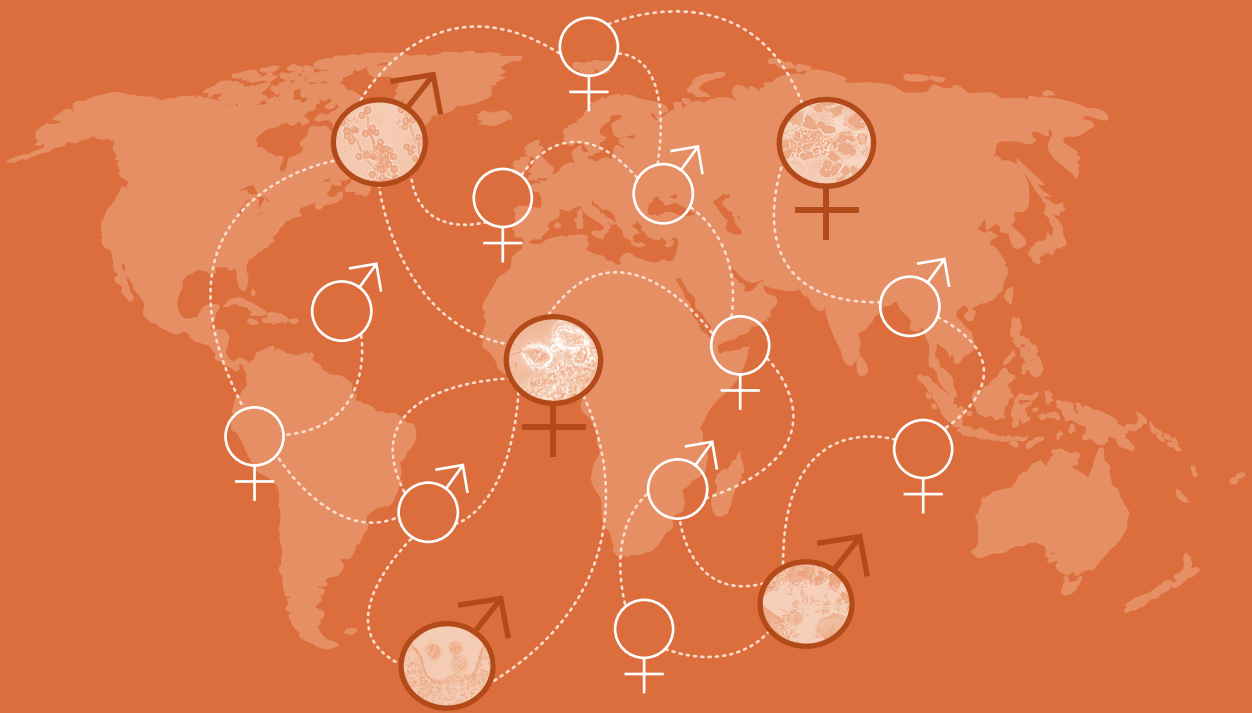
PERIODIC PRESUMPTIVE TREATMENT FOR SEXUALLY TRANSMITTED INFECTIONS

EXPERIENCE FROM THE FIELD AND RECOMMENDATIONS FOR RESEARCH



World Health Organization

London School of Hygiene & Tropical Medicine

Population Council

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ABBREVIATIONS

AIDS	acquired immunodeficiency syndrome
HIV	human immunodeficiency virus
HSV-2	herpes simplex virus type 2 (genital herpes)
PCR	polymerase chain reaction
PPT	periodic presumptive treatment
STI	sexually transmitted infection
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
WHO	World Health Organization

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The WHO Department of Reproductive Health and Research including the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), helps people to lead healthy sexual and reproductive lives. The Department endeavours to strengthen the capacity of countries to enable people to promote and protect their own sexual and reproductive health and that of their partners, and to have access to, and receive, high-quality sexual and reproductive health services when needed. HRP is the main instrument within the United Nations system for research in human reproduction, bringing together health-care providers, policy-makers, scientists, clinicians and consumer and community representatives to identify and address priorities for research aimed at improving sexual and reproductive health.

The Clinical Research Unit, LSHTM, is a WHO Collaborating Centre for Prevention and Control of Sexually Transmitted Infections. The LSHTM is Britain's national school of public health and a leading postgraduate institution in Europe for public health and tropical medicine. It is one of the highest-rated research institutions in the United Kingdom of Great Britain and Northern Ireland with a focus on the health of populations as a framework for its research and training. The Population Council is an international, nonprofit, non-governmental organization that conducts biomedical, social science, and public health research on global issues, including sexual and reproductive health, HIV and AIDS, and population trends. Headquartered in New York City (NY, USA), the Population Council has 19 offices in Africa, Asia, and Latin America and works in 60 countries.

We are grateful to the researchers who shared their experiences from various regions of the world. The technical consultation was also enriched by the attendance of non-health-care community members who had participated in some of the field studies conducted in Africa and Asia.

EXECUTIVE SUMMARY

In any society, sexually transmitted infection (STI) rates are highest among those with frequent change of sexual partner, particularly when they have poor access to health care. For this reason, STI control efforts – while endeavouring to provide basic prevention and treatment services for the general population – must also ensure that they reach sex workers and their clients with effective interventions. Control of transmission in commercial sex networks reduces secondary transmission, and has been shown to have impact at broader population levels.

Successful efforts to achieve STI control among sex workers and their clients range from direct clinical interventions to structural interventions that reduce vulnerability (empowerment models) and increase condom use (100% condom-use policies). Clinical interventions based on syndromic management of STIs work well for sex workers with symptoms but miss the majority of STIs which are asymptomatic. Regular screening visits can help identify asymptomatic infections if sensitive laboratory tests are available, but this is uncommon in low-resource settings.

Another approach to dealing with asymptomatic STIs within these population groups involves providing antibiotic treatment for relevant bacterial STIs on a presumptive basis, either on a one-time basis or repeatedly at predetermined intervals. This is known as one-time or periodic presumptive treatment. Interventions for STIs using this method have been carried out – mainly among sex workers – in many parts of the world. Although individual programmes have been evaluated, there has not been any systematic global appraisal.

To remedy this, an international technical consultation was held in London, the United Kingdom, in September 2005. The objectives of this consultation were to:

- review experience with periodic presumptive treatment for STIs in developing countries;
- identify the conditions under which periodic presumptive treatment might be an effective element of an STI control and human immunodeficiency virus (HIV) prevention strategy;
- produce guidelines on the use of periodic presumptive treatment for STIs; and
- make recommendations for further research in this field.

Presumptive treatment is defined as one-time treatment for a presumed infection in a person, or a group of people, at high risk of infection. Presumptive treatment for STIs is often given at repeated intervals, in which case it is known as *periodic presumptive treatment*. Other STI treatment strategies include *syndromic case management*, which treats pathogens known to cause signs and symptoms with which a person presents, and *laboratory-based diagnosis and treatment*.

These approaches are in fact complementary. While syndromic case management depends on signs and symptoms, presumptive treatment addresses the more problematic asymptomatic infections as well as symptomatic infections in persons presumed to be at high risk and with high probability of infection.

