Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men (Review)

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TABLE OF CONTENTS

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ABSTRACT

Background
There is a need for female-controlled methods of HIV prevention. Vaginal microbicides, substances inserted into the vagina to prevent women acquiring HIV and sexually transmitted infections (STIs) from men, could be useful in this regard. One potential vaginal microbicide is the widely used spermicide, nonoxynol-9 (N-9).

Objectives
To determine the safety and effectiveness of N-9 in preventing vaginal acquisition of HIV infection by women from men.

Search strategy
Extensive searches of electronic databases, conference abstracts, reference lists of relevant studies and contact with experts and funders.

Selection criteria
Randomised controlled trials meeting pre-determined quality criteria with HIV infection as the outcome.

Data collection and analysis
Data were extracted by one reviewer and checked by the another. Any discrepancies were adjudicated by a third reviewer.

Main results
Five trials were included in the review and four contributed to a meta-analysis. Overall, the risk of HIV infection was not statistically significantly different among women receiving N-9 (relative risk [RR] 1.12, 95% CI 0.88-1.42; p=0.4). The risk of genital lesions was statistically significantly greater among women receiving N-9 (RR 1.18, 95%CI 1.02-1.36; p=0.02).

Authors' conclusions
There is no evidence that nonoxynol-9 protects against vaginal acquisition of HIV infection by women from men. There is evidence that it may do harm by increasing the frequency of genital lesions.

PLAIN LANGUAGE SUMMARY

The spermicide nonoxynol-9 does not prevent women becoming infected with sexually transmitted infections, and when used very frequently has been shown to cause open genital sores (which may theoretically increase the chance of acquiring sexually transmitted HIV infection)."

BACKGROUND

The epidemic of HIV infection and sexually transmitted infections (STI) in the developing world is characterised by high incidence and high prevalence in many populations. It is apparent that STIs facilitate the transmission of HIV (Buve 1993). In recent years the rapid spread of HIV worldwide among women has underscored their particular risk of infection. Women are particularly vulnerable to HIV infection for a number of reasons. Male-to-female transmission seems to be more efficient than female-to-male transmission (Padian 1991), STIs are more difficult to diagnose and are often unrecognized in women (Wilkinson 1998), and the subordinate social and cultural status of women in many developing countries makes it difficult for them to initiate sexual practices which would reduce the likelihood of HIV infection. Although male condoms provide good protection against HIV when used consistently, many women find it difficult to convince their male partners to use a condom for every sexual encounter (De Zoysa 1996). The urgent need for female-controlled HIV prevention strategies has been recognized for some time, and focus has now been placed on the development of safe and effective microbicides (Elias 1996).

Microbicides are compounds formulated as gels, films, foams, suppositories, or creams and which, when inserted into the vagina, will prevent male-to-female transmission of HIV and other STIs. One of the important concepts in vaginal microbicide development is that it is a female-controlled method that does not necessarily require negotiation with a male sexual partner for use. A perfect microbicide product would be safe and highly effective, it would not be messy, and it would be insertable several hours before coitus.

Several products are currently undergoing human testing. Different approaches to microbicide development are being explored. Among these are substances that: a) kill or otherwise immobilize pathogens (surfactants); b) block infection by creating a barrier between pathogens and the vagina or rectum; and c) prevent viral replication once the pathogen has entered the body. Only the first group, the surfactants, are in advanced testing (effectiveness studies against STIs and HIV), whilst the others are still undergoing Phase I and Phase II trials.

Although one review of one potential vaginal microbicide, the widely used spermicide nonoxynol-9 (N-9), has been published (Cook 1998), this review included observational studies, focussed on STIs and suggested N9 is protective, concluded that the data on HIV was inconsequential, and did not follow Cochrane methods (Roddy 1998b). Here, we provide a systematic review and meta-analysis of the randomised controlled trials that have studied the potential role of N-9 as a prophylactic against HIV infection. A separate Cochrane review studies the role of N-9 as a prophylactic against STIs.

OBJECTIVES

To determine the safety and effectiveness of N-9 in preventing vaginal acquisition of HIV infection by women from men.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trials (RCTs) comparing an N-9-containing vaginal microbicide with a placebo or with no treatment.

Types of participants

Women in any setting.

Types of intervention

N-9 containing vaginal microbicides.

