment problematic.

Against this background, we sought to design and implement effective STD preventive and curative services that would be acceptable to high-risk women living in this mining community, and to look for evidence of an affect on STD prevalence in the wider community. Data are thus presented on two distinct populations: women at risk who received project services, and miners living in the area of the intervention. The project sought to improve STD services for the former, and to measure changes in STD rates among the latter – a group that received no direct intervention as a result of the project. The prevalence of STD among miners was carefully measured from cross-sectional samples before and after initiation of services for the women and through monitoring of health-facility use to test the hypothesis that provision of services for high-risk women has an impact on STD prevalence in the community. We were confident that provision of services, including monthly presumptive treatment with a highly effective antibiotic, would reduce morbidity due to the common curable STD among the women using the services.

In this study, emphasis was placed on designing a feasible intervention that could be replicated outside of a research setting. To assess important operational aspects of service provision, including feasibility and acceptability of the services to the women, no incentives to attend the services other than the services themselves were offered. The follow-up rates reported represent actual use patterns of a socially marginalized and highly mobile population, but introduce potential bias when analyzing trends. The decision not to artificially stimulate attendance to maintain a cohort may increase the applicability of the findings. The results

suggest that provision of services for high-risk women can have a significant effect on STD rates in the larger community, even when the women use the services irregularly.

Despite loss to follow-up, the exposure to and burden of STD faced by the women participants can be characterized to a certain extent; the prevalence of curable STDs including *N gonorrhoeae*, *C trachomatis*, *T pallidum*, and GUD was high, with one half of the women testing positive for at least one of these infections at their first visit. The lack of acceptable, effective services for these women may partially explain these high rates of curable conditions.

The rate of repeated exposure to STD pathogens was also high. After initial presumptive treatment, the incidence of gonococcal and/or chlamydial infection was more than 12% among women who returned for their initial monthly follow-up visits. If STD exposure continued at this rate, prevalence would be expected to return to baseline levels within several months. Rapid return to initial prevalence rates following one-time presumptive treatment has been described elsewhere, [13,14] and emphasizes the importance of sustaining preventive and curative efforts.

During the intervention period, we documented significant reductions in STD prevalence and increases in condom use that were robust to a subgroup analysis of women who attended the clinic consistently. These changes act to reduce a woman's burden of disease; even with continued STD exposure, early treatment shortens the duration of any new infection, thereby reducing the risk of complications in these women, whereas condom use acts at the primary prevention level to limit exposure. At the community level, the impact of a reduction in STD prevalence among high-risk women can be significant for STD control. Because a male partner's risk of infection is proportional to STD prevalence among his sex partners, transmission opportunity in high-risk encounters would be reduced. Because of the dynamic nature of STD transmission, reduced STD incidence and prevalence in men would decrease subsequent risk for their casual and regular partners. [11]

Core-group theory maintains that interventions reaching persons with the highest rate of partner change will have the greatest effect on community STD prevalence. [31] Data from three sources support the finding of a decrease in STD prevalence in this mining community during the intervention period. As expected, significant decreases in prevalence were documented in women participating in the intervention, while miners in the intervention area experienced marked decreases in prevalence of the same STDs that decreased most significantly in these women (i.e., ulcers and chlamydia). Finally, outpatient STD attendance rates from mine hostels near the intervention site decreased significantly compared with more distant hostels, with the effect again being the strongest for GUD.

An apparent seasonal effect may partially explain the smaller reductions seen with gonorrhea. Women were significantly more likely to have a gonococcal infection detected during the Easter holiday, a time of travel, than at other times. The follow-up screening of miners was conducted immediately after this period, and may reflect increased transmission, perhaps seeded from imported cases. This observation is consistent with experience from mass treatment trials [13,14] and the known transmission dynamics of gonorrhea, including a high efficiency of transmission, short incubation period, and long duration of infectivity. Because of its more volatile epidemiology, gonorrhea may be more resistant to control measures, including monthly presumptive treatment, than other bacterial STDs.

Concerns regarding presumptive treatment include development of antibiotic resistance and an inadvertent promotion of a false sense of security that could impede adoption of preventive behavior. Within the limitations of this intervention research, we examined both of these issues. Azithromycin was chosen for its efficacy against the common bacterial pathogens in the community and for its single orally administered dose. Monthly treatment was given under direct observation, which minimized the possibility of subtherapeutic doses due to poor compliance. Clinical trials [22- 25] have shown high cure rates for 1g azithromycin for *H ducreyi*, *C trachomatis*, and *N gonorrhoeae*; however, some advisors have recommended 2g azithromycin for gonorrhea [22] which, although poorly tolerated, may delay the development of resistance. In this series, the monthly urine LCRs served as a test-of-cure by which the effectiveness of the antibiotic treatment could be monitored. Gonorrhea and chlamydia were eliminated from the genital tract of all infected women who returned for follow-up visits (n=81, gonorrhea; n=50, chlamydia), although several women had positive results on consecutive visits. Given the high incidence of infection with these organisms, it is likely that most persistent positive results were reinfections versus treatment failures; however, as with any strategy involving antibiotic treatment, ongoing surveillance is indicated to detect emerging resistance.

Because of a concern that monthly treatment might have a negative impact on the adoption of preventive measures, adequate risk-reduction education was provided from the start of the intervention, and reported condom use with clients increased significantly with women's use of services. This finding is consistent with a prevention-care synergy reported elsewhere [37] whereby provision of curative services reinforced the adoption of preventive measures. As STD prevalence falls and condom use increases, however, the rationale for an intensive intervention such as presumptive treatment diminishes. Additional research could help define the optimal duration and frequency of presumptive treatment under changing epidemiological and behavioral conditions.

In summary, we have presented evidence that provision of STD prevention and curative services to a core group of high-risk women may contribute to a reduction in community STD prevalence. Computer modelling [44] and cost-benefit analysis suggest that decreases in STD prevalence that were measured during the short intervention period may have a significant impact on HIV transmission, resulting in a high margin of potential benefit to intervention costs. Of course, improved health-care services and public-health interventions are not substitutes for structural changes that could influence the environmental determinants of disease transmission. [45] To the extent that migrant labor practices separate families, they create a high-risk environment for STD and HIV transmission. Public health measures to lower prevalence in the short term must be seen within this context as temporary measures.

We have also shown that periodic presumptive treatment, combined with preventive education and syndrome management of symptomatic women, is a viable option for STD service delivery in this population of high-risk women. Although there may be other options (e.g., screening and treatment), these must take into account the high prevalence and continued high levels of exposure to STDs, and the asymptomatic nature of the majority of infections. In the absence of accurate, affordable screening tests for women, periodic presumptive treatment – at least in the short term – may be an appropriate curative approach for similar populations of high-risk women.

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Chapter 6

STI declines among sex workers and clients following outreach, one time presumptive treatment, and regular screening of sex workers in the Philippines

Teodora Elvira Wi

Epi R Ramos

Richard Steen

TA Esguerra

MCR Roces

MC Lim-Quizon

Graham Neilsen

Gina Dallabetta

Abstract

Objectives

This intervention linked research aimed to reduce prevalence of *Neisseria gonorrhoeae* (Ng) and *Chlamydia trachomatis* (Ct) among female sex workers by means of one round of presumptive treatment (PT), and improved prevention and screening services.

Methods

A single round of PT (azithromycin 1 g) was given to all female sex workers reached during a 1 month period of enhanced outreach activity. Routine sexually transmitted infection (STI) screening services were successfully introduced for two groups of unregistered sex workers who work in brothels (BSWs) and on the street (SSWs). No changes were made to existing screening methods for registered sex workers (RSWs) or lower risk guest relations officers (GROs). Cross sectional prevalence of Ng and Ct was measured by PCR on three occasions, and stratified by type of sex work. Ng/Ct prevalence was assessed twice in clients of BSWs.

Results

Prevalence of Ng and/or Ct at baseline, 1 month post-PT, and 7 months post-PT was BSWs: 52%, 27%, 23%; SSWs: 41%, 25%, 28%; RSWs: 36%, 26%, 34%; GROs: 20%, 6%, 24%, respectively. Ng/Ct declines 1 month post-PT were significant for all groups. 6 months later prevalence remained low for BSWs (p=0.001), and SSWs (p=0.05), but had returned to pre-intervention levels for the other groups. Prevalence of Ng/Ct among clients of BSWs declined from 28% early in the intervention to 15% (p=0.03) 6 months later.

Conclusions

In this commercial sex setting, one round of PT had a short term impact on Ng/Ct prevalence. Longer term maintenance of STI control requires ongoing access to effective preventive and curative services.

Sex work carries occupational risks, not least of which is frequent exposure to sexually transmitted infections (STI). STI prevalence among sex workers in low income countries often surpasses 50% and may reach 80–90% when chronic viral infections are included. [1] Sex workers also face extremely high risk of sexually acquired HIV infection with incidence rates as high as 17 per 100 person months. [2] Yet it is estimated that only 16% of sex workers in low and middle income countries have access to even basic HIV prevention services. [3]

Sex workers, once infected, can transmit STIs and HIV to a far larger number of susceptible clients, who serve as efficient "bridge" groups for even wider transmission. [4] Because of this multiplier effect, effective interventions with sex workers and their clients can avert many more infections than would be prevented by general population strategies alone. [4.5] Empirical data from Asia and Africa confirm that interrupting transmission in commercial sex networks can lead to large reductions in community HIV and STI prevalence, and reverse rapidly growing epidemics [6-11]

Both condom promotion and STI case finding are important for decreasing STI and HIV transmission in sex work settings. [12-16] Case finding is expensive, however, and commonly available methods for identifying STIs in women are neither sensitive nor specific. Presumptive treatment in high risk populations is an alternative that has been shown to contribute to community STI control in several settings. [17-19]

By definition, however, presumptive treatment strategies are temporary measures; as prevalence falls, the epidemiological justification for the intervention weakens. [19] In order to maintain reduced prevalence, other control measures – condom promotion, effective screening, and treatment programmes – must be in place.

In the Philippines, a network of social hygiene clinics (SHCs) provides STI screening and treatment for registered female "entertainment workers" in over 140 cities, in some sites screening over 1000 women weekly. The effectiveness of these services is unclear, however. Cervical Gram stain, used in SHCs to screen for gonorrhoea and chlamydia, has low sensitivity to detect infection, [20] and clinical examinations are not done systematically. Moreover, some categories of entertainment workers are exempt from regular checkups, and most freelance sex workers are either not eligible or avoid the system entirely. Despite these limitations, HIV prevalence remains low in the Philippines even among sex workers. [21] Curable STI rates are high, however, with predominantly non-ulcerative patterns. [21,22]

Angeles City is a priority area for STI control and HIV prevention. Formerly the site of a large US military base, the city's numerous "entertainment establishments" now attract foreign tourists and local men. At the time of the intervention, an estimated 2000–2500 women were

working as sex workers in Angeles. Registered sex workers (RSWs) employed by licensed establishments receive weekly check-ups at the local SHC. Unregistered sex workers who work in brothels (casas) or on the street typically have more clients, poorer access to services, and higher STI prevalence. [23,24] In a recent study in Angeles, gonorrhoea prevalence was 38% among unregistered compared to 15% among RSWs, while chlamydial infection was similar in the two groups (37% v 35%); the majority of these infections were asymptomatic. [25,26]

To address gaps, preventive and curative interventions targeting all categories of sex workers in the "entertainment industry" in Angeles City were strengthened. The objective of this intervention research was to evaluate changes in STI prevalence following implementation of these interventions.

Methods

This intervention was implemented between January and October 2001. The first intervention objective was to rapidly reduce the prevalence of *Neisseria gonorrhoeae* (Ng) and *Chlamydia trachomatis* (Ct) by providing a single round of presumptive treatment (PT) to female sex workers. The second was to maintain reduced Ng/Ct prevalence by strengthening preventive and curative services.

Evaluation of the interventions consisted of cross sectional assessments of behaviour, gonococcal, and chlamydial prevalence among female sex workers and clients. Ethics review committees of the Department of Health / Philippine Council for Health Research and Development, and Family Health International approved the study protocol.

Intervention phase 1—a single round of presumptive treatment

All female sex workers in Angeles City were offered PT during a 1 month period. In order to reach the widest population of sex workers, peer educators from the SHC and several non-governmental organisations (NGOs) extended outreach to both registered and unregistered sex workers. At recruitment staff explained the objectives of the intervention and the benefits and limitations of PT to potential participants. They explained that treatment was only effective for a few specific STIs, that participation in the programme was voluntary, and was not a substitute for other preventive measures. Participants who agreed were given a supervised 1 g dose of azithromycin as PT for gonococcal and chlamydial infections with a small snack to reduce gastrointestinal side effects. Any participant with signs or symptoms consistent with vaginitis or genital ulcer received additional treatment based on national guidelines. Condom use was promoted and condoms demonstrated and supplied at each outreach and clinic encounter.

Intervention phase 2—strengthened clinical services

Recommendations were made for improving existing screening methods used with RSWs at SHC, and for establishing satellite clinics for unregistered sex workers who did not have access to services. Figure 1 shows the recommended STI management algorithm for sex worker visits. In fact, changing existing SHC services proved difficult and screening continued using existing methods (based on Gram stained cervical smears) that permitted rapid processing of hundreds of women per day. The recommended algorithm was implemented only at the new satellite clinics serving unregistered sex workers.

Figure 1 STI management algorithm.
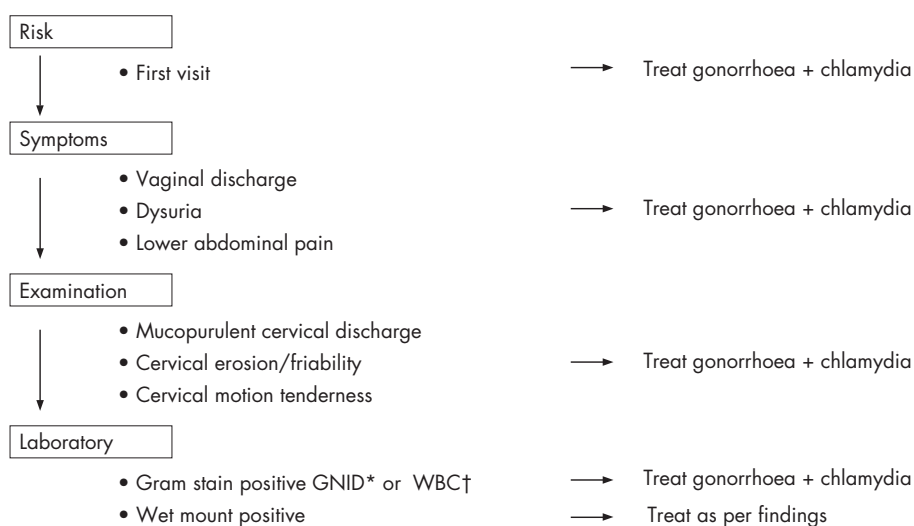
*Gram negative intracellular diplococci; more than 20 white blood cells per high power field.

Intervention assessments

Three cross-sectional behavioural and STI surveys of sex workers were conducted: round one (R1) at the time of PT, R2 1 month later, and R3 7 months after PT. Two cross-sectional surveys of clients were carried out at the time of the second and third sex worker surveys.

Female entertainment workers who had sexual intercourse during the week before interview were systematically recruited as follows.

Among sex workers with health certificates (municipal registration):

- Registered sex workers (RSWs) are establishment based, generally work in "go-go" bars catering to foreigners and possess health certificates issued by SHC. Every fifth RSW attending SHC for routine visits was eligible.

- Guests relations officers (GROs) work in karaoke bars with a largely Filipino clientele, and possess health certificates. Every third GRO contacted by study staff at their workplace was eligible.

Among sex workers without health certificates (unregistered):

- Street based sex workers (SSWs) serving mostly Filipino clients were approached in streets, parks, theatres, and cruising areas. SSWs were asked to refer their peers (snowballing technique).

- Brothel based sex workers (BSWs) serving primarily Filipino clients were recruited in brothels and at a satellite clinic established in their community.

Table 1 Demographic and behavioural characteristics of female sex workers (n = 1130*) at first contact, Angeles City, Feb–Oct 2001

	RSW	No	GRO	No	SSW	No	BSW	No
Age median (years)	22	570	22	204	23	204	20	152
Range	16–41		17–45		16–47		16–44	
Marital status		570		204		204		152
Single	72.3%		39.7%		38.7%		76.3%	
Married or live-in	14.4%		53.4%		51.5%		11.2%	
Separated or widow	13.3%		6.9%		9.8%		12.5%	
Educational level		570		204		204		152
Elementary or none	25.3%		8.8%		27.5%		33.6%	
High school or above	74.7%		91.2%		72.5%		66.4%	
Partners/week mean (median)	2.1 (1)	570	1.1 (1)	204	2.6 (1)	204	17.8 (19)	152
Range	1–15		1–4		1–30		1–65	
Condom use last sex	63.2%	570	6.9%	204	35.8%	204	59.2%	152
Every time last week	54.6%	570	5.9%	204	23.0%	204	22.4%	152
Condom use at last sex by partner type								152
Paying regular partners	69.4%	206	11.1%	18	53.3%	60	47.8%	92
Non-paying regular partners	17.2%	93	5.9%	185	9.9%	121	16.7%	12
Non-regular partner	68.5%	409	23.1%	13	67.9%	81	59.2%	147

RSW, registered sex workers; GRO, guest relations officers; SSW, street based sex workers; BSW, brothel based sex workers.
*Includes first contact by individual sex worker in any survey round, excludes repeat contacts.

Results

Outreach and presumptive treatment

In all, 1938 female entertainment workers accepted PT, close to the estimated sex worker population of 2000–2500 in Angeles.

Cross sectional surveys

The baseline survey (R1) was done at the time of PT in February/March 2001, R2 in March/April, and R3 in October. The total sample included 1651 sex worker contacts during three

rounds. The proportion of women surveyed at rounds R2 and R3 who reported having received PT during round 1 was 50% and 17% (RSW), 75%, and 33% (GRO), 63% and 32% (SSW), and 79% and 70% (BSW), respectively.

Demographic and behavioural characteristics

Table 1 summarises demographic and behavioural characteristics of 1130 women sampled at least once during the three rounds. No significant differences were found among women attending for the first time during initial and subsequent survey rounds. Reported numbers of sex partners during the week before baseline interview varied with BSW having significantly higher numbers of partners – including more non-regular and paying regular clients – than other groups (p=0.001). Numbers of non-paying regular partners was similar across groups (range 0-3).

At the PT contact (R1), 44% of women reported using a condom the last time they had sex. Condom use varied by category of sex worker and partner type.

STI prevalence

Table 2 shows gonococcal and chlamydial prevalence rates. One month post-PT (R2), prevalence of gonorrhoea and/or chlamydial infection (Ng/Ct) was reduced by 28% (36.3% to 25.8%, p=0.02) for RSW, 70% (20.0% to 6.0%, p=0.002) for GRO, 39% (41.0% to 25.0%, p=0.02) for SSW, and 47% (51.6% to 26.6%, p=0.001) for BSW.

Table 2 Prevalence of gonorrhoea (Ng) and chlamydia (Ct) by group and by survey round, Angeles City, Feb–Oct 2001

	R1 (Baseline)	R2 (1 month follow up)	p (R2:R1)	R3 (7 month follow up)	p (R3:R1)
All sex worker groups					
Ng	18.3%	11.9%	**0.004**	15.2%	0.15
Ct	28.6%	15.1%	**<0.001**	22.0%	**0.01**
Ng and/or Ct	36.7%	22.1%	**<0.001**	29.2%	**0.007**
RSW					
Ng	16.2%	14.4%	0.6	17.0%	0.8
Ct	26.5%	16.9%	**0.02**	25.0%	0.7
Ng and/or Ct	36.3%	25.8%	**0.02**	33.7%	0.5
GRO					
Ng	8.0%	1.0%	**0.05**	7.0%	0.8
Ct	18.0%	5.0%	**0.007**	19.0%	0.8
Ng and/or Ct	20.0%	6.0%	**0.002**	24.0%	0.4
SSW					
Ng	23.0%	11.0%	**0.02**	15.0%	0.15
Ct	35.0%	20.0%	**0.02**	23.0%	0.06
Ng and/or Ct	41.0%	25.0%	**0.02**	28.0%	**0.05**
BSW					
Ng	30.5%	18.1%	**0.05**	16.4%	**0.01**
Ct	40.0%	16.0%	**<0.001**	17.2%	**<0.001**
Ng and/or Ct	51.6%	26.6%	**<0.001**	23.0%	**<0.001**
BSW clients		R1 (baseline)		R2 (6 month follow up)	p (R2:R1)
Ng		12.6%		6.0%	0.1
Ct		24.1%		11.0%	**0.02**
Ng and/or Ct		27.6%		15.0%	**0.03**

RSW, registered sex workers; GRO, guest relations officers; SSW, street based sex workers; BSW, brothel based sex workers.
Note: differences significant at p<0.05 in bold.

At the second assessment 6 months later (R3), Ng/Ct prevalence was maintained at the reduced level for BSW (23.0%, p=0.001) and SSW (28.0%, p=0.05) but had returned to pre-intervention levels for RSW (33.7%) and GRO (24.0%).

Greater reductions in Ng/Ct prevalence at round 2 were seen among less mobile groups (a higher proportion of whom had received PT 1 month earlier). Table 3 presents Ng/Ct prevalence rates for sex workers who had received PT during the initial intervention phase compared to those who had not.

Table 3 Prevalence of gonorrhoea (Ng) and/or chlamydia (Ct) stratified by exposure to PT at R1, by group and survey round, Angeles City, Feb–Oct 2001

	R1 (baseline)	No	R2 (1 month follow up)	No	R3 (7 month follow up)	No
RSW		204		236		300
All	36.3%		25.8%	61/236	33.7%	101/300
PT at R1			**19.3%**	23/119	29.4%	15/51
No PT at R1			**32.5%**	38/117	34.5%	86/249
GRO		100		100		100
All	20.0%		6.0%	6/100	24.0%	24/100
PT at R1			**1.3%**	1/75	27.3%	9/33
No PT at R1			**20.0%**	5/25	22.4%	15/67
SSW		100		100		100
All	41.0%		25.0%	25/100	28.0%	28/100
PT at R1			**17.2%**	11/64	**18.8%**	6/32
No PT at R1			**38.9%**	14/36	**32.4%**	22/68
BSW		95		94		122
All	51.6%		26.6%	25/94	23.0%	28/122
PT at R1			**23.0%**	17/74	**14.1%**	12/85
No PT at R1			**40.0%**	8/20	**43.2%**	16/37

RSW, registered sex workers; GRO, guest relations officers; SSW, street based sex workers; BSW, brothel based sex workers.
Note: differences significant at p<0.05 in bold.

Differences in prevalence compared to baseline were significant for all groups at R2 but only for BSW and SSW 6 months later (R3). Exposure to prevention interventions was comparable for all groups (based on outreach reports). Reported condom use at last sex increased slightly overall but differences were significant only for RSW (p=0.01).

STI screening improved greatly for BSW and SSW (who previously had no access) while there were no changes in existing services for RSW and GRO. As a result, the former were more likely to receive treatment for STI during the post-PT period. Only 2–3% of RSW screened by Gram stain at SHC were treated for infection each month, similar to treatment rates before the intervention. In comparison, 21% of BSW screened at newly established clinics using the clinical/laboratory algorithm (fig 1) received treatment during the first month, gradually declining to 8% 6 months later.