This publication describes some experiences using *one-time presumptive treatment* for STIs among sex workers. In the three cases from Cambodia, Madagascar, and the Philippines, presumptive treatment was offered within established STI care services, although one-time presumptive treatment has also on occasion been delivered outside of routine STI services. In some of the cases considered, rapid reductions in prevalence of gonococcal and chlamydial infections were found following the presumptive treatment. Longer-term benefits were often difficult to distinguish from the benefits provided by the other components of the STI care package.

However, most of the descriptions of cases in this publication involve *periodic presumptive treatment* among sex workers within the context of existing STI services. A programme administering periodic presumptive treatment to female sex workers based within geographically self-contained mining communities in South Africa, for instance, found that prevalences of gonococcal and chlamydial infections declined in the women following the intervention. Among the miners in

the area, both the rates of genital ulcer disease and urethral discharge fell sharply. Chancroid, which had been the leading genital ulcer among both miners and sex workers at the beginning of the programme, was effectively eliminated.

Randomized controlled trials among sex workers in Benin, Ghana, and Kenya are also described. The Kenyan trial sought to find whether periodic presumptive treatment might lead to a reduction in the incidence of HIV infection. No effect was found, possibly because the area (Nairobi) had been the focus of STI control efforts for many years and already had relatively low STI rates – particularly genital ulcer disease prevalence and HIV incidence. There was, however, an association between new cases of HIV and some STIs – in particular, pre-existing genital herpes. The Benin-Ghana trial showed no significant impact of periodic presumptive treatment for decreasing gonococcal and chlamydial prevalence and HIV incidence in female sex workers overall, but suggested (although the reasons remain unclear) that periodic presumptive treatment may be more beneficial for HIV-seronegative sex workers than for those who are HIV-seropositive.

A community-based programme in India is also described. This programme combines intensive community-mobilization work with services including syndromic case management, regular health checks, and periodic presumptive treatment. It uses an integrated approach to sexual and reproductive health, emphasizing the importance of peer education and the active involvement in the programme of the sex workers themselves. Based on the available (although limited) data, the provision of periodic presumptive treatment within a comprehensive package of services appears (in some settings) to be effective for reducing gonococcal and chlamydial infections.

The case of the Lao People's Democratic Republic is also included in the publication. In this case, periodic presumptive treatment was provided – in the absence of regular STI services – for sex workers in three provinces. Rates of gonococcal and chlamydial infections fell significantly during the intervention. The findings suggested that there is a good rationale for administering periodic presumptive treatment (as was done in this case) in situations where the prevalence of STIs is high and where STI services are lacking – *provided* there is a credible commitment to introduce and maintain such services. The presumptive treatment offered would then be of a transitional nature.

In its guidelines, the publication stresses that presumptive treatment should not be seen as a magic bullet, and cautions against promoting it as a stand-alone method isolated from other prevention and care interventions. Overall (and based on accumulated experience), however, periodic presumptive treatment can be considered as a component of STI services for sex workers. This component should be included within a package of services, including syndromic case management, regular screening for syphilis, and the promotion of condom use. One-time presumptive treatment may be suitable for an emerging outbreak of STIs in a particular area.

Sexually transmitted pathogens to be included in a periodic presumptive treatment intervention should include *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Treponema pallidum*, where these are prevalent. Periodic presumptive treatment should be considered particularly in areas of high chancroid prevalence. Presumptive treatment for trichomoniasis can also be added, although evidence-based knowledge on its effectiveness is weaker and this treatment would increase the number of medications and likely incidence of side-effects.

While there is a reasonable quantity of evidence for the effectiveness of periodic presumptive treatment among female sex workers, other core groups have not been researched. The publication recommends that studies be carried out on the effectiveness of the strategy, under varying conditions, e.g. among male sex workers, among men who have sex with men, among regular clients of sex workers, and among other men at high risk of STIs. Other recommendations for research focus on the effect of presumptive treatment on other pathogens, such as *Trichomonas vaginalis*. As a viral infection, genital herpes is not curable by

antibiotics, but mention is made of ongoing studies to see whether suppressing genital herpes with antiviral drugs can help control the spread of HIV. Regarding this impact on HIV, more research is needed (including research through modelling), on the effect of periodic presumptive treatment on HIV acquisition and transmission.

Concern was expressed about the development of resistant strains – particularly of *Neisseria gonorrhoeae* and *Treponema pallidum* – especially when drugs are used as monotherapy in periodic presumptive treatment. The possibility of developing resistance requires careful monitoring. There should also be monitoring of resistance to common STI drugs, such as azithromycin, in pathogens other than those causing STIs. Combination therapy using single-dose regimens (azithromycin plus cefixime, for example) is recommended to minimize the development of resistance. Such regimens can be administered under supervision (directly observed treatment) to minimize the problem of non-compliance which is a contributor to rapid development of resistant strains of organisms.

It was also proposed that mathematical modelling be undertaken, to ascertain the optimum prevalence threshold for commencing periodic presumptive treatment, and that the results be validated by field research. Modelling should also be conducted to assess the optimum periodicity of periodic presumptive treatment, as well as to determine at what point such treatment might be stopped and to find the minimum level of coverage needed to achieve success.

In summary, periodic presumptive treatment should be considered – as an interim measure – as a component of STI prevention and control programmes for appropriate populations, such as sex workers with poor or inadequate access to health-care services and at high risk of STIs. This approach should be combined with concurrent plans to establish good services, including outreach services. Once adequate services are established and/or infections are controlled to lower prevalence levels, periodic presumptive treatment interventions should be discontinued.

1. INTRODUCTION

There is substantial evidence that the presence of the classic sexually transmitted infections (STIs) facilitates transmission of the human immunodeficiency virus (HIV). The treatment and control of these STIs has thus become a component of HIV prevention and is considered to be a cost-effective one.

Certain population subgroups are at increased risk of repeatedly acquiring and transmitting STIs, often related to occupational (sex work) and other identifiable factors (migration, displacement, or mobility). Therefore, interventions which reduce the prevalence of STIs in such populations – and, in so doing, decrease their risk of becoming infected with or transmitting HIV – need to be devised and evaluated. Strategies that have proven successful include targeted condom policies (100% condom use), peer education and empowerment, and several direct STI control interventions. The latter include regular screening services for sex workers or other high-risk populations where adequate laboratory facilities exist. Where this is not possible, an alternative is to provide immediate treatment for STIs on a presumptive basis, and to repeat the treatment at regular predetermined intervals. This approach is known as periodic presumptive treatment.

Interventions using periodic presumptive treatment have been carried out – predominantly among sex workers – in many parts of the world. Several of these have been evaluated. However, until now no systematic global appraisal of all the programmes had been carried out to obtain a better understanding of the potential role of periodic presumptive treatment in controlling STIs and preventing HIV transmission.

To achieve this goal, a consultation organized by the World Health Organization (WHO) Department of Reproductive Health and Research, the Clinical Research Unit, London School of Hygiene and Tropical Medicine, and the Population Council was convened in London from 29 to 30 September 2005. This technical consultation considered the important lessons already learnt from interventions in which significant STI outcomes had been measured and those which had shown minimal change following the use of periodic presumptive treatment strategies. Participants examined the impact of periodic presumptive treatment – under a range of conditions – upon the prevalence of specific STIs and on HIV transmission, and considered such factors as STI epidemiology, risk context, and mix and periodicity of interventions.

The technical consultation was attended by programme managers, researchers in STI control, and representatives from partner agencies with experience of STI programmes and research at country level. Also present were modelling experts, health economists and non-health-care members of the community with whose cooperation interventions using periodic presumptive treatment had been carried out.