Types of outcome measures

Outcome measures include: a) effectiveness as measured by new infections with HIV and b) safety as measured by presence of genital lesions.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

Search strategies detailed below were used to identify studies in electronic databases.

Abstracts from international and major national HIV/AIDS and STI conference and meetings (including unpublished, non-peer-reviewed data) were also searched. We included foreign language journals in our search.

The following electronic databases were searched:
AIDSLINE (1980- May 2002)
EMBASE (1974- January 2002)
MEDLINE/Pubmed(1966- May 2002)
Cochrane Library (2002, Issue 2)

Known published studies (including reviews) were examined along with their reference lists. Researchers and funding agencies were also contacted to identify further trials.

For MEDLINE we used the following strategy (last run on June 25, 2001) with the results detailed:

1. Microbicide - (title word)
2. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject)
3. Microbicides - (title word) AND clinical study - (subject)

4. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND safety (subject)
5. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND HIV (subject)
6. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND STD (subject)
7. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND effectiveness (subject)
8. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND administration (subject)
9. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND dosage (subject)
10. Nonoxynol-9 - (subject) OR spermicides - (subject) AND clinical trial (subject) AND delivery (subject)

For AIDSLINE (June 21 2001) we used
1. Nonoxynol-9 - (subject) OR Spermicides - (subject) AND clinical trial (subject)
2. Microbicides - (title word) AND clinical trial - (subject)
3. Microbicides - (title word) AND clinical study - (subject)
4. Microbicides - (subject) AND randomised - (subject)
5. Nonoxynol-9 - (subject) AND HIV (subject) AND clinical trial (subject)
6. Nonoxynol-9 - (subject) AND sexually transmitted (subject) AND clinical trial (subject).

METHODS OF THE REVIEW

Study selection

Studies identified in the search were initially reviewed by title and abstract by two reviewers. Those identified as being of potential interest were further assessed using the full text to develop a list of RCTs. Having agreed on our list of trials one reviewer checked each trial carefully for quality according to criteria used by the Cochrane HIV/AIDS Group (http://hivinsite.ucsf.edu/cochrane/). A second reviewer checked the results. All five identified RCTs were subsequently included in the review.

Data extraction

One reviewer extracted data on the relevant outcome measures and a second reviewer checked this. Any discrepancies were adjudicated by a third reviewer.

All five trials were entered into a meta-analysis and a fixed effects model was used as the test for heterogeneity was not significant.

DESCRIPTION OF STUDIES

Roddy 1998 conducted a double blind RCT among 1,170 HIV-negative, female sex workers in Cameroon. They compared 70 mg N-9 in a film with a placebo film. 2,290 women were screened, 1,317 enrolled and 1,292 randomised (the balance had indeterminate HIV status). Of these, 1,170 returned at least once for follow-up and hence were included in the primary analysis. These women had been sex workers for around 4 years (at least 4 partners per month), rarely used contraception (about 12%), often douched (about 25%), frequently used other vaginal substances (around 45%), and only about half reported using a condom with their last client. Around 10% had gonorrhoea, and 10% had chlamydia infection at screening. About 25% reported oral sex and about 16% anal sex. All women were urged to use, and were provided with, male condoms during the study and were advised to insert the film prior to each episode of intercourse. All were regularly screened and treated for STIs, and all regularly received intensive counseling for HIV prevention. Women were randomised by computer generated permuted blocks of eight. Allocation was concealed by opaque envelope. The placebo product was identical in appearance to the N-9 product. Women were interviewed monthly during follow-up, and 73% were followed-up for 1 year with a mean follow-up of 14 months. Withdrawals and reasons for withdrawal were similar in each arm of the trial. At these follow-up visits women were examined by colposcope for genital lesions. Condom use was reported by 90%, around 10% reported oral sex and around 5% reported anal sex during the study (rates were similar in each trial arm).

Kreiss 1992 did an unblinded RCT in Nairobi, Kenya, among 116 HIV negative female sex workers. They compared 1000 mg N-9 in a sponge (Today Sponge) with placebo glycerine vaginal suppository or cream (as no placebo sponge could be manufactured). 138 women were randomised, but 22 did not return for follow-up and were excluded from the primary analysis. Commercial sex workers in this area average 34 partners per week. Prevalence of gonorrhoea was around 20%, and chlamydia was around 12%. All women received male condoms, STI treatment, and regular HIV prevention advice. Women were randomised by computer-generated list, but the method of allocation concealment was not reported. Those randomised to sponge were advised to insert it prior to the first partner each day, to replace it after every 2-3 partners, and to remove it 6 hours after the last partner. Mean follow-up was for 14-17 months (range 1-46 months), with a mean of 9 follow-up visits. Condom use was reported as about 60%, with 90% compliance with the intervention, and no anal or oral sex.