Among clients of BSWs sampled 1 month after the PT (n=100) and again 6 months later (n=100), Ng/Ct prevalence declined 46%, from 27.6% to 15.0% (p=0.03) (table 2).

Discussion

This intervention-linked research assessed several intervention components introduced to strengthen existing STI control efforts among sex workers in Angeles. Our findings suggest that (1) one-time presumptive treatment can help reduce STI prevalence for rapid but short term control, that (2) ongoing STI screening using sensitive methods, together with outreach and condom promotion are important for sustaining STI reductions, and that (3) interventions that effectively reduce STI prevalence among sex workers can have broader public health effects, extending at least to their clients.

In Angeles, as elsewhere, conditions of sex work influence vulnerability, risk, and STI prevalence. Differences between types of sex work proved important for orienting services. Five out of six women (RSW and GRO) reached during the month-long PT intervention phase were already "in the system," receiving some form of regular STI screening through social hygiene clinics. The remaining women worked in brothels or on the street and, being unregistered, did not have access to services. Importantly for STI control, these unregistered sex workers reported more clients, had the lowest condom use, and highest STI rates. [23-26]

It was not difficult to reach these sex workers. Outreach efforts by peers and NGOs were highly effective in mobilising large numbers of both registered and unregistered sex workers for PT and in promoting services. Peer involvement and community mobilisation are critical factors in uptake of interventions with sex workers. [27,28] Organised sex workers are also better able to demand condom use and safer working conditions, and to resist abusive conditions such as harassment and trafficking. [28]

Presumptive treatment reduced STI prevalence in the short term. One round of presumptive treatment was followed by significant STI declines in all groups 1 month later, similar to experience reported elsewhere. [29] In Angeles, however, rapid turnover among some groups of sex workers quickly diluted the effect of one time PT. Frequent arrival of new sex workers into an area argues for incorporating PT and/or screening into routine sex worker services along with outreach efforts to reach new sex workers.

Sustaining lower STI rates clearly requires more than one time presumptive treatment. By the final assessment round, 7 months post-PT, Ng/Ct prevalence remained low for BSW and SSW but had returned to baseline for RSW and GRO. It is not possible to say with certainty which intervention components were responsible for these differing outcomes. Exposure to condom promotion was similar for all groups and no significant changes in reported condom use (except RSW) or numbers of partners were measured for any group over the short intervention period. One apparent difference was the higher rate of treatment at the newly established

screening services for unregistered sex workers compared to rates at SHC. Sensitive screening criteria (fig 1) were successfully introduced in newly established services for BSW and SSW. Established routines at SHC proved difficult to change, however, and treatment rates for RSW and GRO remained low.

Notably, unregistered BSWs, who initially had the highest rates of risk behaviours and infection, had the lowest STI prevalence at the end of the evaluation period, and STI prevalence had fallen an equivalent amount among their clients as well. Since only 5% of these clients reported condom use at last sex with their regular non-commercial partners, lower STI prevalence in this bridge population should also benefit women with lower risk behaviour.

Holmes et al drew similar conclusions in Olongapo City, Philippines, in 1967, although the sequence of interventions was different. [30] Weekly screening of registered sex workers by gonococcal culture, and treatment of contacts named by US Navy servicemen reduced gonorrhoea prevalence among registered sex workers from 11.9% to 4.0% within 4 months, and gonorrhoea incidence in servicemen at nearby Subic Bay fell by half. A single round of "selective mass treatment" (comparable to presumptive treatment) had a temporary additional benefit that was not sustainable without other interventions.

In Angeles, as in Olongapo more than 30 years earlier, presumptive treatment facilitated STI control by bringing down STI rates rapidly, but benefits were short lived without additional intervention. Regular STI screening using sensitive methods appears to contribute to longer term control. Regular contact with health services also allows for a relationship that can encourage safer behaviours including condom use. [1,6] In both places, important public health benefits – lower STI burden for sex workers and halving of rates among male bridging groups – were evident.

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Periodic presumptive treatment of curable STIs among sex workers: a systematic review

Richard Steen

Matthew Chersich

Antonio Gerbase

Graham Neilsen

Annika Wendland

Francis Ndowa

Eli A Akl

Ying-Ru Lo

Sake J de Vlas

Abstract

Background

Unprotected sex work remains a major driver of HIV / sexually transmitted infection (STI) epidemics in many countries. STI treatment can lower disease burden, complications and prevalence of HIV cofactors. Periodic presumptive treatment (PPT) has been used with sex workers to reduce their high burden of largely asymptomatic STIs. The objective of this review is to assess benefits and harms of PPT among female sex workers.

Methods

We searched MEDLINE for studies related to sex work and STIs during 1990–2010, extracted data from eligible studies in duplicate and conducted meta-analysis by study design using random effects models.

Results

Two thousand, three hundred and fifteen articles were screened, 18 studies met inclusion criteria and 14 were included in meta-analyses. One published randomized controlled trial (RCT) reported significant reductions of gonorrhoea (*Neisseria gonorrhoeae*) [rate ratio (RR) 0.46, 95% confidence interval (CI) 0.31–0.68] and chlamydia (*Chlamydia trachomatis*) (RR 0.38, 95%CI 0.26–0.57), but no effect on serologic syphilis (RR 1.02, 95%CI 0.54–1.95). Similar results were seen for *N. gonorrhoeae* and *C. trachomatis* in pooled analyses, including data from one unpublished RCT and across study designs, and correlated with initial prevalence ($R^2=0.155$). One observational study reported genital ulcer disease (GUD) declines in sex workers, and two reported impact among male client populations for *N. gonorrhoeae* [odds ratio (OR) 0.60, 95% CI 0.38–0.94], *C. trachomatis* (OR 0.47, 95% CI 0.31–0.71) and GUD (OR 0.21, 95% CI 0.11–0.42). No studies reported evidence of risk compensation or antibiotic resistance.

Conclusion

PPT can reduce prevalence of gonorrhoea, chlamydia and ulcerative STIs among sex workers in whom prevalence is high. Sustained STI reductions can be achieved when PPT is implemented together with peer interventions and condom promotion. Additional benefits may include impact on STI and HIV transmission at population level.

Unprotected sex work remains a major driver of HIV and sexually transmitted infection (STI) epidemics, particularly in low-income and middle-income countries. Yet several countries have succeeded in raising condom use in commercial sex, reducing STIs and stabilizing or reversing their HIV epidemics. [1-3] Common programme elements of successful interventions with sex workers include peer outreach, sex worker mobilization, condom promotion and improved STI services. [4,5] Interventions that reduce STI prevalence complement condom programmes which aim to reduce rates of reinfection. When implemented in a supportive environment, such 'combination' interventions have reported high uptake and utilization of services by sex workers, increased condom use, reduced STI prevalence and other positive health and social outcomes. [6,7]

Most STIs in women are asymptomatic, however, and sensitive screening tests are expensive and rarely available in low-income and middle-income settings. For these reasons, periodic presumptive treatment (PPT) has been used with sex workers to reduce their high burden of largely hidden infections. PPT is defined as treatment of curable STIs based on sex workers' high risk and prevalence of infection, rather than on symptoms, signs or results of laboratory tests. PPT is, thus, similar to other forms of epidemiologic treatment, including treatment of identified sex partners of STI index cases.

An expected direct benefit to sex workers is reduced STI-related morbidity, including pelvic inflammatory disease, infertility, ectopic pregnancy, sepsis and adverse pregnancy outcomes. At population level, reduced prevalence among sex workers may also slow transmission to clients and their regular partners. [8] To the extent that STIs amplify HIV transmission – estimated cofactor effects range from two to four for discharges to 25 or more for ulcerative STIs, lower STI prevalence may also reduce efficiency of HIV transmission. [9] A 2005 WHO consultation reviewed experience from nine countries and recommended that PPT be considered as part of a package of services to rapidly reduce STI prevalence in sex work settings, particularly where STI control is poor. [10]

The main objective of this systematic review of PPT among sex workers is to assess evidence of benefits and harms in controlled trials and under field conditions. Primary outcomes of interest include reduced STI prevalence among sex workers themselves and improved STI control among male client or general population groups. Changes in reported condom use by sex workers and adverse effects associated with PPT were also reviewed.

Methods

The systematic review of PPT forms part of a WHO initiative to develop evidence-based guidelines for HIV/STI interventions with sex workers. A guidelines development working group and a Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodologist (E.A.A.) guided the process. Population, Intervention, Comparison, Outcomes (PICO) questions were drafted for PPT and other interventions involving sex workers. [11] This review follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. [12]

Eligibility criteria

We included studies of female sex workers or their clients that took place in low-income or middle-income countries. Randomized controlled trials (RCTs), cross-sectional surveys with adjusted analyses, cohort and time series were eligible if they reported STI or HIV outcomes of a PPT intervention in female sex workers using a drug regimen with high cure rates for *Neisseria gonorrhoeae* (gonorrhoea), *Chlamydia trachomatis* (chlamydia), *Treponema pallidum* (syphilis), *Haemophilus ducreyi* (chancroid) or genital ulcer disease (GUD). Trials in which the control arm was another PPT regimen or STI screening were excluded.

Search strategy

MEDLINE was searched in September 2010 for relevant articles published between 1990 and 2010 using the following search terms: prostitution or prostitut* or 'sex work*' and HIV or STI or STD or 'sexually transmitted disease' or 'sexually transmitted infection' or syphilis or 'chlamydia' or gonor*. References of review articles were reviewed; conference abstracts and unpublished reports were searched through Gateway, National Library of Medicine, researchforsexwork.or and clinicaltrials.gov. First authors and experts in the field were contacted to obtain information on unpublished work, forthcoming manuscripts and research in progress.

Review

Titles and abstracts were first screened to determine whether the study involved female sex workers, took place in a low-income or middle-income country and referred to STIs or HIV. Subsequent steps involved full-text review of the remaining articles to determine whether the study included a PPT intervention and to assess its design and methods. In all stages, two researchers (R.S. and M.C.) evaluated the studies independently and differences were reconciled. Quality of evidence was assessed using GRADE methods (Supplementary Table S1, http://links.lww.com/QAD/A194). For randomized trials, information is presented on allocation

concealment and blinding procedures, whereas for observational studies we report, where available, cohort retention and whether the primary objective of these studies was the same as the review's objectives.

Data extraction and analysis

Data from studies that met inclusion criteria were extracted in duplicate using a standardized data collection form. Extractions were compared and differences reconciled. Interventions and outcomes were evaluated using an outcome framework that considered direct effects on sex worker morbidity, indirect benefits and risks. Evidence of a broader public health effect – a change in STI prevalence among client populations – was also sought.

STIs assessed consisted of *N. gonorrhoeae* (gonorrhoea), *C. trachomatis* (chlamydia), *T. pallidum* (syphilis), *H. ducreyi* (chancroid) and GUD. Other STI/reproductive tract infections reported in a few studies – *Trichomonas vaginalis* and bacterial vaginosis – were excluded from analysis, as they are not sensitive to the antibiotic regimens used in most studies. As HIV does not respond to antibiotic treatment, any reported results were treated as secondary outcomes. Other secondary outcomes included reported condom use and evidence of antimicrobial resistance.

A series of meta-analyses, stratified by study design, summarize outcome effects of PPT on each STI. We examined heterogeneity using the I^2-statistic which describes the percentage of total variation across studies that is due to heterogeneity other than chance [13]. An I^2-value of 50–75% was interpreted as indicating moderate heterogeneity and a value of more than 75% as showing pronounced study heterogeneity. The inverse variance method of Review Manager 5 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen) was used to combine different effect measures and construct forest plots. [14] Evidence was graded using GRADEpro software (Computer program version 3.2 for Windows), as described by the Cochrane Collaboration. [15]

Results

The initial search identified 2315 articles and two reports with detailed data on several PPT interventions. Figure 1 illustrates the results of screening at each stage of the review.
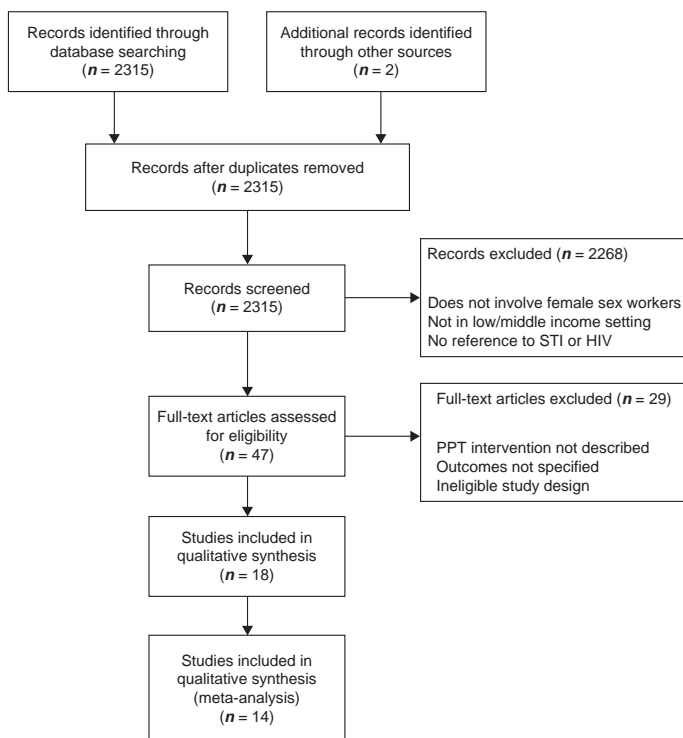
Fig. 1. Identification of evidence. STI, sexually transmitted infection.

Eighteen studies, spanning 10 countries, met inclusion criteria for the qualitative analysis. Five RCTs were identified, two from peer-reviewed publications [16,17] and three from two reports and a modelling article. [10,18,19] Observational studies included four peer-reviewed cross-sectional studies assessing PPT exposure and STI outcomes, adjusted for confounding [7,20 -22], and eight peer-reviewed cohort or time series studies of sex workers receiving PPT. [23-30] Four studies were excluded from meta-analysis: one published RCT lacking a non-PPT comparison group [17], one unpublished RCT with incomplete outcome data [10], one time series with a small convenience sample [26] and one cross-sectional study without disaggregated *N. gonorrhoeae* and *C. trachomatis* outcomes. [22] One RCT without a non-PPT comparison group was included as a cohort study. [19] One modelling study provided data for an unpublished RCT. [31]

Study characteristics and main outcomes of studies included in the meta-analysis are summarized in Supplementary Tables S1 and S2 (http://links.lww.com/QAD/A194). Most studies provided azithromycin 1G or azithromycin 1G with cefixime 400mg or azithromycin 1G with ciprofloxacin 500mg, all single-dose treatments that can be administered under direct observation. Two included studies used combined regimens with ampicillin or amoxicillin in combination with probenicid and/or clavulanic acid.

Changes in sexually transmitted infection prevalence and/or incidence

All studies reported some change in STI prevalence and/ or incidence over the course of the study (Supplementary Table S2, http://links.lww.com/QAD/A194). In all but one, overall declines were reported in the primary curable STIs that were measured, most commonly *N. gonorrhoeae* and *C. trachomatis*. The few studies that included results for GUD also reported declines [18,24]. Results for *Trep. pallidum* and *Trich. vaginalis* were variable and their interpretation complicated by additional treatment (for syphilis or trichomoniasis based on symptoms or screening). One study from Indonesia reported overall rising syphilis trends among sex workers of whom a small proportion had received PPT. [21]

Efficacy of periodic presumptive treatment in experimental studies

One randomized trial from Kenya reported significantly lower rate ratios for *N. gonorrhoeae* [rate ratio (RR) 0.46, 95% confidence interval (CI) 0.31-0.68] and *C. trachomatis* (RR 0.38, 95% CI 0.26-0.57) in the PPT group compared with control (Figs 2 and 3) [7,16,19,20,23-25,27-30]. No significant differences were seen for *Trep. pallidum* (Fig. 4) [7,16,20,21,24], or for GUD or HIV. The quality of this study was rated as high with no serious inconsistency, indirectness, imprecision or other limitation for the main STI outcomes (*N. gonorrhoeae* and *C. trachomatis*). Quality of evidence was rated down for *Trep. pallidum*, GUD and HIV due to imprecision (wide CIs), and additionally for HIV due to indirectness.

Preliminary results from a second, unpublished RCT were available from authors [10,18]. Pooled effects from both RCTs were calculated for *N. gonorrhoeae* (RR 0.50, 95% CI 0.24-1.03) and for *C. trachomatis* (RR 0.38, 95% CI 0.19-0.77) with low heterogeneity across studies.

Effectiveness of periodic presumptive treatment in observational studies

Three observational studies provide adjusted effect measures for PPT in sex worker populations that were exposed to interventions with a PPT component [7,20,21]. Quality of this evidence is rated as moderate (observational design without inconsistency, imprecision, indirectness or other limitations). Figures 2–4 depict pooled adjusted odds ratios (OR) for *N. gonorrhoeae* (OR 0.54, 95% CI 0.27-1.06), *C. trachomatis* (OR 0.53, 95% CI 0.32-0.88) and *Trep. pallidum* (OR 0.86, 95% CI 0.58-1.26).

A fourth study reported that sex workers who received PPT three or more times in the past 6 months had lower combined prevalence of *N. gonorrhoeae* and/or *C. trachomatis* (OR 0.54, 95% CI 0.42-0.7, P<0.001). These results were not disaggregated by pathogen and are, thus, not reflected in the forest plots for *N. gonorrhoeae* or *C. trachomatis* [22].

Effectiveness of combined interventions including periodic presumptive treatment

Other studies (cross-sectional time series and cohorts) report on combined interventions that included a PPT component [23-30]. Common to these studies conducted under nonexperimental, real-world conditions is relatively high initial STI prevalence. The cohort studies also report high population turnover and loss to follow-up, introducing potential bias in long-term outcomes. Reports of short-term (1–3 months) and longer term (up to 9 months) outcomes with reasonable follow-up rates, however, show large declines (Figs 2 and 3). Quality of this evidence was upgraded from low (observational design) to moderate based on large effect size.
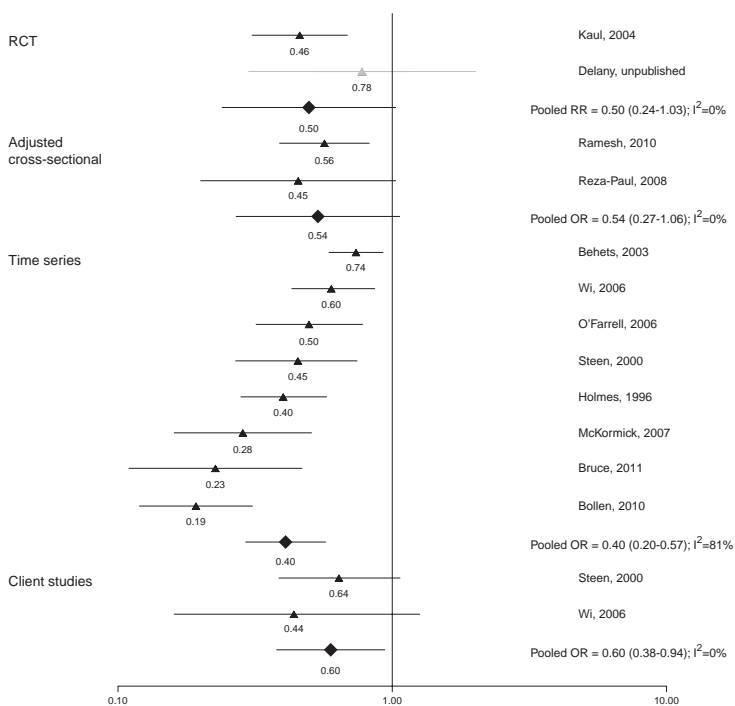
Fig. 2. Meta-analyses of the effect of periodic presumptive treatment on gonorrhoea grouped by study type. OR, odds ratio; RCT, randomized control trial. Adapted from [7,16,19,20,23–25,27–30].
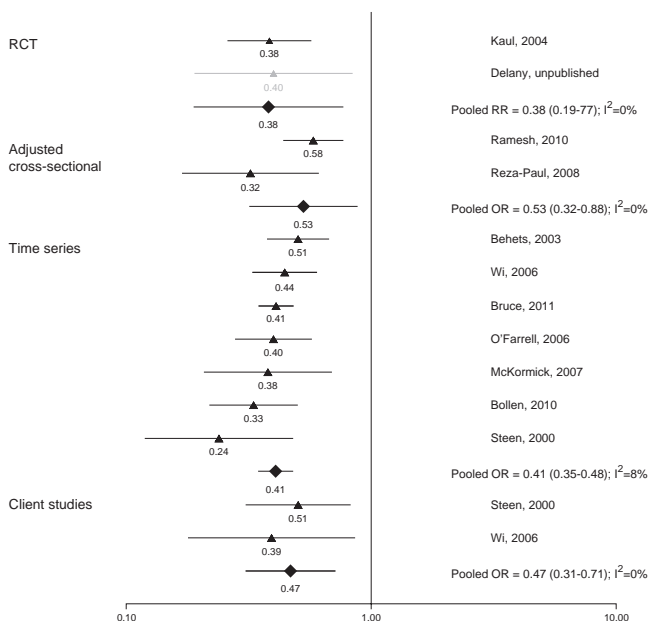
Fig. 3. Meta-analyses of the effect of periodic presumptive treatment on chlamydia grouped by study type. OR, odds ratio; RCT, randomized control trial; RR, rate ratio. Adapted from [7,16,19,20,24,25,27–30].

Evidence of broader public health impact

Finally, several studies report STI results from men, who are likely or actual clients of sex workers, providing evidence of public health impact beyond the group of sex workers exposed to the intervention (Figs 2–4). [24,27] In South Africa, a significant decline in curable STIs was measured over 9 months, larger for ulcerative STIs than for *N. gonorrhoeae* and *C. trachomatis.* [24] Both cross-sectional surveys and ongoing STI surveillance among migrant mine workers showed an effect gradient with lower STI rates measured closer to the intervention site. In the Philippines, cross-sectional prevalence of gonorrhoea and chlamydia among clients of brothel-based sex workers were less than half as high as they were before the intervention. [27]
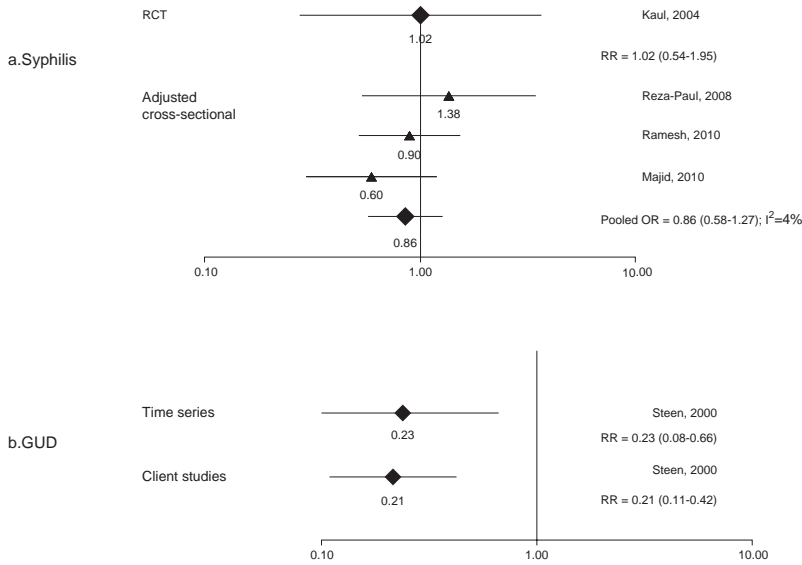
Fig. 4. Meta-analyses of the effect of periodic presumptive treatment on syphilis and genital ulcers grouped by study type. GUD, genital ulcer disease; OR, odds ratio; RCT, randomized controlled trial; RR, rate ratio. Adapted from [7,16,20,21,24].