This publication summarizes the deliberations of the technical consultation, which covered current knowledge on periodic presumptive treatment and experiences to date with interventions, including the conditions that seem to be the most favourable for such interventions to work well. Further research is clearly needed in this field – including research employing possible modelling with current field data. Recommendations for research, as well as guidelines for those carrying out programmes with periodic presumptive treatment, were formulated and are presented in the final section of this publication.

2. OBJECTIVES

The objectives of the consultation were to:

- review global experiences with presumptive treatment (including periodic presumptive treatment) for sexually transmitted infections among populations considered at high risk of infection in developing countries;
- identify conditions under which periodic presumptive treatment might be an effective component of strategies for STI control, including the prevention of HIV infection;
- produce guidelines for periodic presumptive treatment as a component of STI control interventions; and
- advise on further research issues and considerations for modelling in this field.

3. PARTICIPANTS AND METHODOLOGY

Thirty-eight participants attended the two-day workshop (see Annex 2). Their areas of expertise included epidemiology, surveillance, behavioural science, clinical medicine, health economics, mathematical modelling, and STI and HIV/AIDS programme development and implementation in developing countries. All had had experience with interventions involving presumptive treatment as a component, and nearly all the known presumptive treatment projects were represented. Two non-health-care community representatives also attended the workshop. Nine of the participants were based in the WHO African Region, a further nine in the WHO South-East Asia Region, thirteen in the WHO European Region, six in the WHO Region of the Americas, and one in the WHO Western Pacific Region.

On the first day of the workshop, participants presented research studies and programmes involving presumptive treatment in developing countries. Plenary discussions followed each presentation.

On the second day, group discussions focused on the objectives listed in Section 2 above. One group considered policies and principles for presumptive treatment of STIs, a second group looked at programmatic and operational issues, and a third group examined research issues and modelling. Further plenary discussion on the reports of these three groups resulted in the formulation of recommendations and guidelines.

4. WHAT IS PERIODIC PRESUMPTIVE TREATMENT?

4.1 Definitions

Presumptive treatment is a one-time treatment given for a presumed infection in a person, or group of people, at high risk of infection. Presumptive treatment is often given at regular intervals, in which case it is known as *periodic presumptive treatment* (PPT).

The *syndromic approach*, on the other hand, is based on the presence of consistent groups of symptoms and easily recognized signs caused by a single pathogen or a mixture of pathogens. Syndromic case management of STIs treats for those pathogens shown to be the consistent causes of the signs and symptoms with which a person presents.

4.2 A continuum of approaches

Syndromic case management of STIs, by definition, treats symptomatic STI cases, and the treatment covers the organisms commonly responsible for each syndrome. By contrast, presumptive treatment is a form of asymptomatic treatment and addresses one of the main problems of STI control: STIs frequently manifest no symptoms. The two approaches would thus appear to be largely complementary; in practice, however, there is often an overlap.

In many settings, syndromic case management incorporates a lower threshold for treatment and may include some form of risk-based assessment to identify and treat additional infections that may not be causing the presenting symptom (such as cervical infections under certain circumstances when a woman presents with vaginal discharge). Such risk-based assessment may be based, for example, on locally validated risk factors for STIs or, for sex workers, if the last sexual intercourse was not protected.

For example, an STI clinic for sex workers may routinely treat presumptively those who have not attended for a check-up for at least six months (whether or not they have symptoms), or who report having had more than a given number of sexual partners in the previous week, or who admit to having not used condoms with non-regular partners in the recent past. The lower the threshold for a decision to treat, the closer to presumptive treatment such management becomes. There is, therefore, a continuum of treatment approaches – from "pure" syndromic case management to presumptive treatment.

Presumptive treatment has sometimes been adopted among groups or individuals especially prone to a particular infection or set of infections, and where screening with sensitive laboratory tests is difficult, expensive, not cost-effective, or impractical. In the absence of symptoms, clinical signs, or laboratory results, presumptive treatment is based on high prevalence and repeated risk of exposure.

The exact composition of a group being presumptively treated periodically – for instance, female sex workers in a particular town – may change over time, as individuals enter or leave the group. Some members of the group, therefore, may receive only occasional or irregular treatment. However, the public health objective is to identify newcomers through outreach efforts, thus ensuring high levels of coverage and uptake, and maximizing population-level impact.

5. SEX WORKER POPULATIONS

Sex worker populations in many settings often have high rates of STIs, many of which are easily curable. This is especially true in settings where rates of consistent condom use in sex work are low. For this reason, presumptive treatment has been included among STI interventions for sex worker populations in recent years. Since clients and regular non-client partners of sex workers also frequently have high rates of STIs (including HIV infection) and therefore act as a bridge for transmission to the general population, the use of presumptive treatment to control STIs may have potential benefits for both individuals and the public.[1] The experience of using presumptive (and especially periodic presumptive) treatment for STIs among sex workers was the main focus of the technical consultation.

6. EXPERIENCES OF ONE-TIME PRESUMPTIVE TREATMENT FOR STIs AMONG CORE GROUPS

Angeles City, Philippines

A single round of presumptive treatment with the broad-spectrum antibiotic, azithromycin, was given to all sex workers who could be reached during one month.[2] At the same time, preventive and curative STI services were strengthened – as were outreach efforts and peer education. Cross-sectional measurements of the prevalences of gonococcal and chlamydial infections were conducted before the intervention, after one month, and after six months. The measurements were stratified according to the type of sex work – brothel-based, street-based, and registered (bar-based) sex workers, as well as so-called 'guest relations officers'.

After one month, the prevalence of gonococcal and chlamydial infections had declined by 47% among brothel-based sex workers, 39% among street sex workers, 28% among registered sex workers and 70% among the 'guest relations officers'. Six months after the intervention, prevalence remained lower than baseline among brothel-based sex workers and street-based sex workers – the two groups for whom existing screening services were successfully strengthened – but had returned to baseline levels for the other groups. Gonococcal and chlamydial prevalences were also measured among a sample of clients of brothel-based sex workers in whom rates at follow-up were found to be 46% lower compared to baseline.

The greatest benefit was seen for brothel-based and street-based sex workers who had the highest prevalence before the intervention. Higher rates of coverage were possible among brothel-based sex workers who were less mobile than other types. The rapid turnover of sex workers required continuous outreach to promote services.

The Angeles City experience suggests that:

- one-time presumptive treatment can help reduce STI prevalence for rapid but short-term control;
- ongoing STI services – including outreach, condom promotion, and clinical check-ups – are important for sustaining STI reductions; and
- interventions that effectively reduce STI prevalence among sex workers can have broader public health effects, extending at least to their clients.

Antananarivo and Tamamave, Madagascar

Curable STIs are common among sex workers in Madagascar where most of the sex work is street-based and mobile.[3] The study sought to identify effective STI management strategies for sex workers and improve basic STI services in partnership with the sex workers. Presumptive treatment – consisting of 1 gram of azithromycin and 500 milligrams of ciprofloxacin – was administered. The combined prevalence of gonococcal and chlamydial infections

was observed to fall (by 27% – from 30% at baseline to 22% two months after treatment). The rate of trichomoniasis declined (by 28% – from 53% to 38%) over the same period, and the rate of syphilis also fell (by 59% – from 29% to 12%).