Van Damme 2001 did a triple-blind RCT among 765 HIV-negative female sex workers from Benin, Cote d'Ivoire, South Africa, and Thailand. They compared 52.5 mg N-9 as a gel (COL-1492; Advantage S) with placebo (vaginal moisturiser; Replens) of the same components (except the N-9) and identically packaged. 892 women were randomised with 765 attending at least one follow-up visit and hence included in the primary analysis. In the introductory phase of the trial all women were colposcoped at all visits but not during the full phase III trial. Women were aged over 18 years (16 years in South Africa) and were recruited directly from place of work, via STI clinics, or through clinics for sex workers.

Condom use varied from around 100% in Thailand to less than 50% in South Africa. Anal sex varied from 40% in South Africa to less than 5% in Cote d'Ivoire. Approximately 5% of women had gonorrhoea, and 5% had chlamydia at baseline. Condom use was promoted and STI treatment provided at all visits. Women were asked to use male condoms for each episode of intercourse and to apply the gel for every episode if they had cleaned the vagina after the last intercourse (there was no limit to the number of gels used each day). In all, 68% of women remained in the study at 48 weeks.

Roddy 2001 did an unblinded RCT among 1,241 HIV negative women (not sex workers) in Cameroon. They compared N-9 100 mg in a gel (Conceptrol contraceptive gel) with no gel (i.e. the comparison was gel plus condoms vs condoms alone). Women were aged over 17 years, typically single, with high education, had 1-2 partners in the preceding month, and averaged 3 coital acts per week. Around 40% douched, and around 5% had gonorrhoea and chlamydial infection at screening. All women received male condoms and strong HIV prevention messages together with treatment for any STIs. These were women with symptoms of STIs and were recruited from 10 clinics and 10 pharmacies (they also had STIs before). Women were randomly assigned by computer generated random number list in permuted blocks of 4, 8 and 12. During the study, condom use was reported by approximately 85% of women and gel use was reported by 76%; sexual activity was not reported to have changed during the study. Follow-up was carried out for up to 6 months. There were no routine gynaecological examinations.

Richardson 2001 did a double blind RCT among 278 female sex workers in Mombasa, Kenya. They compared 52.5mg N-9 gel (COL-1492; Advantage S)with a placebo gel (very similar to the N-9 carrier gel). About half of the women were married, median age was 28 years and median duration of sex work was 3 years. Reported median weekly sex acts was 2. Douching was reported by 86% and 29% used lubricants for sex. Most (94%) returned for at least one follow-up visit and the median folow-up was for 50.1 weeks. At 12 weeks, 69% of the N-9 group and 61% of the placebo group were still being followed-up. Women were seen monthly and had a full clinical examination with colposcopy and evaluation for STIs and HIV. Median compliance with N-9 was reported to be 75%, but only 34% reported 100% compliance. In addition, 50% of the N-9 group reported 100% condom use.

METHODOLOGICAL QUALITY

All five trials were generally of fair to high quality.

Two of the studies (Kreiss 1992 and Roddy 2001) were unblinded because suitable placebo products could not be produced.

The study by Kreiss used a non-standard measure of outcome (number of events/number of visits) and these data are not included in the meta-analysis.

RESULTS

All five trials were included in the review and four contributed to the meta-analysis.

Roddy 1998 reported 48 HIV infections among 595 women receiving N-9 and 46 HIV infections among 575 women receiving placebo film. Women receiving N-9 film were more likely to have genital lesions, most of which were on the vulva and included excoriation, fissures, and ulcers (129/410 vs 107/393). There was little difference in the rate of HIV infection (around 5 per 100 woman-years) between placebo and film groups with, and without, ulcers.