Stratified meta-analysis by initial prevalence (*Neisseria gonorrhoeae* and *Chlamydia trachomatis*)

Given the wide range of baseline STI prevalence in the different studies, *N. gonorrhoeae* and *C. trachomatis* results from the meta-analyses are stratified by initial prevalence in Fig. 5 [7,16,19,20,23-25,27-30].

In two thirds of studies, including all RCT data points, in which initial prevalence of gonorrhoea or chlamydia was between 5 and 20%, reported OR/RR clustered around 0.5 (range 0.32-0.78). Where *N. gonorrhoeae* or *C. trachomatis* was greater than 20%, larger effects of PPT were measured.
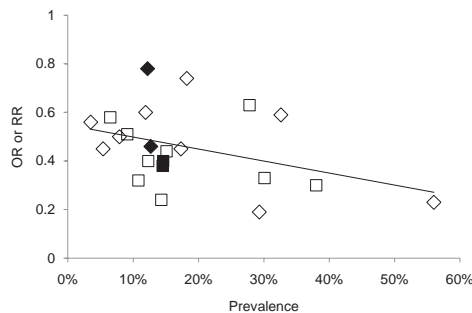
Legend: diamond=NG, square=CT, black=RCT, white=observational, line=trend (r^2=0.155)

Fig. 5. Stratified analysis by initial prevalence of gonorrhoea and chlamydia. Diamond represents *Neisseria gonorrhoeae* (NG); square represents *Chlamydia trachomatis* (CT); black colour represents randomized controlled trial (RCT); white colour represents observational studies; line represents trend ($r^2 = 0.155$). OR, odds ratio; RR, rate ratio. Adapted from [7,16,19,20,23–25,27–30].

Discussion

A considerable body of evidence permits assessment of PPT, as an intervention component for STI control. Results from 15 studies using a range of study designs show consistent reductions on the order of 50% where gonorrhoea and chlamydia are prevalent. More limited data suggest an even larger effect on ulcerative STIs in chancroid-endemic settings, as well as potential impact on STI transmission beyond sex workers themselves. Results for syphilis are mixed, however, with no effect measured in one RCT. We were unable to identify sufficient evidence to assess effects of PPT on HIV infection, quality of life or adverse effects, including antibiotic resistance.

Some limitations were identified in nearly all studies. The few RCTs were conducted under conditions of relatively good STI control, limiting the amount of change that could be demonstrated as well as the types of STIs that could be studied. Studies with less rigorous designs were more often carried out in areas with poorer STI control, yet potential confounding limits differentiation of PPT effects from those of other intervention components, particularly condom use. Despite these limitations, this review found a high degree of consistency in the direction of effect for gonorrhoea and chlamydia across geographic regions and study designs.

The evidence shows that PPT works, first and foremost, to reduce existing high burden of two STIs that cause significant morbidity among many sex workers. Efficacy in reducing prevalence of gonorrhoea and chlamydia – common infections with severe reproductive tract sequelae – was demonstrated in controlled trials, with effectiveness under field conditions supported across study designs. Without intervention, such infections would go largely untreated, leading to many preventable cases of pelvic inflammatory disease, infertility and ectopic pregnancy.

Apart from averting morbidity among sex workers themselves, PPT addresses several important obstacles to STI control in low-income and middle-income countries. First, it offers an effective approach to the problem of asymptomatic STIs in women, at least those at very high risk. In the absence of sensitive and affordable screening tests, PPT, thus, complements standard symptom-dependent case management approaches. Second, PPT addresses the core epidemiology underlying STI transmission and control. Reducing STIs among sex workers has long been known to interrupt transmission to and beyond clients, contributing to broader STI control. [32,33] Data supporting such public health impact were reported in two studies in this review. [24,27]

Although fewer studies have reported on PPT for ulcerative STIs (which were not prevalent in many sites), the magnitude of effect may be even greater than for *N. gonorrhoeae* and *C. trachomatis*. Rapid control of chancroid in one study suggests that elimination of select STIs

may be a feasible objective, as has been achieved in Thailand and elsewhere following effective interventions with sex workers. [34] Given the importance of ulcerative STIs – and chancroid specifically – as HIV cofactors, and their close association with sex work and male noncircumcision, the contribution of PPT to GUD control could also contribute significantly to HIV prevention. [31]

Given the lack of clear evidence for an effect on syphilis – despite reported effectiveness of azithromycin in at least incubating and early stages – other control strategies are advisable. Syphilis serology is a feasible and affordable screening test and many programmes that provide PPT also offer periodic (usually 6-monthly) screening with rapid plasma reagin or other nontreponemal test. Syphilis screening also provides a useful surveillance indicator to monitor STI transmission trends among sex workers. [5]

Furthermore, given the strong association between curable STIs, particularly genital ulcers and HIV acquisition and transmission, improved STI control due to PPT may also slow HIV transmission. Although hard evidence is lacking – the one published study that tried to measure it had insufficient power to do so – such an indirect effect of PPT on HIV is supported by empirical evidence and modelling. [9,31] In a recent study in Indonesia, higher HIV incidence was measured among sex workers who had not received PPT during the previous 6 months, as well as among those who had active syphilis or genital ulcers in the past year. [35] To the extent that specific ulcerative and other STIs are cofactors that facilitate HIV acquisition and transmission, removing those cofactors – through a combination of condoms, PPT and other STI interventions – would reduce HIV transmission efficiency. Modelling supports such a potential impact on HIV transmission, depending largely but not solely on prevalence of ulcerative chancroid. [31]

Although this review did not identify any harm related to PPT, several cautions are warranted. Nearly all programmes made efforts to reinforce condom use as PPT was introduced and only one study reported a decrease in reported condom use (vaginal prostate-specific antigen also decreased, however). [19] Nevertheless, programme implementers should recognize the potential for risk compensation, promote the primary importance of consistent condom use and monitor behavioural trends.

No study reported increases in antibiotic resistance associated with use of PPT, although few attempted to monitor it and existing surveillance is inadequate. The risk of developing resistance may be low, however, given current PPT regimens – azithromycin and cefixime are both highly active against *N. gonorrhoeae* and, as single dose treatments, can be given under observation, eliminating the risk of ineffective treatment. Nonetheless, antimicrobial sensitivity

should be regularly monitored by STI programmes, regardless of specific interventions, to ensure continuing high levels of cure.

These findings have implications for programming of targeted interventions with sex workers and for related operations research. Feasibility of implementing at scale is one important consideration. Although most early reports of PPT come from interventions that were implemented in one or several communities, reports describing experience with PPT as part of large-scale implementation efforts have appeared since 2008. [7,20-22,29] The Avahan India AIDS Initiative rapidly scaled-up targeted interventions including PPT, reaching more than 300,000 sex workers in six states over 5 years. [7,20,36] In Indonesia, PPT was rolled out in government clinics with non-governmental organization-supported peer outreach in 10 districts with large sex work networks. [21,22,29]

Other operational considerations relate to decisions about where and how to introduce PPT. Where STI prevalence among sex workers is high and alternative methods for detecting and treating asymptomatic STIs are not feasible or affordable, adding PPT can strengthen efforts to reduce morbidity and control transmission. However, less benefit has been reported in a few sites where effective STI interventions were in place and prevalence was already low. [10] This argues for implementing PPT as a short-term control measure, to be phased out once conditions have improved and prevalence has declined, assuming other measures are in place to maintain control. The heterogeneous and dynamic conditions of sex work itself that determine exposure and rates of reinfection – including numbers of clients, condom use and STI prevalence – are, thus, factors that would influence the optimal frequency and duration of PPT for STI control. These and other operational issues have been investigated through operations research and mathematical modelling and are the subject of a separate review. [18,31,37]

In conclusion, PPT can rapidly reduce prevalence of gonorrhoea, chlamydia and ulcerative STIs among sex workers. When implemented together with peer interventions, condom promotion and other clinical services, additional potential benefits include reinforced condom use, reduced HIV cofactors and impact on transmission at population level. Greater short-term impact can be expected where rates of condom use are low and prevalence of curable STIs is high. As these conditions improve, reduced STI prevalence may be sustainable with less intensive interventions.

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Chapter 8

Periodic presumptive treatment of curable sexually transmitted infections among sex workers: recent experience with implementation

Richard Steen

Matthew Chersich

Sake J de Vlas

Abstract

Purpose of review

Curable sexually transmitted infections (STIs) are common occupational hazards for female sex workers in low-income and middle-income countries. Yet, most infections are asymptomatic and sensitive screening tests are rarely affordable or feasible. Periodic presumptive treatment (PPT) has been used as a component of STI control interventions to rapidly reduce STI prevalence.

Recent findings

Six recent observational studies confirm earlier randomized controlled trial findings that PPT reduces gonorrhoea and chlamydia prevalence among sex workers. One modelling study estimated effects on *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Haemophilus ducreyi*, and HIV prevalence at different levels of PPT coverage and frequency, among sex workers who take PPT and among all sex workers. Important operational issues include use of single-dose combination antibiotics for high cure rates, conditions for introducing PPT, frequency and coverage, and use of PPT together with other intervention components to maximize and sustain STI control and reinforce HIV prevention.

Summary

PPT is an effective short-term measure to rapidly reduce prevalence of gonorrhoea, chlamydia, and ulcerative chancroid among female sex workers. It should be implemented together with other measures – to increase condom use, reduce risk and vulnerability – in order to maintain low STI prevalence when PPT is phased out.

Introduction

Curable sexually transmitted infections (STIs) are common occupational hazards for female sex workers in low-income and middle-income countries. [1] Combined prevalence of gonorrhoea (*Neisseria gonorrhoeae*), chlamydia (*Chlamydia trachomatis*), and syphilis (*Treponema pallidum*) among sex workers frequently surpasses 30–50%. [2] In settings with large HIV epidemics and weak STI control, ulcerative chancroid (*Haemophilus ducreyi*) remains an important HIV cofactor. [3]

High STI prevalence, when combined with frequent partner change in sex work networks, also influences transmission dynamics at population level. Upstream transmission in sex work networks is capable of generating high STI incidence, which drives downstream transmission among lower risk populations (Fig. 1). Interventions that have raised condom use and reduced STI prevalence among sex workers have also documented downstream impact on male 'bridge' groups and general populations. [4-6] Importantly, the public health benefits of controlling curable STIs extends to HIV prevention. [7]
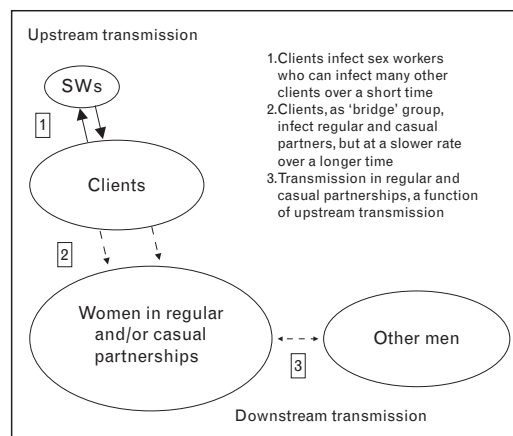

FIGURE 1. Sexually transmitted infections/HIV transmission dynamics within and beyond sex work networks. 1, clients infect sex workers (SWs) who can infect many other clients over a short time; 2, clients, as 'bridge' group, infect regular and casual partners, but at a slower rate over a longer time; 3, transmission in regular and casual partnerships is a function of upstream transmission.

For these reasons, intervention programmes often offer STI treatment to symptomatic sex workers in addition to promoting condom use. However, a major weakness of STI services in resource-limited settings is the lack of sensitive screening methods to identify and treat asymptomatic and unrecognized STIs. Two of the most common curable STIs – gonorrhoea and chlamydia – are asymptomatic in the majority of women with infection, and common vaginal symptoms have low predictive value for STIs. Furthermore, ulcerative STIs, which may be painless and internal, frequently go unnoticed. Many curable STIs are thus missed, leading to serious and life-threatening sequelae including pelvic inflammatory disease, infertility, ectopic pregnancy, sepsis, and congenital infections.

Periodic presumptive treatment

Periodic presumptive treatment (PPT) is an STI treatment strategy that extends treatment to sex workers on the basis of their high risk and prevalence of infection, rather than limiting it to those with symptoms, signs, or positive diagnostic tests. [2] As such, it is analogous to epidemiologic treatment of identified sex partners of STI index cases, or presumptive treatment of fever with antimalarials in endemic areas.

The efficacy of PPT has been demonstrated in one published randomized controlled trial (RCT), which measured significant reductions of *N. gonorrhoeae* [relative risk (RR)=0.46; 95% confidence interval (CI)=0.31-0.68] and C. trachomatis (RR=0.38; 95% CI=0.26-0.57), but no effect on serologic syphilis [RR=1.02; 95% CI=0.54-1.95]. [8] Based on available evidence, a 2005 WHO technical consultation recommended that PPT be considered, in areas with high STI prevalence, as part of a package of services for sex workers that includes condom promotion, syndromic case management, and regular screening for syphilis. [9] Additionally, involving sex workers in outreach and other peer interventions was strongly recommended to increase uptake and utilization of services and to reinforce primary prevention. [9]

Beyond the benefit to individual sex workers in need of treatment, PPT is promoted as a temporary measure to rapidly reduce population prevalence in areas of poor STI control. [2,9] As STI prevalence declines and subsequent risk decreases, however, many programmes have attempted to reduce the frequency of PPT, or withdraw it entirely, relying on other interventions to maintain low prevalence. Such operational issues have received recent attention in the literature and are the focus of this review.

Methods

This article reviews the recent literature to identify factors that are important in implementing interventions with sex workers that include a PPT component. We conducted a MEDLINE search of articles from 2008 to 2011 with search terms related to sex work, STI, and presumptive treatment. Studies describing PPT interventions and outcomes were searched for information on operational issues including choice of antibiotic regimen, appropriate conditions for introducing PPT, PPT frequency and coverage, and use of PPT together with other intervention components to maximize and sustain STI control and reinforce HIV prevention.

Recent evidence of periodic presumptive treatment effectiveness

Six observational studies included data on PPT interventions and outcomes, three from Indonesia, two from India, and one from Papua New Guinea. [10-12,13,14,15] One modelling study included earlier data from South Africa, Benin, Ghana, and Laos. [16] All studies reported STI prevalence reductions among female sex workers. The efficacy and effectiveness of PPT was recently assessed in a systematic review. [17]

One time-series study among Indonesian brothel-based sex workers included PPT (azithromycin 1 g + cefixime 400 mg), syndromic treatment and condom promotion [10]. *N. gonorrhoeae* decreased by 44% (P<0.01) and 79% (P<0.01) at two sites, and *C. trachomatis* by 25% (P=0.13) and 70% (P=0.01), after 15 months. *N. gonorrhoeae* and/or *C. trachomatis* prevalence among sex workers who received PPT at least once was lower than for newcomers (19.6 versus 35.9%, P<0.01).

Two population-based, cross-sectional, bio-behavioral studies from Indonesia examined associations between STIs and previous PPT after adjusting for condom use and other factors. [11,12] One reported that female sex workers who received PPT (azithromycin 1 g + cefixime 400 mg) three or more times in the past 6 months had lower combined prevalence of *N. gonorrhoeae* and/or *C. trachomatis* [adjusted odds ratio (aOR) 0.54; 95% CI=0.42-0.7]. [11] The second study measured syphilis prevalence and associated factors among female sex workers in 10 cities of Indonesia in 2007, compared with earlier surveillance in 2003 and 2005. [12] Prevalence of active syphilis was lower among those who had received at least one dose of PPT (azithromycin 1 g + cefixime 400 mg) compared with those who had not received PPT (3.9 versus 6.0%; P=0.008).

In Mysore district, India, PPT was introduced as part of sexual health services that were an integral part of a community-led structural intervention to empower sex workers and strengthen HIV/STI prevention. [13] STI prevalence declined from baseline to follow-up 2 years later: *N. gonorrhoeae* from 5 to 2% (P=0.03); *C. trachomatis* from 11 to 5% (P=0.001); and *Treponema pallidum* from 25 to 12% (P<0.001). Reductions in *N. gonorrhoeae* (aOR 0.45, 95% CI=0.20-1.02) and *C. trachomatis* (aOR 0.32, 95% CI=0.17-0.61) were associated with self-report of having received PPT (prepackaged and color-coded as a 'grey pack').

Elsewhere in Karnataka state, India, targeted interventions also included peer outreach with promotion of condoms and services; sexual health services for female sex workers and their regular partners, syndromic case management, speculum examination, PPT (azithromycin 1 g + cefixime 400mg) every 3–6 months, and syphilis screening. [14] Compared with baseline, reductions were measured in the prevalence of *N. gonorrhoeae* and/or *C. trachomatis* (8.9 versus

7.0%, P=0.02) and high-titre *T. pallidum* (5.9 versus 3.4%, P=0.001). Reductions in *N. gonorrhoeae* and/or *C. trachomatis* were associated with self-report of receiving PPT 'grey pack', P<0.001.

In Papua New Guinea, female sex workers received a 3 monthly oral combination of amoxicillin with clavulanic acid, probenecid, and azithromycin. [15] Nine months later, after three PPT rounds, significant declines were measured for *N. gonorrhoeae* from 56 to 23% (P<0.001) and for *C. trachomatis* from 38 to 16% (P=0.001).

Antibiotic regimens

PPT based on monthly azithromycin 1g alone was first used empirically in South African mining communities in 1996. [9] Based on reported reductions of *N. gonorrhoeae*, *C. trachomatis* and genital ulcers, PPT protocols using azithromycin at different treatment intervals were adapted for the Philippines and Laos. [9] RCT evidence supports the efficacy of monthly PPT with azithromycin 1 g for *N. gonorrhoeae* and *C. trachomatis*. [8]

Subsequent PPT interventions have employed combination regimens – azithromycin 1 g and either cefixime 400 mg or ciprofloxacin 500 mg – to maximize cure rates, particularly for gonorrhoea. It is argued that risk of developing antimicrobial resistance to *N. gonorrhoeae* would be minimized by administering, under observation, two single-dose antibiotics that are highly effective against *N. gonorrhoeae*. The importance of using an effective regimen was highlighted in one study from Indonesia, which reported an increase in *N. gonorrhoeae* /*C. trachomatis* following substitution of less effective antibiotics. [10]

Introducing periodic presumptive treatment

Conditions related to sex work – including condom use, STI prevalence, and incidence – are important factors in deciding when and how to start PPT. Several recent studies were conducted in areas where sex workers were already reached by outreach, condom and STI interventions, and STI prevalence had declined to moderate or even low levels (Fig. 2, white symbols). [13,14] Others, where PPT was initiated at the start of interventions when STI prevalence was higher, reported larger STI declines (Fig. 2, black symbols). [10,15]
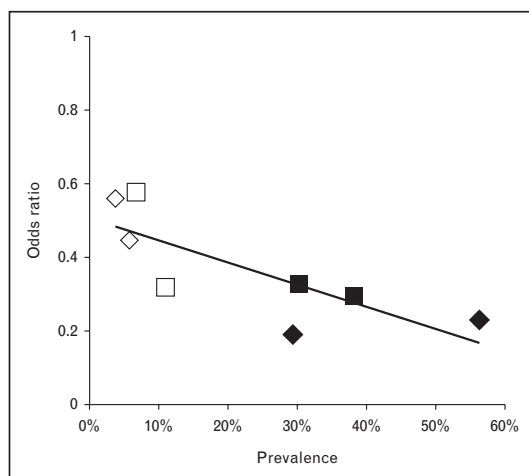
FIGURE 2. *N. gonorrhoeae* and *C. trachomatis* declines (odds ratios) as a function of initial prevalence. diamonds, *N. gonorrhoeae*; rectangles, *C. trachomatis*; black, new intervention; white, established intervention.

STI surveillance can identify epidemiologic hotspots, pockets of poor STI control that may be driving larger epidemic spread. PPT is most beneficial in such settings, and may have little or no effect if STIs are already well controlled. The Benin/Ghana RCT (described in the WHO report and article by Vickerman et al. [16]) demonstrates this point. [9] In a setting with greater than 90% reported condom use with last client, and where sex workers had access to regular STI screening and treatment, chlamydia prevalence was only 3.2% when PPT was introduced. Adding PPT resulted in no additional reduction of *C trachomatis* prevalence (data not shown).

Frequency and coverage of periodic presumptive treatment

STI incidence, a function of exposure and condom use, determines how often PPT may need to be given to control transmission. Recent studies report on interventions with quarterly PPT, whereas earlier studies (including one RCT) provided PPT monthly. Vickerman et al. [16] used mathematical modelling to estimate the effect of PPT at different frequencies and levels of coverage. Assuming an azithromycin-based PPT regimen, the model estimated that control of *N. gonorrhoeae* and *H. ducreyi* would improve by increasing PPT frequency from quarterly to monthly, at which point little additional benefit would be gained by giving PPT more frequently.

In India (including the two studies reported here), targeted interventions initially offered PPT at sex workers' first visit, then for sex workers who failed to attend clinical checkups for more than 6 months. [18] Subsequent operations research showed that 50% of new *N. gonorrhoeae* / *C. trachomatis* infections occurred within 3 months of PPT, and guidelines were revised to recommend quarterly PPT. [19]

Coverage of interventions is another important determinant of STI outcomes. The Vickerman et al. model assumed low PPT coverage (only 10% of sex workers reached by the intervention, based on Johannesburg data) as a starting point. The effect of reaching a larger proportion of sex workers was estimated for *N. gonorrhoeae* and *H. ducreyi* among sex workers reached by the intervention and for all sex workers. The model estimated that PPT interventions can effectively reduce STI prevalence among all female sex workers – a population effect related to reduced STI transmission in sex work networks – when coverage levels surpass 30% of the sex worker population.

Coverage rates well above 30% have been reported. Reza-Paul et al. [13] examined STI and behavioral outcomes as a function of programme exposure following initiation of a community-led intervention. Within 2.5 years, more than 90% of sex workers reported having been visited by a peer educator, having visited the project drop-in centre and dedicated sexual health clinic, and having received presumptive STI treatment. The study measured substantial increases in self-reported condom use with all sexual partners in addition to significant reductions in STI prevalence. Programme exposure was associated with increased condom use with last client, with visiting the clinic and with receiving PPT. *N. gonorrhoeae* and *C. trachomatis* reductions were in turn significantly associated with PPT after adjusting for condom use and other covariates. Fig. 3 [13] is a simplified version of the causal pathways to reduced STI prevalence described in the article.
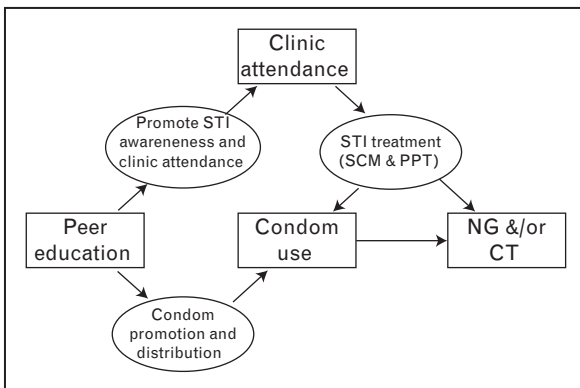

FIGURE 3. Causal pathways. CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*; PPT, periodic presumptive treatment; SCM, syndromic case management; STI, sexually transmitted infection. Adapted from [13■■].