From the point of view of the health-care system, presumptive treatment (compared to a risk-assessment-based treatment approach) was found to be cost-effective at levels of gonococcal and/or chlamydial infections of 36% prevalence or higher.

Some of the lessons learnt and concerns raised during the study were that presumptive treatment might encourage risk-taking. In addition, some sex workers queried the need to come to a clinic when drugs could easily be purchased at a local pharmacy.

Sihanoukville, Cambodia

A pilot project for 100% condom use in brothels was set up in Sihanoukville in 1998. The project led to the eventual introduction of a 100% condom-use policy in sex work throughout Cambodia. This approach was combined with syndromic case management of STIs for the general population, following a similar national policy in Thailand. The project consisted of condom promotion in all sex establishments, hotels, and guest houses; a mandatory monthly visit for brothel-based female sex workers (also known as 'direct sex-workers') to their local STI clinic; constant health education, including through outreach work; and peer education.

In the STI case management component of the project, the following protocol was followed.

- All first-time visitors were given presumptive treatment for gonococcal and chlamydial infections.
- Follow-up visitors were treated for cervical infection depending on the result of a risk assessment and clinical examination.

Subsequently, the protocol was amended for economic reasons, and presumptive treatment for first-time visitors was not given.

The overall strategy of tackling STIs (including HIV infection) was later scaled up to cover the whole country and was found to be effective in reducing HIV prevalence – both directly, through the encouragement of condom use, and indirectly, through lower rates of STIs. However, since presumptive treatment was discontinued early in the project, not much can be inferred about its contribution to lowering rates of STIs.

However, some relevant issues did emerge. These included the question of how to reach so-called 'indirect' sex workers – those working in the entertainments sector, such as in massage parlours, hair salons, bars and night clubs – as opposed to brothel-based sex workers. The mobility of many sex workers – a phenomenon observed in many countries – was considered an obstacle to effective STI control. It was also realized that health-care staff needed better training and monitoring.

7. EXPERIENCES OF PERIODIC PRESUMPTIVE TREATMENT FOR STIs AMONG CORE GROUPS

Periodic presumptive treatment has been applied both in the context of settings where there are no existing services for STI care – or where there is only limited access to services – as well as in settings that offer good access to services.

7.1 Periodic presumptive treatment within the context of existing STI services

Several interventions involving periodic presumptive treatment within the context of existing accessible STI services have been attempted in the following settings.

South African mining communities

Periodic presumptive treatment was administered in three projects – Carletonville, Lechabile and Lesedi – and the effects on STIs were measured in studies conducted between 1996 and 2001.[4–6]

Periodic presumptive treatment was first used at the Lesedi and Lechabile projects in the Free State, followed by the Mothusimphilo project in the Carletonville area and other mining districts. In all sites, mobile clinics were deployed in areas frequented by sex workers and their clients near mine hostels.[7] Peer educators encouraged women at high risk to visit the clinics for medical examination, treatment and counselling. Presumptive treatment of 1 gram of azithromycin was given to cover the common curable STIs, and STI prevalence was repeatedly measured. Monthly rates of new STIs were also calculated for the miners, from syndromes reported by the mine clinics.

During the first nine months of the intervention in Lesedi, significant reductions in both ulcerative and non-ulcerative STIs were measured among participating women. STI incidence rates for miners were also examined, with miners stratified according to their closeness to the intervention sites. STI incidence rates among miners were lowest in the areas immediately covered by the project (less than 2 kilometres), higher in areas at intermediate distance (2–5 kilometres) and highest in more distant areas (more than 5 kilometres). As the intervention expanded, subsequent surveillance among miners documented STI declines in these more distant areas.

Among women attending the clinic in the Carletonville mining area, the prevalence of gonorrhoea was 20.6% at the first visit and 2.3% ($P < 0.001$) at the fourth monthly visit (reflecting a reduction of 89%). For *Chlamydia trachomatis*, the figures were 20.6% at the first visit and 8.6% ($P = 0.001$) at the fourth visit (a reduction of 58%). Within two months of the project's launch, quarterly STI incidence rates among miners at a large complex near the intervention site fell from 54 per 10 000 to 24 per 10 000 ($P < 0.001$) for genital ulcer disease (a reduction of 55%), and from 56 per 10 000 to 30 per 10 000 ($P < 0.001$) for urethral discharge (a reduction of 46%).

On the other hand, cross-sectional surveys conducted at the community level among sex workers, men and women in the community, and miners in Carletonville did not demonstrate a reduction in STI rates. This evidence suggests the need to achieve sufficient coverage with the periodic presumptive treatment intervention in order to achieve a population-level effect.

Beginning in 2000 at Lesedi, periodic presumptive treatment was 'tapered' – that is, its frequency was reduced – in this case from monthly to quarterly.[8] Rates of genital ulcer disease remained low at all sites for both the women and the miners, although rates of urethral discharge were highly variable and actually rebounded in some areas. Condom use may have been a factor in this rebound, which was observed in places where rates of reported condom use at last sex were less than 60% – but not in other places (Mothusimphilo) where reported condom use was greater than 70%.

Chancroid was the leading organism recovered from genital ulcers of both miners and sex workers at baseline.[9] Among women returning for follow-up visits to the clinic, who had previously received periodic presumptive treatment with azithromycin, the only organism causing genital ulcer dis-

ease that was detected was herpes simplex virus type 2 (HSV-2). Six weeks into the intervention, chancroid was no longer detected – even among women attending the clinic for the first time.

Conclusions

- Good coverage is important. The fact that the mining areas were geographically self-contained, with relatively little interaction with more distant towns, was thought to have contributed to the success of the intervention.
- There were concerns, as in other projects, about possible negative effects of periodic presumptive treatment on condom use by sex workers, as well as about the possibility of development of azithromycin resistance. The former was successfully addressed through peer education (significant increases in condom use were measured), and the latter through directly-observed treatment and the monitoring of antibiotic resistance patterns.
- The question of whether to administer periodic presumptive treatment monthly or quarterly was examined through operational research. Based on the results (including moderate rebound of some STIs), an intermediate frequency of periodic presumptive treatment of every two months was instituted.
- Since successful tapering of periodic presumptive treatment is likely to depend on rates of condom use, other high-risk sexual behaviours and access to clinical services, a flexible approach is now being used at Lesedi and the other intervention sites, depending on rates of condom use and other high risk sexual behaviours. Based on the risk assessment, the frequency of periodic presumptive treatment may be monthly for new attendees, once every two months or even discontinued altogether for those who have been in the programme for some time and are consistent condom users.
- Condom use increased progressively from 3% to 30% during the initial study period, when large STI declines were measured. It was not possible, however, to determine how much of the observed outcomes were due to condom promotion or other intervention components – as compared to periodic presumptive treatment alone.
- The large decrease in chancroid suggested that it could be eliminated quickly from a self-enclosed group such as a mining community. Targeting groups at high risk could be an effective strategy for controlling chancroid in areas where it is endemic. It is reasonable to suppose that such a strategy could also reduce HIV incidence in areas with a high prevalence of chancroid.

Hillbrow sex worker intervention, Johannesburg, South Africa

Although a high prevalence of STIs has been observed in sex worker populations in the South African cities of Durban and Johannesburg, provision of health services to sex workers presents a challenge because of the clandestine nature of sex work in the country.