Kreiss 1992 reported 27 HIV infections among the 60 women receiving N-9 and 20 infections among the 56 receiving placebo. N-9 sponge use was associated with an increased frequency of genital ulcers (relative risk [RR] 3.3, p<0.0001). These ulcers were most frequently identified on the vulva. Spermicide-attributed complaints, mainly vulvar irritation, burning, and ulceration, were reported by 47% of N-9 users compared with 7% of placebo users.

Van Damme 2001 reported 59 HIV infections among the 376 women receiving N-9 and 45 infections among the 389 women receiving placebo. HIV incidence was 48% higher in the N-9 group (RR 1.48, 95%CI 1.01-2.19), and this effect was observed in 3 of 4 study centres. This finding was unconfounded by anal sex. The estimated number of women experiencing genital lesions (from proportions given in the paper) was 132 in the N-9 group and 117 in the placebo group. Incidence of lesions was greater among women who used the gel most frequently (close to double that among low users). There was a significant association between genital lesion with epithelial breach and HIV infection (RR 2.1, 95%CI 1.3-3.2).

Roddy 2001 reported 5 HIV infections among the 622 women receiving N-9 and 4 HIV infections among those in the control group. Women were not examined in this study and so there is no report of genital lesions. It is reported that 214 women in the N-9 group and 215 in the control group had at least one adverse event, but the nature of these events is not specified.

Richardson 2001 reported 12 HIV infections among N-9 users and 16 among placebo users (adjusted RR 0.7, 95% CI 0.3-1.5). Genital lesions causing epithelial disruption were reported by 21 N-9 users and 22 placebo users (adjusted RR 1.0, 95%CI 0.5-2.0).

Overall, combining these data, the risk of HIV infection was greater, although not statistically significant, among women receiving N-9 (relative risk [RR] 1.12, 95% CI 0.88-1.42; p=0.4).

The risk of genital lesions was also greater, at a statistically significant level, among women receiving N-9 (RR 1.18, 95%CI 1.02-1.36; p=0.02).

DISCUSSION

N-9 is a nonionic detergent that has been used for around 50 years as a spermicide. It has in vitro and some in vivo activity against STIs and HIV. It also protects macaques against intra vaginal challenge with simian immunodeficiency virus (Miller 1992). Observational studies have suggested that N-9 may protect against HIV infection (Cook 1998). Trials have however been inconclusive, and some concern has been raised about the potential for increased rates of genital ulceration among N-9 users, particularly frequent users (Roddy 1998b).

Our systematic review and meta-analysis of the five available high-quality randomised controlled trials shows that N-9 is associated with higher rates of HIV acquisition when compared with placebo (but without reaching statistical significance), and that women using N-9 also have higher rates of genital ulceration. As these trials all included high levels of male condom promotion and use and regularly screened for, and treated for STIs, we can conclude that N-9 use does not add to these HIV prevention strategies.

It is notable that in the trials that included high-risk sex workers, relatively high rates of HIV incidence were measured despite high levels of reported male condom use and despite regular screening for, and treatment of, STIs. There was, therefore, sufficient power overall in these trials to detect an effect of N-9 on HIV transmission, but no effect was seen. It seems reasonable to conclude that N-9 is unlikely to provide substantial (if any) protection among women using male condoms at lower rates and unable to access STI treatment, the situation more typically found in developing countries.

Most genital ulcers or lesions were observed on the vulva, away from the sites of highest concentration of N-9. The aetiology of these lesions is somewhat uncertain although some studies have indicated that N-9 causes imbalance in the normal vaginal flora leading to a higher incidence of Candida vaginitis, which may in turn lead to vaginitis. Direct erosive or hypersensitivity effects may also be important. Finally other STIs, such as reactivation of genital herpes, may play a role. That the lesions may not be entirely due to N-9 is suggested by Van Damme 2001 where the placebo group showed increasing rates of genital lesions with increasing frequency of use. However, the potential role of N-9, and the role of these lesions in increasing the risk of HIV acquisition is shown in the same trial where genital lesion rates were higher among reported high N-9 users than among high-use placebo users and there was an association between lesions that breached the epithelium and HIV infection.

Therefore, there seems to be little if any role for N-9 as an HIV prophylactic. As these trials were mainly done in high-risk female sex workers working in high HIV prevalence areas and with high rates of partner change, it would be unwise to generalise the findings of potential harm to lower risk women using N-9 occasionally as a spermicide.

