

**Summary Statement Title:**

**Individual-level, population-level, and multilevel interventions for preventing sexually transmitted infections: Evidence and implications for public health**

**Quality Assessment Rating: 7 (moderate)**

**Review on which this summary statement is based:**

Manhart, L.E., & Holmes, K.K. (2005). **Randomized controlled trials of individual-level, population-level, and multilevel interventions for preventing sexually transmitted infections: What has worked?** *Journal of Infectious Diseases*, 191, S7-S24.

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*This is a summary statement written to condense the work of the authors of this systematic review, referenced above. The intent of this summary is to provide an overview of the findings and implications of the full review. For more information on individual studies included in the review, please see the review itself.*

**Review content summary**

This review of 41 randomized trials aimed to examine individual-level, population-level, and multi-level interventions to prevent sexually transmitted infections (STI). Outcomes of interest included those targeting individuals (28 interventions), groups (9 interventions), and communities (4 interventions). The review also examined biological markers of prospectively measured STI outcomes in all studies. In 22 included trials (54%), interventions resulted in reduced acquisition, transmission, or complications of STIs; however, only one of these studies reported intervention efficacy against sexual transmission of HIV. The four interventions most often used included behavior change, vaccination, use of topical microbicides and prophylactic, curative, or suppressive therapy. The review authors stress that public health agencies must give more attention to rigorous evaluation of the effectiveness of successful intervention strategies during scale-up and implementation in new settings, as well as trials of new interventions.

**Comments on this review's methodology**

This is a methodologically moderate systematic review. Inclusion criteria were clearly stated. A search strategy was employed and included: bibliographic databases searches on MEDLINE and the Cochrane Central Register of Controlled Trials; recent unpublished presentations through 2003; and searching reference lists of included publications. The search strategy could have been made more comprehensive by including additional databases and other sources of published literature, contacting key experts, and hand searching relevant journals. A thorough outline of interventions ordered by level of intervention (individual, group, or community), modality of intervention (e.g., behavior change, vaccine, topical microbicide, or treatment), and type of outcome measured (acquisition, transmission, or complications) was presented in tables. While methodological quality of the review's studies was considered, it was not assessed independently. Throughout their discussion of individual studies, review authors did not use study quality to weight their recommendations.

**Why this issue is of interest to public health**

Since 1997 there has been a gradual but widespread escalation in the rates of chlamydial and gonococcal infection along with outbreaks of infectious syphilis and a rise in both new HIV diagnoses and in HIV incidence estimates for men who have sex with men.<sup>1</sup> The best example of STI resurgence in Canada is the reported rate of gonorrhea. In 1997 the declining trend in both sexes reversed, so that Canada in 2000 was back to a rate of 20.1 per 100,000 population, an increase of 35% since 1997.<sup>1</sup> Previously considered rare in Canada, infectious syphilis is also on the rise with 463 cases reported in Canada for 2002, and a staggering 1493 cases reported in 2006.<sup>1</sup> Notably, the STI resurgence is occurring in high-risk populations (e.g., sex trade workers, intravenous drug users) for which traditional public health interventions (partner notification and treatment, screening, health promotion) are less effective. In light of the asymptomatic nature of a number of STIs, and the fact that previous STI infection increases risk of a subsequent STI, preventive efforts prove undeniably valuable.<sup>1,2</sup>

**Evidence and implications**

Evidence points presented in the table below are not ranked (or weighted) according to strength.