To complement existing services provided by local primary health-care clinics, a cluster-randomized controlled trial was conducted to determine the acceptability, feasibility, and cost effectiveness of hotel-based STI treatment and prevention services for high-risk women in 12 hotels in Hillbrow, a district of the City of Johannesburg. In addition, the trial compared the effectiveness of two STI treatment strategies – periodic presumptive treatment and syndromic case management – in reducing the prevalence of chlamydial and gonococcal infections.

A mobile clinic, staffed by a trained primary health-care nurse and counsellor and operated daily for three to four days a month, was introduced into the 12 hotels. All high-risk women working in the hotels were invited by trained outreach workers to attend the clinic for free STI treatment, counselling, and condoms.

Five-hundred-and-forty sex workers completed an enrolment visit and at least one subsequent visit and were included in the outcome analysis. In terms of total visits

made, 292 sex workers (54%) completed two follow-up visits, and 171 (32%) completed three follow-up visits. The interval between visits was the same (approximately two months) for the intervention and control groups.

HIV prevalence at baseline was 60%. In the results from a pooled analysis, gonococcal prevalence decreased from 12.1% to 4.4% ($P = 0.048$) (a reduction of 64%) in the intervention group and from 17.1% to 11.5% (a reduction of 33%) in the control group. The reduction in prevalence differed significantly (OR = 0.57, $P = 0.019$) between the groups, and the greatest reduction was seen among those who attended at least three clinic visits (OR = 0.08, $P = 0.016$). The prevalence of chlamydial infections decreased by 69% (from 14.7% to 4.6%) in the intervention group and by 23% (from 14.1% to 10.9%) in the control group – these reductions in prevalence were not statistically significantly different (OR = 0.69, $P = 0.08$).

A mathematical model which was fitted to the epidemiological data projected that over a period of one year the intervention averted 2450 gonococcal and chlamydial infections (range, 2304–2997) and 451 ulcerative STIs (range 321–529). This resulted in a 3.1% (range, 2.3–3.7%) drop in HIV incidence among the sex workers, from 33.7 (range, 30.3–35.9) to 32.6 (range, 29.2–35.1) HIV infections per 100 person-years, and a 2.0% (range, 1.6–2.6%) drop in the district's incidence from 6.2 (range, 5.3–7.5) to 6.1 (range, 5.2–7.3) HIV infections per 100 person-years. The intervention averted 53 (range, 41–65) HIV infections, and 1413 DALYs (range,1246–1684). Without periodic presumptive treatment, the model projects that both arms of the intervention would have averted 45 (range, 34–55) HIV infections.[10] The provision of periodic presumptive treatment to sex workers in six of the hotels increased the number of HIV infections that were averted.

For the whole intervention, the economic cost per HIV infection averted was US$ 2093 (range, US$ 1384–3635), or US$ 78 (range, US$ 53–121) per DALY averted. If sex workers had been treated only using syndromic case management, then the averted cost per DALY increases to US$ 85. The incremental cost of adding periodic presumptive treatment to the intervention was US$ 31 per DALY averted.

Conclusions

- Qualitative research demonstrated that the mobile clinics were acceptable to women in terms of their service quality, accessibility, and efficacy, and that the clinics positively influenced health-seeking behaviours, health awareness, and condom use.
- Periodic presumptive treatment contributed substantially to the reduction in curable STIs, and modelling suggests that expanding periodic presumptive treatment coverage to all sex workers and their clients in the district could increase the impact tenfold, decreasing the HIV incidence among sex workers and the general population by up to 22% and 29%, respectively.

Nairobi, Kenya

A randomized controlled trial in Kenya sought to establish whether periodic presumptive treatment would reduce not only the incidence of STIs but also of HIV infection.[11] HIV-seronegative female sex workers in Nairobi were assigned either 1 gram of azithromycin each month, or a placebo. All the women were counselled and given free condoms and access to STI services. Urine tests for bacterial STIs were conducted monthly, and fuller STI and behavioural assessments were performed every six months. Groups were well matched at baseline for sexual risk-taking and STI-rates. Annual incidence rates of STIs, including HIV infection, were as shown in Table 1.

Conclusions

- In the intervention (periodic presumptive treatment) arm, reduced rates were observed for *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis*.

Table 1

Annual incidence of STIs in the two arms of the Kenyan randomized controlled trial

Pathogen	Annual incidence in treatment group (%)	Annual incidence in control group (%)	Statistical effect
HIV	4.0	3.2	Not significant
Neisseria gonorrhoeae	4.7 (urine PCR) 2.6 (cervical PCR)	12.7 (urine PCR) 5.7 (cervical PCR)	$P < 0.001$ P .02
Chlamydia trachomatis	6.3 (urine PCR) 1.1 (cervical PCR	14.5 (urine PCR) 6.5 (cervical PCR)	$P < 0.001$ $P < 0.001$
Trichomonas vaginalis	11.3 (culture)	20.4 (culture)	$P < 0.001$
Treponema pallidum (syphilis)	3.9	3.8	Not significant

- No effect was found on HIV incidence. However, there was a strong association between new cases of HIV and an earlier STI. This may reflect the time-lag to seroconversion after infection with HIV *at the same time as* infection with another STI. If this is the case, then the principal manner in which STIs facilitate HIV transmission (within this context of generally good STI control) is likely to be through the increased infectivity of a sex partner who is coinfected with HIV and an STI. STI treatment for those infected with HIV is, therefore, an important HIV prevention strategy.

Cotonou and Porto-Novo, Benin and Accra, Ghana

In the context of a dedicated clinic for sex workers, a randomized controlled trial was conducted among sex workers in Accra in Ghana and in Cotonou and Porto-Novo in Benin in 2001–2002.[12] Two randomization strategies were employed: community-cluster randomization in Accra and outlying areas of Cotonou and Porto-Novo, and standard 1:1 randomization for the other parts of the Benin sites. Sex workers were enrolled at special clinics which have been operating in West Africa since the 1990s.

There was monthly follow-up of the participants in the trial, who attended the clinic at enrolment and at months 3, 6 and 9, at which times cervical samples were collected for gonococcal and chlamydial polymerase chain reaction testing. During the other months, the participants were visited by the study personnel in their community. The control group received placebo, while the treatment group received 1 gram of azithromycin at month 1, and 500 milligrams of ciprofloxacin at months 2 and 3. This three-month cycle was repeated over the total of nine months. All treatments and placebo were taken under direct supervision. The results were adjusted for age, nationality, city, and the type of randomization being used.

Adjusted prevalences of gonorrhoea decreased from 13.5% to 7.3% (RR = 0.57; $P = 0.009$) in the treatment group (a reduction of 46%). In the control group, the prevalence fell from 16.2% to 11.8% (RR = 0.90; $P = 0.49$) (a reduction of 27%). There was no significant difference, however, in the fall in prevalence between the two arms of the trial (RR = 0.70, $P = 0.18$). After the study ended, periodic presumptive treatment was not routinely administered, but prevalences continued to fall among sex workers in Cotonou, reaching 3.7% in 2005.

However, there was an interesting finding related to sex workers who were HIV-seronegative at baseline. In this group, adjusted gonorrhoea prevalence fell sharply in the treatment group, from 11.0% to 3.1% (RR = 0.16; $P < 0.001$), but considerably less so in the control group, from 8.8% to 6.3% (RR = 0.78; $P = 0.54$). In this case involving HIV-seronegative sex workers, there was a significant difference in the fall in prevalence between the two groups (RR = 0.32; 95% CI 0.11–0.94; P = 0.038). Among those who were HIV-seropositive at baseline, the adjusted prevalence of gonorrhoea showed no significant declines in both groups.