The feasibility of implementing combined interventions including PPT on a large scale, with high coverage and utilization by sex workers, has been demonstrated by the Avahan India AIDS Initiative. [18] Over 2.7 million clinical visits by 431,434 individuals, including 331,533 female sex workers, were captured by an individual tracking system. [20] The number of visits per person increased annually from 1.2 in 2005 to 8.3 in 2009. The proportion attending clinics more than four times per year increased from 4% in 2005 to 26% in 2009 (P<0.001), and the proportion seeking regular STI checkups increased from 12 to 48% (P<0.001).

Implementing periodic presumptive treatment as part of a package of interventions

As described above, PPT is generally introduced together with other condom and STI interventions. Promotion of correct and consistent condom use during penetrative sex remains one of the most important prevention components for sex worker interventions. [4] Concern has been raised that some interventions, such as male circumcision, may undermine condom use, however. Such risk compensation has been raised as a possible negative effect of PPT. For this reason, most studies describe condom promotion interventions implemented alongside PPT, and all recent studies reported condom use increases (Fig. 4). [10,13,14,15]

Condom and STI interventions are also needed to maintain reduced prevalence once short-term interventions like PPT bring them down. Although PPT-specific data are limited, studies show that low STI prevalence can be maintained if sex worker condom use is high enough and other STI services are available. 100% condom use programmes, for example, have been able to maintain very low incidence and prevalence of curable STIs using combinations of outreach, condom promotion, and STI services. [4] Others have adapted protocols that combine PPT at a sex workers' first visit with clinical and laboratory-based screening at subsequent visits. [13,14]

Interventions should, thus, adapt to changing STI transmission dynamics. Figure 4 fits data from four recent PPT studies with condom use trends to a conceptual implementation timeline beginning under conditions of low condom use and poor STI control. [10,15] In this scenario, in which intervention coverage and condom use are high, the additional benefits of PPT in reducing and maintaining low STI prevalence may decrease to the point wherein PPT can be phased out. [13,14]
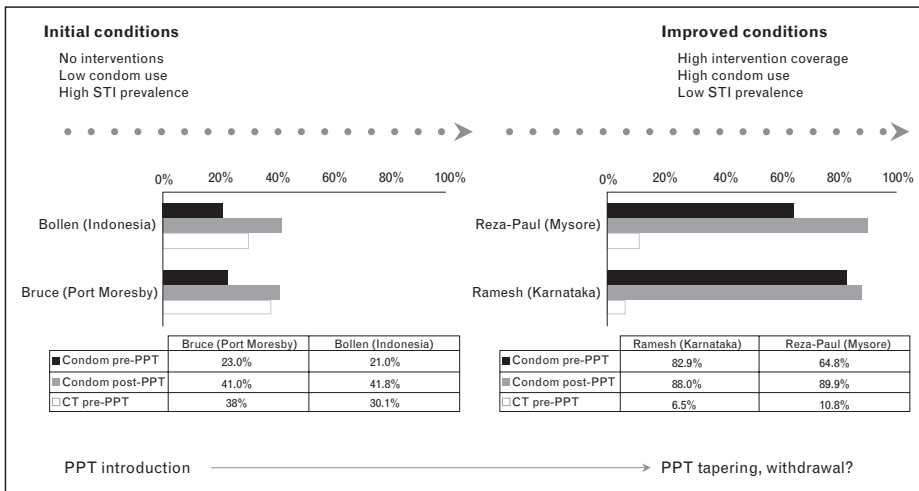
FIGURE 4. Intervention timeline: condom use, sexually transmitted infections (STI) prevalence and periodic presumptive treatment (PPT) [10■,13■■,14■,15■]. Left: early interventions under conditions of low condom use and high STI prevalence [10■,15■]. Right: established interventions with high condom use and reduced STI prevalence [13■■,14■].

There is little reported evidence of the effects of tapering or withdrawing PPT once STI prevalence has declined, however. Based on limited empirical evidence, the 2005 WHO consultation suggested 10% combined *N. gonorrhoeae / C. trachomatis* prevalence and 70% reported condom use (by sex workers with last client) as thresholds for tapering or withdrawing PPT. Several recent studies cautioned that without increasing condom use, STIs would likely rebound if PPT were withdrawn. [10,15]

Potential contribution to HIV prevention

In places where STIs are poorly controlled, adding PPT to interventions with sex workers can strengthen HIV prevention by lowering the prevalence of STI cofactors. The model by Vickerman et al. [16] estimates a moderate-to-strong impact on HIV transmission, PPT interventions with sufficient coverage (40%) and follow-up (2 years) could noticeably decrease sex worker HIV incidence (>20%). Larger effects were modelled in simulations that included chancroid due to the high HIV cofactor effect of genital ulcers.

Limited empirical data support this indirect effect on HIV. Ramesh et al. [14] reported reductions in HIV prevalence (19.6 versus 16.4%, P=0.04). Reza-Paul et al. [13] reported that although overall HIV prevalence remained stable, detuned assay suggested a decline in recent HIV infections, and lower HIV prevalence was measured among women without a regular partner. Finally, in a study among Indonesian sex workers, Morineau et al. [21] demonstrated higher HIV incidence among those not receiving PPT for STIs during the previous 6 months, as well as sex workers who had active syphilis or genital ulcers in the past year.

Conclusion

PPT has been shown to reduce *N. gonorrhoeae* and *C. trachomatis* prevalence among sex workers. Earlier studies and modelling suggest a larger effect on ulcerative chancroid, and population-level impact on STI/HIV transmission. Considerable experience implementing PPT in over a dozen countries supports the feasibility of PPT and provides evidence to guide important operational decisions. High coverage of PPT, given at sufficient frequency and as part of broader interventions with sex workers, could make a substantial contribution to strengthen overall STI control and HIV prevention.

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Pursuing scale and quality in STI interventions with sex workers: initial results from Avahan India AIDS Initiative

Richard Steen

Vittal Mogasale

Teodora Elvira Wi

Aman Kumar Singh

Angela Das

Celine Daly

Bitra George

Graham Neilsen

Virginia Loo

Gina Dallabetta

Abstract

Background

Migration, population mobility, and sex work continue to drive sexually transmitted epidemics in India. Yet interventions targeting high incidence networks are rarely implemented at sufficient scale to have impact. India AIDS Initiative (Avahan), funded by the Bill and Melinda Gates Foundation, is scaling up interventions with sex workers and other high-risk populations in India's six highest HIV prevalence states.

Methods

Avahan resources are channelled through state level partners (SLPs) to local level non-governmental organisations (NGOs) who organise outreach, community mobilisation, and dedicated clinics for sex workers. These clinics provide services for sexually transmitted infections (STIs) including condom promotion, syndromic case management, regular check-ups, and treatment of asymptomatic infections. Sex workers take an active role in service delivery. STI capacity building support functions on three levels. A central capacity building team developed guidelines and standards, trains state-level STI coordinators, monitors outcomes, and conducts operations research. Standards are documented in an Avahan-wide manual. State-level STI coordinators train NGO clinic staff and conduct supervision of clinics based on these standards and related quality monitoring tools. Clinic and outreach staff report on indicators that guide additional capacity building inputs.

Results

In 2 years, clinics with community outreach for sex workers have been established in 274 settings covering 77 districts. Mapping and size estimation have identified 187 000 sex workers. In a subset of four large states covered by six SLPs (183 000 estimated sex workers, 65 districts), 128 326 (70%) of the sex workers have been contacted through peer outreach and 74 265 (41%) have attended the clinic at least once. A total of 127 630 clinic visits have been reported, an increasing proportion for recommended routine check ups. Supervision and monitoring facilitate standardisation of services across sites.

Conclusion

Targeted HIV/STI interventions can be brought to scale and standardised given adequate capacity building support. Intervention coverage, service utilisation, and quality are key parameters that should be monitored and progressively improved with active involvement of sex workers themselves.

Migration, population mobility, and sex work continue to drive sexually transmitted epidemics in India as elsewhere. [1] Yet interventions targeting networks with the highest HIV incidence are rarely implemented at sufficient scale to have public health impact. [2] For the South East Asia region, for example, only an estimated 19% of sex workers (SWs), 5% of injecting drug users, and 1% of men who have sex with men have access to even basic prevention services. [3]

In India, reports from the early 1990s found high HIV prevalence among migrant populations, sex workers, their clients, and patients with sexually transmitted infections (STI), particularly those with genital ulcers. [4–7] Less than a decade later, six states had surpassed 1% antenatal HIV prevalence, with some districts reporting over 3%. [8] Sex work continues to drive existing epidemics while helping to seed new ones in mobile, highly vulnerable communities. In 2000, cross sectional, population-based surveys identified variable but high levels of STIs and HIV: in coastal Andhra Pradesh, 68.2% of sex workers had at least one curable STI and 48.5% were HIV positive. Among long distance truck drivers and helpers surveyed in southern states, 10.7% had a genital ulcer and 10.9% HIV. [9–11]

Since 2003, the India AIDS Initiative (Avahan), with funding from the Bill and Melinda Gates Foundation, has been working to scale up HIV prevention interventions in six high prevalence states. Additional interventions address clients and partners of sex workers, injecting drug users and their partners, and truck drivers along national highways.

This paper focuses on Avahan STI interventions with sex workers – female, male, and transgender – and outlines implementation challenges and attempted solutions during the initial scale-up phase of clinic and community based interventions. We describe STI capacity building inputs, present interim process and outcome data on key scale-up parameters, and discuss plans for strengthening these initial efforts.

The challenge of scale

The population living in India's six high prevalence states was 291 million in 2001. To reduce HIV transmission in these states, effective public health interventions would need to be supported on a massive scale.

Early on, Avahan identified priorities for strengthening the prevention response, including saturating coverage of sex worker populations, fostering community mobilisation, providing a comprehensive package of services, and improving data collection. To address these areas, the Avahan design provides funding through separate subprojects for (1) direct implementation of interventions; (2) capacity building of implementing agencies in community mobilisation, communication, and clinical interventions; and (3) monitoring and evaluation.

For direct implementation of interventions, Avahan works through state level non-governmental organisation (NGO) partners who in turn contract with local NGOs to organise peer outreach, community mobilisation, and dedicated clinics for sex workers. The primary target populations for interventions are sex workers, their clients and regular partners. Through other funding mechanisms, high risk males are reached through hot spot interventions, occupation group stratification, and condom social marketing.

Initial estimates and targets were developed and later refined based on local mapping and size estimation using several methodologies. A total of 116 districts were chosen for interventions taking into account both prevalence and existing coverage, including an estimated 267 000 sex workers. The typology of sex work was found to vary greatly within and across states, however, requiring local adaptation of strategies and targets. Approaches appropriate for female, male, and transgender sex workers in a range of urban and rural settings, including brothels, lodges, pilgrimage sites, street, and home based, were needed.

Ensuring quality at this scale was a priority for planners and collaborating state AIDS control societies (SACS). NGO implementing partners generally had little experience organising STI interventions or, frequently, clinical services of any kind. State level NGO partners were chosen based on demonstrated ability to manage large HIV, STI, or reproductive health programmes, but few had ever developed clinical services for sex workers. National STI guidelines were based on World Health Organization (WHO) syndromic standards, but did not include specific protocols for sex workers. Even less guidance was available on how to provide services for male or transgender sex workers.

Initial capacity building needs were thus to define an essential STI service package, to develop clear standards and tools, and to provide the necessary support to enable partners to scale up high quality services in diverse settings. An added challenge was to do this retrospectively, as most state level partners had already started establishing clinics and training staff months before STI capacity building support was in place.

Developing an essential STI service package

Avahan's STI strategy aims to reduce the prevalence of common curable STIs that facilitate HIV transmission, and to reinforce general STI/HIV prevention efforts in doing so. Peer outreach, community mobilisation, promotion of condoms and STI services have been effective elsewhere in decreasing STI/HIV rates among sex workers. [12] The challenge was how to scale up such interventions rapidly while ensuring quality.

Project clinics are expected to provide an "essential service package" for sex workers designed to recognise and treat curable STIs and reinforce condom use. The main case management components of the services are syndromic case management, regular screening, and presumptive treatment for asymptomatic infections. Regular screening involves promotion of monthly check-ups for sex workers to detect signs of STI by speculum/bimanual examination, and twice yearly serological testing and treatment for syphilis. Presumptive STI treatment (azithromycin plus cefixime) is recommended quarterly. While monthly check-ups are promoted, the programmatic target is at least one clinic visit per sex worker every 3 months.

State level partners and local level NGOs adapt the essential service package to local conditions; mapping and micro-planning are carried out to identify sites and methods – appropriate outreach, fixed or satellite clinics, health camps, mobile services – to maximise coverage and access. These clinical services are linked to peer based outreach in order to promote utilisation, reinforce prevention, and facilitate follow up and partner treatment.

Clinic and outreach services are provided within the context of community led structural interventions (CLSI), which builds active involvement and ownership of sex workers in all aspects of interventions. This includes progressively increasing participation of sex workers in (1) daily clinic activities related to medical visits and clinic administration, (2) management of drop-in centres (DIC), (3) peer outreach and education in the community, and (4) building a supportive environment through community based organisations, self-help groups, and income schemes. Additional capacity building support for CLSI is provided by Care International.

Capacity building to support scale up

STI capacity building support is provided by Family Health International (FHI) in collaboration with the World Health Organization (WHO). The aim is to build capacity of state level partners to provide effective STI services. Technical assistance is organised on three levels. A central STI capacity building team develops guidelines, standards, and tools; trains and supports STI technical coordinators working for the state level partners; monitors outcomes and conducts operations research. State level STI coordinators train their NGO clinic staff and conduct supervision based on these standards and related quality monitoring tools. Clinic and outreach staff report on indicators that guide additional capacity building inputs. The sequence of major STI capacity building activities is illustrated in figure 1.
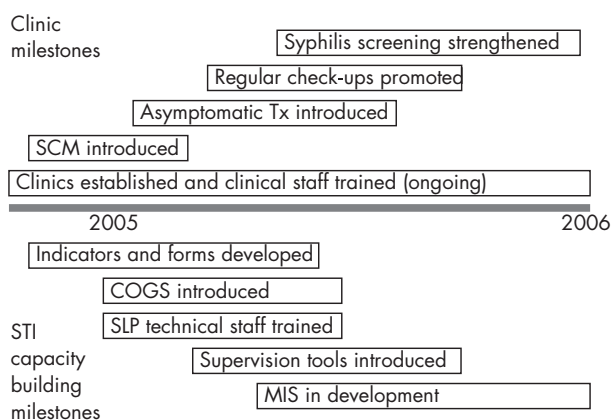
Clinic
milestones

| Syphilis screening strengthened |

| Regular check-ups promoted |

| Asymptomatic Tx introduced |

| SCM introduced |

| Clinics established and clinical staff trained (ongoing) |

2005   2006

| Indicators and forms developed |

| COGS introduced |

STI
capacity
building
milestones

| SLP technical staff trained |

| Supervision tools introduced |

| MIS in development |

Figure 1 STI capacity building timeline.

A manual, Clinic Operational Guidelines and Standards (COGS), was developed which defines common approaches for STI prevention, detection and care, and standards of service delivery for dedicated sex worker clinics. Realistic standards were developed based on participatory assessments, field experience, existing national guidelines, and expert inputs. The COGS forms the basis for training and supervision and serves as a benchmark against which performance of clinics can be monitored. The manual addresses STI clinic operations (set-up, staffing, community involvement, coordination with outreach, logistics support); clinical management with detailed protocols and standards; health education and counselling; laboratory support; infection control; ethical standards, confidentiality and right of refusal; monitoring, evaluation, and reporting; and technical support and supervision. Explicit recommendations on counselling of sex workers, HIV testing, and referral linkages including HIV related support services are included.

The COGS, along with tools for training, supervision and monitoring, was introduced during training of state level technical coordinators. STI capacity building staff make field visits at least quarterly to each state level partner, during which joint supervisory visits to clinics are made. The primary purpose of these visits is to reinforce the capacity of state level technical coordinators to provide support and supervision to frontline service providers, rather than to attempt to provide that support directly. The state level technical coordinators, responsible for up to 20 clinics, are expected to visit each clinic monthly. During these visits, mentoring and supervision are carried out to improve performance of the clinical teams.

Scale-up progress and a first look at key indicators

Since October 2003, clinic and community based interventions for sex workers have been progressively built up in 77 districts. In most of these, mapping and size estimation have been carried out to identify sites where sex work is negotiated or takes place, to estimate numbers of sex workers and to plan local interventions.

Avahan intervention areas currently include an estimated 187 000 sex workers. This represents an estimated 30% to 65% of female sex workers in the six states; together with interventions of government and other donors, estimated state coverage is 85-90%. Avahan intervention areas include about 40 000 male and transgender sex workers, for estimated state-wide coverage of 60-70%. In one large state with an estimated 33 000 sex workers, 9000 (27%) are male or transgender.

As of December 2005, 294 fixed and satellite clinics for sex workers, linked to outreach and community mobilisation were operational. Avahan partners continue to identify more dispersed communities with smaller numbers of sex workers, and attempt to extend services to reach them. This requires flexibility in programming and service delivery including part time satellite clinics, mobile units, and temporary health camps. Despite these challenges of diversity and scale, services are increasingly standardised; state level partners base services on uniform clinical protocols, follow COGS standards and are using comparable monitoring and supervision tools. Box 1 describes standardisation of STI services in one state.

Data on scale-up indicators are currently reported differently by different state level partners as a result of different management and service delivery approaches. Adoption of standard definitions of core indicators; methods for tracking individual patients at STI clinics; and use of a web based reporting system of core indicator data, including patient level records, are under way. At this stage, however, available indicators reported by state level partners include:

- Outreach contacts are currently reported as either first time contacts or registration of new sex workers. Several contacts with a peer worker may be needed before the sex worker agrees to participate in the intervention; s/he is then given a registration card with a unique number (pseudonyms are commonly used).

- Uptake of clinic services is tracked in a more consistent way across state projects. Clinics report the number of sex workers attending the clinic for the first time, extracting data from clinic registers.

- Continuation is measured differently across sites. All clinics report repeat visits, and ratios of repeat to new visits can be calculated. Some sites report clinic visits for routine checkups separately.

Box 1 Standardising clinical services in Tamil Nadu

Tamil Nadu AIDS Initiative (TAI), an Avahan state level partner, developed its STI programme with input from state experts, key populations (sex workers, men who have sex with men, and transgenders) and the Avahan STI capacity building team.

Forty programme clinics are operational near places where key populations (estimated 33 000) live and work. Standardisation is achieved by contracting with two medical college affiliated agencies, which manage STI clinics in collaboration with implementing NGO partners and communities. Technical training is on site and hands on, and includes training on attitudes and communication skills of clinic staff.

TAI clinics are closely linked to community outreach and have drop-in centres (DICs) attached. In many sites, female, male, and transgender sex workers share clinic/DICs; in some larger sites, separate services are organised for MSM/transgenders. In all, coordination meetings involving clinic and community staff are held every 1–2 weeks to motivate and coordinate outreach work as well as to keep clinic staff informed about community attitudes. Doctors and nurses hold regular community dialogues and the community is involved in monitoring clinic quality.

Assessments by the STI capacity building team have found STI management to be highly standardised across sites with COGS based systems in place, records complete and accurate, and supportive supervision conducted by TAI technical coordinators and management agencies. In addition, innovative steps are being taken to improve quality and promote high levels of utilisation. Seventy per cent of sex workers contacted by peers (58% of total population estimate) have attended clinic at least once and this indicator is closely followed by NGO peer outreach workers and clinic teams.

Summary prepared by Dr Lakshmi Bai and the TAI STI team

Despite differences in current reporting, some patterns and trends emerge from the data of four large states (Andhra Pradesh, Karnataka, Maharashstra, and Tamil Nadu). Issues related to access and utilisation include the following.

How many sex workers are being reached compared to the estimated population?

Using either first contact or registration data from six SLPs (183 000 estimated sex workers in 65 districts), 128 326 (70%) have been contacted at least once through peer outreach.

Are sex workers coming to the clinic?

Based on first visit data from clinic registers, 74 265 sex workers have attended clinic at least once. This represents 58% of sex workers contacted by peer workers or 41% of the estimated sex worker population in the intervention districts (fig 2).
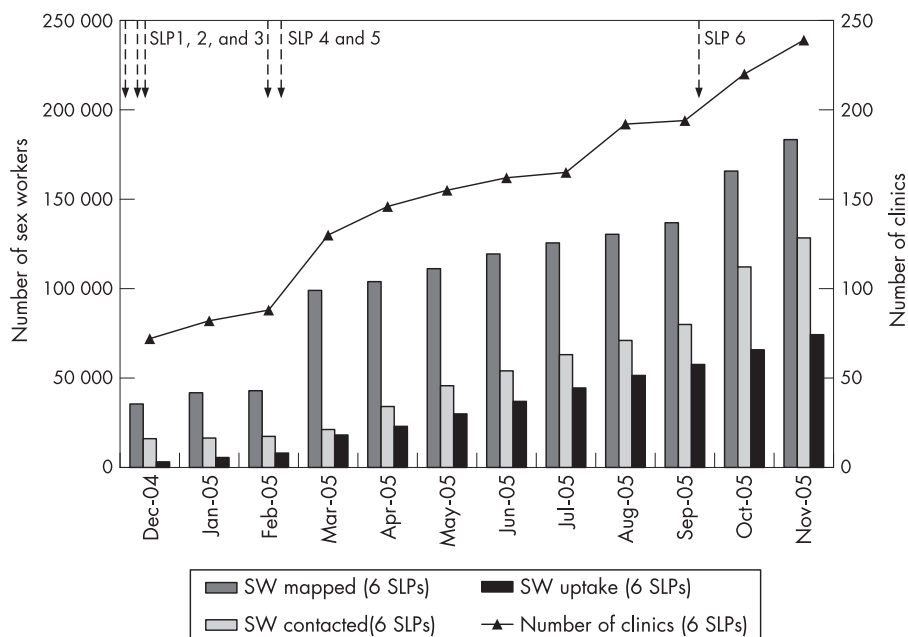
Figure 2 Outreach contacts and new clinic visits in relation to number of clinics and estimated SW populations (*six state level partners).

Continuation is more difficult to describe without individual patient tracking. A total of 127 630 clinic visits have been reported. Among five SLPs (132 000 estimated sex workers in 51 districts) reporting 50 748 new clinic visits, a total of 90 025 clinic visits have been made (0.8 return visits per sex worker) during the first year. This crude ratio is increasing as more sex workers return for recommended routine check-ups.

Data from five SLPs describe 51 637 STI related syndromic diagnoses, 48% with vaginal discharge, 18% with lower abdominal pain (presumptive pelvic inflammatory disease), 8% with genital ulcers, and 27% with other diagnoses. A significant declining trend of ulcerative STIs ($p<0.0001$) relative to other syndromes is apparent (fig 3).

