Population-based biomedical sexually transmitted infection control interventions for reducing HIV infection

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This review did not find evidence to support the hypothesis that interventions to control sexually transmitted infections are an effective HIV prevention strategy at the population level. However, some of the interventions studied reduced the prevalence of syphilis and gonorrhoea at the population level.

RHL commentary by Low N

1. INTRODUCTION

It has been reported that bacterial and viral sexually transmitted infections (STIs) increase the transmissibility of and susceptibility to HIV (1). Hence, it has been postulated that treating people with STIs could contribute to reducing HIV transmission. There are about 30 million people living with HIV infection, two thirds of whom live in sub-Saharan Africa (2). There are about 340 million new cases of curable sexually transmitted infections (chlamydia, gonorrhoea, syphilis, trichomoniasis) each year (3). The majority of these also occur in sub-Saharan Africa. Because of the common route of transmission through sexual networks, interventions against STIs need to be targeted to whole populations. Grosskurth and colleagues conducted the first cluster randomized population-based trial in Mwanza, United Republic of Tanzania, from 1991 to 1994, providing improved routine health-care services for syndromic management of people with symptoms of STIs (4). They found that the incidence of HIV infection two years later was 42% lower in villages receiving the intervention compared with those that did not.

The primary objective of this Cochrane review was to determine the impact of population-based biomedical STI interventions on the incidence of HIV infection in the general population. Secondary objectives were to determine the impact of the intervention on: STI incidence; utilization of STI treatment services and partner treatment rates; quality of STI treatment services; and safer sexual behaviour, including condom use. This is an update of a Cochrane review that was first published in 1998 and last updated in 2004 (5).

2. METHODS OF THE REVIEW

The literature search was comprehensive and is unlikely to have missed important studies. The review authors' search included six major electronic databases including The Cochrane Library from 1980 to 16 August 2010, selected conference abstracts and trials registers without language or geographical restrictions. The results of the searches were screened by independent reviewers. Two authors selected studies for inclusion from 46 full text articles. Two authors extracted the data and assessed the risk of bias using the Cochrane Collaboration tool.

The authors included community-randomized controlled trials studying a population-based intervention with
HIV incidence as the primary outcome. Excluded were: individually randomized trials, trials in sub-populations such as sex workers, injection drug users, men who have sex with men, adolescents, etc., and interventions that the review authors described as 'primarily behavioural in nature'. The authors used the following definitions:

- 'Population-based biomedical STI interventions' as programmes and activities that include treatment or prophylaxis of STIs with antibiotics, antiviral medications or devices such as condoms or diaphragms. Such programmes and activities may or may not encompass other population-based STI interventions.
- Community as 'a group of villages, an arbitrary geographical division, or the catchments population of a group of health facilities'. The authors excluded studies that were based on schools, bars, restaurants, community centres or any other similar venues. Also excluded were studies that were focused on a single high-risk subpopulation, such as sex workers or men who have sex with men.

The above definitions are important for defining the scope of this review. Population-based biomedical STI interventions clearly focused on STI treatment for the general population by improving routine services (4) or by providing mass treatment (6). Since then, integrated interventions have become more common with information, education and communication (7) and peer-led education (8) to promote behavioural change in addition to STI services. Furthermore, the target population for the behavioural intervention by Gregson et al. comprised sex workers and their clients (8), which was not apparent from the text of the review.

Additional information in the 'reasons for exclusion' would have been helpful to explain why some studies providing improved STI services were excluded for being 'primarily behavioural'. The details provided about included trials in the text, tables and figures were not always consistent so the studies were sometimes difficult to compare.

The authors synthesized the results using fixed or random effects meta-analysis to estimate pooled risk ratios (RR) with 95% confidence intervals (CI). Heterogeneity was assessed using chi-square tests and the I-squared statistic. The authors report the importance of intracluster correlation coefficient to take into account the effect of clustering for the primary outcome. Original data were used for the STI outcomes because data on intracluster coefficients were not available. The results would have been easier to understand with some additional explanation, for example: (i) that applying the intracluster correlation coefficient results in numbers of events and denominators in the forest plots that differ from those in the original publications; (ii) how original results presented as incidence rates per 100 person years are converted to risks; and (iii) for each STI outcome, the diagnostic definition, the sub-population tested and whether pooled results refer to prevalence or incidence.

3. RESULTS OF THE REVIEW

The review includes four cluster randomized controlled trials conducted in sub-Saharan Africa. One new trial (8) has been added, while two from the previous review have been excluded based on the revised inclusion criteria. The approximate total number of participants in the four trials were: 11 000 adults in 12 communities in eastern Zimbabwe (men aged 17–54, women aged 15-44 years) (8); 12 000 women and men aged 15–54 years in 12 communities in Mwanza, United Republic of Tanzania (4); 20 000 women and men aged 13–65 years in 18 communities in Masaka, Uganda (7); 14 000 women and men aged 15–59 in 10 communities in Rakai, Uganda (6). The authors rated the risk of bias for most of the domains of allocation, blinding and loss-to-follow-up as low but noted a high risk of 'other biases' in all trials.

