Population-based interventions for reducing sexually transmitted infections, including HIV infection (Review)

Sangani P, Rutherford G, Wilkinson D

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

http://www.thecochranelibrary.com

TABLE OF CONTENTS

Population-based interventions for reducing sexually transmitted infections, including HIV infection (Review)

Sangani P, Rutherford G, Wilkinson D

This record should be cited as:
Sangani P, Rutherford G, Wilkinson D. Population-based interventions for reducing sexually transmitted infections, including HIV infection. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD001220. DOI: 10.1002/14651858.CD001220.pub2.

This version first published online: 19 July 2004 in Issue 3, 2004.
Date of most recent substantive amendment: 26 February 2004

ABSTRACT

Background
Sexually transmitted infections (STI) are common in developing countries. The World Health Organisation (WHO) estimates that in 1999, 340 million new cases of syphilis, gonorrhoea, chlamydial infection and trichomoniasis occurred. Human immunodeficiency virus (HIV) infection is also common in developing countries. UNAIDS estimates that over 95% of the 40 million people infected with HIV by December 1999 live in developing countries (UNAIDS 2003). The STI and HIV epidemics are interdependent. Similar behaviours, such as frequent unprotected intercourse with different partners, place people at high risk of both infections, and there is clear evidence that conventional STIs increase the likelihood of HIV transmission. Several studies have demonstrated a strong association between both ulcerative and non-ulcerative STIs and HIV infection (Cameron 1989, Laga 1993). There is biological evidence, too, that the presence of an STI increases shedding of HIV, and that STI treatment reduces HIV shedding (Cohen 1997, Robinson 1997). Therefore, STI control may have the potential to contribute substantially to HIV prevention.

Objectives
To determine the impact of population-based STI interventions on the frequency of HIV infection, frequency of STIs and quality of STI management.

Search strategy
The following electronic databases were searched for relevant randomised trials or reviews:
1) MEDLINE for the years 1966 to 2003 using the search terms "sexually transmitted diseases" and "human immunodeficiency virus infection"
2) The Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness and the Cochrane Clinical Trials Register, in the most recent issue of the Cochrane Library
3) The specialist registry of trials maintained by the Cochrane Infectious Diseases Group.
4) EMBASE

The abstracts of relevant conferences were searched, and reference lists of all review articles and primary studies were scanned. Finally, authors of included trials and other experts in the field were contacted as appropriate.

Selection criteria
Randomised controlled trials in which the unit of randomisation is either a community or a treatment facility. Studies where individuals are randomised were excluded.

Data collection and analysis
Two reviewers independently applied the inclusion criteria to potential studies, with any disagreements resolved by discussion. Trials were examined for completeness of reporting. The methodological quality of each trial was assessed by the same two reviewers, with details recorded of randomisation method, blinding, use of intention-to-treat analysis and the number of patients lost to follow-up, using standard guidelines of the Cochrane Infectious Diseases Group.

Main results
Five trials were included.

Frequency of HIV infection: In Rakai, after 3 rounds of treatment of all community members for STIs, the rate ratio of incident HIV infection was 0.97 (95%CI 0.81 to 1.16), indicating no effect of the intervention. In Mwanza, the incidence of HIV infection in the intervention groups (strengthened syndromic management of STIs in primary care clinics) was 1.2% compared with 1.9% in the control groups (OR=0.58, 95% CI 0.42-0.70), corresponding to a 38% reduction (95%CI 15% to 55%) in HIV incidence in the intervention group. In the newest trial by Kamali et al, the rate ratio of behavioral intervention & STI management compared to control on HIV incidence was 1.00 (0.63-1.58, p=.98). These are consistent with Rakai data showing no effect of intervention.

Frequency of STIs: In both Mwanza and Rakai, there was no significant reduction in gonorrhoea, chlamydia, urethritis, or reported STI symptoms among intervention communities. The prevalence ratio of syphilis between intervention and control groups in Rakai was 0.8 (95%CI 0.71-0.89), of trichmoniasis was 0.59 (0.38-0.91), and of bacterial vaginosis was 0.87 (0.74-1.02). In Mwanza, the prevalence of serologically diagnosed syphilis in the intervention community was 5% compared with 7% in the control community at the end of the trial (adjusted relative risk 0.71 (95%CI 0.54-0.93). In Kamali et al, there was a significant decrease in gonorrhoea and active syphilis cases. Rate ratio for gonorrhoea was 0.29(0.12-0.71, p=0.016), active syphilis was 0.53(0.33-0.84,p=0.016). There was a trend towards significance with intervention on the use of condoms with the last casual partner; the rate ratio was 1.27(1.02-1.56,p= 0.036).

Quality of treatment: In Lima, following training of pharmacy assistants in STI syndromic management, symptoms were recognised as being due to an STI in 65% of standardised simulated patients (SSPs) visiting intervention and 60% of SSPs visiting control pharmacies (p=0.35). Medication was offered without referral to a doctor in most cases (83% intervention and 78% control, p=0.61). Of those SSPs offered medication, only 1.4% that visited intervention pharmacies and only 0.7% of those that visited control pharmacies (p=0.57) were offered a recommended regimen. Similarly in only 15% and 16% of SSP visits respectively was any recommended drug offered. However, education and counseling were more likely to be given to SSPs visiting intervention pharmacies (40% vs 27%, p=0.01). No SSPs were given partner cards or condoms. In Hlabisa, following the intervention targeting primary care clinic nurses (strengthened STI syndromic management and provision of STI syndrome packets containing recommended drugs, condom, partner cards and patient information leaflets), SSPs were more likely to be given recommended drugs in intervention clinics (83% vs 12%, p<0.005) and more likely to be correctly case managed [given correct drugs, partner cards and condoms] (88% vs 50%, p<0.005). There were no significant differences in the proportions adequately counseled (68% vs 46%, p=0.06), experiencing good staff attitude (84% vs 58%, p=0.07), and being consulted in privacy (92% vs 86%, p=0.4). There was no strong evidence of any impact on treatment-seeking behaviour, utilisation of services, or sexual behaviour in any of the four trials.

Authors' conclusions
There is limited evidence from randomised controlled trials for STI control as an effective HIV prevention strategy. Improved STI treatment services have been shown to reduce HIV incidence in an environment characterised by an emerging HIV epidemic (low and slowly rising prevalence), where STI treatment services are poor and where STIs are highly prevalent. There is no evidence for substantial benefit from treatment of all community members. The addition of the Kamali trial to the existing evidence supports the data from the Rakai trial of no effect. There are, however, other compelling reasons why STI treatment services should be strengthened, and the available evidence suggests that when an intervention is accepted it can substantially improve quality of services provided. The Kamali trial shows an increase in the use of condoms, a marker for improved risk behaviors. Further community-based randomised controlled trials that test a range of alternative STI control strategies are needed in a variety of different settings. Such trials should aim to measure a range of factors that include health seeking behaviour and quality of treatment, as well as HIV, STI and other biological endpoints.

BACKGROUND

Sexually transmitted diseases (STI), including HIV, are common in developing countries. The World Health Organisation (WHO) estimates that in 1999, 340 million new cases of syphilis, gonorrhoea, chlamydial infection and trichomoniasis occurred. Disease burden is highest in sub-Saharan Africa, where the combined incidence of these four infections is estimated at 257 per 1000 population at risk (WHO 2001). In addition, UNAIDS estimates that over 95% of the 40 million people infected with HIV by December 2003 live in developing countries (UNAIDS 2003). A large proportion (69%) of these people live in sub-Saharan Africa. Both STIs and HIV have substantial impact. For example, STIs, excluding HIV, collectively rank second in importance among dis-

eases for which intervention is possible among women aged 15-44 years (World Bank 1993, WHO 2001), and it is projected that in Zambia for example, HIV infection may increase child mortality three-fold early in the next century (UNAIDS 1999).