The HIV/AIDS epidemic continues to grow and spread. Despite the known and demonstrated effectiveness of a variety of prevention and care strategies, we do need more strategies, especially those controlled by women. As such, it is important that research into other potential microbicides continues apace and that large scale, high quality randomised controlled efficacy trials start soon.

AUTHORS' CONCLUSIONS

Implications for practice

In the context of condom use and STI treatment, N-9 cannot be recommended to prevent vaginal acquisition of HIV by women from men, as its use does not reduce the risk of acquiring HIV infection, and its use is associated with a higher risk of genital lesions.

Implications for research

Further trials of N-9 as prophylaxis against HIV are therefore unjustified. Trials of alternative vaginal microbicides are urgently required and will benefit from the methodological lessons learned from the N-9 trials.

POTENTIAL CONFLICT OF INTEREST

Gita Ramjee was an investigator in one of the cited trials.

SOURCES OF SUPPORT

External sources of support

- HRP-UNDP/UNFPA/WHO/World Bank Special Programme in Human Reproduction, Geneva SWITZERLAND
- California HealthCare Foundation USA

Internal sources of support

- Adelaide University, Adelaide AUSTRALIA
- University of South Australia AUSTRALIA
- South African Medical Research Council SOUTH AFRICA

REFERENCES

References to studies included in this review

Kreiss 1992 *{published data only}*

Kreiss J, Ngugi E, Holmes KK, Ndinya-Achola J, Waiyaki P, Roberts PL, Ruminjo I, Sajabi R, Kimata J, Fleming TR, Anzala A, Holton D, Plummer F. Efficacy of nonoxynol-9 contraceptive sponge use in preventing heterosexual acquisition of HIV in Nairobi prostitutes. *JAMA* 1992;**268**(4):477–482.

Richardson 2001 *{published data only}*

Roddy 1998 *{published data only}*

Roddy RE, Zekeng L, Ryan KA, Tamoufe U, Weir SS, Wong EL. A controlled trial of nonoxynol-9 film to reduce male to female transmission of sexualy transmitted diseases. *New England Journal of Medicine* 1998;**339**(8):504–510.

Roddy 2001 *{published data only}*

Roddy RE, Zekeng L, Ryan KA, Tamoufe U, Tweedy KG. Nonoxynol-9 provides no prophylaxis for urogenital gonorrhoea and chlamydial infection: randomised controlled trial.

Van Damme 2001 *{published data only}*

Van Damme. Effectiveness on HIV-1 transmission of COL-1492, a nonoxynol-9 vaginal gel, among female sex workers.

Additional references

Buve 1993

Buve A, Laga M, Piot P. Sexually transmitted diseases: where are we now?. *Health Policy and Planning* 1993;**8**:277–281.

Cates 1985

Cates W, Farley TMM, Rowe PJ. Worldwide patterns of infertility: is Africa different?. *Lancet* 1985;**2**(8455):596–598.

Cook 1998

Cook RL, Rosenberg MJ. Do spermicides containing nonoxynol-9 prevent sexually transmitted infections?. *Sexually Transmitted Diseases* 1998;**25**(3):144–150.

De Zoysa 1996

De Zoysa I, Sweat M, Denison J. Faithful but fearful: reducing HIV transmission in stable relationships. *AIDS* 1996;**10**(Suppl.):S197–S203.

Elias 1996

Elias C, Coggins C. Female-controlled methods to prevent sexual transmission of HIV. *AIDS* 1996;**10**(Suppl):S43–S51.

Miller 1992

Miller CJ, Alexander NJ, Gettie A, Hendricks AG, Mark PA. The effect of contraceptives containing nonoxynol-9 on the genital tract trasnmission of simian immunodeficiency virus in rhesus macaques. *Fertility and Sterility* 1992;**57**:1126–1128.

Padian 1991

Padian NS, Shoboski SC, Jewell NP. Female-to-male transmission of human immunodeficiency virus. *JAMA* 1991;**266**:1664–1667.

Roddy 1998b

Roddy RE, Schulz KF, Cates W. Microbicides, meta-analysis, and the N-9 question. *Sexually Transmitted Diseases* 1998;**25**(3):151–153.

Wilkinson 1998

Wilkinson D, Ramjee G, Strum W. Unrecognized genital ulcer diseases among rural South African women. *International Journal of STD and AIDS* 1998;**9**:494–495.