Looking forward

In 2 years, Avahan partners have made measurable progress. Large numbers of sex workers are being reached by peer outreach workers and many have attended the clinic at least once. Despite rapid scale up, however, potential impact at this early stage is limited by partial uptake of services and variable rates of continuation. For example, the recommended monthly schedule of clinic visits is far from being reached, although many sites are approaching a more realistic programmatic target of one clinic visit per quarter.
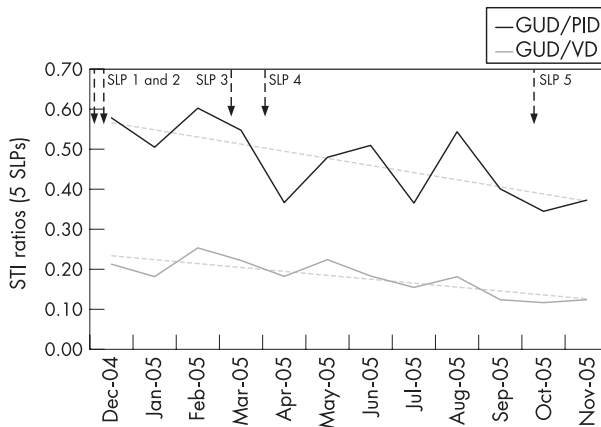
Figure 3 Proportion of ulcerative to non-ulcerative STI syndromes (five SLPs).

Quality has not yet been adequately measured although progressive improvement has been documented at capacity building visits. Moreover, analysis of clinic data suggests some positive trends; ulcerative STIs, prevalent among underserved sex workers in India, are declining relative to other STI syndromes. Ongoing surveillance will help to validate these trends.

Meanwhile, a platform has been established for reaching the highest risk and most vulnerable populations. Looking forward, a number of new capacity building challenges can be seen as the focus shifts to consolidation and improvement of services.

Continued scale-up support will be needed as partners establish new clinics and outreach to previously unidentified areas where sex work is common. At least three new districts will be added in addition to new satellite or mobile clinics in existing Avahan supported districts. As new service delivery models are used to reach more dispersed groups of sex workers, capacity building support (including operations research) will be needed to evaluate and adapt standards.

All partners are addressing barriers to coverage and uptake. The highest clinic utilisation rates have been seen in communities with active sex worker involvement in both outreach and clinic activities, and where there is good coordination and interaction of clinic and outreach staff (box 2). Additional efforts include local advocacy with police and gatekeepers, promotional events, and incentive schemes to motivate peer educators and sex workers.

Box 2 Community mobilisation in Mysore, Karnataka

A community based programme in Mysore is run by the Karnataka Health Promotion Trust (KHPT), another Avahan state level partner. Community outreach and clinical services reach networks of female, male, and hijra (transgender) sex workers, and their partners. The programme emphasises peer education, empowerment, and involvement of the sex workers.

Clinical services include syndromic case management, counselling, regular health checks, and treatment for asymptomatic STIs. Medicines, with condoms and prevention information, are pre-packaged in six colour coded syndromic packs—white for genital ulcers, grey for cervicitis, etc.

Active community involvement in Mysore translates into high rates of clinic utilisation. Sex workers themselves participated early by mapping local hot spots with population size estimations at different times of the day. This information was used to develop outreach plans jointly with the sex workers, a first step in development of a peer network in the community. The community also played a major part in conducting a community based behavioural and STI prevalence survey. Outreach teams were trained in sampling methods, contacted peers and accompanied them to the clinic, achieving high levels of participation in the survey.

Through involvement in these early activities, a growing number of peers and community members became more actively involved in other activities including selection of a location and staff for the clinic, establishment of a local community based organisation and advocacy with police. These efforts in turn further strengthened community involvement in the clinic and utilisation of services.

Summary prepared by Dr Sushena Reza Paul and the Mysore STI team

Following a first clinic visit, continuation depends on sex workers appreciating the value of the services. The concept of routine check-ups to stay healthy is being actively promoted, but this will require more attention as interventions mature. DIC – with facilities for resting and washing on the same premises as the clinic – provide additional incentive for regular attendance.

Another priority is to expand the range of clinical services to better meet sex workers' needs. In the initial phase, clinical services emphasised STIs while also treating minor ailments. As quality of these basic services improves, clinical staff and sex workers are asking for additional services such as family planning, and HIV related counselling and care. Prophylaxis and management of opportunistic infections and tuberculosis case finding are also planned.

Better referral systems are needed. With high rates of HIV infection, the need to improve access to antiretroviral treatment (ART) for sex workers is growing. As India increases capacity to provide ART in hospitals, referral linkages with Avahan clinics can be developed.

Finally, there are evolving data needs. Introduction of the computerised monitoring system with individual level data will facilitate standardisation and quality assurance through timely reporting and feedback to technical staff and project managers. Additional surveillance and operations research are planned.

In summary, initial experience under Avahan suggests that scale-up of quality STI/HIV services with sex workers is feasible, but requires active community participation and coordinated capacity building efforts. In the face of rapid transmission seen among the most vulnerable and highest risk networks, such investments would likely be well worth the effort. [13]

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Looking upstream to prevent HIV transmission:
can interventions with sex workers alter the course
of HIV epidemics in Africa as they did in Asia?

Richard Steen

Jan AC Hontelez

Andra Veraart

Richard G White

Sake J de Vlas

Abstract

Background

High rates of partner change in 'upstream' sex work networks have long been recognized to drive 'downstream' transmission of sexually transmitted infections (STIs). We used a stochastic microsimulation model (STDSIM) to explore such transmission dynamics in a generalized African HIV epidemic.

Methods

We refined the quantification of sex work in Kisumu, Kenya, from the 4-cities study. Interventions with sex workers were introduced in 2000 and epidemics projected to 2020. We estimated the contribution of sex work to transmission, and modelled standard condom and STI interventions for three groups of sex workers at feasible rates of use and coverage.

Results

Removing transmission from sex work altogether would have resulted in 66% lower HIV incidence (range 54–75%) and 56% lower prevalence (range 44–63%) after 20 years. More feasible interventions reduced HIV prevalence from one-fifth to one-half. High rates of condom use in sex work had the greatest effect, whereas STI treatment contributed to HIV declines at lower levels of condom use. Interventions reaching the 40% of sex workers with most clients reduced HIV transmission nearly as much as less targeted approaches attempting to reach all sex workers. Declines were independent of antiretroviral therapy rollout and robust to realistic changes in parameter values.

Conclusion

'Upstream' transmission in sex work remains important in advanced African HIV epidemics even in the context of antiretroviral therapy. As in concentrated Asian epidemics, feasible condom and STI interventions that reach the most active sex workers can markedly reduce the size of HIV epidemics. Interventions targeting 'transactional' sex with fewer clients have less impact.

Introduction

The concept of 'core transmission' is fundamental to the epidemiology of sexually transmitted infections (STIs). [1] The basic reproductive number (R_0) that determines whether an STI will spread or die out within a population depends on rates of sexual partner change. [2] As sexual behaviour is highly heterogeneous, however, with most people having few sexual partners, high rates of partner change in sub-populations are required to sustain transmission. A high reproductive number within active sub-populations can serve as an engine for epidemic growth, whereas wider sexual mixing – 'bridging' between high and lower-risk populations – facilitates dissemination to others at lower risk.

HIV prevalence rates among sex workers and clients are generally several times higher than among lower-risk women and men. [3] Higher prevalence, more frequent contact with uninfected, susceptible individuals and higher transmission efficiency – due to high prevalence of ulcerative and other STI cofactors – potentially raise HIV incidence in core-bridge networks orders of magnitude above that in the general population. Such a large incidence differential is analogous to a transmission pump that can sustain overall prevalence at high levels. The implication for prevention, perhaps as relevant for HIV today as it was for cholera in nineteenth century London, is that epidemics may be controlled by intervening effectively at the level of the pump. [4]

Empirical evidence from Thailand, Cambodia and elsewhere in Asia – where interrupting core transmission resulted in rapid deflation of HIV epidemics – supports this approach. [5-7] Common components of such interventions include peer-based outreach to attain high coverage, condom programming and STI services that address both symptomatic and asymptomatic infections. These have also been successful in parts of Africa – Kinshasa, Nairobi, Abidjan, South African mining communities – although implemented on a more limited geographic scale. [8-13] Programmes that address structural conditions of sex work and offer more comprehensive HIV and reproductive health services may be even more effective. [14-16]

Yet, exception has been made for highly generalized epidemics in sub-Saharan Africa (SSA). Some argue that since most infections now take place between couples or regular partners, the fraction attributable to sex work must be low. [17] The concept of 'self-sustaining' generalized epidemics – initially ignited by, but now largely independent of sex work – has taken hold, leading to a wide diffusion of prevention resources in an effort to cover large populations with a range of interventions. [18]

Mathematical modelling has been used to estimate the effect of individual interventions – from 'behaviour change' to STI treatment, male circumcision and antiretroviral therapy (ART) – on HIV epidemic spread in SSA. [19-22] Implicit in many models is the assumption of reaching high levels of coverage in the general population. Less attention has been paid to modelling the effect of targeting itself – focusing a few proven prevention interventions on small sub-populations at high risk of HIV acquisition and transmission – as a prevention strategy. [13,23,24]

The study uses an established microsimulation model (STDSIM) to explore the effect that targeting sex workers could have on HIV epidemics in SSA, using an updated and refined version of an existing model quantification for Kisumu, Kenya. [25–27] Condom use and STI treatment interventions are simulated at varying levels of coverage among sex worker populations, assuming no change in interventions or behaviour among the general population. Our aim is to explore transmission dynamics and related intervention effects in a generalized epidemic setting, not to make specific predictions for Kisumu. To do this, we take a counterfactual approach – simulating introduction of a range of interventions with sex workers in the year 2000, where the model fit is close to data points from the 4-cities study – and estimate the impact on HIV epidemics 10 and 20 years later. This approach also permits estimation of changes in HIV incidence and prevalence separately from ART, which is a more recent factor with independent effects on both. [22] Programmatic implications, including potential synergies of implementing targeted interventions together with ART rollout, are also examined.

Methods

Model description

STDSIM, a stochastic individual-based microsimulation model, has been used extensively to study HIV and STI epidemics in SSA. [28–32] STDSIM simulates the natural history and transmission of HIV and other STIs in a population consisting of individuals with characteristics that can change over time. The formation and dissolution of heterosexual relationships and transmission of STIs during contacts between sexual partners are modelled as stochastic events. STDSIM allows the simultaneous and interactive simulation of several different STIs, with different HIV cofactor effects, and against which different prevention and treatment interventions can be applied.

An STDSIM quantification was previously fit to demographic, behavioural and epidemiological data for Kisumu as part of the 4-cities study. [23-27] We used the same quantification with four improvements. First, we updated HIV transmission probabilities used in 4-cities modelling to lower values that resulted from a recent systematic review (Table S1 in supplementary materials, http://links.lww.com/QAD/A462). [33] Secondly, in the quantification of sex work, we used the mean number of clients per week (1.6) and centile ranges from survey data, rather than the median (1.0) as reported by Morison et al. [27] and used by Orroth et al. [25] Also, assumptions about the coverage and effectiveness of STI treatment were revised downward based on recent programme evaluation data. [34] Finally, we refined the simulation of commercial sex to include three categories of sex workers with different rates of partner change (numbers of clients), as explained in the following paragraph. More details on the above changes are provided in the supplementary materials (http://links.lww.com/QAD/A462).

Data suggest that approximately 3% of women aged 15–49 in Kisumu engage in some form of sex work. [35] Behavioural data derive from population-based surveys using standardized questionnaires with a broad definition of sex work – any exchange of sex for money, gifts or favours in the past year. Yet, sex workers in the 4-cities study reported widely divergent mean numbers of clients in the past week – 1.6 in Kisumu, 3.3 in Yaounde, 4.0 in Ndola and 11.9 in Cotonou. We explored heterogeneity of client numbers by disaggregating into three sub-populations of sex workers, maintaining an overall sex worker population size of 2–3% and a mean of 1.6 clients per week. On the basis of the observed geometric distribution of the survey data, we defined a low activity group (L=60% of all sex workers) with 0.6 clients, a medium group (M=30%) with 2.2 clients and a high group (H=10%) with 5.7 clients per week. In programmatic terms, these groups may approximate commonly observed patterns of sex work, from overt, full-time, self-identified 'professional' (H) and their somewhat less active peers (M), to covert, occasional, non-identifying or 'transactional' (L). We aggregate H and M groups in some analyses to compare the effect of targeting the 40% of more highly active sex workers (HM) to that of reaching all sex workers (HML).

Client demand – the proportion of men who buy sex and their number of sex worker contacts per year – was calculated to arrive at the sex worker activity levels described above. Client population sizes were maintained from the 4-cities quantification (31% of men 15–49), as was their distribution among married and unmarried men. We increased the frequency of visiting sex workers from 12 to 18 times per year for the more active group (5% of men) and from one to three times per year for a less active group (26% of men) after examining alternative assumptions (see Table S3 in supplementary materials, http://links.lww.com/QAD/A462).

HIV is introduced first as outside infections (at an ongoing rate of 1.9% for male and 1.7% for female immigrants) in 1980, and in four sex workers in 1984.

Simulated interventions

Simulations were run to explore the contribution of sex work to HIV and STI transmission and the potential effect of targeting sex workers with different condom and STI treatment interventions. First, the hypothetical independence of HIV epidemics from sex work was explored by completely removing the possibility of transmission through sex work abruptly in 2000. To this end, sex work continues in the model but we assume 100% condom protection without failure. Although unrealistic, these assumptions permit exploring the plausibility of epidemics persisting where sex work exists but has no role in transmission – the null hypothesis behind sex work as a continuing transmission factor. Simulations examine the effect of removing transmission potential for all sex workers and for subsets of highly active sex workers. The population-attributable fraction (PAF) of sex work in HIV transmission in these settings was estimated for the years 2010 and 2020 using the formula $1 * (\text{HIV}_{\text{incidence without sex work}}/\text{HIV}_{\text{incidence with sex work}})$.

Second, after restoring transmission potential to commercial sex, we introduced standard, feasible interventions at different levels of utilization and coverage among sex workers assuming no change in other interventions or behaviour among the general population. These include the following:

- Targeted condom programmes, which have been shown to raise reported condom use in commercial sex to 80–90% or more. [7,14,15]

- Targeted STI treatment, which includes both sensitive STI screening and periodic presumptive treatment (PPT), or either of them, covering both symptomatic and asymptomatic STIs. Coverage rates of 60% or more have been described for such interventions. [36,37]

For each scenario, we modelled interventions – first condom use alone, then condom use with STI treatment – at different levels of coverage, and determined HIV incidence and prevalence in the general population 10 and 20 years after their introduction. As before, we estimate the effect of feasible interventions applied to different sex worker sub-populations.

After making the above changes, STI transmission probabilities were refitted within a priori ranges as was done in the original 4-cities model (Table S2 in supplemental materials, http://links.lww.com/QAD/A462) in order to arrive at similar STI prevalences to those observed. STI co-factor estimates for HIV transmission and acquisition were not changed.

Simulation results were based on the average of 400 runs for each scenario to minimize stochastic variability. [25] The epidemiology of HIV transmission at population level was examined by linking HIV transmission events over time from sex workers and clients to subsequent 'downstream' infections in other partners.

Alternative explanations for findings were explored in scenario analysis varying key parameters including sex worker and client population sizes and partner change rates, multiplying each parameter value by 3/2 and 2/3, respectively (Table S3 in supplemental materials, http:// links.lww.com/QAD/A462). A scenario that includes assumptions about ART rollout based on Kenyan programme data was run to explore whether this influenced the main findings. ART coverage until 2010 was fit to coverage levels reported by WHO using two sub-models representing an individual's demand for ART and the capacity of the health system to meet this demand (section S3.2 in supplemental materials, http://links.lww.com/QAD/A462). [22]

Results

The baseline model quantification (Fig. 1) describes simulated HIV prevalence trends from 1980 to 2020 compared to data points from antenatal clinic surveys.
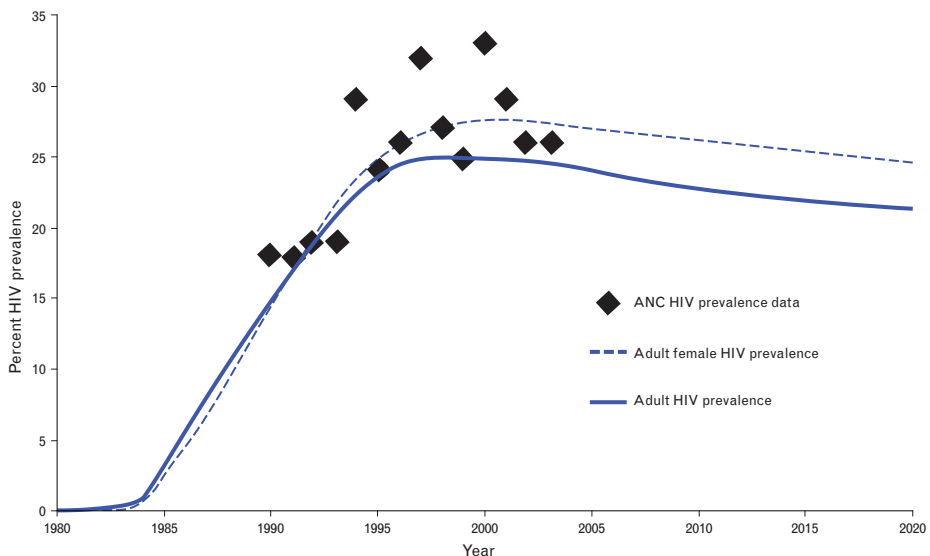

Fig. 1. Model fit to data: HIV prevalence. ANC, antenatal clinic.

Figure 2 shows that complete blocking of transmission in sex work in 2000 would have resulted in 66% lower HIV incidence (54–75% lower in 95% of runs) and 56% lower prevalence (44–63% lower in 95% of runs) by 2020 compared to the same scenario without intervention.

Overall HIV incidence declines from 3.6% in 2000 to 1.8% in 2010 and 1.1% in 2020; HIV prevalence falls from 24.9% in 2000 to 16.0% in 2010 and 9.4% in 2020 (continuing to below 5% by 2033 and 2.1% in 2050). The estimated PAF for all sex work (HML) is 45.6% in 2010 (PAF_{2010}) and 66.4% in 2020 (PAF_{2020}). HIV incidence reductions are almost identical for the HM sub-group (PAF_{2010}=43.7%, PAF_{2020}=64.4%), suggesting that most transmission is attributable to sex work with high numbers of clients. In contrast, blocking transmission in the L sub-group with lowest client numbers has only a marginal effect on the epidemic.
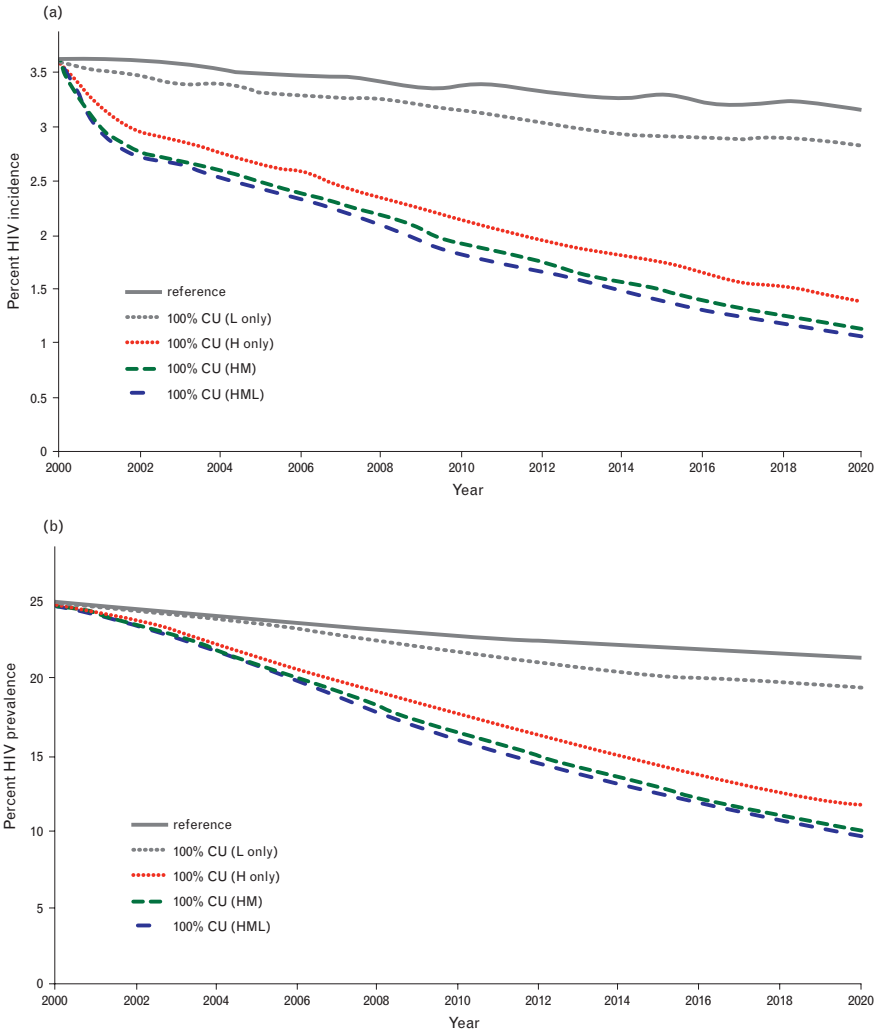

Fig. 2. HIV (a) incidence and (b) prevalence, after removing transmission in sex work for different sex worker sub-groups. CU, condom use; H, high activity sex worker group; L, low activity sex worker group; M, medium activity sex worker group. Removing transmission from sex work is simulated by applying 100% condom use without failure.

The response to more realistic interventions in sex work is shown in Fig. 3. Increases in condom use and STI screening resulted in reduced transmission and a progressive decline in HIV prevalence in all scenarios. At 70–85% condom use, HIV prevalence is reduced by 25–29% after 10 years and 46–52% after 20 years. Again, intervening in high (H) and medium (M) activity sex work accounts for nearly all of the estimated HIV declines.
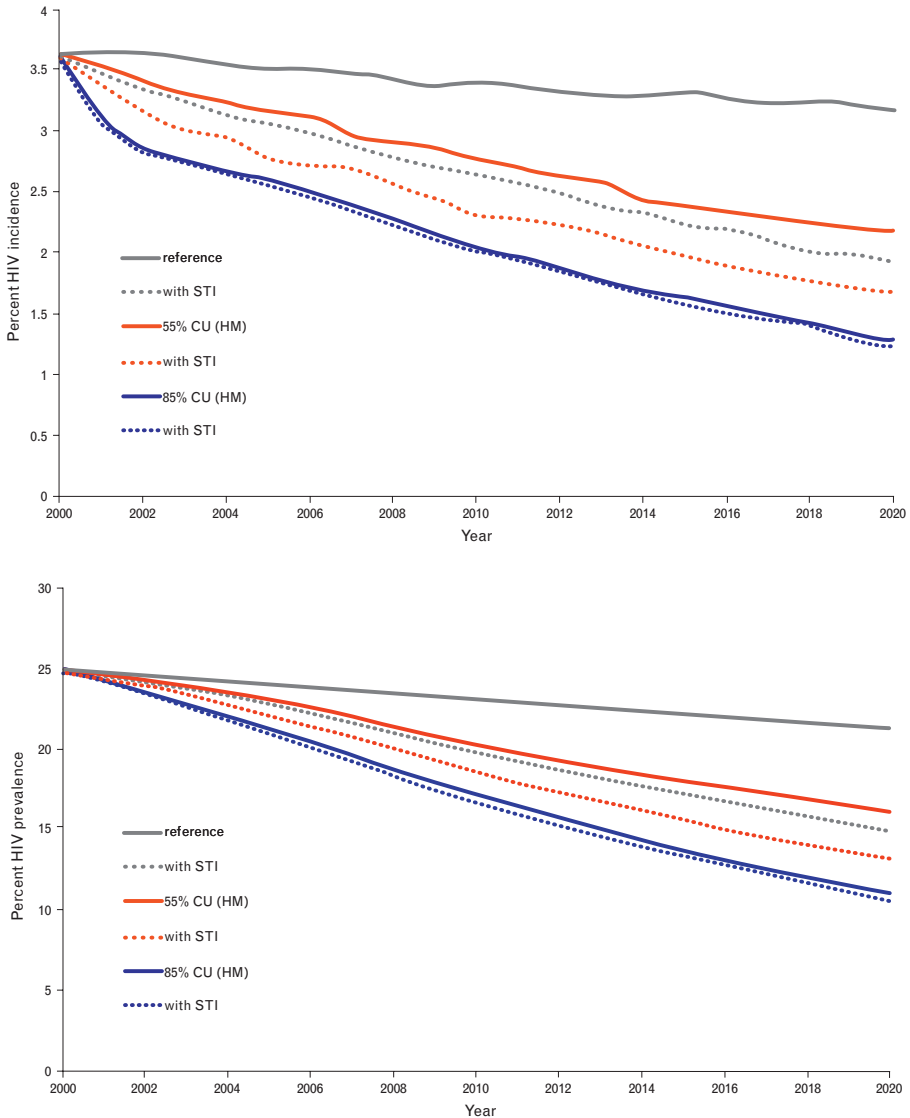

Fig. 3. HIV (a) incidence and (b) prevalence, at different levels of condom use (HM) with and without STI screening/PPT. CU, condom use; HM, combined H and M sex worker groups (high and medium activity); PPT, periodic presumptive treatment; STI, sexually transmitted infection. Solid line indicates condom use in sex work (HM) and dotted line indicates STI treatment (60% sex worker coverage) at different levels of condom use in sex work.