What's the evidence?	Implications for practice and policy:
<p><b>1. Individual-level: Prevention of Acquisition (23 interventions)</b></p> <p><b>1.1. Behaviour change (4 studies)</b>  The most frequently used approach for behaviour change was risk reduction counselling and these studies show mixed results:</p> <p>1.1.1. Participants receiving counselling experienced a significantly greater reduction in STIs (20%) over a 12-month period as compared with those receiving didactic messages (p=0.008). In this study, participants with ≥ 3 partners were 1.9 times more likely to have incident STI than those who had fewer partners and those who had ≥ 6 episodes of unprotected sex with an occasional partner were 1.9 times more likely to have incident STI than those who had fewer such episodes.</p> <p>1.1.2. Participants receiving counselling were no more or less likely to acquire STIs than controls (p=0.20 for each of men and women). In this study, participants receiving counselling were less likely than controls to have unprotected sex at 3 months (p&lt;0.05) and no more or less likely than controls to have unprotected sex at 5 months.</p> <p>1.1.3. Participants who received counselling were no more or less likely to experience a reduction in STI than those receiving health information (OR 0.8, 95%CI 0.53 to 1.20).</p> <p>1.1.4. Participants receiving more intensive counselling with booster sessions were no more or less likely to acquire HIV than those who received less frequent sessions (OR 0.8, 95%CI 0.66 to 1.08). However, participants in this study receiving more frequent counselling were less likely to have unprotected anal intercourse than controls (OR 0.9, 95%CI 0.79 to 0.94), less likely to have unprotected anal intercourse between sero-discordant men who have sex with men (MSM) (OR 0.9, 95%CI 0.78 to 0.94), and less likely to have unprotected receptive anal intercourse with HIV-positive partners or those for whom HIV status is unknown (OR 0.8, 95%CI 0.71 to 0.89).</p> <p><b>1.2. Oral antimicrobial prophylaxis (2 studies)</b></p> <p>1.2.1. Participants receiving prophylactic minocycline experienced greater reductions in incident gonorrhoea than those receiving placebos. However, men who received the prophylaxis but who acquired gonorrhoea were more likely to have drug-resistant strains of the infection. No effect size data was provided.</p> <p>1.2.2. Participants receiving monthly azithromycin were significantly less likely to acquire gonorrhoea, chlamydial infection, or trichomoniasis, but no more or less like to acquire HIV. No effect size data was provided.</p> <p><b>1.3. STI vaccines or passive immunization (7 studies)</b></p> <p><b>1.3.1. Inactivated hepatitis B virus (HBV) vaccine (3 studies)</b>  High levels (85%-100%) of vaccine efficacy were reported, particularly after administration of all 3 doses. Participants receiving the vaccine were also significantly less likely to acquire HBV compared with those receiving placebos.</p> <p><b>1.3.2. Immunoglobulin against hepatitis C virus (HCV) (1 study)</b>  Participants who received intramuscular injections of serum immunoglobulin every 2 months were significantly less likely to acquire HCV than those who received placebos (p=0.02)</p> <p><b>1.3.3. Herpes simplex virus type 2 (HSV-2) vaccine (2</b></p>	<p><b>1. Individual-level</b></p> <p>1.1. Although trials of individual level interventions are more common than group-level and community-level interventions, the evidence is not clear as to effectiveness</p> <p>1.1.1. There is some evidence to support the use of counselling interventions that include at least 2 sessions, however, the optimal number and intensity of counselling sessions needed to produce a positive effect on the incidence of STI is not clear.</p> <p>1.1.2. Prophylactic treatments appear to be successful in reducing the incidence of STI, however, the extent to which this intervention affects antimicrobial resistance is a concern and more research is needed.</p> <p>1.1.3. Although numerous trials of topical microbicides have been carried out there does not appear to be any net benefit and several trials reported evidence of harm through the induction of genital lesions.</p> <p>1.1.4. Partner treatment may be a promising intervention to prevent transmission of STIs, however, only two out of four interventions showed positive effect.</p>

## studies)

Results were mixed regarding the efficacy of HSV-2 vaccines. Participants in one study who received the vaccine were no more or less likely to acquire HSV-2 than controls. In another study, participants who received the HSV-2 vaccine were significantly less likely to acquire HSV-2 than controls ( $p=0.01$ ;  $p=0.02$ )

### 1.3.4. Human papillomavirus (HPV-16) vaccine (1 study)

In one study, the HPV-16 vaccine was 100% efficacious in preventing acquisition of the virus in young college women.

## 1.4. Topical microbicides inserted vaginally (10 studies)

Results across these interventions are mixed with regard to their effectiveness in preventing various STIs.

### 1.4.1. Gonococcal Infection

In 4 studies, participants who received microbicides were significantly less likely to acquire gonorrhea than controls, at least in the short term. In one of these studies, the treatment effect noted at 6 months was no longer noted at 12 months. In 4 studies, participants who received microbicides were no more or less likely to acquire gonorrhoea. In 2 studies, participants receiving microbicides were significantly more likely to acquire gonorrhoea.