TABLES

Characteristics of included studies

Study	**Kreiss 1992**
Methods	Unblinded RCT
Participants	116 female sex workers in Kenya
Interventions	1000mg N-9 sponge and placebo products
Outcomes	Gonorrhoea and chlamydia and genital lesions and HIV
Notes	All women received male condoms, STI treatment and condoms
Allocation concealment	D – Not used

Study	**Richardson 2001**
Methods	Double blind RCT
Participants	278 female sex workers in Kenya
Interventions	52.5mg N-9 gel and placebo
Outcomes	HIV, other STIs and genital lesions

Notes	All received male condoms, STI treatment and counselling
Allocation concealment	B – Unclear

Study	**Roddy 1998**
Methods	Double blind RCT
Participants	1170 female sex workers in Cameroon
Interventions	70mg N-9 film and placebo film
Outcomes	Gonorrhoea and chlamydia and genital lesions and HIV
Notes	All women received male condoms, STI treatment and HIV prevention messages
Allocation concealment	A – Adequate

Study	**Roddy 2001**
Methods	Unblinded RCT
Participants	1241 low risk non-sex working women (women with STI symptoms) in Cameroon
Interventions	100mg N-9 gel and non-users
Outcomes	Gonorrhoea and chlamydia infection (combined) and HIV
Notes	Comparison here is gel plus condoms vs condoms alone
Allocation concealment	D – Not used

Study	**Van Damme 2001**
Methods	Triple blind RCT
Participants	765 female sex workers from various African and Asian countries
Interventions	52.5mg N-9 gel and placebo gel
Outcomes	Gonorrhoea and chlamydia infection and genital lesions and HIV
Notes	All women received counselling about HIV and condom use, and were treated for STIs
Allocation concealment	A – Adequate

ANALYSES

Comparison 01. N-9 vs placebo

Outcome title	**No. of studies**	**No. of participants**	**Statistical method**	**Effect size**
01 HIV infection	4	3454	Relative Risk (Fixed) 95% CI	1.12 [0.88, 1.42]
02 Genital lesion	3	1795	Relative Risk (Fixed) 95% CI	1.18 [1.02, 1.36]

INDEX TERMS

Medical Subject Headings (MeSH)

Coitus; HIV Infections [*prevention & control; transmission]; Nonoxynol [*therapeutic use]; Randomized Controlled Trials; Spermatocidal Agents [*therapeutic use]

MeSH check words

Female; Humans; Male

COVER SHEET

Title	Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men
Authors	Wilkinson D, Ramjee G, Tholandi M, Rutherford G
Contribution of author(s)	DW developed the protocol, extracted data and wrote the first draft of the review. GR developed the protocol and contributed to the review. MT did the search, extracted data and contributed to the review. GWR developed the protocol and contributed to the review.
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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
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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 N-9 vs placebo, Outcome 01 HIV infection

Review: Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men

Comparison: 01 N-9 vs placebo

Outcome: 01 HIV infection

Study	N-9 n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Richardson 2001	12/139	16/139		14.4	0.75 [0.37, 1.53]
Roddy 1998	48/595	46/575		42.1	1.01 [0.68, 1.49]
Roddy 2001	5/622	4/619		3.6	1.24 [0.34, 4.61]
Van Damme 2001	59/376	45/389		39.8	1.36 [0.95, 1.95]
Total (95% CI)	1732	1722		100.0	1.12 [0.88, 1.42]
Total events: 124 (N-9), 111 (Placebo)					
Test for heterogeneity chi-square=2.61 df=3 p=0.46 I^2 =0.0%					
Test for overall effect z=0.90 p=0.4					

Analysis 01.02. Comparison 01 N-9 vs placebo, Outcome 02 Genital lesion

Review: Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men

Comparison: 01 N-9 vs placebo

Outcome: 02 Genital lesion

Study	N-9 n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Richardson 2001	21/139	22/139		9.1	0.95 [0.55, 1.65]
Roddy 1998	129/370	107/382		43.5	1.24 [1.01, 1.54]
Van Damme 2001	132/376	117/389		47.5	1.17 [0.95, 1.43]
Total (95% CI)	885	910		100.0	1.18 [1.02, 1.36]
Total events: 282 (N-9), 246 (Placebo)					
Test for heterogeneity chi-square=0.82 df=2 p=0.66 I^2 =0.0%					
Test for overall effect z=2.29 p=0.02