The addition of STI treatment interventions (including screening for asymptomatic infections or PPT) adds little benefit in terms of HIV reductions when rates of condom use are high (70–85%). However, at lower rates (40–55%), adding STI treatment is roughly equivalent to increasing condom use 15 percentage points – 40% condom use with STI treatment comparable to 55% condom use alone.

Finally, we ran all simulations in a quantification that included progressive rollout of ART as has been described for Kenya (Fig. 4). [31] ART scale-up started in 2003; by 2010, 50% of those eligible (at CD4$^+$ cell counts of <350cells/ml) were on treatment, with universal access (coverage of >80%) achieved in 2014 and maintained thereafter.

Compared to ART alone, HIV prevalence in 2020 was 23, 42 and 46% lower when condom use among more highly active sex workers (HM) increased to 55, 70 and 85% in 2000, and HIV incidence declined 33, 53 and 63% more than in the ART-only scenario. The complementary of the two interventions is also apparent – with ART, the effect on HIV prevalence of raising condom use to 85% (HM: 8.4% by 2020) is greater than that of completely blocking transmission without ART (HM: 10.0%; Fig. 2b).
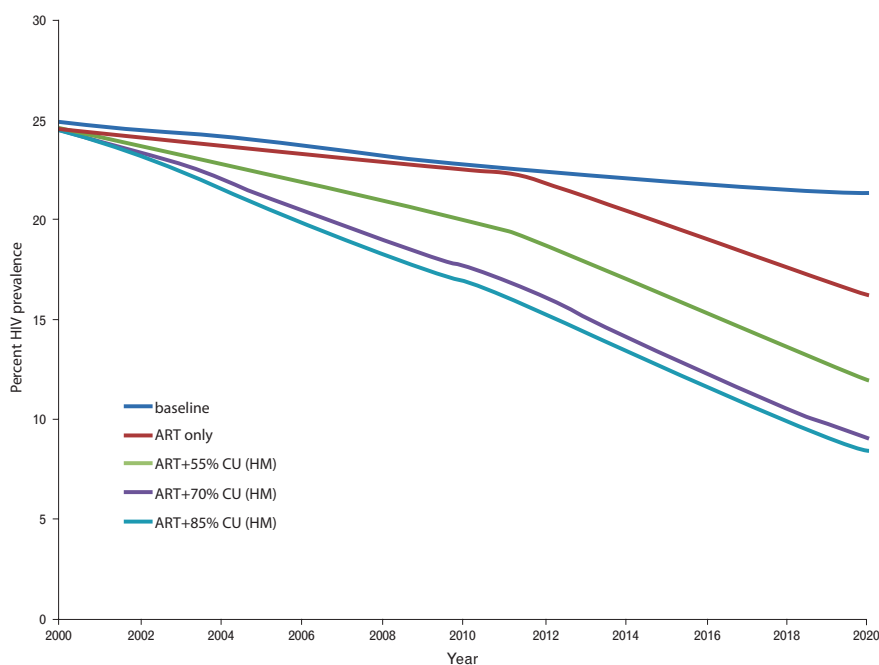

Fig. 4. HIV prevalence at different levels of condom use (HM) in ART rollout scenario. The ART scale-up started in 2003, and by 2010, 50% of those eligible (at CD4$^+$ cell counts of ≤350 cells/μl) were on treatment. Universal access under this rate of scale-up (coverage of >80%) in the model is achieved in 2014 and maintained thereafter. The condom use interventions started in 2000. ART, antiretroviral therapy; CU, condom use; HM, combined H and M sex worker groups (high and medium activity). ART prevalence estimates are slightly lower than baseline (without ART) due to small differences in modelling stages of HIV infection to permit detailed modelling of CD4$^+$ patterns (see Hontelez et al. [31]).

Discussion

The study explores the role of sex work and the potential impact of targeted prevention interventions in a generalized African HIV epidemic. The simulation of sex work in the 4-cities model was refined based on available data without changing assumptions about general population sexual behaviour. Our baseline parameters and assumptions thus reflect early conditions and interventions in Kisumu, which have undoubtedly changed since 2000. The estimates from this study were used to generate insights into transmission dynamics and potential interventions in a generic generalized epidemic setting, not to describe HIV and STI trends in Kisumu today.

Our findings suggest that sex work – in the absence of effective interventions – remains an important driver of HIV transmission, even in generalized or 'hyper-endemic' epidemics such as Kisumu's. By analysing transmission chains (HIV transmission events), we estimate that approximately 60% of HIV infections can be linked to sex work in 2000, 20 years after the start of the epidemic, subsequently levelling off to nearly 50% in 2010 and beyond. Without this continued infusion of new infections from sex work after 2000, the model estimates that HIV prevalence in the general population would be 30% lower in 2010 and 56% lower in 2020.

As in Asia – where preventing transmission in sex work has already reversed large HIV epidemics in several countries – interrupting 'upstream' transmission would have obvious benefits. These include facilitating ART scale-up and universal access to services by reducing the number of people who need them, as well as raising the possibility of eliminating new HIV infections altogether. We estimate that HIV incidence in the modelled scenario could be reduced to 0.1% (and prevalence below 2%) by 2040 by increasing condom use rates in sex work, beginning in 2013, to levels comparable to those reported from Asia (85%), while continuing to scale up ART (explorations beyond period shown in Figure S2, http://links.lww.com/QAD/A462). Given the magnitude of such potential benefits, further research into their relevance to African settings should be a high priority.

We also examined the effect of interventions targeted to different groups of sex workers. Most behavioural surveys define sex work broadly as the exchange of sex for material gain, in cash or in kind, yet often report that many respondents who meet this definition neither self-identify as sex workers nor have many partners. Such surveys, in casting a wide net, tend to 'dilute' the core group with large numbers of 'sex workers' with relatively low rates of partner change. We disaggregated sex workers by reported client numbers to analyse the effect of targeting different groups. Although interventions have a large impact when applied to all sex workers, nearly all of this effect remains if only the 40% of sex workers with highest rates of partner

change are reached. From a programme perspective, this would be similar to targeting only the most overt sex workers – who are often easiest to identify – without reaching the more numerous and hard-to-reach 'transactional' or 'occasional' sex workers. Blocking transmission from these sex workers – who account for a disproportionate number (79%) of client contacts and most sex work-linked transmission events (91%) – completely would be expected to reduce general population HIV prevalence by 28% at 10 years to 53% after 20 years, with overall incidence reductions of 44 and 64%, respectively.

It is, of course, unrealistic to assume that transmission in sex work, even among smaller subpopulations, can be blocked completely. We therefore modelled several basic interventions among sex workers that have been shown to be feasible and effective. Condom use as expected is the most effective way to interrupt transmission in commercial sex networks. Empirical data from Kinshasa, Nairobi, Abidjan, Cotonou, Thailand, Cambodia, India and elsewhere associate condom use rates of 80–90% reported by sex workers with declining HIV rates. [8-11,14-16] Actual use may be lower than reported, however. Simulations at different levels of condom use (85, 70 and 55%) in our model showed large impact on transmission, even when only highly active sex workers were targeted. Again, from a programme perspective, this is an important finding as the feasibility of increasing coverage and condom use among a subset of easily identifiable sex workers is much greater than trying to reach all sex workers.

Sexually transmitted infection screening and treatment interventions were simulated as an adjunct to condom programmes, assuming effective treatment of both symptomatic and asymptomatic infections, with 60% sex worker coverage every 3 months. Such interventions can be implemented either as laboratory-based screening (with sensitive diagnostics) or PPT, feasible interventions with well documented outcomes. [3,12] The simulated STI intervention in the model was found to be highly synergistic with condom use – raising the impact of 40% condom use to the equivalent of 55% condom use alone, if 60% of sex workers also received STI screening or presumptive treatment. As expected, the additional benefit of STI treatment diminishes as rates of condom use in sex work increase reducing STI/HIV exposures.

We also explored alternative explanations for the findings by varying several key assumptions (supplementary materials, http://links.lww.com/QAD/A462). Sex worker partner change rates reinforce findings, with higher rates contributing more to transmission. Findings are also resilient to varying client population sizes and contact rates. In addition, the analysis including ART rollout using Kenyan data (Fig. 4) showed an additive, complementary effect on HIV incidence and prevalence. This is an important area for further research.

In conclusion, our findings suggest that, similar to concentrated epidemics in Asia, generalized African HIV epidemics may not be self-sustaining in the absence of high-incidence 'upstream' transmission from sex work. Moreover, feasible interventions that focus on small but highly active sex work networks may be highly efficient in controlling transmission in such epidemics. Basic interventions that address condom use and curable STIs in sex work appear to be core elements of an effective prevention response even in contexts where ART is being rolled out. Intervention-linked research should be prioritized to confirm these findings in other generalized epidemic settings.

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Chapter 11

General discussion

Preventing HIV through targeted STI control

This thesis explores the role of sex work in STI and HIV transmission, important epidemiological interactions and implications for control of these interrelated epidemics. The main research question asks whether, as a general rule, *scaling up basic condom and STI interventions with sex workers and their clients has substantial impact on HIV transmission?* An important corollary is whether regional deviation from this approach – non-targeted interventions in generalised African epidemics – can be justified on epidemiological grounds.

11.1 Key findings in relation to the research questions of this thesis

STI control is defined in Chapter 2 in standard epidemiological terms of decreased incidence and prevalence outcomes. Control may be relative to earlier prevalence levels or absolute (elimination/eradication), as measured in the general population or among sub-populations believed to be important in STI transmission dynamics. *Targeting* refers mainly to populations involved in sex work, recognising that other populations may also be prioritised by programmes for related or other reasons.

We begin by exploring the feasibility of control interventions and potential benefits to sex workers themselves. We then explore effects of core group dynamics on transmission of common curable STIs and HIV – clients, for example, infect sex workers who can infect many other clients, and also act as a bridge to extend transmission to lower risk partners outside sex work. The underlying hypothesis explored in questions 2 and 3 relates to these dynamics – that (upstream) transmission in sex work determines to a large extent how much subsequent (downstream) transmission occurs among the population at large. To what degree such dynamics provide necessary and sufficient conditions for epidemic spread and maintenance are also considered, along with implications for control programmes.

Question 1: Is control of curable STIs among sex workers feasible?

High STI burden among female sex workers is reversible, and subsequently preventable, by reaching sex workers with appropriate interventions and services

Sex workers have an extremely high burden of STIs. [1,2] This represents first and foremost a major health problem for sex workers as individuals, directly affecting many women – estimated at from less than one percent to as high as seven percent of women of reproductive age in different areas of the world. [3] Untreated, common STI sequelae and major complications – including pelvic inflammatory disease, infertility, ectopic pregnancy, sepsis and congenital infections – account for a substantial burden of morbidity and mortality. Better control of STI transmission in sex work would thus provide important benefits to sex workers themselves. But to what extent can the prevalence of common STIs among sex workers actually be reduced?

We show through original field research (Chapters 5, 6 and 9) and systematic reviews (Chapters 7 and 8) that the high STI burden among female sex workers is reversible, and subsequently preventable, by reaching sex workers with appropriate interventions and services. Two general observations are striking across regions and studies – the high prevalence of curable STIs among sex workers before, and the large degree of change possible following interventions. Chapter 3 reviews relevant experiences from Asia and a recent systematic review documents evidence from Africa. [4] The potential magnitude of prevalence reductions among sex workers following intervention depends on several factors – including the specific STIs, populations and interventions considered. We estimate short-term prevalence reductions of more than fifty percent for gonorrhoea and chlamydia by meta-analysis of intervention studies (Chapter 7), with some sites reporting declines exceeding eighty percent. Reductions of ulcerative STIs may be even greater, with elimination of chancroid reported from some sex work settings, progressive syphilis declines in others.

Intervention components – peer outreach, condom programming and STI services – are feasible and remarkably consistent across countries and regions. We distinguish (Chapters 2 and 3) between *direct* and *structural* interventions, where the former are those that act directly on the probability of transmission during sexual contact – condom use (to reduce exposure) and STI treatment (to shorten duration of infectiousness and cofactor effects). Structural interventions, on the other hand, may influence transmission by changing conditions under which sex work takes place – reducing vulnerability, removing barriers and making direct interventions easier to adopt, more frequently applied or more effective. Considerable evidence, particularly from Asia (Chapter 3), supports the importance of structural interventions. [5] Peer-based outreach and interventions facilitate both direct and structural interventions and provide a critical link between the sex worker community and public health interventions and services.

Among direct interventions, increasing condom use in sex work to high levels appears to be most important for STI control. At a population level, condoms effectively reduce the infectiousness of STI pathogens – a critical determinant of epidemic growth – by blocking potential exposures. Where this has been achieved in sex work to levels above 80-90%, prevalences of HIV and common curable STIs among sex workers have declined rapidly. Structural interventions – *100% condom use policies* in several Asian countries and *community-led structural interventions* in India – enable high condom use by ensuring supportive conditions in sex work settings.

STI treatment is a second direct intervention. While condom use reduces STI exposure and incidence, STI treatment acts on existing prevalent infections. By shortening the duration of infectiousness through effective treatment, the chain of infection can be interrupted and risk of complications to the individual reduced. STI treatment thus complements condom use interventions by reducing existing STI burden among sex workers, while condom use prevents reinfection. This complementarity decreases over time as prevalence falls and condom use rises to high levels, permitting less intensive treatment interventions to maintain low STI prevalence (Chapter 10).

Providing effective STI treatment to female sex workers entails several important challenges, however. As for all women, STIs are often asymptomatic making detection difficult. Furthermore, the most common genital complaint of vaginal discharge is usually due to non-sexually transmitted reproductive tract infections (RTI), and is poorly predictive of STI. Lastly, except in the case of syphilis, there are few affordable and sensitive laboratory methods for detecting common STIs.

Chapters 5 though 9 explore alternative approaches to treating asymptomatic infections through the use of periodic presumptive treatment (PPT), which bases treatment on risk of infection rather than laboratory or symptom-based methods. Two field studies (Chapters 5 and 6) and a systematic review (Chapter 7) provide evidence that PPT can rapidly reduce prevalence of common curable STIs by half or more. Interventions such as PPT should be implemented as part of a package of services (Chapters 8 and 9) that reach sex workers through peer-based outreach, include strong support for increasing condom use, and address both symptomatic and asymptomatic STIs. It is thus as part of such a combination of interventions, not as a stand-alone intervention, that PPT results should be considered.

We thus recommend that targeted interventions with sex workers be scaled up first and foremost in order to reduce the high burden of common curable STIs and avert serious morbidity and mortality among sex workers. Direct interventions should include peer-based outreach, condom programming and STI services which address both symptomatic and asymptomatic STIs, and should be supported by structural interventions to reduce vulnerability, enable condom use and facilitate participation and ownership by sex workers. Provision of more comprehensive services – related to HIV, family planning, drugs and alcohol, violence, etc – addresses sex workers' broader health and social needs and, in doing so, may also increase participation and engagement of sex workers in the interventions.

Question 2: Does controlling curable STIs in sex work improve STI control in the general population?

Interventions which reduce STI prevalence among sex workers also reduce STIs among clients, and rapid country-level STI declines follow large-scale interventions in sex work

Beyond addressing STI morbidity among sex workers themselves is the broader public health objective of controlling STI transmission among the population as a whole. Core group theory, supported by extensive empirical evidence, suggests that controlling transmission in sex work is a critical step in efforts to improve overall STI control. [6] Not only are STI prevalence rates consistently higher among sex workers and their clients (usually measured as men who report sex work contacts or whose occupation, often involving migration or mobility, is considered 'high risk') compared to the general population, but high rates of partner change generate high incidence facilitating spread within and beyond sex work networks. Targeted approaches to disease control arguably have important advantages, including the efficiency of achieving population-wide impact by intervening within relatively small sub-populations. But do such approaches work for control of common STIs beyond the sex work networks that they target?

We show first of all, through intervention studies and a systematic review (Chapters 5-7), that interventions which reduced STI prevalence among sex workers also had effects on clients or men living in nearby communities. We also present strong evidence in a review from Asia (Chapter 3) of rapid country-level declines in STI incidence and/or prevalence after large-scale interventions in sex work were implemented. We pursue the question further for the special case of chancroid (Chapter 4) where elimination has been achieved in several countries by interrupting transmission in sex work.

We present field research conducted in South Africa (Chapter 5) and the Philippines (Chapter 6), which demonstrated that interventions which effectively reduced STI incidence and prevalence among sex workers also slowed transmission within and beyond sex work networks. In both studies, the main focus of the research was on condom/STI interventions for sex workers, including a PPT component. No new interventions were introduced for men who were nevertheless monitored for changes in STI incidence and prevalence. In South Africa, reductions in both STI incidence and prevalence – approximately 80% for ulcerative and 40 to 50% for non-ulcerative STIs – were measured among migrant mine workers living near the area of the sex worker intervention. In the Philippines, clients were sampled at sex work venues (prior to entering brothels) and found to have 46% lower prevalence of gonorrhoea and/or chlamydia in cross-sectional surveys conducted after the intervention compared to the pre-intervention baseline.

The strongest empirical evidence of public health benefit is national programme data, mostly from Asian countries that have implemented 100% condom use programmes (100% CUP). Four countries (Thailand, Cambodia and, to a lesser extent, Myanmar and Mongolia) have documented national-level STI declines and two others (China and Vietnam) at provincial levels following implementation of 100% CUP (Chapter 3). In Thailand, STI incidence – gonorrhoea, syphilis, chlamydia, chancroid and lymphogranuloma venereum (LGV) case reports – declined by 95% within 10 years, leading to elimination of chancroid and LGV. Cambodia reported low prevalence of gonorrhoea (0%), syphilis (3.0%) and chlamydia (1.8%) among police in 2001 (when reported condom use in sex work was 97%); corresponding rates measured in 1996 among police and military – who reported 43% and 66% condom use with sex workers – were gonorrhoea (5.0%), syphilis (6.6%) and chlamydia (2.1%).

Pursuing these observations further, important epidemiological patterns have relevance for control programmes. The degree of STI control is related to the reproductive rate (R_0) of the organism and thus to three key factors – the inherent infectiousness of the organism (ß), the average duration of infection (D), and rates of partner change (c) in specific populations. [6]

The latter effectively determines the size of the sub-population that can support transmission. Observed STI declines among sex workers appear to follow expected patterns with 'sex work dependent' STIs like chancroid, which require high rates of partner change (estimate 15-20 per year), declining most rapidly following intervention. Chlamydia, at the opposite extreme, requires a relatively low rate of partner change (estimate 2-3 per year), has a much broader population base and is thus less sensitive to interventions in sex work, while gonorrhoea and syphilis fall between these extremes. Empirical evidence, with few exceptions, generally follows these patterns of control – chlamydia prevalence, for example, remains high in many Asian countries, although syphilis control continues to be problematic in Mongolia.

A related question concerns the level of intervention required in sex work to influence STI transmission at general population level. Asian country data (Chapter 3) suggests that when self-reported condom use by sex workers exceeds 80-90%, STI transmission declines while this is less apparent at rates of 60-70% or below. Condom use is not the only factor, however, as countries documenting improved STI control also provide STI services to sex workers. Through modelling (Chapter 10), we estimate that STI services are most important when condom use in sex work is low, by reducing prevalence, and thus transmission opportunities during subsequent unprotected sex.

We recommend that interventions with sex workers be prioritised, not only for the direct benefits to sex workers themselves, as discussed under Question 1, but as an essential strategy for controlling STIs in the general population. In countries with low rates of male circumcision where ulcerative STIs are common, improved control of ulcerative STIs, including chancroid elimination, are feasible targets. In other countries where non-ulcerative STIs predominate, reductions of at least fifty percent in gonorrhoea and chlamydia prevalence appear to be feasible.

Question 3: Does control of curable STIs among sex workers slow HIV transmission?

Rapidly expanding HIV epidemics have been halted and reversed by intervening effectively to reduce transmission in sex work. Appropriate targeting appears to be both necessary and sufficient to reduce HIV prevalence in the general population.

HIV epidemics spread most rapidly and reach their largest size in the presence of three factors which directly increase transmission probabilities – where sex work is largely unprotected by condoms, many clients are uncircumcised, and ulcerative STIs are prevalent. The epidemiological argument for this is developed in Chapters 2 and 3, and is perhaps best illustrated by an early observation from Kenya where over forty percent of uncircumcised men

with genital ulcer seroconverted to HIV after a single sex worker contact. [7] Changing one or more of these conditions may well serve to interrupt HIV transmission beginning within sex work networks where, due to high rates of partner change, HIV and other STIs can spread most efficiently. Male circumcision is a potential intervention to disrupt this triad, albeit requiring high uptake among half the sexually active population. We consider here the other two factors – condom use in sex work and ulcerative STIs – extending earlier discussions to estimate the impact of STI control in sex work on the transmission of HIV.

We have shown in the previous section that basic condom and STI interventions in sex work contribute to improved STI control, most markedly for ulcerative STIs like chancroid and syphilis. Controlling STIs in sex work through targeted interventions thus removes two of three critical conditions for rapid HIV transmission – high rates of exposure are directly reduced by increasing condom use, and ulcerative and other STIs decline rapidly, even where men remain uncircumcised. Moreover, such targeted interventions are highly efficient, requiring coverage of from about one percent of the adult female population in some areas, up to 5-7 percent in others. [3] The question is whether such interventions are as effective for HIV as they are for other STIs?

We show, as demonstrated most dramatically in Asia, that rapidly expanding HIV epidemics have been halted and reversed by intervening effectively to reduce transmission in sex work. Chapter 3 presents evidence supporting such change in Thailand, Cambodia, Myanmar and West Bengal, India. In all cases, reported condom use in sex work increased from low levels to above 80-90 percent and significant reductions in ulcerative STIs were documented, despite no change in male circumcision status. In addition, China and Mongolia, with similar conditions but much lower-level HIV epidemics, appear to have controlled HIV in sex work and averted wider HIV transmission using similar approaches.

