Randomized controlled trials of interventions to prevent sexually transmitted infections:
learning from the past to plan for the future

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CRD summary
The authors found that most of a wide range of interventions were efficacious in preventing infection with at least one STI. Treatment interventions and vaccines showed the greatest effects. Shortcomings in the review process, a lack of patient and study details, limited outcome data and wide variation among the included studies mean the authors’ conclusions should be interpreted with caution.

Authors’ objectives
To assess the effectiveness of interventions aimed at the prevention of sexually transmitted infections (STIs) other than the human immunodeficiency virus (HIV).

Searching
PubMed was searched from January 2004 to December 2009 for randomised controlled trials (RCTs) published in English. Search terms were reported. Additional studies published earlier were identified and considered for inclusion from another review (Manhart and Holmes 2005).

Study selection
Eligible studies were RCTs that evaluated the effectiveness of interventions to prevent transmission or acquisition of prospectively evaluated laboratory confirmed STIs. Trials with HIV as the only endpoint and trials designed to prevent STI-related pregnancy, puerperal and neonatal morbidity and other STI-related complications were excluded.

In the included studies, interventions were categorised as behavioural (risk reduction counselling, skills building), vaginal microbicides (nonoxynol-9 or cellulose sulfate gel mostly targeted at female sex workers), vaccines (passive and active, mostly assessed in USA and other high-income countries), treatment (periodic presumptive treatment, enhanced syndromic treatment, post exposure prophylaxis), partner services (undertaken in industrialised countries), physical barrier methods (male or female condom, diaphragm or gel given in low- to middle-income countries), male circumcision (undertaken in sub-Saharan Africa) and multicomponent interventions (provision of peer risk reduction counseling, youth-friendly clinical STI services, family planning and STI case management provided to schools, health facilities and communities in Africa). Some behavioural interventions were compared to risk reduction counseling or health promotion control conditions. All participants in trials of physical barrier methods received male condoms. No other details on control groups were provided.

Three reviewers independently undertook study selection.

Assessment of study quality
Follow-up rates, adherence to treatment, ongoing risk behaviours and analysis techniques were assessed.

The authors did not state how quality assessment was undertaken.

Data extraction
Data were extracted on incidence or prevalence of laboratory documented STIs according to intervention type. When multiple intervention estimates were presented, adjusted rather than crude estimates were extracted. Estimates were extracted on intention-to-treat analyses rather than per protocol analyses. The last available time point was extracted where outcomes were assessed at multiple time points.

The authors did not state how many reviewers performed data extraction.
Methods of synthesis
Studies were synthesised qualitatively in narrative format by counting the numbers of studies that found positive, adverse and no effects on risk.

Results of the review
Ninety-three publications reporting data from 74 RCTs that evaluated 75 STI prevention interventions (numbers of participants not reported) were included in the review. The authors reported that study quality was high overall. Follow-up rates ranged from 30% to 100%.

Behavioural interventions: Seventeen (reported as 18 in a table) out of 27 interventions found positive effects on STI risk. One intervention showed negative effects and nine showed no effect. Positive effects ranged from 9% to 83%. Subgroup analyses included individual versus group therapy, skills building interventions versus interventions without skills building and risk reduction counseling control groups versus general health promotion control groups. Where reported, adherence rates ranged from 47% to 100%.

Physical barrier methods: Four studies found no effects on STI risk when compared with standard male condoms with or without risk reduction information and education. Where reported, adherence rates ranged from 7% to 97%.

Vaginal microbicides: Three out of 12 studies found a positive effect on STI risk. Two studies found an adverse effect and seven studies found no effect. Where reported, adherence rates ranged from 47% to 90%.

Male circumcision: Three out of four studies found a positive effect on STI risk and one study found no effect.

Partner services: Four out of seven studies found a positive effect on STI risk and three studies found no effect. Where reported, adherence ranged from 25% to 88%.

Treatment: Seven of eight studies found a positive effect on STI risk and one study found no effect. Positive effects ranged from 30% to 60% reduction in risk. Where reported, adherence ranged from 70% to 100%.

Vaccines and passive immunization: Ten out of 12 studies found a positive effect on STI risk and two studies found no effect. Where reported, adherence ranged from 76% to 100%.

Multicomponent interventions: One study found an adverse effect on STI risk as a result of a multicomponent intervention. Adherence rates were not reported.

Where possible, the authors reported outcomes for different STI infections.

Authors’ conclusions
Fifty-nine per cent of interventions demonstrated efficacy in preventing infection with at least one STI. Treatment interventions and vaccines showed the greatest effects. Future prevention efforts should focus on enhancing adherence within interventions, integrating new technologies, ensuring sustainable behaviour change and conducting implementation research.

CRD commentary
The review addressed a clear research question. Inclusion criteria appeared appropriate. Limited searching of one electronic database was undertaken with appropriate search terms but restricted to studies in English, so language and publication bias could not be excluded. Studies identified from this search were added to those published in a previous review (Manhart and Holmes 2005). Appropriate methods were described for selection of studies, but methods for data extraction and quality assessment were not reported. The number of participants was not reported, so the sample size was unclear. For most RCTs, the nature of interventions received by the control groups was not reported. The quality of the included studies was assessed. Follow-up rates appeared generally high, but adherence to interventions and changes from baseline in risk-taking behaviour were not reported for all studies. The authors acknowledged poor reporting in the included studies. Most analyses took into account the contribution of person-time, whether correlated data methods were used and testing frequency. Qualitative synthesis in narrative format was appropriate as studies varied widely; the authors counted the numbers of studies that found positive effects on STI risk and where possible the range of
reduction in risk. Some of the intervention results (such as male circumcision and vaccines) included reference numbers for studies not included in the included studies for the review.

Shortcomings in the review process, a lack of patient and study details, limited outcome data and wide variation among the included studies mean the authors’ conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that the extent to which findings from RCTs of individual STI prevention approaches were generalisable to non-study settings and the feasibility of population-level scale-up of these individual interventions were unclear; they suggested that implementation research should continue to assess these carefully.

**Research:** The authors stated that future efforts should focus on enhancing adherence within interventions, integrating new technologies, ensuring sustainable behaviour change and conducting implementation research.

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Manhart LE, Holmes KK. Randomised controlled trials of individual-level, population-level, and multilevel interventions for preventing sexually transmitted infections: what has worked? Journal of Infectious Diseases 2005; 191(suppl 1):S7-S24

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