STIs and HIV are interdependent. Similar behaviours, such as frequent unprotected intercourse with different partners, place people at high risk of both infections, and there is clear evidence that certain bacterial and viral STIs increase the likelihood of HIV transmission. Several observational studies have demonstrated a strong association between ulcerative and non-ulcerative STIs and HIV infection (Cameron 1989, Laga 1993). There is biological evidence, too, that the presence of an STI increases shedding of HIV, and that STI treatment reduces HIV shedding (Cohen 1997, Robinson 1997).

Prevention of HIV infection depends on promotion of safer sexual behaviour (e.g. having fewer sexual partners), use of condoms, and the early and effective treatment of STIs. Therefore, STI control has the potential to contribute substantially to HIV prevention, because up to 90% of new HIV infections may be attributable to STIs as co-factors in the early phase of an HIV epidemic (Robinson 1997), and because substantial and sustained changes in sexual behaviour are difficult to attain.

STI control by itself will reduce illness. STIs are responsible for a considerable burden of acute illness and a substantial proportion become chronic and complicated, causing chronic pelvic pain, ectopic pregnancy, infertility and death (Wasserheit 1989).

To have maximal impact, STI interventions will likely need to be applied to whole populations. In this way the "mass effect" of the intervention on HIV transmission can be anticipated. The mass effect refers to the combined effect of reducing HIV shedding among HIV infected people who have an STI, and reducing the susceptibility of HIV-uninfected people with an STI to acquiring HIV infection (Mabey 1996). If coverage of an intervention is high enough it may achieve the "mass effect" whereby the overall level of transmission of STIs in the population is reduced.

Potential community-level STI interventions include campaigns aimed at promoting safer sexual behaviour and better STI treatment-seeking behaviour, improved STI treatment services (including improved attitudes of care providers, improved case management and contact treatment), integration of STI case findings in family planning and antenatal care services, STI screening programmes, and mass treatment of whole communities for STIs.

OBJECTIVES

To determine the impact of population-based STI interventions on the incidence of HIV infection.

To determine the effect of population-based STI interventions on the following outcomes:

- reduction in the incidence and prevalence of HIV infection
- reduction in the incidence and prevalence of STIs
- increase in the utilisation of STI treatment services and improved rates of partner treatment
- improvement in the quality of STI treatment services
- increase in safer sexual behaviour in the community, including increased condom use

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised controlled trials in which the unit of randomisation was either a community or a treatment facility. Studies in which individuals were randomised were excluded.

The term community was interpreted to include a group of villages, an arbitrary geographical division, or the catchment population of a group of health facilities.

Types of participants

General adult populations and people with STIs

Types of intervention

Any population-based STI intervention including, but not exclusive to: 1) information, education and communication campaigns aimed at promoting safer sexual behaviour, increased condom use, and better STI treatment-seeking behaviour, 2) improved STI treatment services, 3) integration of STI case finding into family planning, antenatal care and other health services, and 4) mass treatment of whole communities (that is, all individuals symptomatic and asymptomatic in a community who meet the study's criteria for treatment for STI).

Types of outcome measures

1. Frequency of HIV infection:

- incidence and prevalence of HIV infection in a representative community sample

2. Frequency of STIs:

- incidence and prevalence of STIs in a representative community sample

3. Quality of STI treatment:

- proportion of STI patients correctly examined
- proportion of STI patients correctly treated, compliant and cured
- proportion of STI patients given partner notification cards
- proportion of STI patients given condoms

- proportion of STI patients counseled about STIs and HIV infection

4. Treatment-seeking behaviour and utilisation of services:

- proportion of patients with an STI that seek care
- duration of symptoms among STI patients
- proportion of (asymptomatic) partners of index cases treated

5. Safer sexual behaviour:

- proportion of people in a representative sample that report a reduction in rate of partner change
- proportion of people in a representative sample reporting regular condom use with casual partners
- increase in average age of sexual debut

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The trials registers of The Cochrane Infectious Diseases Group and the Cochrane Collaborative Review Group on HIV Infection and AIDS were searched for relevant trials (published, in press or in progress). The topic search terms used were acquired immunodeficiency syndrome, HIV infections, human immunodeficiency virus infection, immunologic deficiency syndromes, sexually transmitted diseases, venereal disease, drug screening. Full details of the review group's methods and the journals hand-searched are published in The Cochrane Library in the section on Collaborative Review Groups.

The reviewers searched the Cochrane Controlled Trials Register, published on The Cochrane Library (2000, Issue 1). This is a compilation of about 220,000 published trials identified by hand-searching by various individuals within The Cochrane Collaboration. Full details of the sources and methods used are published in The Cochrane Library.

The following databases were also searched: MEDLINE 1966-2003 EMBASE 1980-2003, using the search strategy defined by the Cochrane Collaboration, and detailed in appendix 5c of The Cochrane Handbook. The specific topic search terms used were acquired immunodeficiency syndrome, HIV infections, human immunodeficiency virus infection, immunologic deficiency syndromes, sexually transmitted diseases, venereal disease, drug screening, community/tw (text word).

Dates of latest searches:

- Cochrane Infectious Diseases Group Trials Register: May 2003
- Cochrane Collaborative Review Group on HIV infection and AIDS Trials Register: May 2003
- CCTR: May 2003
- MEDLINE: May 2003
- EMBASE: May 2003

External referees were asked to check the completeness of the search strategy and to identify any additional unpublished, ongoing or planned trials.

The abstracts of relevant conferences, as indexed in AIDSLINE, were searched and reference lists of all review articles and primary studies were scanned. Finally, authors of included trials and other experts in the field were contacted.

METHODS OF THE REVIEW

Two reviewers independently applied the inclusion criteria to potential studies, with any disagreements resolved by discussion. Trials recognised as randomised controlled clinical trials were examined for completeness of reporting. The methodological quality of each trial was assessed by the same two reviewers, with details recorded of randomisation, allocation method, blinding, use of intention-to-treat analysis and the number of patients lost to follow-up using standard guidelines of the Cochrane Infectious Diseases Group.

DESCRIPTION OF STUDIES

Grosskurth et al randomised 12 communities and their associated primary care clinics in Mwanza, Tanzania, to receive improved STI case management, or not to receive it. The intervention comprised establishing a STI reference clinic in the district, staff training, regular supply of basic drugs, regular supervision of clinic staff, and STI health education. The 12 communities were paired based upon baseline HIV and STI prevalence and risk factors for infection, proximity to roads, geography, and prior STI clinic attendance rates. In each pair one community was randomly chosen to receive the intervention and the other to serve as the control. Outcomes were measured among approximately 12000 adults aged 15-54 years (1000 randomly selected from each community, residing within a 90 minute walk of each clinic). HIV incidence (004 Grosskurth) and STI prevalence (005 Mayaud) were measured two years post-intervention.