### 1.4.2. Chlamydial Infection

In 6 studies, participants who received microbicides were no more or less likely to acquire chlamydia than controls. In 1 study, participants who received microbicides were significantly more likely to acquire chlamydial infection than controls.

### 1.4.3. HIV (4 interventions)

In 3 studies, participants receiving microbicides were no more or less likely to acquire HIV than controls. In one study, participants receiving microbicides were significantly more likely to acquire HIV than controls.

### 1.4.4. Syphilis

In 1 study, participants receiving microbicides were no more or less likely to acquire syphilis than controls

### 1.4.5. Trichomoniasis

In 1 study, participants receiving microbicides were no more or less likely to acquire trichomoniasis than controls.

### 1.4.6. Bacterial Vaginosis (BV)

In 1 study, participants receiving microbicides were no more or less likely to acquire BV than controls

## 1.5. Adverse effects

In 3 of 10 studies, participants receiving microbicides were significantly more likely to experience adverse effects (symptomatic irritation, genital ulcer disease, vulvitis, genital lesions) than controls.

## 2. Individual level: Prevention of Transmission (4 interventions)

All 4 of these interventions involve curative or suppressive therapy.

2.1. Results across these four studies are mixed.

2.1.1. Participants whose partners received tinidazole were less likely to experience recurrence of vaginal trichomoniasis than those whose partners received a placebo ( $p<0.001$ )

2.1.2. Partner-delivered therapy provided by participants who provided their partners with azithromycin for chlamydial infection were no more or less likely to transmit the STI than those whose partners self-referred (OR 0.80, 95% CI 0.62 to 1.05).

2.1.3. Administering valacyclovir to HSV-2-positive members of serodiscordant couples reduced transmission to HSV-2-negative partners (HR 0.52, 95% CI 0.27 to 0.99,  $p=0.04$ ).

<p>2.1.4. Partners of participants with gonococcal and/or chlamydial infection experienced less persistence of or reinfection of these STIs (<math>p=0.04</math>) with treatment. Partners of participants with gonorrhoea experienced less persistence of or reinfection with gonorrhoea (<math>p=0.02</math>) with patient-delivered partner therapy.</p> <p><b>3. Individual level: Prevention of Complications (1 intervention)</b></p> <p>3.1. Participants who received screening for endocervical chlamydial infection by ELISA and culture were 56% less likely to have incident pelvic inflammatory disease (PID) than those who did not. The true reduction in risk of acquiring PID ranged between 12% and 80% less likely (RR=0.44, 95% CI 0.20 to 0.88).</p>	
<p><b>4. Group-level: Prevention of Acquisition (9 interventions)</b></p> <p><b>4.1. Behaviour change</b></p> <p>Behaviour change counselling produced mixed results.</p> <p>4.1.1. Participants exposed to a 4 session group counselling intervention experienced no more or less lower rates of STIs, sexual activity with more than one partner, or condom use than did those exposed to only 2 counselling sessions.</p> <p>4.1.2. Participants in a 7 session small group risk reduction intervention reported fewer STI symptoms than controls (<math>p=0.001</math>) but were no more or less likely to have gonococcal or chlamydial infections at 12 months compared to controls. In the same study, male participants receiving the intervention were less likely to have gonorrhoea than controls (<math>p&lt;0.03</math>)</p> <p>4.1.3. Participants receiving a 3 session counselling intervention experienced a greater reduction in STI rates compared with controls (<math>p=0.004</math>)</p> <p>4.1.4. Participants in 6 small group sessions were no more or less likely to acquire STIs than controls.</p> <p>4.1.5. Participants receiving 16 sessions of small group counselling experienced greater reductions in STIs at 12 months post intervention compared with controls (<math>p=0.05</math>)</p> <p>4.1.6. Participants receiving behaviour change interventions experienced reductions in STIs and pregnancy rates as compared with controls (OR 0.71, 95%CI 0.51 to 0.99).</p> <p><b>4.2. Oral microbial prophylaxis</b></p> <p>4.2.1. Participants receiving azithromycin were no more or less likely to acquire gonococcal or chlamydial infection than controls.</p> <p><b>4.3. Female condom provision</b></p> <p>4.3.1. In two studies participants for whom female and male condoms were made available were no more or less likely to acquire STIs than those in control group receiving male condoms only.</p>	<p><b>4. Group-level interventions</b></p> <p>4.1. There is insufficient evidence to determine whether group-based interventions are effective in preventing the acquisition of STI.</p>
<p><b>5. Community-level: Mixed Modal (4 interventions)</b></p> <p>5.1. Multi-component interventions included school-based education, reproductive health services for youth, condom distribution &amp; community activities</p> <p>5.2. Participants exposed to community level interventions experienced no difference in incidence of HIV or HSV-2 or prevalence of STIs as compared with control</p>	<p><b>5. Community-level</b></p> <p>5.1. There is insufficient evidence to determine whether mixed modal or mass treatment community-level interventions are effective in preventing the acquisition or transmission of STIs.</p> <p>5.2. All five trials of community- based interventions took place in Africa and it is not clear how the findings are transferable to the Canadian context .</p>
<p><b>6. Community-level: Syndromic or mass treatment</b></p> <p>6.1. Participants exposed to information, education and communication and syndromic management of STIs as compared with controls, experienced greater reductions in incident active syphilis (IRR 0.25, 95%CI 0.27 to 0.98) and gonorrhoea (IRR 0.25, 95% CI 0.10 to 0.64), but no difference in HIV -1, infection, chlamydial infection, genital ulcers, or urethral discharge.</p>	