Prevalence rates of *Chlamydia trachomatis*, which had been lower at baseline than those of gonorrhoea, did not decline. There was also no impact on HIV incidence and, in any event, the trial was not powered to assess such an impact.

Among clients, gonorrhoea prevalence decreased in both groups – from 2.0 to 1.6% among clients visiting sex workers cluster-randomized to the intervention group and from 3.9 to 1.9% among clients visiting sex workers cluster-randomized to the placebo group. However, the reduction in prevalence did not differ significantly between the groups. Chlamydial prevalence also slightly decreased in both groups ($P > 0.05$).

Conclusions

- Periodic presumptive treatment is probably not recommended when other control measures have been successful. Condom use among sex workers, for instance, has risen – over time – to levels now over 90% with the last client, and over 80% of female sex workers always using condoms with their clients in both Benin and Ghana, and STI rates have progressively fallen.
- During the trial, the syndromic case management of STIs (which included a gynaecological examination for the detection of signs of infection, not only symptoms) continued to be available to all participants. Of those in the placebo group, 37% had received at least one dose of ciprofloxacin in the context of syndromic case management – thus reducing the ability to evaluate the effectiveness of periodic presumptive treatment.

Mysore, India

A community-based programme in Mysore, India, operated by the Karnataka Health Promotion Trust uses periodic presumptive treatment as part of its integrated approach to sexual and reproductive health. Its strategy is to address sex work as a whole, and to bring in overlapping sex networks – including male sex workers, *hijra* (transsexual) sex workers, and male partners of sex workers. The programme provides outreach work, referrals, and clinical services. These clinical services include syndromic case management, counselling, regular health checks, and periodic presumptive treatment. Quarterly periodic presumptive treatment for gonococcal and chlamydial infections – with doses of 400 milligrams of cefixime and 1 gram of azithromycin – is given on the first visit to the clinic, and also if the last treatment for an STI was at least three months earlier.

Medicines for syndromic treatment, including periodic presumptive treatment, are provided in six colour-coded packs, according to the presumed infection. A blue pack, for instance, is for male urethritis and contains azithromycin 1 gram, cefixime 400 milligrams and metronidazole 2 grams. A white pack is given for genital ulcer disease. A red pack contains acyclovir 400 milligrams per day for five days for herpes simplex type 2 (HSV-2) ulcers. A grey pack is given for cervicitis (which is also used for periodic presumptive treatment), a green pack for vaginitis, and a yellow pack for pelvic inflammatory disease.

In August 2004 (six months after the programme was launched) a behavioural and biological study – involving 429 randomly selected female sex workers – was conducted. Approximately 15% reported having taken medicines for STIs regularly, and 45% had received periodic presumptive treatment. Only 21% said they always used condoms with

Table 2
STI prevalences among those who had and those who had not received periodic presumptive treatment

Pathogen	Prevalence among those who had received PPT (%)	Prevalence among those who had not received PPT (%)	Odds ratio [95% Confidence Interval]
HIV	27.5	24.2	Not statistically significant
N. gonorrhoeae	4.2	8.1	2.0 [0.9–4.7] $P = 0.1$
C. trachomatis	5.7	14.5	2.8 [1.4–5.7] $P = 0.005$
T. vaginalis	28.7	36.5	1.4 [0.9–2.2] $P = 0.09$
T. pallidum	28.7	21.5	Not statistically significant
HSV-2	69.0	60.7	Not statistically significant

clients, and 91% had never used a condom with a regular sexual partner. Comparisons were made of the differences in prevalences between those who had received periodic presumptive treatment and those who had not. The results are shown in Table 2.

Conclusions

- The major thrust of this programme is on involvement and participation of the sex workers at every stage. Community mobilization, access to, and utilization of services and active advocacy to create an enabling environment are key elements of the programme.
- The provision of periodic presumptive treatment was associated with lower rates of chlamydial infection.

7.2 Periodic presumptive treatment outside of routine STI services

One case of periodic presumptive treatment being administered where STI services were lacking – from the Lao People's Democratic Republic – was presented. Such a strategy has also been used with sex workers in Indonesia, Papua New Guinea, and Viet Nam.[13]

The Lao People's Democratic Republic

A group of 442 female sex workers, known as "service women", were selected for the study in the three border provinces of Khammouane, Oudomxai, and Savannakhet. Sex workers in these areas were highly mobile, and STI services were altogether lacking. Baseline samples showed high prevalences among the sex workers of either gonococcal or chlamydial infection or both (42.7% in Oudomxai, 39.9% in Khammouane and 22.7% in Savannakhet). Periodic presumptive treatment was administered using 1 gram of azithromycin at baseline and at monthly intervals over three months in Khammouane; at days 1, 30 and 90 in Oudomxai; and at days 1, 60 and 90 in Savannakhet. After three months, and following either the two or three rounds of treatment, respectively, the prevalence rates in the three provinces had fallen – to 12.3% in Oudomxai (a reduction of 71%), to 21.9% in Khammouane (a reduction of 45%), and to 17.0% in Savannakhet (a reduction of 25%). Overall, cervical infection declined from 32.4% (95% CI 28.1–36.9) to 18.0% (95% CI 14.5–22.1) over the three months ($P < 0.001$).[14]

Following the introduction of this project, the cost of STI drugs fell by 80%, making the intervention sustainable in

financial terms. To be effective, periodic presumptive treatment would need to have been administered once every two to three months.

It is probable that local STI clinics will not be available in these provinces in the foreseeable future, and other options for treating STIs need to be considered urgently. The inclusion of male clients and other sexual partners in treatment strategies would be important.

Conclusions

- There is a good argument for periodic presumptive treatment to be administered, as it was in the Lao People's Democratic Republic, in situations where the prevalence of STIs is high and where services are lacking, provided there exists a credible commitment to introduce STI services. The periodic presumptive treatment offered would then be of a transitional nature, while services were being established.

8. CONCLUSIONS, RECOMMENDATIONS AND PRIORITIES FOR FURTHER RESEARCH

8.1 Uses of presumptive treatment and periodic presumptive treatment for STI control

Based on accumulated experience, presumptive treatment can be considered as a component of STI services – particularly for sex workers. Where presumptive treatment is provided, the health benefit to individuals should be its primary objective. Public health benefits, while potentially significant, would be a secondary objective.

Presumptive treatment for STIs should not be regarded as a 'magic bullet'. Rather, it should be seen as one way to quickly reduce STI prevalence while other preventive and curative services are being established. In all cases, it was stated that it was important to improve access to STI services as a solution in the longer term.

Rapid reductions in prevalence of gonococcal and chlamydial infections following presumptive treatment were demonstrated in Madagascar and the Philippines. The long-term benefit of one-time presumptive treatment within a package of STI services is more difficult to disentangle from the benefits stemming from the services delivered. However, there is no reason to believe that a one-time presumptive treatment would have any sustainable benefit unless it were part of a more comprehensive intervention package.