Wawer et al conducted a randomised controlled single-masked community-based trial of intensive STI control via home-based mass antibiotic treatment in Rakai, Uganda. Ten community clusters were randomly assigned to intervention (treatment of all consenting adults aged 15-59 years with azithromycin, ciprofloxacin, and metronidazole, irrespective of symptoms) or control (treatment with vitamins/antihelminthic drugs). Treatment was given as single dose under direct observation every 10 months. The ten community clusters each comprised 4-7 contiguous villages that

encompassed social and sexual networks. Clusters were grouped into blocks based on projected HIV prevalence and were paired based on HIV prevalence. Communities and participants were blinded to the intervention, but study personnel were not. Participants included all permanent resident adults aged 15-59 years who consented to the trial. Participants comprised an open cohort, including newly arrived residents at each study round. All households were visited every 10 months at which time treatment was given, biological samples for HIV and STI taken, and a questionnaire administered. All participants in both arms of the study received identical education on HIV prevention, confidential HIV counseling and testing services, free condoms, and free health care. All participants were also advised to seek treatment for STI symptoms between study rounds. Mass treatment was provided to over 80% of eligible adults present in the community each study round. Results of the first three study rounds were presented as the Data Safety and Monitoring Board (DSMB) invoked a predetermined stopping rule at this stage. Outcome measures were HIV incidence and STI prevalence.

Kamali et al randomised all adults living in 18 communities in the Masaka district of rural Uganda to three groups. The total population was 96000 aged 13 and older. The aim was to assess the effect of different interventions on the primary outcome, the incidence of HIV. The secondary outcomes were the incidence of other STDs. These included herpes simplex type 2, active syphilis, and prevalence of gonorrhoea & chlamydia, reported genital ulcers and markers of behavioral change. Group A received behavioural interventions alone consisting of information, education. Group B received behavioral and STI interventions and Group C received the routine government health services. The study communites were individually matched in triplets by the type of main road passing through, distance from the district capital and quality of the local government health facility. They formed a total of 6 triplets. Interventions were tested at baseline (April 1994-November 1996), round 2 (December 1996-December 1998) and round 3 (January 1999-June 2000) with questionnaires and laboratory testing.

Garcia et al randomised 180 pharmacies randomly selected from a list of 2 546 pharmacies, to either receive or not receive education on STI recognition, management, and prevention counseling, in Lima, Peru. The sample of 180 was stratified to reflect the proportion of pharmacies in each district of the city. All 180 received a baseline visit from two standardised simulated patients (SSP) and an interviewer, 90 received the intervention, and then all 180 received two more visits from different SSPs and an interviewer. One male and one female SSP visited each pharmacy pre- and post-intervention. Males reported having either urethritis or genital ulcer, and females reported either vaginal discharge or pelvic inflammatory disease. They filled in a standardised form following each pharmacy visit to record information such as diagnosis, treatment offered, referral to doctor, recommendations for sexual contacts, and risk reduction counseling. The intervention comprised an eight-hour training course on STI-HIV management and prevention, but, as only 21 of 90 invited pharmacies attended, a 1.5-2 hour training session was offered on site in the pharmacies. In all, 50 (56%) pharmacies received one or both interventions. Outcome measures included diagnoses given, referral to a doctor advised, use of recommended treatment regimens, and prevention counseling offered. No biological outcomes were measured.

Harrison et al randomised five matched pairs of primary care clinics (10 clinics in all) in the rural Hlabisa district, South Africa, to an intervention or routinely available STI management. The intervention comprised training and supervising clinic nurses in comprehensive syndromic management of STIs and the use of STI syndromic packs. Packs comprised recommended drugs for a specific syndrome, condoms, contact cards, and written health information. Outcome measures included the proportion of SSPs given recommended drugs, correctly case managed, adequately counseled, reporting good staff attitude, and consulted in privacy. No biological outcomes were reported.

METHODOLOGICAL QUALITY

Grosskurth et al: Study was randomised between pre-determined village pairs with pairing dependent on geographical characteristics, proximity to roads, and baseline HIV prevalence. The study was unmasked.

Wawer et al: Study was block randomised. Allocation was concealed from participants but not from study personnel. Intention to treat analyses were used.

Garcia et al: Study was stratified randomised. Allocation to training or not could not be concealed from the pharmacies, but allocation was concealed from SSPs. Intention-to-treat analyses were used.

Harrison et al: Study was randomised with pairing dependent on prevalence of syphilis in pregnant women attending clinics, socio-demographic characteristics of surrounding communities, and geography. Allocation was concealed from the investigators only prior to the intervention. SSPs were not explicitly told which clinics had received the intervention, but this information could not be hidden from them.

Kamali et al: Study was randomised by communities with matching done in triplets based on geographical characteristics.

RESULTS

1. Frequency of HIV infection.

In Rakai, after three rounds of mass treatment the fully adjusted rate ratio of incident HIV infection in intervention versus control communities was 0.97 (95%CI 0.81 to 1.16), indicating no effect of the intervention. In a secondary paper comparing the Rakai and

Mwanza trials the results have also been expressed as a (non-significant) 3% reduction in HIV incidence (95%CI 16% reduction to 19% excess) (004 Grosskurth).

In Mwanza, the incidence of HIV infection in the intervention groups was 1.2% per 100 person years compared with 1.9% per 100 person years in the control groups; the adjusted relative risk was 0.58 (95%CI 0.42-0.70), (004 Grosskurth). In a fully adjusted analysis this corresponds to a 38% reduction (95%CI 15% to 55% reduction) in HIV incidence in the intervention group (004 Grosskurth).

In Masaka, the rate ratio after three rounds of follow-up of group B vs. control was 1.00 (0.63-1.58,p=.98), indicating no effect of the intervention. Because the data is presented as incidence rate ratios per person years at risk and thus, this outcome variable could not be included in the meta-analysis.

2. Frequency of STIs

In Rakai, there was no significant reduction in gonorrhoea, chlamydia, urethritis, or reported STI symptoms between trial groups. The prevalence ratio of syphilis between intervention and control groups at the end of the trial was 0.80 (0.71-0.89), of trichmoniasis 0.59 (0.38-0.91), and of bacterial vaginosis 0.87 (0.74-1.02).

In Mwanza, there was no significant reduction in gonorrhoea, chlamydia, overall urethritis, or reported symptoms between trial groups. The prevalence of serologically-diagnosed syphilis in the intervention community was 5% compared with 7% in the control community at the end of the trial (adjusted relative risk 0.71, 95%CI 0.54-0.93). Prevalence of reported symptomatic urethritis was 1.6% in intervention and 2.5% in control communities (adjusted relative risk 0.51, 95%CI 0.24-1.10).

In Masaka, there was a significant decrease in gonorrhoea and active syphilis cases. Rate ratios respectively were 0.29 (0.12-0.71,p= 0.016 and 0.53(0.33-0.84,p=0.016). There was not a significant decrease in chlamydia prevalence; rate ratio was 0.99 (0.70-1.41,p=0.94). he syphilis data is presented as incidence rate ratios per person years at risk and thus, this outcome variable could not be included in the meta-analysis.

3. Quality of treatment

In Lima, following the intervention, symptoms were recognised as being due to an STI in 65% of SSPs visiting intervention and 60% of SSPs visiting control pharmacies (p=0.35). Medication was offered without referral to a doctor in most cases (83% intervention and 78% control, p=0.61). Of those SSPs offered medication, only 1.4% that visited intervention pharmacies and only 0.7% of those that visited control pharmacies (p=0.57) were offered a recommended regimen. Similarly, in only 15% and 16% of SSP visits respectively was any recommended drug offered. However, education and counseling were more likely to be given to SSPs visiting intervention pharmacies (40% vs 27%, p=0.01). No SSPs in either group were given partner cards or condoms.