<p>6.2. Participants exposed to mass treatment were no more or less likely than controls to experience reduction in incidence of HIV, gonorrhoea, chlamydial infection, BV, or syphilis after 20 months</p> <p>6.3. Pregnant participants exposed to mass treatment experienced reductions in early neonatal mortality (RR 0.83, 95%CI 0.71 to 0.97); infant ophthalmia (RR 0.37, 95%CI 0.20 to 0.70); low birth weight (RR 0.68, 95%CI 0.53 to 0.86); but not preterm delivery (RR 0.77, (95%CI 0.56 to 1.05).</p> <p>6.4. Participants exposed to syndromic treatment experienced lower incidence of HIV infection as compared with controls (RR 0.58, 95%CI 0.42 to 0.79).</p>	
<p><b>7. Methodological Issues with included studies</b></p> <p>7.3. All of the included studies included no more than 95 participants, which may affect generalizability. Furthermore, a number of studies did not report their loss-to-follow-up data (n=17)</p> <p>7.4. Studies varied widely in their settings, populations and interventions which makes it difficult to draw meaningful comparisons</p> <p>7.5. The narrative summary is not weighted according to primary study quality</p> <p>7.6. Results from the 4 trials presented at international conferences in 2002–2003, are used in the narrative summary, but should be interpreted with caution as they are not yet published and have not yet been peer reviewed.</p> <p>7.7. The community-level interventions (n=5), along with some group- and individual-level interventions were conducted in developing countries. This may affect their generalizability to other populations</p> <p>7.8. This review is limited to RCTs; however, other designs may have provided valuable evidence</p>	<p><b>7. Program Evaluation and Research</b></p> <p>7.1. High quality evaluation and research is needed to add to the body of knowledge on this issue. This should include:</p> <p>7.1.1. Evaluating the effectiveness of successful intervention strategies during scale-up and implementation in new settings.</p> <p>7.1.2. Trials with larger sample sizes and stronger power.</p> <p>7.1.3. Trials that focus on duration of follow-up and sustaining effects beyond 6-12 months.</p> <p>7.1.4. Trials that explore the implications of interventions on the phase of epidemic or within different sexual networks</p> <p>7.1.5. Systematic review updates that include the results of studies currently underway.</p> <p>7.1.6. Implementation and evaluation of effective individual level STI prevention interventions (e.g., patient delivered therapy to partners) in different settings.</p> <p>7.1.7. Trials that focus on whether specific behavioral interventions have different effects in populations with different baseline prevalence' of STIs and on the incidence of STIs of different infectiousness.</p> <p>7.1.8. Systematic reviews that include trials with passive follow-up (versus active testing), nonrandomized designs (e.g., before after observation studies), or intermediate outcomes (e.g., screening rates).</p> <p>7.2. Given the potentially high cost of research, consideration should be given to prioritizing and selecting interventions to study.</p>
<p><b>8. Cost benefit or cost-effectiveness information</b></p> <p>8.1. No cost related information was included in the review.</p>	<p><b>8. Cost benefit or cost-effectiveness information</b></p> <p>8.1. Future research should include cost effectiveness of interventions.</p>
<p><b>General Implications</b></p> <ul style="list-style-type: none"> <li>• A number of studies were patient-focused (n=7) and will require scaling up in order to be used as population-based interventions. Scaled up versions of interventions will then need to be examined in terms of their implementation in different settings.</li> <li>• Because the included studies delivered interventions mostly at the individual-level (28/41) conclusions are based largely on this study design.</li> <li>• While the review authors conclude that twenty-two of the 41 included studies (54%) successfully reduced acquisition, transmission, or complications of STI, and 1 intervention showed efficacy against sexual transmission of HIV, the findings of the quality assessment of these studies were not reported.</li> </ul> <p><b>Research Implications</b></p> <ul style="list-style-type: none"> <li>• There is a significant gap in RCTs that use objective outcome measures for STI and HIV infection prevention among MSM.</li> <li>• No randomized trials in this review examined structural interventions, and few evaluated STI screening.</li> <li>• Rigorous program evaluation and high quality research studies should be conducted in order to add to the body of knowledge on this issue. This should include evaluating the effectiveness of successful interventions that have been scaled-up and / or implemented in new settings.</li> </ul>	
<p><b>Legend:</b> CI – Confidence Interval; OR – Odds Ratio; RR – Relative Risk  **please see the <i>health-evidence.ca</i> glossary of terms (found under 'How to Use This Site') for definitions</p>	