A related question is whether such interventions can work as well in advanced generalised epidemics in Africa? Successful interventions with sex workers have been reported from Africa – in Kinshasa, Nairobi, Abidjan, Dakar, Cotonou, and South African mining areas – yet few have been implemented on a large scale. [8-16] As a result, apart from Kenya, and perhaps Senegal and Benin, there is little evidence of country-level impact on HIV epidemics comparable to Asia. [8,9,15]

This question remains an important one, although it may seem more notional than germane to the challenges of controlling large epidemics – why indeed should transmission dynamics differ fundamentally by geographic region? Certainly interventions anywhere require adaptation to local conditions, but these are generally operational concerns that rarely conflict with

epidemiological principles or challenge the underlying rationale of proven interventions. Yet, the sidelining and stagnation of targeted STI control efforts in Africa, exacerbated by policy shifts and marginal funding in that region, do in fact beg exception from global experience. The resulting neglect of what in Asia are considered fundamental interventions lies behind the fractured paradigm of STI control (Chapter 2) and, arguably, persistence of HIV and related STI epidemics in Africa. It is beyond the scope of this thesis to review the reasons underlying this exceptional view of African HIV epidemics. Africa-focused research – undermining STI cofactors, elevating the importance of general population factors such as male circumcision and concurrent sexual partnerships, to cite just three examples – has consistently neglected to integrate evidence from other regions or to reconcile findings with divergent global experience. Regional priorities and external funding support a 'know your epidemic' approach that conforms to meandering research streams despite serious challenges to their validity, interpretation and operational feasibility [17-20]

We explored the question – can proven interventions work as well in generalised epidemics – further in Chapter 10 by modelling a range of targeted interventions with sex workers in the context of a generalised African HIV epidemic. The contribution of sex work was estimated by removing HIV/STI transmission potential from sex work completely, which had a substantial impact on HIV transmission, even in the context of ART scale-up. More importantly from a programme perspective, feasible condom and STI interventions in sex work, assuming realistic rates of use and coverage, were complementary, particularly at lower rates of condom use, reducing the size of the simulated HIV epidemic by up to one-half over twenty years. An additional important finding of this modelling work was that nearly all of the estimated reductions in HIV incidence and prevalence could be attributed to interventions with only 40% of sex workers who had the highest number of clients. Even within interventions focusing on sex work, additional targeting based on rates of partner change, apparently a critical epidemiologic factor, makes a difference. This 'dose-effect' of targeting further strengthens the validity of core group theory.

Control and reversal of HIV epidemics thus likely require effective interventions with core and bridge populations whose rates of partner change are high enough to sustain transmission. Appropriate targeting appears to be both necessary and sufficient to reduce HIV prevalence in the general population, as argued further below (Section 11.2). We thus recommend that interventions with sex workers described above, particularly those with large numbers of clients, receive high priority, not only for STI control, but as fundamental components of HIV prevention, and regardless of stage or classification of HIV epidemic.

11.2 Additional considerations referring to other ongoing work

The link between sex work and wider transmission of STIs is not new. It has been alluded to in general terms since at least the late fifteenth century when syphilis followed military deployments and spread rapidly through Europe. With advances in germ theory and modern epidemiology during the nineteenth century, the role of sex work in the spread of first syphilis and then of other STIs, and the factors determining it were more fully described. [21] Understanding of this dependence has advanced considerably over the last half century as a number of 'less developed' countries, beginning with Sri Lanka and China, have documented large reductions in their STI burden. At least half a dozen other Asian countries report similar success – achieving STI control levels comparable in some cases to developed countries – by implementing strategies that make sex work safer.

Similarly, the relationship between poor STI control and HIV transmission has been a focus of research for over three decades (Chapter 2). [19] We describe the important triad of uncircumcised males, unprotected sex work, and ulcerative STIs (Figure 11.1), which can be considered as ideal conditions or a 'perfect storm' for HIV transmission. We see these three conditions as not merely important and closely interrelated, but likely necessary and sufficient conditions for development and maintenance of large HIV epidemics. The importance of these factors was first described in the 1980s and later supported by modelling work in the 4-cities study. [7,22,23] Chapter 3 reviews historical data on chancroid to argue, not only that the largest HIV epidemics developed in countries where male circumcision was uncommon, but that ulcerative STIs (predominately chancroid), under conditions of low condom use in sex work, were critical and interrelated cofactors. Low-level HIV epidemics in countries like Sri Lanka, or in Europe, where men are not circumcised but STI control, both in sex work and overall, is strong, argue against the male foreskin being a sufficient condition for rapid HIV transmission on its own. Rather, it is the interaction between non-circumcision and genital ulcers which permits the highest HIV transmission efficiency. This is illustrated (Figure 11.1) by the estimated magnitude of HIV cofactor effects – 25 to 300 times for chancroid (plus foreskin) compared to 2-3 times for the male foreskin alone. [24]

Figure 11.1 Interaction between male foreskin and chancroid facilitates HIV transmission
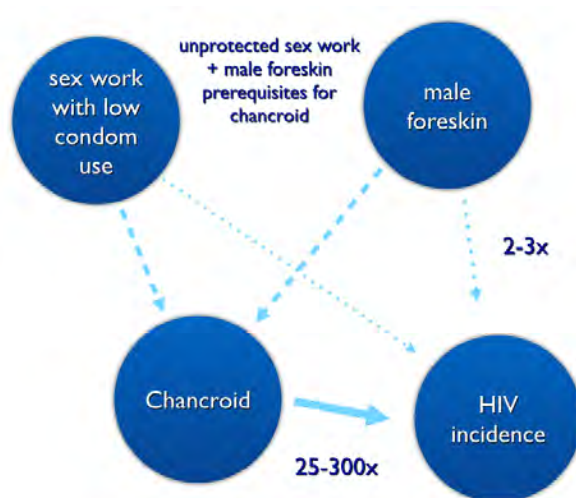
The relationship between these factors is of critical importance to understanding transmission dynamics and planning interventions. Ulcerative STIs, particularly chancroid, spread rapidly through and beyond sex work networks where many clients are uncircumcised and don't use condoms. Either condom use in sex work or male circumcision at high enough rates results in fewer genital ulcers and elimination of chancroid, thus slowing HIV transmission. High rates of condom use in sex work have been achieved within months to years in a number of countries, whereas the time needed to circumcise a high proportion of sexually active males (or neonates) is projected to require decades. [25]

As mentioned, the 4-cities study, conducted in the late 1990s, included modelling work that highlighted chancroid as a probable critical cofactor in development of large HIV epidemics. Then and now, however, reliable data on chancroid are scarce, a major limitation for STI control efforts. There are several reasons for this. Chancroid is very difficult to culture, limiting diagnosis to few centres with strong laboratory capacity. [26] On the other hand, chancroid quickly disappears in areas where condom use in sex work rises to high levels (Chapter 4). Chancroid was the major ulcerative STI identified in a number of sub-Saharan African cities – those with low male circumcision rates and unprotected sex work – early in their epidemics. [7] As the standard of care improved in these locations – often sites of large and well-funded intervention trials – the 'disappearance' of chancroid was noted, and research attention shifted to other ulcerative STIs, especially HSV-2. [19] Yet, chancroid clearly still persists as a cause of genital ulcers. [27] Without reliable surveillance data from remote 'interior' areas, where conditions have generally changed little and interventions are weak, there is little basis to suggest that chancroid has been eliminated as a public health problem. On the contrary, from a

public health perspective, it may be safer to assume, until data demonstrate otherwise, that 'perfect storm' conditions persist in remote areas – particularly those that attract migrant labour and sex work. High population mobility to and from such high-transmission areas may continue to sustain larger epidemics.

Differing conditions in areas with established interventions and more remote areas likely also explains divergent research findings reported in the literature. This is particularly apparent in studies that have attempted to assess the contribution of common curable STIs to development of HIV epidemics. Although one randomised controlled trial in Mwanza, Tanzania reported significant effect of STI interventions on HIV incidence, several others – in rural Uganda and Nairobi, Kenya – failed to confirm this finding. [19,28] Perhaps the most notable difference among the sites was the higher prevalence of STIs, particularly ulcerative chancroid, in Mwanza. In Nairobi, chancroid had already been eliminated while its prevalence was very low in the rural Ugandan districts. In all sites, differences between intervention and control groups, where a relatively high standard of care was offered to all participants, was likely sufficient to eliminate chancroid and reduce overall STI rates. Such trial results clearly cannot be generalised to more remote sites lacking any interventions at all.

Another important issue that receives little serious attention is that of 'bridge' populations – both the clients and regular partners of sex workers. For a number of reasons, common wisdom has been to focus intervention efforts on sex workers themselves, rather than spread them thinly in an attempt to reach large numbers of men who purchase sex, a group that is furthermore quite difficult to identify. In addition to being more numerous, clients tend to guard their anonymity and to be less receptive to interventions than sex workers. In addition, partner notification and treatment strategies, where attempted for STIs or HIV, generally fail with clients whom sex workers are unable or unwilling to identify. Regular sex partners, however, present a different situation. Recent research on the 'emotional' (regular) partners of sex workers raises questions about the importance of this group in sustaining transmission in and beyond sex work, and suggests room for carefully designed interventions. [29] These should be systematically evaluated and their contribution to control estimated and explored, including by adapting existing transmission models such as STDSIM.

11.3 Implications for policy and programmes including insights from modelling

The main findings of this thesis argue for greater policy and programme support for interventions with sex workers in order to improve control of HIV and other STIs. At policy level, this includes structural interventions to increase condom use in sex work and to reduce vulnerability among sex workers. Sex workers should be involved not only as beneficiaries but as active participants in policy change and programme improvement.

What specifically should be included in the programmatic response? First and foremost, condom programming – adequately supported by structural changes in sex work rather than only individual behavioural change interventions – has been shown to have the strongest effect on sexual transmission. Where rates of condom use reported by sex workers with last client surpass 80%, epidemics of HIV and several STIs appear to collapse (Chapter 3).

Second, STI treatment is important to reduce existing STI burden and prevent complications. It also serves to reduce HIV transmission efficiency during exposures when condoms are not used or fail. Our modelling (Chapter 10) suggests that at high rates of condom use, STI screening or presumptive treatment (at 60% coverage) have little additional effect on HIV outcomes. At lower rates of condom use, however, adding these STI interventions was estimated to be equivalent to increasing condom use by 15 percentage points.

Programmes should also strive to provide other services that sex workers need or value. Experience shows that the more services meet sex workers' perceived needs, the more likely they will be to utilise them and contribute actively to interventions. Commonly requested services include family planning and other sexual and reproductive health services, HIV counseling, testing, treatment and support, drug and alcohol treatment and interventions addressing violence. Our modelling explored the effect of ART provision together with basic condom and STI services and found them to be complementary. Experience from India (Chapter 8) demonstrates that services can be scaled up quickly following a common minimum programme then progressively extended to provide more comprehensive services and referrals. Balance is important, however. Narrowly conceived programmes with single interventions – to increase condom use, for example, or test sex workers for HIV – run the risk of alienating sex workers. Programmes should build trust by involving sex workers in decisions about how to provide services, especially those, like HIV testing, which may feel threatening.

Several programmatic considerations are critical to maximising the public health impact of interventions. Programmes should attempt to reach high coverage of the most active sex workers. Our modelling work estimates that most of the effect of interventions on HIV

transmission is achieved by reaching sex workers with the most clients (highest rates of partner change). Determinations about levels of risk are impractical and unethical to make on an individual basis, however. Any sex worker who asks for services should receive them. On the other hand, programmes must decide how to allocate resources, beginning with decisions about which areas to target with outreach and peer interventions. More effort should go into attaining high coverage in areas with overt, full-time, high-volume sex work, for example, than to identifying hidden part-time sex workers with few clients.

Mapping and population size estimates facilitate this kind of targeting, especially when carried out with the participation of sex workers themselves. Epidemiologic data can also help to identify areas where interventions are needed, or need strengthening. Interviewing male STI patients about where they might have acquired infection has been used in Thailand and elsewhere to locate areas of high transmission or weak programme implementation.

Strengthening STI surveillance is thus important for several reasons. First, even basic surveillance based on syndromic case reports should permit monitoring of trends and identification of areas with high risk of sexual transmission. Second, STI trends provide a tool for monitoring the effectiveness of the programme response.

11.4 Recommendations for modelling and related research

This thesis has drawn on insights from modelling and includes original work involving a stochastic model (STDSIM) and a previously published quantification of a generalised HIV epidemic in Kisumu, Kenya (Chapter 10). [22] This section includes observations about the limitations of current modelling and recommendations for future work, with specific attention to STDSIM.

Earlier models of sex work and STI transmission include limited data on clients and other male partners, limited ability to disaggregate client behaviour with respect to choosing sex workers (associative/dissociative mixing) and other partners, wide ranges for STI transmission probabilities and considerable uncertainty about the coverage, effectiveness and impact of existing STI interventions. In some cases, conservative assumptions about such parameters may have resulted in underestimation of the contribution of sex work to STI/HIV transmission.

With respect to STDSIM, quantifications of STI/HIV transmission would benefit from additional research and model adaptation in each of these areas. Some of these can be addressed by extending the model, others are hampered by lack of reliable data to inform parameter values.

Main recommendations for improving the quantification of sex work in STDSIM include:

1. Support research into client population size and behaviour, specifically the proportion of men at different ages and partner status who buy sex, how often, their tendencies to choose the same or different sex workers, and their likelihood of using condoms in different situations. Alternative methods to household surveys need to be found to reduce selection bias since the highest risk men are unlikely to be found at home.

2. Extend behavioural modules related to sex work to permit different types of mixing between sex workers, clients and regular partners. Consistency in being a client and in choosing the same or different sex workers are likely important factors in transmission. The model should be able to simulate both one-off and regular client contacts, informed by data and ideally disaggregated by age group and marital status.

3. Validate assumptions about STI biological parameters through review of recent literature, where available, and taking into account available STI surveillance data from specific countries.

4. Develop better estimations of STI treatment interventions, and validate, as in recommendation 3 with country data.

11.5 Main conclusions and directions for future research

We conclude that transmission of STIs, including HIV, is largely dependent on high-incidence upstream transmission in sexual networks with high rates of partner change, most commonly seen in sex work. The theoretical construct of core transmission is well founded in models of sexual transmission dynamics and supported globally by extensive empirical evidence. It should be seen as a fundamental principal behind the epidemiology and control of sexually transmitted infections rather than as a relative factor dependent on cultural factors, prevalence level or stage of specific sexually transmitted epidemic. Control efforts should ensure adequate coverage of sex work networks with proven and feasible interventions without diverting resources to less efficient efforts among the general population.

We further justify this main conclusion with the following responses to specific research questions, addressing the individual and public health benefits for sex workers themselves and for the general population.

1. The often high STI burden among female sex workers is reversible, and subsequently preventable, by reaching sex workers with appropriate interventions and services

2. Interventions which reduce STI prevalence among sex workers also reduce STIs among clients, and rapid country-level STI declines follow large-scale interventions in sex work

3. Rapidly expanding HIV epidemics have been halted and reversed by intervening effectively to reduce transmission in sex work. Appropriate targeting appears to be both necessary and sufficient to reduce HIV prevalence in the general population.

An extensive body of literature describes these targeted interventions, which, in the case of HIV, are highly complementary to broader programme efforts such as HIV testing and treatment (Chapters 2, 7, 8 and 10). While the latter are important to care for the pool of individuals already infected, the former serves to 'turn off the tap', averting new infections that otherwise continue to accumulate, weighing down treatment programmes and health systems. This potential complementarity is perhaps best illustrated by the experience of Thailand and Cambodia, which with declining numbers of new infections, have been able to reach high ART coverage and can consider the elimination of new HIV infections as a feasible strategy (Chapter 3).

Future research should address conditions and factors which facilitate or hinder the control of STIs in sex work settings. These include:

1. Intervention-linked research to strengthen targeted interventions in sex work

2. Improved STI surveillance with attention to genital ulcers as markers of high HIV transmission potential

3. Estimation of client population sizes and sex work seeking behaviour and better modelling behaviour of sex workers and clients, as detailed in section 11.4

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Summary

This thesis explores the role of sex work in STI and HIV transmission, important epidemiological interactions and implications for control of these interrelated epidemics. The main research question asks whether, as a general rule, scaling up basic condom and STI interventions with sex workers and their clients has substantial impact on HIV transmission? An important corollary is whether regional deviation from this approach – largely non-targeted interventions in generalised African epidemics – can be justified on epidemiological grounds.

We begin by exploring the feasibility of STI control interventions and potential benefits to sex workers themselves (first research question). We then explore effects of core group dynamics on transmission of common curable STIs and HIV – clients, for example, infect sex workers who can infect many other clients, and also act as a bridge to extend transmission to lower risk partners outside sex work. The underlying hypothesis explored in the second and third research questions relates to these dynamics – that (upstream) transmission in sex work networks determines to a large extent how much subsequent transmission occurs (downstream) among the population at large. To what degree such dynamics provide necessary and sufficient conditions for epidemic spread and maintenance is also considered, along with implications for control programmes.

Chapter 2 examines STI control from a policy perspective, describing a fractured paradigm where funding and strategy are largely dominated by attention to one disease. HIV, we argue, should be addressed within an STI control paradigm, not the other way around. Sexually transmitted infections differ from influenza or other infectious diseases where risk and transmission potential are distributed fairly uniformly across large populations. STI control thus requires effective interventions with much smaller 'core' populations whose rates of partner change are high enough to sustain transmission. A large body of empirical evidence, partially laid out in later chapters, suggests that effective, appropriate targeting is necessary and often sufficient to reduce prevalence in the general population. The crux of this proposition, central to this thesis, can be summarised as follows. STI control is a public health outcome measured by reduced incidence and prevalence. The means to achieve this, well supported in the literature, includes targeting and outreach to populations at greatest risk; promoting and providing condoms and other means of prevention; effective clinical interventions; an enabling environment; and reliable data.

Appropriate targeting, referring foremost to populations involved in sex work, is fundamental to a public health paradigm of STI control. As sex work is a universal and heterogeneous phenomenon, so the contribution of sex work to transmission of HIV and other sexually transmitted infections follows universal principles that play out in variable but predictable patterns, often requiring adaptation of interventions to local context. Adapting targeted interventions is one thing, however. Exceptional responses – where STI control fundamentals are disregarded and prevention resources are disseminated widely over large populations at variable risk – are quite another.

Chapter 3 describes an alternative to the fractured paradigm – a more balanced and effective response to HIV and other STIs in Asia – with focus on ten countries. The chapter begins by examining the explosive emergence of Asian HIV epidemics from urban pockets – Bangkok and Chiang Mai in Thailand, Mumbai and Pune in India – characterised by migration, unprotected sex work and high STI prevalence, and describes the role of targeted interventions in controlling them. The triad of unprotected sex work, male foreskin and chancroid is introduced here as creating ideal conditions for HIV transmission. Historically associated with development of large-scale HIV epidemics, we argue that such conditions may be necessary and sufficient to sustain high HIV prevalence in populations.

The Asian response typically follows an intact STI control paradigm with primary focus on core transmission in sex work. All ten countries report increasing condom use trends in sex work. In the seven countries where condom use exceeds 80%, surveillance and other data indicate declining HIV trends or low and stable HIV prevalence with declining STI trends. All four countries with national-level HIV declines among sex workers have also documented significant HIV declines in the general population. While all interventions in sex work included outreach, condom programming and STI services, the largest declines were found in countries that implemented structural interventions on a large scale. Rapid epidemic control creates other opportunities. Thailand and Cambodia, having controlled transmission early, are closest to providing universal access to HIV care, support and treatment and are exploring HIV elimination strategies.

Chapter 4 continues this argument and explores the potential effect of eliminating chancroid, an ulcerative STI strongly associated with both HIV acquisition and sex work. *Haemophilus ducreyi*, the causative organism of chancroid, is biologically vulnerable and occupies a precarious epidemiological niche. Both simple, topical hygiene and male circumcision greatly reduce risk of infection, and antibiotics provide rapid cure. *H. ducreyi* depends on sexual networks with high rates of partner change for its survival, thriving in environments characterised by male mobility

and intensive commercial sex activity. Elimination of *H. ducreyi* infection from vulnerable groups results in disappearance of chancroid from the larger community.

Eradication of chancroid is a feasible public health objective. Chancroid is in fact frequently dismissed as having already 'disappeared' based on limited data from a few research sites. As with other infectious diseases, however, verification of 'elimination' requires reliable surveillance data covering sites – especially underserved areas with favourable conditions for transmission – where the disease, and enhanced HIV transmission, are likely to persist. Protecting sex workers and their clients from exposure and improving curative STI services are among proven strategies that could be employed.

Chapters 5 and 6 present original intervention-linked research which focus on reducing the high burden of common curable STIs commonly found among sex workers. They address a major STI control challenge – that of detecting asymptomatic STIs among women in the absence of accurate and affordable screening tests. We evaluate the effect of one intervention component – periodic presumptive treatment (PPT) – implemented as a part of targeted condom and STI interventions in two quasi-experimental studies, demonstrating benefit to sex workers themselves (research question 1) and to clients and high-risk men (research question 2) in intervention areas. We conclude that provision of STI treatment services, including PPT, to core groups of women at high risk may significantly reduce their burden of disease, and may contribute to reduction in community STI prevalence.

Chapters 7 and 8 broaden the focus on approaches to asymptomatic STIs among female sex workers with two systematic reviews. Chapter 7 reviews studies of PPT efficacy/effectiveness. We estimate short-term prevalence reductions of more than fifty percent for gonorrhoea and chlamydia by meta-analysis of intervention studies, with some sites reporting declines exceeding eighty percent. Reductions of ulcerative STIs may be even greater, with elimination of chancroid reported from some sex work settings, progressive syphilis declines in others. We conclude that sustained STI reductions can be achieved when PPT is implemented together with peer interventions and condom promotion. Additional benefits may include impact on STI and HIV transmission at population level. Chapter 8 considers important operational issues including use of single-dose combination antibiotics for high-cure rates, conditions for introducing PPT, frequency and coverage, and use of PPT together with other intervention components to maximise and sustain STI control and reinforce HIV prevention. The main recommendation is that PPT be implemented together with other measures – designed to increase condom use, reduce risk, and vulnerability – in order to maintain low STI prevalence when PPT is phased out.

Chapter 9 is a feasibility paper that describes large scale implementation of STI control interventions including PPT in India. In two years, clinics with community outreach for sex workers were established in 274 settings in 77 districts. Mapping and size estimation identified 187 000 sex workers; 70% were contacted through peer outreach and 41% attended the clinic at least once. We conclude that targeted HIV/STI interventions can be brought to scale and standardised given adequate capacity building support. Intervention coverage, service utilisation, and quality are key parameters that should be monitored and progressively improved with active involvement of sex workers themselves.

In Chapter 10, We used a stochastic microsimulation model (STDSIM) to explore STI/HIV transmission dynamics in a generalised African HIV epidemic. We refined the quantification of sex work in Kisumu, Kenya, from the 4-cities study, introduced interventions with sex workers in 2000 and projected epidemics to 2020. We estimated the contribution of sex work to transmission, and modelled standard condom and STI interventions for three groups of sex workers at feasible rates of use and coverage. Removing transmission from sex work altogether would have resulted in 66% lower HIV incidence and 56% lower prevalence after 20 years. More feasible interventions reduced HIV prevalence by one-fifth to one-half. High rates of condom use in sex work had greatest effect, while STI treatment contributed to HIV declines at lower levels of condom use. Interventions reaching the 40% of sex workers with most clients reduced HIV transmission nearly as much as less targeted approaches attempting to reach all sex workers. We conclude that 'upstream' transmission in sex work remains important in advanced African HIV epidemics even in the context of ART. As in concentrated Asian epidemics, feasible condom and STI interventions reaching the most active sex workers can markedly reduce the size of HIV epidemics. Interventions targeting 'transactional' sex with fewer clients have less impact.