In Hlabisa, following the intervention, SSPs were more likely to be given recommended drugs in intervention clinics (83% vs 12%, p<0.005) and more likely to be correctly case managed (given correct drugs, partner cards, and condoms: 88% vs. 50%, p<0.005). There was no significant difference in the proportions adequately counseled (68% vs 46%, p=0.06), experiencing good staff attitude (84% vs 58%, p=0.07) or being consulted in private (92% vs 86%, p=0.4).

4. Treatment-seeking behaviour and utilisation of services

In Hlabisa, the monthly mean number of STI patients attending intervention clinics increased, but this was almost entirely due to changes in one clinic. The proportion of patients seeking treatment within seven days of symptom onset was similar in the two groups after adjustment for baseline differences (p=0.08). The proportion of patients treated that reported being asymptomatic partners was higher in control than intervention clinics for women (10% vs 3%, p=0.001) but not for men (6% vs 7%, p=0.57).

In Rakai, of those reporting STI symptoms between rounds of mass treatment, 20% of those living in intervention communities and 16% of those living in control communities reported seeking treatment.

5. Safer sexual behaviour

In Rakai there was no significant change in the variables used to measure safer sexual behaviour. At the end of the trial, 14% of residents of intervention communities and 11% of residents of control communities reported condom use in the preceding six months, and 5.5% vs 4.1% reported consistent condom use with a primary partner.

In Mwanza, there was no difference in condom use, reported lifetime number of sexual partners, and partners during the past year between intervention and control communities either before or after the intervention.

In Masaka there was a trend towards a significant outcome for increase in condom use with last partner, rate ratio was 1.27 (0.83-1.80p=0.24). Otherwise there were no signficant changes for the other outcomes measured of reported genital ulcers, reported urethral discharge or reported vaginal discharge, all of which are markers for STI prevalence.

DISCUSSION

This review demonstrates that there is limited evidence from community-based randomised controlled trials for the effectiveness of STI control as an HIV prevention strategy. Indeed of the five trials that we identified, only three reported HIV incidence as an

outcome measure, and only in one of these was HIV incidence reduced among intervention communities.

There is evidence for the impact of the STI control interventions tested in these three trials on the incidence and prevalence of STIs and reproductive tract infections such as bacterial vaginosis. In both the Masaka and Rakai trials, rates of syphilis fell significantly, as did rates of trichomoniasis. Futhermore, Kamali et al observed significant reduction in the rates of gonorrhoea. In one study, there was a borderline decrease in bacterial vaginosis.

The findings from the two trials that did not measure biological outcomes, but rather studied quality of STI treatment, provide additional insight. In Lima, as only 21 of 90 invited pharmacies attended a training session, a variation on the intended intervention was designed and implemented. Clearly, it is important to develop and design interventions that suit local circumstances. Both before and following the intervention in Lima the quality of STI treatment, assessed through the use of simulated patients (SSPs), seemed to be very poor, and did not increase among SSPs visiting intervention pharmacies. However, more positively, some improvement in the quality of counseling was observed. It is unclear whether the failure to show an effect was due to poor uptake of the intervention or failure of the intervention to have an impact, or both.

In Hlabisa, the combination of health worker training and supervision, together with provision of STI treatment packs, resulted in substantial improvements in the proportion of SSPs given correct drug treatment, comprehensively case managed, and appropriately counseled.

The Mwanza and Rakai trials have limited data available to allow an exploration of proximal factors that may be important in the chain of causality. For example, there are some (but incomplete) data on STI prevalence and incidence, and there are few data on health-seeking behaviour and quality of care in these settings. In contrast, in the Lima and Hlabisa trials there is good information on the importance of developing a strong local intervention and of the beneficial impact that interventions may have on quality of STI treatment. We do not know, however, what effect these interventions might have on rates of STI and HIV in the community.

Initially, the differing outcomes of the Rakai and Mwanza trials were perplexing. Now, with the addition of the Kamali data, which studied a population similar to Rakai, the conclusion that STI interventions have little to no effect on HIV incididence in communities where the HIV epidemic is stabilzed is strengthened. We did see differences in these two trials in terms of STI incidence, and that could be explained by the fact that in the Rakai trial the STI intervention was mass treatment, regardless of symptoms of STI's. In the Kamali trial, we see a direct relationship and positive effect of the behavioural intervention on incidence of STI's, specifically syphilis and gonorrhoea. The study design in Kamali et al supports this becasue those patients with symptoms would be treated. In a design such as Wawer et al, where there is mass treatment, people are getting treated in a constant fashion so rates are difficult to interpret. Why did the Rakai and Mwanza trials, both testing a community-based STI control strategy, deliver apparently contradictory results? It is clear that the two trials were actually testing quite different interventions: strengthened primary care STI syndromic management in Mwanza, and rounds of mass community treatment, irrespective of symptoms, in Rakai. In fact, the successful Mwanza intervention was the behavioral counselling that accompanied STI treatment. Also the HIV epidemic in the two settings was quite different, with the HIV epidemic in Rakai relatively mature compared to an evolving epidemic in Mwanza. In a setting like Rakai where HIV prevalence was quite high (16%) and had spread beyond high risk groups into the more general population, the role of STIs in HIV spread is reduced and hence the role of STI control in HIV control will be somewhat less important. In fact, in a subanalysis of the Rakai data, the population attributable fraction for STI in HIV transmission was only 10% (Hudson 2001, Hayes, 1997). This could be because in more mature epidemics the bulk of transmission occurs between serodiscordant couples in which the HIV-negative partner is repeatedly exposed (Hudson 2001, Gray 1999). The possibly important role of STIs such as herpes and bacterial vaginosis, which were not treated by the interventions tested in both trials, should be considered. Also, it is likely that symptomatic STIs (targeted in Mwanza) are relatively more important as facilitators of HIV spread compared with asymptomatic STIs (targeted in Rakai), due to the increased inflammatory response associated with them. Furthermore, in Rakai, STIs may have been reintroduced more easily than in Mwanza because of the lack of high quality, continuously available treatment services (Grosskurth 2000).

AUTHORS' CONCLUSIONS

Implications for practice

There is limited evidence from randomised controlled trials for STI control as an effective HIV prevention strategy. The addition of the fifth trial (Kamali et al) further supports this conclusion. Improved STI treatment services have been shown to reduce HIV incidence in only one trial and in a particular environment characterised by an emerging HIV epidemic (low and slowly rising prevalence), where STI treatment services were poor, and where STIs were highly prevalent. There is no evidence for benefit from mass treatment of communities, at least for the regimen tested in Rakai. There are, however, other compelling reasons why STI treatment services should be strengthened, and the available evidence suggests that when a health service intervention is effectively implemented, it can substantially improve quality of STI service provision, at least in the short term.

Implications for research

Further community-based randomised controlled trials that test a range of alternative STI control strategies are needed in a variety of different settings.

POTENTIAL CONFLICT OF INTEREST

We certify that we have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of the review (e.g. employment, consultancy, stock ownership, honoraria, expert testimony).

ACKNOWLEDGEMENTS

The protocol for this review was developed as an activity of both The Cochrane Infectious Diseases Group and the Cochrane HIV/AIDS Group. Thanks to the Department for International Development, UK for financial support as we began this review.

We would like to thank Professor Richard Hayes and Dr Heiner Grosskurth for their helpful comments and also Ms Kay May Madeleine Kwok for her hand search of International AIDS Conference abstracts.