There was no evidence of a reduction in HIV incidence when the results of all trials were pooled (RR 0.93, 95% CI 0.67–1.31, random effects model, I-squared 51%). One individual trial showed statistical evidence of a reduction in HIV incidence, with an adjusted RR of 0.58 (95% CI 0.42–0.79) (4). There was no statistical evidence of a reduction in any of the other individual trials. The results were presented separately with the three trials providing improved STI care (pooled RR 0.88, 95% CI 0.52–1.49, I-squared 67%) and the mass treatment trial (RR 1.02, 95% CI 0.71–1.46).
There was evidence of a reduction in the prevalence of any syphilis diagnosis in the intervention group at the end of the trial in two trials (pooled RR 0.88, 95% CI 0.80–0.96, I-squared 12%). Grosskurth measured active syphilis (4), and Wawer measured both current and past syphilis (6). The incidence of high titre (rapid plasma reagin test ?1:8) active syphilis fell in another trial (7) (RR 0.53, 95% CI 0.33–0.84).

Two trials measured the prevalence of gonorrhoea and chlamydia in a subset of the study populations (6, 7). There was evidence of a reduction in the prevalence of gonorrhoea (pooled RR 0.49, 95% CI 0.31–0.77, I-squared 0.0%). For chlamydia, the authors report a pooled RR of 1.03 (95% CI 0.77–1.36, I-squared 0.0%), comparing prevalence at the end of the trial in intervention compared with the control arm. In the original publication by Wawer et al., the intervention did seem to have had an effect on chlamydia (6). However, the baseline chlamydia prevalence was higher in the intervention (4.0%) than in the control arm (2.2%) (prevalence ratio 1.50, 95% CI 1.08–2.08). At the last assessment, chlamydia prevalence had fallen in the intervention arm (to 2.4%) and increased (to 2.6%) in the control group.

One trial (6) reported on trichomonas prevalence in the intervention compared with the control group (adjusted RR 0.59, 95% CI 0.71–0.91) and bacterial vaginosis (adjusted RR 0.87, 95% CI 0.74–1.02) at the end of the trial.

Data on two sexual behaviour measures were combined. Regular condom use increased in those receiving the intervention (pooled RR 1.2, 95% CI 1.04–1.3, I-squared 80%, 3 trials). There was an increase in the proportion of people reporting two or more sexual partners in the past year. All four studies measured the percentage of people (pooled RR 1.1, 95% CI 1.01–1.1, I-squared 0.0%, 4 trials). No results for two stated objectives were presented: utilization of STI treatment services or quality of STI treatment services.

3.1 Effects of specific interventions

4. DISCUSSION

The findings of this review do not support the hypothesis that STI control interventions can serve as an effective HIV prevention strategy at the population level. The interventions do, however, have an effect at the population level on certain STI. For example, the interventions studied reduced the prevalence of syphilis and gonorrhoea. There was insufficient evidence to draw conclusions about their effect on chlamydia, trichomonas and bacterial vaginosis.

4.1 Applicability of the results

The findings of the review are applicable to resource-poor settings with limited health-care infrastructure. All the trials were conducted in sub-Saharan Africa and included rural areas and small towns. The lack of an effect on HIV incidence is probably generalizable to settings where HIV infection has become endemic or where STI prevalence is low. The trial which showed a reduction in HIV incidence was the first to be done and was conducted in rural Tanzania when HIV prevalence was relatively low (4%) but the prevalence of curable, particularly ulcerative STI was high (4). The reasons for the differences between the results of the Mwanza and subsequent trials have been discussed extensively. The consensus of opinion is that HIV transmission in the later three trials was established, baseline prevalence ranged from 10% to >20%, and much of the exposure to HIV infection occurred within discordant couples. The fraction of new HIV infections attributable to STI co-infections in these settings was likely to be much lower than in Mwanza.

4.2 Implementation of the intervention

Strengthening of STI treatment services should be promoted because of the potential benefits in reducing the prevalence of curable STI. The STI interventions in Mwanza, Masaka and eastern Zimbabwe focused on feasible and sustainable activities in existing health services to improve the delivery of syndromic
management through training of health-care staff, regular supplies of treatment and condoms and supervisory visits (4, 7, 8). Periodic mass treatment as evaluated in Rakai, Uganda, is not a sustainable intervention at the population level but did provide treatment for asymptomatic as well as symptomatic STIs (6). Syndromic management for potential STIs is not appropriate in all settings, especially where the prevalence of STIs is low and overtreatment of symptoms not caused by STIs might do more harm than good.

It is not possible to disentangle the contributions of the parts of the interventions aimed at changing sexual behaviour from those providing STI treatment. All communities in both intervention and control groups of all trials received ongoing health education activities. It is not clear whether or not the intensive information, education and communication activities targeted to the whole population in Masaka and to sex workers and their clients in eastern Zimbabwe provided additional benefits.

4.3. Implications for research

Further research should be conducted to evaluate the benefits of improved STI case management in Asia and the Americas as well as in sub-Saharan Africa. The effectiveness of partner notification and the balance of benefits and harms in resource-poor settings should be further investigated. Partner notification offers substantial benefits for case-finding and preventing STI re-infection in index cases, even if an effect on reducing STI prevalence at the population level has not been shown (9). Partner notification was not stressed as a component of the STI interventions in the trials in this review. The role of point-of-care tests for the diagnosis of syphilis, chlamydia and gonorrhoea as part of STI control programmes also merits further investigation in settings where the specificity of syndromic diagnosis needs to be improved, or where syndromic management is of limited value (10).

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References

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