## References used to outline issue

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1. Patrick DM, Wong T, Jordan RA.(2000). Sexually transmitted infections in Canada: Recent resurgence threatens national goals. *The Canadian Journal of Human Sexuality*. 9(3), 149-165.
2. Public Health Agency of Canada.(2006). Canadian guidelines on sexually transmitted infections. Retrieved from [http://www.phac-aspc.gc.ca/std-mts/sti\\_2006/pdf/Guidelines\\_Eng\\_complete\\_06-26-08.pdf](http://www.phac-aspc.gc.ca/std-mts/sti_2006/pdf/Guidelines_Eng_complete_06-26-08.pdf)

## Other quality reviews on this topic

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- Elwy, A.R., Hart,G.J., Hawkes, S., & Petticrew, M. (2002). Effectiveness of interventions to prevent sexually transmitted infections and human immunodeficiency virus in heterosexual men: A systematic review. *Archives of Internal Medicine*, 162(16), 1818-1830.
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## Related links

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- Association of Medical Microbiology and Infectious Disease Canada <http://www.ammi.ca/index.php>
- Canada Communicable Disease Report <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/>
- Canadian Guidelines on Sexually Transmitted Infections <http://www.phac-aspc.gc.ca/std-mts/sti-its/index-eng.php>
- Canadian Guidelines for Sexual Health Education [http://198.103.98.171/publicat/cgshe-ldnemss/cgshe\\_toc-eng.php](http://198.103.98.171/publicat/cgshe-ldnemss/cgshe_toc-eng.php)
- The College of Family Physicians of Canada. (2007). *Common STIs and tips on prevention* <http://www.cfpc.ca/local/user/files/%7BCA955980-76FB-45E9-BF43-502FD7BED4198%7D/STIS.pdf>
- The Sex Information and Education Council of Canada [http://www.sieccan.org/pdf/sexual\\_health\\_qs.pdf](http://www.sieccan.org/pdf/sexual_health_qs.pdf)
- Society of Obstetricians and Gynaecologists of Canada <http://sexualityandu.ca/professionals/sti.aspx>

## Suggested citation

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Robeson, P., McRae, L., Dobbins, M. (2010). Risk of infection after nasal colonization: Evidence and implications for public health. Hamilton, ON: McMaster University. Retrieved from [http://www.health-evidence.ca/documents/16300/Manhart\\_2005\\_Summary\\_Statement\\_-\\_English.pdf](http://www.health-evidence.ca/documents/16300/Manhart_2005_Summary_Statement_-_English.pdf)

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