SOURCES OF SUPPORT

External sources of support

- European Commission (Directorate General XII) BELGIUM
- California HealthCare Foundation USA

Internal sources of support

- Adelaide University AUSTRALIA
- University of South Australia AUSTRALIA

REFERENCES

References to studies included in this review

001 Wawer *{published data only}*
Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N, Wabwire-Mangen F, Li C, lutalo T, Nalugoda F, Gaydos CA, Moulton LH, Meehan MO, Ahmed S, the Rakai Project Study Group and Gray RH. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. *Lancet* 1999;**353**(9152):525–535.

002 Garcia *{published data only}*
Garcia PJ, Gotuzzo E, Hughes JP, Holmes KK. Syndromic management of STDs in pharmacies: evaluation and randomised intervention trial. *Sexually Transmitted Infections* 1998;**74**(Suppl 1):S153–S158.

003 Harrison *{published data only}*
Harrison A, Abdool Karim SS, Floyd K, Lombard C. Lurie M, Ntuli N, Wilkinson D. Syndrome packets and health worker training improve quality of sexually transmitted disease case management in rural South Africa: results of a randomised controlled trial. *AIDS* 2000; **in press**.

004 Grosskurth *{published data only}*
Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Senkoro K, Mayaud P, Changalucha J, Nicoll A, ka-Gina G, Newell J, Mugeye

K, Mabey D, Hayes R. Imapct of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995;**346**:530–36.

005 Mayaud *{published data only}*

Mayaud P, Mosha F, Todd J, Balira R, Mgara J, West B, Rusizoka M, Mwijarubi E, Gabone R, Gavyole A, Grosskurth H, Hayes R, Mabey D. Improved treatment services significantly reduce the prevalence of sexually transmitted diseases in rural Tanzania: results of a randomised controlled trial. *AIDS* 1997;**11**:1873–1880.

006 Kamali *{published data only}*

Kamali A, Quigley M, et al. Syndromic managment of sexually-transmitted infections and behaviour change interventions on transmissio of HIV-1 in rural Uganda: a community randomised trial. *Lancet* 2003;**vol 361**:645–652.

Additional references

Cameron 1989

Cameron DW, Simonsen JN, D'Costa LJ, Ronald AR, Maitha GM, Gakinya MN, et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989;**ii**:184–9.

Cohen 1997

Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Costello Daly C, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997;**349**:1868–73.

Gray 1999

Gray, et al. Relative risks and population attributable fraction of incident HIV asociated with symptoms and treatable STDs. *AIDS* 1999;**13**:2113–23.

Grosskurth 1995

Grosskurth H, Mosha F, Todd J, Awijaruba E, Klokke A, Senkoro K, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995;**346**:530–6.

Grosskurth 2000

Grosskurth H, Gray R, Hayes R, Mabey D, Wawer M. Control of sexually transmitted diseases for HIV-1 prevention: understanding the implications of the Mwanza and Rakai trials. *Lancet* 2000;**355**:1981–87.

Hayes, 1997

Hayes, et al. Randomized trials of STD treatment for HIV prevention. *Genitourinary Med* 1977;**73**:432–43.

Hudson 2001

Hudson CP. Community-based trials of sexually transmitted disease treatment: repercussions for epidemiology and HIV prevention. *Bull WHO* 2001;**79**:48–58.

Laga 1993

Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. *AIDS* 1993;**7**:95–102.

Mabey 1996

Mabey DC. Sexually transmitted diseases in developing countries. *Trans R Soc Trop Med Hyg* 1996;**90**:97–9.

Mostad 1997

Mostad S, Overbaugh J, DeVange D, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. *Lancet* 1997;**350**:922–927.

Robinson 1997

Robinson NJ, Mulder DW, Auvert B, Hayes RJ. Proportion of HIV infections attributable to other sexually transmitted diseases in a rural Ugandan population: simulation model estimates. *Intl J Epidemiol* 1997;**26**:180–189.

UNAIDS 1999

UNAIDS. Report on the global HIV/AIDS epidemic.

UNAIDS 2003

UNAIDS. AIDS Epidemic Update. Geneva: UNAIDS, 1997.

Wasserheit 1989

Wasserheit J. The significance and scope of reproductive tract infections among Third World women. *Intl J Gynaecol Obstet* 1989;**Suppl 3**:145–168.

WHO 2001

World Health Organization. Global Prevalence and Incidence of Selected Curable Sexually Transmitted Infections: Overview and Estimates. 2001:World Bank, 1993.

World Bank 1993

World Bank. World Development Report.

TABLES

Characteristics of included studies

Study	001 Wawer
Methods	Community randomised trial in Rakai, Uganda
Participants	Approximately 14,000 consenting adults aged 15-59 in 10 community clusters
Interventions	Mass treatment of all participants with azithromycin, ciprofloxacin, and metronidazole
Outcomes	HIV and STD infection

Characteristics of included studies (*Continued*)

Notes	
Allocation concealment	A – Adequate

Study	**002 Garcia**
Methods	Pharmacy randomised trial in Lima, Peru
Participants	360 visits to 180 pharmacies by two standardised simulated patients (SSP)
Interventions	Education on STD recognition, management and prevention counselling
Outcomes	STD diagnosis provided, referral to doctor, use of recommended treatment regimen, preventive counselling offered
Notes	
Allocation concealment	A – Adequate

Study	**003 Harrison**
Methods	Primary care clinic randomised trial in Hlabisa, South Africa
Participants	100 visits to 10 clinics by 10 SSP
Interventions	Training and supervision of clinic nurses in STD syndromic management and use of STD treatment packs
Outcomes	Use of recommended drugs, case management, counseling, privacy and staff attitude
Notes	
Allocation concealment	A – Adequate

Study	**004 Grosskurth**
Methods	Community randomised trial in Mwanza, Tanzania
Participants	Approximately 12,000 adults aged 15-54 in 12 communities
Interventions	Improved STD case management
Outcomes	HIV incidence
Notes	
Allocation concealment	A – Adequate

Study	**005 Mayaud**
Methods	Community randomised trial in Mwanza, Tanzania
Participants	Approximately 12,000 adults aged 15-54 in 12 communities
Interventions	Improved STD case management
Outcomes	STD prevalence
Notes	
Allocation concealment	A – Adequate

Study	**006 Kamali**
Methods	Community randomised trial in rural Uganda
Participants	Approximately 20,000 adults aged 13 - 65 in 18 communities
Interventions	Behavioral interventions including knowledge, skills training and support versus behavioral interventiosn PLUS syndromic STI management versus control group receiving community development and health-related issues chosen by each community

Outcomes	HIV-1 incidence
Notes	
Allocation concealment	B – Unclear

ANALYSES

Comparison 01. Any intervention vs control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV incidence	2	17925	Relative Risk (Fixed) 95% CI	0.84 [0.67, 1.04]
02 STD prevalence	8	49657	Relative Risk (Fixed) 95% CI	0.83 [0.79, 0.86]
03 Quality of treatment	8	1786	Relative Risk (Fixed) 95% CI	2.14 [1.79, 2.55]
04 Treatment seeking behaviour / service use	0	0	Relative Risk (Fixed) 95% CI	Not estimable
05 Safer sexual behaviour	4	24762	Relative Risk (Fixed) 95% CI	1.15 [1.08, 1.22]

Comparison 02. STD mass treatment vs placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV incidence	1	9376	Relative Risk (Fixed) 95% CI	1.02 [0.77, 1.36]
02 STD prevalence	5	26627	Relative Risk (Fixed) 95% CI	0.84 [0.80, 0.88]
03 Quality of treatment	0	0	Relative Risk (Fixed) 95% CI	Not estimable
04 Treatment seeking behaviour / service use	1	11686	Relative Risk (Fixed) 95% CI	1.22 [1.13, 1.32]
05 Safer sexual behaviour	2	23372	Relative Risk (Fixed) 95% CI	1.15 [1.08, 1.23]