A final discussion chapter (Chapter 11) considers the findings in relation to the research questions. We show that the high STI burden among female sex workers is reversible, and subsequently preventable, by reaching sex workers with appropriate interventions and services (Q1). We further demonstrate that interventions which reduced STI prevalence among sex workers have similar effects on clients or men living in nearby communities, and present evidence from Asia of rapid country-level declines in STI incidence and prevalence after large-scale interventions in sex work were implemented (Q2). We show, as demonstrated most dramatically in Asia, that rapidly expanding HIV epidemics have been halted and reversed by intervening effectively to reduce transmission in sex work. We explored the question further by modelling a range of targeted interventions with sex workers in the context of a generalised African HIV epidemic. The large declines in HIV incidence and prevalence estimated in the

model were independent of ART roll-out and nearly entirely attributable to interventions with a minority of sex workers with the most clients. Even within interventions focusing on sex work, additional targeting based on rates of partner change – a 'dose-effect' within targeting itself – further strengthens the validity of core group theory.

We thus recommend that targeted interventions with sex workers be scaled up first and foremost in order to reduce the high burden of common curable STIs and avert serious morbidity and mortality among sex workers. Direct interventions should include peer-based outreach, condom programming and STI services which address both symptomatic and asymptomatic STIs, and should be supported by structural interventions to reduce vulnerability, enable condom use and facilitate participation and ownership by sex workers. Provision of more comprehensive services addressing sex workers' broader health and social needs is also important, and likely increases participation and engagement of sex workers in interventions.

We further recommend that interventions with sex workers be prioritised, not only for the direct benefits to sex workers themselves, but as an essential strategy for controlling STIs in the general population. In countries with low rates of male circumcision where ulcerative STIs are common, improved control of ulcerative STIs, including chancroid elimination, are feasible targets. In other countries where non-ulcerative STIs predominate, reductions of at least fifty percent in gonorrhoea and chlamydia prevalence appear to be feasible.

As with other STIs, control and reversal of HIV epidemics likely require effective interventions with core and bridge populations whose rates of partner change are high enough to sustain transmission. Appropriate targeting appears to be both necessary and sufficient to reduce HIV prevalence in the general population. We thus recommend that interventions with sex workers described above, particularly those with large numbers of clients, receive high priority, not only for STI control, but as fundamental components of HIV prevention, and regardless of stage of HIV epidemic.

Samenvatting

Dit proefschrift gaat in op de rol van prostitutie (of: sekswerk) bij de overdracht van seksueel overdraagbare infecties (STIs) en HIV, belangrijke interacties gezien vanuit een epidemiologische perspectief, en implicaties voor de bestrijding van onderling samenhangende epidemieën. De hoofdvraag was of het opschalen van interventies onder sekswerkers en hun klanten met betrekking tot condoomgebruik en STIs in het algemeen een substantiële impact heeft op HIV-overdracht. Een belangrijk uitvloeisel hiervan is de vraag of regionale afwijkingen van deze benadering – grotendeels selectieve interventies bij gegeneraliseerde Afrikaanse epidemieën – op grond van epidemiologische overwegingen terecht is.

Allereerst kijken we naar de haalbaarheid van interventies ter bestrijding van STIs en de mogelijke voordelen voor de sekswerkers zelf (eerste onderzoeksvraag). Vervolgens komt aan de orde in hoeverre kerngroepdnamiek invloed heeft op de overdracht of gewone, geneesbare STIs en HIV – klanten, bijvoorbeeld, infecteren sekswerkers die vervolgens vele andere klanten kunnen infecteren, en vormen ook een brug naar verspreiding onder partners met een lager risico buiten de wereld van betaalde seks. De onderliggende hypothese die wordt onderzocht in de tweede en derde onderzoeksvragen houdt verband met deze dynamiek – namelijk dat (upstream) overdracht in betaalde-seksnetwerken in hoge mate bepalend is voor de verdere overdracht (downstream) onder de algemene bevolking. We hebben ook onderzocht in welke mate deze dynamiek de voorwaarden schept waaronder een epidemie zich kan verspreiden en consolideren, evenals de implicaties voor bestrijdingsprogramma's.

Hoofdstuk 2 is gewijd aan de bestrijding van STIs vanuit beleidsperspectief en beschrijft een versplinterde aanpak (fractured paradigm) waarbij de strategie en de verstrekking van middelen grotendeels is afgestemd op één ziekte. Wij beargumenteren dat HIV zou moeten worden benaderd vanuit de aanpak voor de bestrijding van STIs en niet andersom. Het verschil tussen STIs en influenza of andere infectieziekten is dat bij de laatste het risicopotentieel en overdrachtspotentieel redelijk uniform zijn verdeeld over grote bevolkingsgroepen. Voor de bestrijding van STIs zijn derhalve effectieve interventies nodig onder veel kleinere kerngroepen waarbinnen de overdracht in stand wordt gehouden door het vele switchen tussen partners. Een grote hoeveelheid empirisch bewijs, dat gedeeltelijk wordt gepresenteerd in de volgende hoofdstukken, geeft ook aan dat een effectieve en doelgerichte benadering nodig is, en dat deze vaak voldoet om de prevalentie onder de algemene bevolking terug te brengen. De kern van

deze veronderstelling, die ten grondslag ligt aan dit proefschrift, kan als volgt worden samengevat. STI-bestrijding is een volksgezondheidsuitkomst in termen van lagere incidentie en prevalentie. De volgende middelen om dit te verwezenlijken zijn goed onderbouwd in de literatuur: streven naar het bereiken van bevolkingsgroepen met het hoogste risico; het promoten en beschikbaar stellen van condooms en andere preventiemiddelen; effectieve klinische interventies; een omgeving die ondersteunend werkt; en betrouwbare data.

Vanuit een maatschappelijk oogpunt is het bereiken van de groepen waar het om gaat essentieel bij STI-bestrijding, in dit geval de groepen sekswerkers. Aangezien sekswerk een universeel en heterogeen fenomeen is, verloopt de bijdrage van sekswerk aan de overdracht van HIV en andere STIs volgens universele principes die vervolgens uitmonden in variabele maar voorspelbare patronen die vaak aanpassing van interventies aan de lokale context vereisen. Het aanpassen van gerichte interventies is echter slechts één kant van de medaille. Er kan ook sprake zijn van uitzonderlijke – waarbij de principes van STI-bestrijding worden genegeerd en de beschikbare middelen voor preventie grotendeels worden aangewend voor grote bevolkingsgroepen met variabel risico.

Hoofdstuk 3 beschrijft een alternatief voor de versplinterde aanpak – een meer uitgebalanceerde en effectievere respons op HIV en andere STIs in Azië – met een focus op tien landen. Allereerst wordt ingegaan op de explosieve uitbraak van Aziatische HIV-epidemieën vanuit stedelijke gebieden – Bangkok en Chiang Mai in Thailand, Mumbai en Pune in India – gekenmerkt door veel migratie, onveilig sekswerk en een hoge prevalentie van STI, en de rol van gerichte interventies om deze in te dammen. Er wordt gesteld dat de triade van onveilig sekswerk, de voorhuid bij mannen en chancroïd (of: zachte sjanker) de ideale voorwaarden creëert voor de overdracht HIV. Gezien het feit dat deze historisch gezien verband lijken te houden met de uitbraak van grootschalige HIV epidemieën, stellen we dat dergelijke voorwaarden noodzakelijk en voldoende kunnen zijn voor het in stand houden van een hoge HIV-prevalentie onder groepen van de bevolking.

De Aziatische respons verloopt typisch volgens een intacte aanpak van de bestrijding van STIs met een grote nadruk op kernoverdracht bij sekswerk. Alle tien landen maken melding van een toegenomen trend in condoomgebruik in sekswerk. In de zeven landen waar het condoomgebruik boven de 80% is, wijzen surveillance en andere data op dalende HIV-trends of een lage en stabiele HIV-prevalentie met afnemende STI-trends. In alle vier landen waarin landelijk een afname van HIV onder sekswerkers is geconstateerd is ook een significante afname van HIV in de algemene bevolking gedocumenteerd. Terwijl alle interventies in sekswerk gebruik maakten van outreach, stimulering van condoomgebruik en STI-

gezondheidsdiensten, werden de grootste afnamen gevonden in die landen waar structurele interventies op grote schaal waren geïmplementeerd. Een snelle beheersing van epidemieën schept andere mogelijkheden. Thailand en Cambodia, waar de overdracht in een vroeg stadium tot staan werd gebracht, zijn het dichtst bij een situatie waarin men universeel toegang heeft tot HIV-zorg, ondersteuning en behandeling. In deze landen is men ook bezig met het verkennen van strategieën om HIV uit te roeien.

Hoofdstuk 4 gaat hier verder op in en onderzoekt wat het effect zou zijn van het uit de wereld helpen van chancroïd, een ulceratieve STI die sterk geassocieerd is met zowel het oplopen van HIV en sekswerk. Haemophilus ducreyi, het organisme dat chancroïd veroorzaakt, is biologisch kwetsbaar en bezet een precaire epidemiologische niche. Het risico op infectie wordt al heel veel kleiner door goede genitale hygiëne en besnijding van de voorhuid, en met antibiotica geneest men snel. H. ducreyi kan alleen overleven in seksuele netwerken waain men vaak van partner ruilt, en bloeit in een omgeving met hoge mobiliteit van mannen en intensieve commerciële seksuele activiteiten. Wanneer H. ducreyi infectie niet langer voorkomt onder kwetsbare groepen verdwijnt ook chancroïd uit de grotere gemeenschap.

De uitroeiing van chancroïd is haalbaar. In feite wordt vaak aangenomen dat het al is 'verdwenen', op basis van beperkte data van een paar onderzoekslocaties. Net als bij andere infectieziekten dient dit echter geverifieerd te worden aan de hand van betrouwbare surveillancedata van locaties waar de ziekte, en toegenomen HIV overdracht, kans maakt te blijven bestaan – vooral gebieden waar weinig aandacht aan wordt besteed en met gunstige condities voor overdracht. Het beschermen van sekswerkers en hun klanten tegen blootstelling en het verbeteren van STI-gezondheidsdiensten gericht op genezing zijn enkele van de bewezen strategieën die zouden kunnen worden toegepast.

Hoofdstukken 5 en 6 presenteren origineel onderzoek naar interventies met een focus op het terugdringen van gewone, geneesbare STIs die gebruikelijk voorkomen onder sekswerkers. Het gaat hier om een grote uitdaging bij de bestrijding van STIs – dat wil zeggen het opsporen van asymptomatische STIs onder vrouwen terwijl er geen accurate en betaalbare screeningtests beschikbaar zijn. We evalueren het effect van een van de componenten van de interventie – periodic presumptive treatment (PPT) – die was geïmplementeerd als onderdeel van gerichte interventies betreffende condoomgebruik en STIs in twee quasi-experimentele studies, en tonen aan dat dit gunstig uitwerkt voor de sekswerkers zelf (onderzoeksvraag 1) evenals hun klanten en mannen met een hoog risico (onderzoeksvraag 2) in de interventiegebieden. We concluderen dat het aanbieden van behandeling van STIs, met inbegrip van PPT, aan kerngroepen van

vrouwen met een hoger risico hun ziektelast significant kan verminderen, en kan bijdragen tot een afname van de STI-prevalentie in de grotere gemeenschap.

Hoofdstukken 7 en 8 verbreden de focus op de benadering van asymptomatische STIs onder vrouwelijke sekswerkers met twee systematische reviews. Hoofdstuk 7 presenteert een review van artikelen over de doelmatigheid/effectiviteit van PPT. In een meta-analysis van interventiestudies komen we uit op een geschatte reductie in de korte-termijn prevalentie van meer dan vijftig procent voor gonorroe en chlamydia, terwijl in sommige locaties een afname van meer dan tachtig procent wordt gezien. De afname in ulceratieve STIs kan zelfs groter zijn, gezien het feit dat eliminatie van chancroïd uit verschillende sekswerk-settings wordt gemeld, en een toenemende afname van syfilis in andere settings. We concluderen dat afname in STIs kan worden doorgezet als PPT wordt geïmplementeerd samen met interventies waarin lotgenoten worden betrokken en promotie van condoomgebruik. Onder de bijkomende voordelen is te noemen een impact op de overdracht van STIs en HIV op bevolkingsniveau. Hoofdstuk 8 besteedt aandacht aan belangrijke operationele zaken zoals het gebruik van single-dose combinaties van antibiotica, waarmee een hoge genezingsgraad kan worden bereikt, randvoorwaarden voor de introductie van PPT, frequentie en dekking, en toepassing van PPT samen met andere interventiecomponenten om de STI-bestrijding te maximaliseren en consolideren en de HIV-preventie te versterken. De belangrijkste aanbeveling is om PPT te implementeren samen met andere maatregelen – gericht op meer condoomgebruik en minder risico en geringere kwetsbaarheid – waardoor de STI-prevalentie lag kan blijven wanneer PPT wordt afgebouwd.

Hoofdstuk 9 betreft een artikel over haalbaarheidsaspecten dat aandacht besteedt aan de grootschalige implementatie in India van interventies ter bestrijding van STIs, met inbegrip van PPT. Binnen het tijdsbestek van twee jaar werden klinieken met community outreach voor sekswerkers opgericht in 274 settings in 77 districten. Met behulp van mapping en size estimation werden 187.000 sekswerkers geïdentificeerd; 70% werd bereikt via lotgenoten en 41% bezocht de kliniek minstens één keer. We concluderen dat schaalvergroting en standaardisatie van gerichte HIV/STI-interventies mogelijk is mits er voldoende bouwcapaciteit is. De volgende cruciale parameters zouden moeten worden gemonitord en zelfs verbeterd met actieve inbreng van de sekswerkers zelf: dekking van de interventie, gebruikmaking van gezondheidsdiensten, en kwaliteit van de zorg.

In Hoofdstuk 10 hebben we een stochastisch microsimulatiemodel (STDSIM) toegepast om de dynamiek van de overdracht van STI/HIV te onderzoeken in een gegeneraliseerde Afrikaanse HIV-epidemie. We verfijnden de kwantificatie van sekswerk in Kisumu, Kenya, op basis van de

4-steden studie, introduceerden interventies met sekswerkers in 2000 en projecteerden epidemieën tot 2020. We hebben geschat in hoeverre sekswerk bijdraagt aan de overdracht, en hebben standaard interventies voor condoomgebruik en STI gemodelleerd voor drie groepen sekswerkers met haalbare gebruiks- en dekkingsgraden. Wanneer er geen sprake zou zijn geweest van overdracht via sekswerk in zijn geheel zou dit hebben geresulteerd in een 66% lagere HIV-incidentie en een 56% lagere prevalentie na 20 jaar. Beter haalbare interventies reduceerden de HIV prevalentie met een vijfde tot een half. Een hoge mate van condoomgebruik in sekswerk gaf het grootste effect, terwijl STI-behandeling bijdroeg tot een afname van HIV-infectie bij lagere percentages van condoomgebruik. Interventies die de 40% sekswerkers met de meeste klanten bereikten reduceerden de HIV-overdracht bijna net zo veel als benaderingen waarmee werd geprobeerd alle sekswerkers te bereiken. We concluderen dat 'upstream' overdracht in sekswerk een belangrijke rol blijft vervullen in progressieve Afrikaanse HIV-epidemieën, zelfs in de context van ART. Net zoals bij de geconcentreerde Aziatische epidemieën, kunnen haalbare interventies met betrekking tot condoomgebruik en STIs die de actiefste sekswerkers bereiken de omvang van HIV-epidemieën aanzienlijk verminderen. Interventies gericht op 'transactional' seks met minder klanten hebben minder impact.

Het afsluitende discussiehoofdstuk (Hoofdstuk 11) relateert de bevindingen aan de onderzoeksvragen. We laten zien dat het veel optreden van STIs onder vrouwelijk sekswerkers omkeerbaar is, en vervolgens te voorkomen, door sekswerkers gerichte interventies en diensten te bieden (onderzoeksvraag 1). We laten ook zien dat interventies die leidden tot een lagere prevalentie van STIs onder sekswerkers dezelfde effecten hebben op hun klanten of mannen die in nabijgelegen buurten, en presenteren bewijs uit Azië dat nadat grootschalige interventies in sekswerk waren geïmplementeerd de incidentie en prevalentie van STIs landelijk snel afnamen (onderzoeksvraag 2). We laten zien, zoals het duidelijkst is aangetoond in Azië, dat zich snel uitbreidende HIV-epidemieën tot staan zijn gebracht en zelfs omgekeerd met behulp van effectieve interventies gericht op het terugdringen van transmissie via sekswerkers. De vraag werd verder onderzocht door middel van het modelleren van een scala aan gerichte interventies met sekswerkers in de context van een gegeneraliseerde Afrikaanse HIV-epidemie. De grote afnamen in de incidentie en prevalentie van HIV die het model aangaf waren onafhankelijk van de ART roll-out en vrijwel volledig toe te schrijven aan interventies waarbij een kleine groep van sekswerkers met de meeste klanten waren betrokken. Zelfs binnen interventies met een focus op sekswerk wordt de validiteit van de kerngroeptheorie nog verder vergroot door middel van aanvullende targeting gebaseerd op de mate waarin van partner wordt gewisseld – een 'dose-effect' binnen de targeting zelf.

In de eerste plaats bevelen we daarom aan om de gerichte interventies met sekswerkers op te schalen, waardoor onder sekswerkers het veelvuldig optreden van gewone geneesbare STIs kan worden verminderd en zowel ernstige morbiditeit als mortaliteit kan worden voorkomen. Directe interventies zouden moeten gebruikmaken van de inzet van lotgenoten, campagnes ter stimulering van condoomgebruik en STI-gezondheidsdiensten die zich richten op zowel symptomatische als asymptomatische STIs. Deze directe interventies dienen te worden ondersteund door structurele interventies gericht op een lagere kwetsbaarheid, toegang tot condoomgebruik en het faciliteren van participatie en eigen bezit van sekswerkers. De beschikbaarheid van meer uitgebreide diensten gericht op de bredere gezondheids- en sociale behoeften van sekswerkers is ook belangrijk, en vergroot waarschijnlijk de participatie en betrokkenheid van sekswerkers bij interventies.

We bevelen verder aan om prioriteit te geven aan interventies gericht op sekswerkers, niet alleen voor hun eigen directe belang, maar ook als een cruciale strategie om STIs onder de algemene bevolking te bestrijden. In landen met een lage graad van besnijden van mannen waar ulceratieve STIs veel voorkomen zijn een betere bestrijding van ulceratieve STIs, met inbegrip van de uitroeiing van chancroïd, haalbare doelen. In andere landen waar niet-ulceratieve STIs meer voorkomen blijkt het mogelijk te zijn de prevalentie van zowel gonorroe als chlamydia minstens te halveren.

Net als bij andere STIs, zijn voor de bestrijding en het terugdringen van HIV-epidemieën waarschijnlijk effectieve interventies nodig met betrokkenheid van kern- en bruggroepen in de bevolking waarin men zo vaak van partner wisselt dat de overdracht in stand wordt gehouden. Juist toegepaste targeting blijkt zowel noodzakelijk en voldoende te zijn om de HIV-prevalentie in de algemene bevolking terug te dringen. Onze aanbeveling is daarom dat interventies gericht op sekswerkers zoals bovenstaand beschreven, vooral diegenen die veel klanten ontvangen, hoge prioriteit krijgen, niet alleen met het oog op de bestrijding van STIs, maar als essentiële componenten van HIV-preventie, en onafhankelijk van het stadium van een HIV-epidemie.

Curriculum Vitae

Richard Steen was born in New York City in 1952. He became interested in medicine, public health and social equality as a medic at the Berkeley Free Clinic in the early 1970s. He completed a degree in Medicine at the State University of New York at Stony Brook in 1979 and a Masters in Public Health at the University of California at Berkeley in 1983.

Richard has worked as a public health clinician and researcher in designing, implementing and evaluating interventions and operations research in areas of STI control and HIV prevention since 1989. This includes capacity building and support to scale up targeted interventions for high-risk populations in countries such as South Africa, Madagascar, the Philippines, India and Indonesia. He has developed guidelines for the World Health Organisation including Sexually Transmitted and other Reproductive Tract Infections: a Guide for Essential Practice, the HIV/AIDS and Sex Work Toolkit and the South-East Asia Regional Strategy for Prevention and Control of STIs. Publications include scientific articles and reviews on STI control, targeted interventions, periodic presumptive STI treatment and related topics.

Since 2003, Richard has worked for WHO at its global headquarters in Geneva, regional office for South-East Asia in New Delhi and country office for the Palestinian Occupied Territories in East Jerusalem. Current work focuses on guideline development, implementation support and modelling related to targeted STI control. Affiliations include Erasmus MC, the University of the Witwatersrand, Johannesburg, South Africa, and the community-based sex worker collectives Durbar Mahila Samanwaya Committee (DMSC Sonagachi), Kolkata, India and Ashodaya Samithi, Mysore, India.

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Portfolio

ERASMUS UNIVERSITEIT ROTTERDAM

Name PhD student: **Richard Steen**		PhD period: **2010-2014**	
Erasmus MC department: **Public Health**		Promoter: **Prof. dr. JH Richardus** Copromotor: **Dr. SJ de Vlas**	

Technical assistance to countries (WHO)		**Year**	**Duration**
Cambodia	Participated as lead writer in external review of National AIDS response	2013	5 weeks
Indonesia	Technical assistance on targeted interventions and STI surveillance	2013	3 weeks
Argentina	Technical assistance on strengthening routine STI reporting	2012	1 week
Uruguay	Technical assistance on strengthening routine STI reporting	2012	1 week
Palestine	Technical advisor for HIV and TB	2011	20 weeks
Mongolia	Technical assistance on strengthening STI reporting	2010	1 week

Normative guidance development			
WHO	Consultation on global estimates of curable sexually transmitted infections	2013	1 week
WHO	Development of road map for strengthening routine STI reporting	2013	10 weeks
WHO	Proposal development for modelling global burden of STIs and their complications	2013	2 weeks
WHO	Review of evidence base to support development of guidelines on sex work and HIV	2011-2012	20 weeks

WHO Western Pacific Region	Review of country data on targeted interventions with sex workers and development of operational guidance on implementation	2011-2012	20 weeks
WHO Eastern Mediterranean Region	Review of country data on targeted interventions with sex workers and men who have sex with men	2011	5 weeks

Presentations

Cambodia	High and overlapping risk and vulnerability: sharper epidemiologic targeting to reach those most likely to acquire and transmit infection	2013	10 hours
Geneva	STI surveillance: strengthening routine reporting	2013	10 hours
Indonesia	Making lokalisasi safer: Preliminary findings from review of interventions in 5 locations	2013	10 hours
Panama	La vigilancia de las ITS	2012	10 hours
Mongolia	STI reporting	2010	10 hours
Abidjan	La modelisation de l'impact des interventions ciblées	2010	10 hours

Article reviews

Lancet		2014	4 hours
STI		2014	4 hours
BMJ P Health		2013	4 hours
Sexual Health		2013	4 hours
STI		2011	4 hours