Periodic presumptive treatment seems to have a greater impact in places where STI control is poor and where sex workers have little access to preventive and curative services. Good coverage is critical for interventions in commercial sex networks. For this reason, more rapid results may be seen where sex networks are relatively self-contained. However, even where mobility is high, interventions can achieve good coverage provided peer outreach efforts identify newcomers for referral to services.

One-time presumptive treatment

Recommendation

- One-time presumptive treatment may be suitable for *an emerging outbreak* of one or more STIs in an area. This has been demonstrated in several places for control of chancroid and syphilis outbreaks, but must be combined with other interventions to sustain control.

Periodic presumptive treatment

Recommendations

- Periodic presumptive treatment for STIs is not a stand-alone intervention, but *should be embedded in a package of services* – including syndromic case management, regular screening for syphilis, and the promotion of condom use.
- In areas of high STI prevalence, in which there is a lack of routine services for STI care, periodic presumptive treatment *can act as a temporary solution to rapidly reduce prevalence*, while STI services are being set up.
- Periodic presumptive treatment *can also be an entry point to STI services* for sex workers who have poor access to health services. This approach can help increase coverage. Initial emphasis on a few intervention components, such as condom use and presumptive treatment, can be developed over time into a more comprehensive package that meets sex workers' broader health needs.

8.2 Approaches to operating periodic presumptive treatment

The programmes and studies considered at the workshop revealed many differences in context and methods. In some south-eastern Asian countries, for example, periodic presumptive treatment was included as part of large-scale public health interventions. Some community-based projects in India and South Africa put more emphasis on local decision-making and participatory approaches.

In Cambodia, there is increasing involvement in decision-making by sex workers. However, the mandating of 100% condom use in all brothels – and the obligation for sex workers to present for monthly check-ups – is primarily directed at brothel owners. These owners face potential penalties for non-compliance.

Overall, the experiences suggest that an involvement of those receiving periodic presumptive treatment in the organization of programmes is beneficial – both for the recipients as well as for the success of the interventions.

Recommendations

- Plans containing periodic presumptive treatment for sex workers should be developed and operated with the participation of the sex worker community in decision-making at each stage. Peer education and peer outreach should be an integral part of such initiatives.
- Barriers to attending the clinic should be analysed and overcome, in order to encourage high attendance rates. This approach may involve taking the services closer to where sex workers live and work. Provision of transportation or other incentives may be considered.
- Efforts should be made to improve attitudes of health-care workers at general health-care facilities, as well as at dedicated clinics for sex workers. Sex workers attending routine health-care services should receive a level of care similar to that which they would be given in dedicated clinics. The choice to establish dedicated clinics or to integrate STI care for sex workers into mainstream care facilities should be made with the sex workers in defined communities. The location of care should also be discussed with potential users of the service.

8.3 Evaluation of the effectiveness of periodic presumptive treatment

Effectiveness

The complexity of trying to exclude the effect of other components of STI services (such as condom promotion and syndromic case management) from the effect of periodic presumptive treatment makes it difficult to assess the effectiveness of periodic presumptive treatment alone. However, data from studies (e.g. in Kenya, Madagascar and South Africa) as well as evidence from other programmes and studies, point to a significant impact on STIs such as gonococcal and chlamydial infections. There was, however, no such impact overall in the Ghana-Benin intervention except among HIV-seronegative participants.

While there is a reasonable amount of evidence for the effect of periodic presumptive treatment among female sex workers, other core groups have not been researched at all.

Recommendation

- Studies should be considered to determine the conditions under which periodic presumptive treatment is most effective and which of the various at-risk populations would benefit most, including female sex workers, male sex workers, transgender sex workers, men who have sex with men, and regular clients and steady partners of sex workers, as well as other persons at high risk of STIs – such as truck drivers, miners, the military, and prisoners.

Cost-effectiveness

Cost-effectiveness studies, with attention to potential social costs and benefits, should be conducted where possible. The additional cost of periodic presumptive treatment is minimal, compared with the cost of an overall package of services. The main costs of periodic presumptive treatment arise in the initial establishment of services. However, it should be understood that incremental costs may be encountered as the intervention becomes more complex. These incremental costs may arise not only from drug costs, but also from administrative and personnel costs – mostly for intensive field work to ensure follow-up of participants at the right time. Modelling of the data from the Hillbrow intervention suggests that periodic presumptive treatment was cost-effective in that setting.

Recommendation

- More cost-effectiveness studies of periodic presumptive treatment are needed to provide more evidence for the role of such interventions in different population groups and prevalence settings.

Mobility

Mobility of sex workers is an obstacle both to good coverage in periodic presumptive treatment programmes and to the accurate evaluation of the effectiveness of periodic presumptive treatment.

8.4 The impact of periodic presumptive treatment on specific STIs

Coverage of specific STIs

Recommendation

- STIs that are treated by periodic presumptive treatment should include gonococcal and chlamydial infections, syphilis and chancroid, where these are sufficiently prevalent. If syphilis is included in periodic presumptive treatment, the intervention should be accompanied by antenatal screening and treatment and, where feasible, the treatment of regular sex partners. Some sites have added presumptive treatment to cover trichomoniasis, although this involves adding an additional medication (usually metronidazole) with potentially higher levels of gastrointestinal side-effects.

Chancroid

Periodic presumptive treatment seems to be particularly effective in sharply reducing the incidence of chancroid in areas where it is prevalent. Because chancroid (an ulcerative STI closely linked to sex work) has been strongly implicated in increasing the risk of HIV transmission, periodic presumptive treatment for chancroid has potential for reducing HIV transmission.

- Periodic presumptive treatment should be considered for relevant key populations in areas of high chancroid prevalence.

Trichomoniasis

More research is needed on the impact of periodic presumptive treatment on trichomoniasis. If metronidazole is given in populations that also frequently consume alcohol, the use of this drug needs to be reconsidered. There is also concern that gastrointestinal side-effects could be increased if azithromycin and metronidazole are used at the same time, and deter sex workers from attending clinics or from complying with their medication.

- Regimens in which the two drugs azithromycin and metronidazole are taken separately or on alternate days need evaluation.

Genital herpes

To date, periodic presumptive treatment has not been conducted for viral STIs such as HSV-2. However, several studies are currently evaluating the effectiveness of HSV-2-suppressive and episodic therapy, using antiviral drugs such as acyclovir and valaciclovir. HSV-2 infection, like chancroid and syphilis, is an ulcerative STI that can greatly increase the probability of HIV transmission if HIV is present in either partner.

- The outcome of ongoing research should provide more data on how best to control HSV-2 to prevent HIV transmission.

HIV transmission

To date, the effect of periodic presumptive treatment on HIV transmission has not been effectively demonstrated. In a Kenyan trial, an effect of periodic presumptive treatment on some STIs was measured, but the intervention did not show impact on HIV incidence. There was also no impact on HIV incidence in the Benin-Ghana trial, although the latter was not powered to assess such an impact. Modelling of the data from the Hillbrow intervention suggests a modest impact on HIV incidence among sex workers.

- Further research – including through modelling – is needed to determine the effect of periodic presumptive treatment on HIV acquisition and transmission. A randomized community trial would probably help to answer this question, but such a study would be difficult to implement and would be costly.

8.5 Operating periodic presumptive treatment programmes

Periodicity, tapering, and the duration of programmes

The optimal periodicity of periodic presumptive treatment will vary from place to place, depending upon STI infection rates, the extent that condoms are not used, and other risk behaviours. Regular periods of no more than three months seem to be optimal. Shorter intervals lead to tighter STI control, but are more expensive because of the increased cost of drugs.