Comparison 03. Improved STD syndromic management vs usual care

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV incidence	1	8549	Relative Risk (Fixed) 95% CI	0.62 [0.44, 0.88]
02 STD prevalence	1	8772	Relative Risk (Fixed) 95% CI	0.72 [0.61, 0.86]
03 Quality of treatment	8	1786	Relative Risk (Fixed) 95% CI	2.14 [1.79, 2.55]
04 Treatment seeking behaviour / service use	0	0	Relative Risk (Fixed) 95% CI	Not estimable
05 Safer sexual behaviour	1	967	Relative Risk (Fixed) 95% CI	1.11 [0.91, 1.35]

INDEX TERMS

Medical Subject Headings (MeSH)

*Developing Countries [statistics & numerical data]; HIV Infections [epidemiology; prevention & control]; Randomized Controlled Trials; Sexually Transmitted Diseases [epidemiology; *prevention & control]

MeSH check words

Humans

COVER SHEET

Title Population-based interventions for reducing sexually transmitted infections, including HIV infection

Authors	Sangani P, Rutherford G, Wilkinson D
Contribution of author(s)	Information not supplied by author
Issue protocol first published	/
Review first published	/
Date of most recent amendment	09 November 2004
Date of most recent SUBSTANTIVE amendment	26 February 2004
What's New	Information not supplied by author
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Prof David Wilkinson Pro Vice Chancellor and Vice President Division of Health Sciences University of South Australia North Terrace, Adelaide South Australia 5000 AUSTRALIA E-mail: david.wilkinson@unisa.edu.au Tel: +61 8 8302 2029 Fax: +61 8 8302 2030
DOI	10.1002/14651858.CD001220.pub2
Cochrane Library number	CD001220
Editorial group	Cochrane HIV/AIDS Group
Editorial group code	HM-HIV

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Any intervention vs control, Outcome 01 HIV incidence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 01 Any intervention vs control

Outcome: 01 HIV incidence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
001 Wawer	101/4927	89/4449		54.0	1.02 [0.77, 1.36]
004 Grosskurth	48/4149	82/4400		46.0	0.62 [0.44, 0.88]
Total (95% CI)	9076	8849		100.0	0.84 [0.67, 1.04]
Total events: 149 (Treatment), 171 (Control)					
Test for heterogeneity chi-square=4.72 df=1 p=0.03 I^2 =78.8%					
Test for overall effect z=1.57 p=0.1					

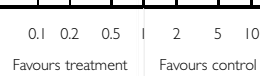
Analysis 01.02. Comparison 01 Any intervention vs control, Outcome 02 STD prevalence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 01 Any intervention vs control

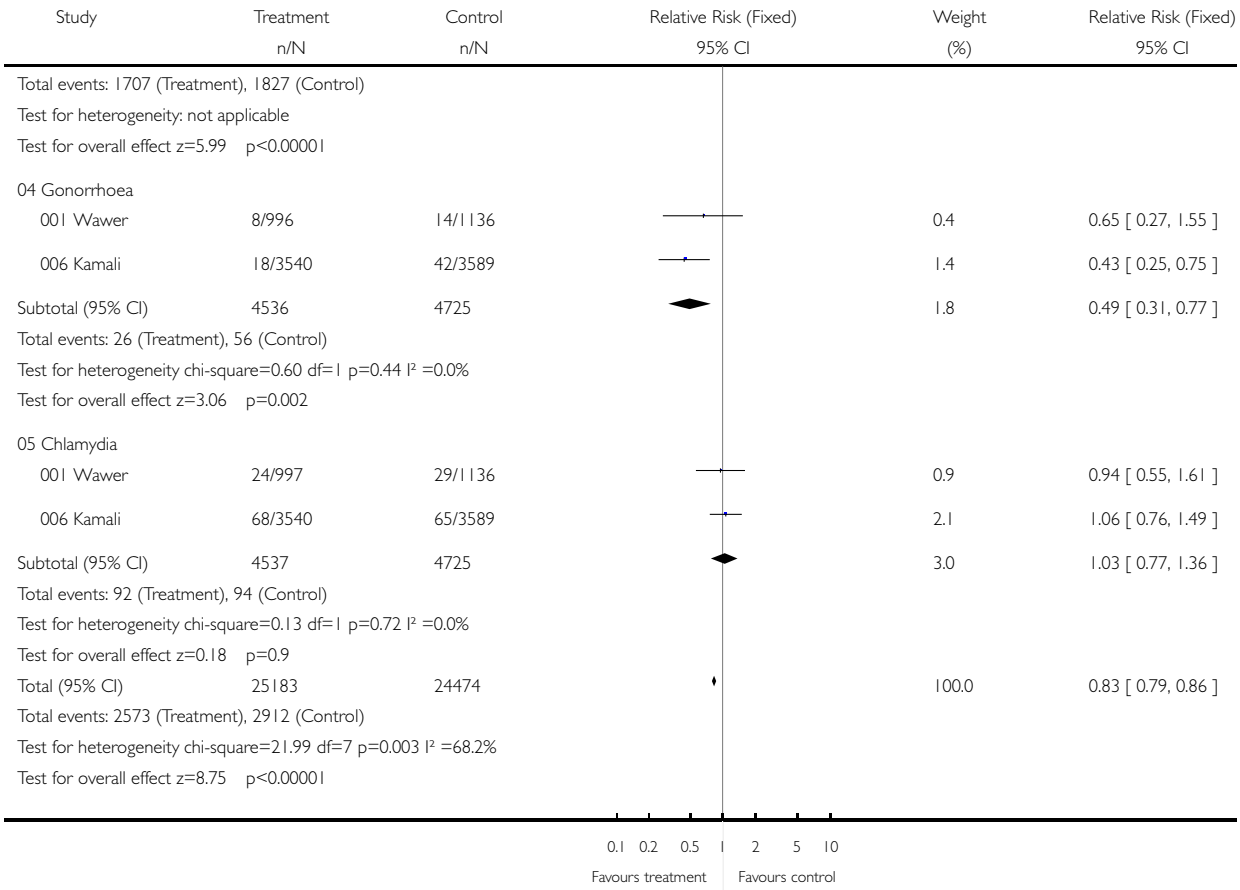
Outcome: 02 STD prevalence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Syphilis					
001 Wawer	352/6238	359/5284		12.9	0.83 [0.72, 0.96]
005 Mayaud	214/4244	315/4528		10.1	0.72 [0.61, 0.86]
Subtotal (95% CI)	10482	9812		23.1	0.78 [0.70, 0.87]
Total events: 566 (Treatment), 674 (Control)					
Test for heterogeneity chi-square=1.46 df=1 p=0.23 I^2 =31.7%					
Test for overall effect z=4.39 p=0.00001					
02 Trichomoniasis					
001 Wawer	182/1968	261/1815		9.0	0.64 [0.54, 0.77]
Subtotal (95% CI)	1968	1815		9.0	0.64 [0.54, 0.77]
Total events: 182 (Treatment), 261 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.86 p<0.00001					
03 Bacterial Vaginosis					
001 Wawer	1707/3660	1827/3397		63.0	0.87 [0.83, 0.91]
Subtotal (95% CI)	3660	3397		63.0	0.87 [0.83, 0.91]



(*Continued . . .*)

(. . . *Continued*)



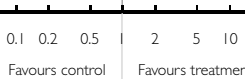
Analysis 01.03. Comparison 01 Any intervention vs control, Outcome 03 Quality of treatment

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 01 Any intervention vs control

Outcome: 03 Quality of treatment

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Number correctly treated					
002 Garcia	2/172	1/176		0.9	2.05 [0.19, 22.36]
003 Harrison	42/48	25/50		22.7	1.75 [1.30, 2.36]
Subtotal (95% CI)	220	226		23.7	1.76 [1.30, 2.38]
Total events: 44 (Treatment), 26 (Control)					
Test for heterogeneity chi-square=0.02 df=1 p=0.90 I^2 =0.0%					
Test for overall effect z=3.68 p=0.0002					
02 Number correctly examined					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 Number given partner notification cards					
× 002 Garcia	0/172	0/176		0.0	Not estimable
003 Harrison	40/48	6/50		5.5	6.94 [3.24, 14.87]
Subtotal (95% CI)	220	226		5.5	6.94 [3.24, 14.87]
Total events: 40 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.99 p<0.00001					
04 Number given condoms					
× 002 Garcia	0/172	0/176		0.0	Not estimable
003 Harrison	40/48	6/50		5.5	6.94 [3.24, 14.87]
Subtotal (95% CI)	220	226		5.5	6.94 [3.24, 14.87]
Total events: 40 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.99 p<0.00001					
05 Number counselled					
002 Garcia	69/172	48/176		44.1	1.47 [1.09, 1.99]
003 Harrison	34/50	23/50		21.4	1.48 [1.04, 2.11]
Subtotal (95% CI)	222	226		65.4	1.47 [1.17, 1.86]
Total events: 103 (Treatment), 71 (Control)					
Test for heterogeneity chi-square=0.00 df=1 p=0.98 I^2 =0.0%					
Test for overall effect z=3.24 p=0.001					



(*Continued . . .*)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	882	904		100.0	2.14 [1.79, 2.55]
Total events: 227 (Treatment), 109 (Control)					
Test for heterogeneity chi-square=30.17 df=5 p=<0.0001 I^2 =83.4%					
Test for overall effect z=8.38 p<0.00001					

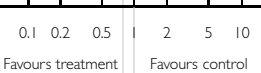
Analysis 01.05. Comparison 01 Any intervention vs control, Outcome 05 Safer sexual behaviour

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 01 Any intervention vs control

Outcome: 05 Safer sexual behaviour

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Reduced frequency of partner change					
001 Wawer	964/6143	826/5543		49.5	1.05 [0.97, 1.15]
004 Grosskurth	138/464	135/503		7.4	1.11 [0.91, 1.35]
Subtotal (95% CI)	6607	6046		56.9	1.06 [0.98, 1.15]
Total events: 1102 (Treatment), 961 (Control)					
Test for heterogeneity chi-square=0.21 df=1 p=0.65 I^2 =0.0%					
Test for overall effect z=1.45 p=0.1					
02 Regular condom use with casual partners					
001 Wawer	848/6143	593/5543		35.6	1.29 [1.17, 1.42]
006 Kamali	156/218	128/205		7.5	1.15 [1.00, 1.31]
Subtotal (95% CI)	6361	5748		43.1	1.27 [1.16, 1.38]
Total events: 1004 (Treatment), 721 (Control)					
Test for heterogeneity chi-square=2.21 df=1 p=0.14 I^2 =54.7%					
Test for overall effect z=5.42 p<0.00001					
03 Average age of sexual debut					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	12968	11794		100.0	1.15 [1.08, 1.22]
Total events: 2106 (Treatment), 1682 (Control)					
Test for heterogeneity chi-square=9.45 df=3 p=0.02 I^2 =68.2%					
Test for overall effect z=4.70 p<0.00001					



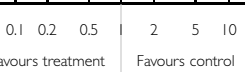
Analysis 02.01. Comparison 02 STD mass treatment vs placebo, Outcome 01 HIV incidence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 02 STD mass treatment vs placebo

Outcome: 01 HIV incidence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
001 Wawer	101/4927	89/4449		100.0	1.02 [0.77, 1.36]
Total (95% CI)	4927	4449		100.0	1.02 [0.77, 1.36]
Total events: 101 (Treatment), 89 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.17 p=0.9					



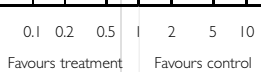
Analysis 02.02. Comparison 02 STD mass treatment vs placebo, Outcome 02 STD prevalence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 02 STD mass treatment vs placebo

Outcome: 02 STD prevalence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Syphilis					
001 Wawer	352/6238	359/5284		15.0	0.83 [0.72, 0.96]
Subtotal (95% CI)	6238	5284		15.0	0.83 [0.72, 0.96]
Total events: 352 (Treatment), 359 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.56 p=0.01					
02 Trichomoniasis					
001 Wawer	182/1968	261/1815		10.5	0.64 [0.54, 0.77]
Subtotal (95% CI)	1968	1815		10.5	0.64 [0.54, 0.77]
Total events: 182 (Treatment), 261 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.86 p<0.00001					
03 Bacterial Vaginosis					
001 Wawer	1707/3660	1827/3397		73.0	0.87 [0.83, 0.91]
Subtotal (95% CI)	3660	3397		73.0	0.87 [0.83, 0.91]
Total events: 1707 (Treatment), 1827 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.99 p<0.00001					
04 Gonorrhoea					



(*Continued . . .*)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
001 Wawer	8/996	14/1136		0.5	0.65 [0.27, 1.55]
Subtotal (95% CI)	996	1136		0.5	0.65 [0.27, 1.55]
Total events: 8 (Treatment), 14 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.97 p=0.3					
05 Chlamydia					
001 Wawer	24/997	29/1136		1.0	0.94 [0.55, 1.61]
Subtotal (95% CI)	997	1136		1.0	0.94 [0.55, 1.61]
Total events: 24 (Treatment), 29 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.22 p=0.8					
Total (95% CI)	13859	12768		100.0	0.84 [0.80, 0.88]
Total events: 2273 (Treatment), 2490 (Control)					
Test for heterogeneity chi-square=11.08 df=4 p=0.03 I^2 =63.9%					
Test for overall effect z=7.82 p<0.00001					

Analysis 02.04. Comparison 02 STD mass treatment vs placebo, Outcome 04 Treatment seeking behaviour / service use

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 02 STD mass treatment vs placebo

Outcome: 04 Treatment seeking behaviour / service use

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Number seeking care					
001 Wawer	1229/6143	909/5543		100.0	1.22 [1.13, 1.32]
Subtotal (95% CI)	6143	5543		100.0	1.22 [1.13, 1.32]
Total events: 1229 (Treatment), 909 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.02 p<0.00001					
02 Symptom duration					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

(*Continued* . . .)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
03 Number of contacts treated					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	6143	5543	♦	100.0	1.22 [1.13, 1.32]
Total events: 1229 (Treatment), 909 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.02 p<0.00001					

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

Analysis 02.05. Comparison 02 STD mass treatment vs placebo, Outcome 05 Safer sexual behaviour

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 02 STD mass treatment vs placebo