Tapering is the process through which the interval between treatments is increased with a view to reaching a stage when periodic presumptive treatment may be discontinued.

Recommendations

- If periodic presumptive treatment is administered, its periodicity should be once every one to three months depending on prevailing risk factors and conditions.
- Without evidence-based information, experts felt that if the prevalence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* combined falls below 10% *and* the rate of condom use is greater than 70%, consideration should be given to tapering, or even ending, the periodic presumptive treatment intervention. However, new participants (sex workers who are new to the area or who are attending for the first time) should still receive one round of presumptive treatment.
- Periodic presumptive treatment should – as a rule – be continued while good, comprehensive, accessible, and affordable services are being established. Tapering should be considered when services are in place and well frequented, and where there is evidence of declining STI prevalence rates.
- STI prevalence and condom use should be monitored regularly, ideally at least every two years. Different methods of evaluation exist depending on available resources.

Inclusiveness

Recommendations

- It is important to reach not only female sex workers in an STI intervention, but also male sex workers, transgender sex workers, and the clients of sex workers.
- As reinfection from regular partners of those treated in periodic presumptive treatment interventions is a major problem, means to extend STI services to the regular sex partners of members of core groups should be put in place.

Training

Recommendation

- Thorough training should be provided. This applies both for staff involved with services for sex workers as well as for sex workers themselves (trained as peer educators).

8.6 Drug resistance

There are serious concerns about the development of resistant strains – particularly of gonorrhoea and also of syphilis – to drugs such as azithromycin that are commonly used as monotherapy in periodic presumptive treatment.

Recommendations

- The possibility of developing resistance needs to be monitored in areas where periodic presumptive treatment, syndromic case management, and other STI services are provided. Pathogens other than those causing STIs also need to be monitored for possible resistance

to medicines used for STIs, such as azithromycin and ciprofloxacin.

- The role of single-dose combination therapy – for instance, of azithromycin together with cefixime – should be considered and evaluated as a means to minimize the development of resistance. Single-dose, directly observed therapy, which eliminates the problem of non-compliance with treatment (a major factor in the development of antimicrobial resistance), should be implemented whenever possible.

8.7 Uses of modelling

Typically in periodic presumptive treatment interventions, female sex workers have been seen every one to three months, irrespective of symptoms, whereupon they were given medication for specific STIs. However, it has not been feasible through operational research to determine the relative effectiveness of different approaches of conducting and terminating periodic presumptive treatment interventions. Modelling can offer a means of determining optimum approaches for an effective periodic presumptive treatment intervention.

Recommendations

- Mathematical modelling should be conducted, to determine the optimum prevalence threshold for initiating periodic presumptive treatment. Results should be validated by field research.
- Modelling should be applied to assess more effectively the optimum interval for periodic presumptive treatment, to determine at what point periodic presumptive treatment might be stopped, and to ascertain the minimum level of coverage needed to achieve success within a given population and setting.
- Modelling should be used to estimate the relative contributions of the various components of the recommended STI control packages targeted at sex workers, including presumptive treatment and condom use.

ANNEX 1. REFERENCES

1. Steen R, Dallabetta G. Sexually transmitted infection control with sex workers: regular screening and presumptive treatment augment efforts to reduce risk and vulnerability. *Reprod Health Matters* 2003;11:74-90.

2. Wi T, Ramos ER, Steen R, Esguerra TA, Roces MCR, Lim-Quizon MC, et al. STI declines among sex workers and clients following outreach, one time presumptive treatment, and regular screening of sex workers in the Philippines. *Sex Transm Infect* 2006;82:386-91.

3. Behets FM, Rasolofomanana JR, Van Damme K, Vaovola G, Andriamiadana J, Ranaivo A, et al. Evidence-based treatment guidelines for sexually transmitted infections developed with and for female sex workers. *Trop Med Int Health* 2003;8:251-8.

4. Olivier E, DeCoito T, Ralepeli S, Leong MG, Porotloane J, Semela M, et al. Maintenance of STD control in a mining community following introduction of a targeted intervention. In: Abstracts, International Congress of Sexually Transmitted Infections of the International Society for Sexually Transmitted Diseases Research and the International Union against Sexually Transmitted Infections, Berlin, 24–27 June 2001.

5. Steen R, Vuylsteke B, DeCoito T, Ralepeli S, Fehler G, Conley J, et al. Evidence of declining STD prevalence in a South African mining community following a core-group intervention. *Sex Transm Dis* 2000;27:1-8.

6. van Dam CJ, Holmes KK. STD prevention: effectively reaching the core and a bridge population with a four-component intervention [editorial article]. *Sex Transm Dis* 2000;27:9-11.

7. Steen R, Olivier E, Mzaidume Z, Rasego B, Moema S, Fehler G, et al. Periodic presumptive treatment as a component of a comprehensive HIV/STD prevention programme in a South African mining community. In: Abstracts, International Congress of Sexually Transmitted Infections of the International Society for Sexually Transmitted Diseases Research and the International Union against Sexually Transmitted Infections, Berlin, 24–27 June 2001.

8. Steen R, Ralepeli S, DeCoito T. Lesedi: services for women at high risk help reduce sexually transmitted infection (STI) prevalence in a South African mining community. In: Makinwa B, O'Grady M, eds. *FHI/UNAIDS best practices in HIV/AIDS prevention collection*. Arlington, VA, and Geneva: FHI/UNAIDS; 2001.

9. Steen R, DeCoito T, Ralepeli S, Morse SA, Fehler HG, Dallabetta G, et al. Rapid control of chancroid in a South African mining community. 13th Meeting of the International Society for Sexually Transmitted Diseases Research (ISSTDR), Denver, Colorado, 1999 (abstract 337).

10. Kumaranayake L, Rees H, Watts C. Are targeted HIV prevention activities cost-effective in high prevalence settings? Results from a sexually transmitted infection treatment project for sex workers in Johannesburg, South Africa. *Sex Transm Dis* 2006;33:S122-32.

11. Kaul R, Kimani J, Nagelkerke NJ, Fonck K, Ngugi EN, Keli F, et al. Monthly antibiotic chemoprophylaxis and incidence of sexually transmitted infections and HIV-1 infection in Kenyan sex workers: a randomized controlled trial. *JAMA* 2004;291:2555-62.

12. Labbé AC, Dzokoto A, Khonde N, Pépin J, Meda H, Asamoah-Adu C, et al. A randomized placebo-controlled trial of routine monthly antibiotics against gonococcal and chlamydial infections among female sex workers in Ghana and Bénin: intention-to-treat analysis. 15th Biennial Congress of the International Society for Sexually Transmitted Diseases Research (ISSTDR), Ottawa, Canada, 27–30 July 2003 (abstract 0335).

13. Joesoef MR, Valleroy LA, Kuntzjoro TM, Kamboji A, Linnan M, Barakbah Y, et al. Risk profile of female sex workers who participate in a routine penicillin prophylaxis programme in Surabaya, Indonesia. *Int J STD AIDS* 1998;9:756-60.

14. O'Farrell N, Oula R, Morison L, Van CT. Periodic presumptive treatment for cervical infections in service women in three border provinces of Laos. *Sex Transm Dis* 2006;33:558-64.

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