Outcome: 05 Safer sexual behaviour

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Reduced frequency of partner change					
001 Wawer	964/6143	826/5543	■	58.2	1.05 [0.97, 1.15]
Subtotal (95% CI)	6143	5543	♦	58.2	1.05 [0.97, 1.15]
Total events: 964 (Treatment), 826 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.19 p=0.2					
02 Regular condom use with casual partners					
001 Wawer	848/6143	593/5543	■	41.8	1.29 [1.17, 1.42]
Subtotal (95% CI)	6143	5543	♦	41.8	1.29 [1.17, 1.42]
Total events: 848 (Treatment), 593 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.08 p<0.00001					
03 Average age of sexual debut					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	12286	11086	♦	100.0	1.15 [1.08, 1.23]
Total events: 1812 (Treatment), 1419 (Control)					
Test for heterogeneity chi-square=9.33 df=1 p=0.002 I^2 =89.3%					
Test for overall effect z=4.31 p=0.00002					

0.1 0.2 0.5 1 2 5 10

Favours treatment Favours control

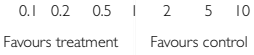
Analysis 03.01. Comparison 03 Improved STD syndromic management vs usual care, Outcome 01 HIV incidence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 03 Improved STD syndromic management vs usual care

Outcome: 01 HIV incidence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
004 Grosskurth	48/4149	82/4400		100.0	0.62 [0.44, 0.88]
Total (95% CI)	4149	4400		100.0	0.62 [0.44, 0.88]
Total events: 48 (Treatment), 82 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.64 p=0.008					



Analysis 03.02. Comparison 03 Improved STD syndromic management vs usual care, Outcome 02 STD prevalence

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 03 Improved STD syndromic management vs usual care

Outcome: 02 STD prevalence

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Syphilis					
005 Mayaud	214/4244	315/4528		100.0	0.72 [0.61, 0.86]
Subtotal (95% CI)	4244	4528		100.0	0.72 [0.61, 0.86]
Total events: 214 (Treatment), 315 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.74 p=0.0002					
02 Trichomoniasis					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 Bacterial Vaginosis					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
04 Gonorrhoea					
Subtotal (95% CI)	0	0		0.0	Not estimable

(*Continued* . . .)

(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
05 Chlamydia					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	4244	4528		100.0	0.72 [0.61, 0.86]
Total events: 214 (Treatment), 315 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.74 p=0.0002					

Analysis 03.03. Comparison 03 Improved STD syndromic management vs usual care, Outcome 03 Quality of treatment

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

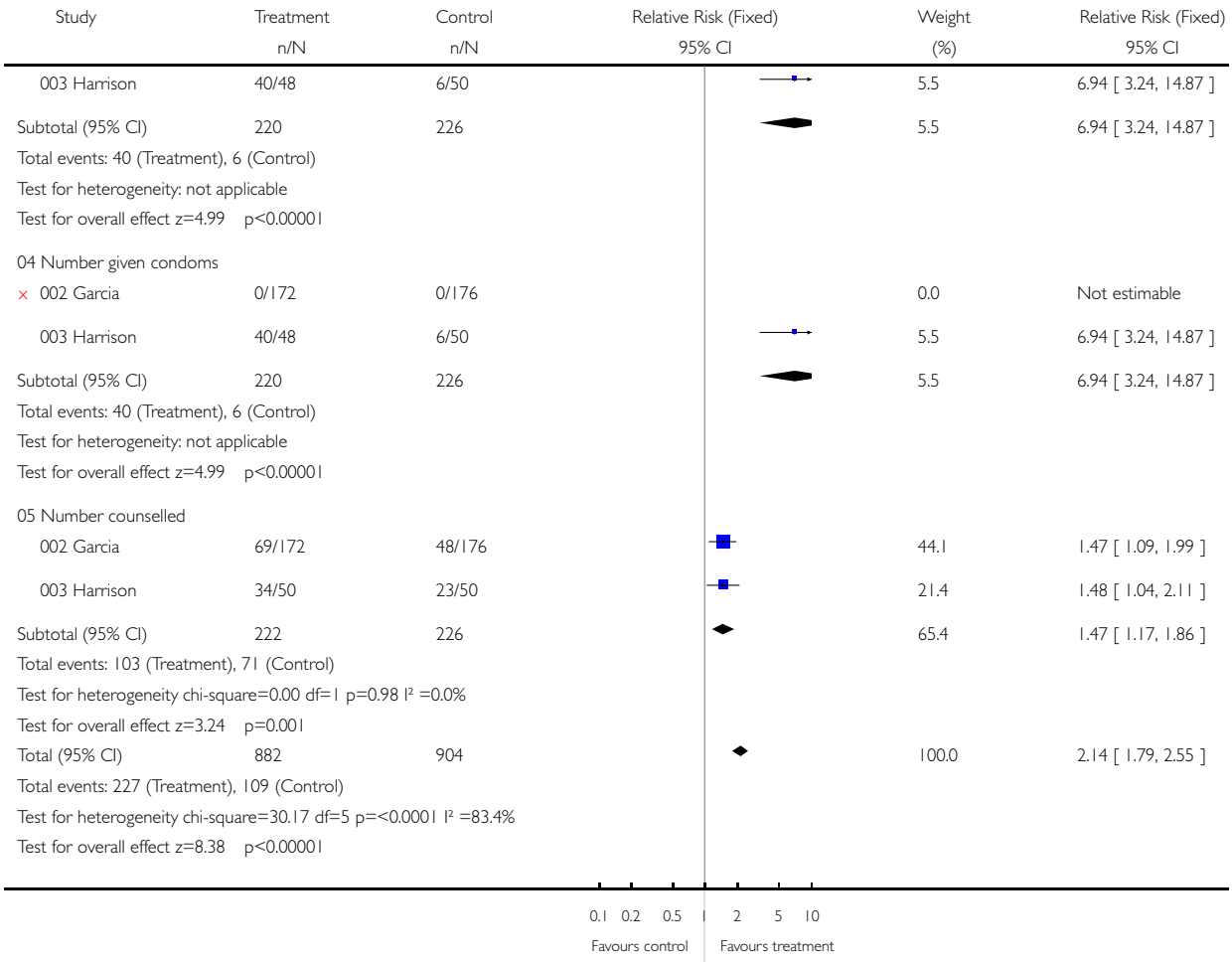
Comparison: 03 Improved STD syndromic management vs usual care

Outcome: 03 Quality of treatment

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Number correctly treated					
002 Garcia	2/172	1/176		0.9	2.05 [0.19, 22.36]
003 Harrison	42/48	25/50		22.7	1.75 [1.30, 2.36]
Subtotal (95% CI)	220	226		23.7	1.76 [1.30, 2.38]
Total events: 44 (Treatment), 26 (Control)					
Test for heterogeneity chi-square=0.02 df=1 p=0.90 I^2 =0.0%					
Test for overall effect z=3.68 p=0.0002					
02 Number cured					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 Number given partner notification cards					
× 002 Garcia	0/172	0/176		0.0	Not estimable

(*Continued* . . .)

(... *Continued*)



Analysis 03.05. Comparison 03 Improved STD syndromic management vs usual care, Outcome 05 Safer sexual behaviour

Review: Population-based interventions for reducing sexually transmitted infections, including HIV infection

Comparison: 03 Improved STD syndromic management vs usual care

Outcome: 05 Safer sexual behaviour

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Reduced frequency of partner change					
004 Grosskurth	138/464	135/503		100.0	1.11 [0.91, 1.35]
Subtotal (95% CI)	464	503		100.0	1.11 [0.91, 1.35]
Total events: 138 (Treatment), 135 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.00 p=0.3					
02 Regular condom use with casual partners					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 Average age of sexual debut					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	464	503		100.0	1.11 [0.91, 1.35]
Total events: 138 (Treatment), 135 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.00 p=0.3