Antibiotic prophylaxis for intrauterine contraceptive device insertion (Review)

Grimes DA, Schulz FK

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A B S T R A C T

Background

Concern about the risk of upper genital tract infection (pelvic inflammatory disease (PID)) often limits use of the intrauterine device (IUD), a highly effective contraceptive. Prophylactic antibiotic administration around the time of induced abortion significantly reduces the risk of postoperative endometritis (Sawaya 1996). Since the risk of IUD-related infection is limited to the first few weeks to months after insertion (Lee 1983; Farley 1992) contamination of the endometrial cavity at the time of insertion (Mishell 1966) appears to be the mechanism, rather than the IUD or string itself. Thus, antibiotic administration before IUD insertion might reduce the risk of upper genital tract infection from passive introduction of bacteria at insertion.

Objectives

To assess the effectiveness of prophylactic antibiotic administration before IUD insertion in reducing IUD-related complications (pelvic inflammatory disease; complaints leading to an unscheduled visit) and discontinuations within three months of insertion.

Search strategy

We used computer searches of MEDLINE, POPLINE, and EMBASE. We also reviewed references lists in original research and review articles. We wrote to experts on several continents to identify unpublished trials.

Selection criteria

We included randomized controlled trials using any antibiotic compared with a placebo.

Data collection and analysis

Two independent reviewers abstracted data. We made telephone calls to investigators to obtain additional information. We assessed the validity of each study using methods suggested in the Cochrane Handbook. We generated 2x2 tables for the principal outcome measures. The Peto modified Mantel-Haenszel technique was used to calculate odds ratios and assessed statistical heterogeneity between studies.

Main results

The odds ratio (OR) for pelvic inflammatory disease was 0.89 (95% Confidence Interval (CI) 0.53 to 1.51) for use of prophylactic doxycycline or azithromycin compared with placebo or no treatment. Use of prophylaxis was associated with a small reduction in unscheduled visits to the provider (OR 0.82; 95% CI 0.70 to 0.98). Use of doxycycline or azithromycin had little effect on the likelihood of removal of the IUD within 90 days of insertion (OR 1.05; 95% CI 0.68 to 1.63). No statistically significant heterogeneity between study results was detected.

Authors' conclusions

Use of either doxycycline 200 mg or azithromycin 500 mg by mouth before IUD insertion confers little benefit. While the reduction in unscheduled visits to the provider was marginally significant, the cost-effectiveness of routine prophylaxis remains questionable. A uniform finding in these trials was the low risk of IUD-associated infection, with or without use of antibiotic prophylaxis.

PLAIN LANGUAGE SUMMARY

Antibiotics for prevention with IUDs

An intrauterine device (IUD) is a small device placed in the womb for long-term birth control. Many people worry about the woman getting pelvic inflammatory disease (PID) with an IUD. This infection can lead to problems in getting pregnant. If PID occurs, it is often within the first few weeks. Antibiotics are sometimes used before inserting an IUD to prevent an infection. This review looked at how well these preventive drugs reduced problems. Such problems include PID, extra health care visits, and stopping IUD use in three months.

We did a computer search for trials that compared an antibiotic to a placebo ('dummy'). We called researchers to get more information. We also wrote to researchers to find other trials.

Women who took antibiotics to prevent infection did not get PID as often as those who had the placebo or no treatment. However, the numbers with PID were low for all groups, so the treatment did not have a major effect. Women who use the drugs for prevention had fewer extra visits for health care. The small difference may not be enough to provide all women with the drugs. Using antibiotics to prevent infection did not change how many women had an IUD removed in three months.

BACKGROUND

Concern about the risk of upper genital tract infection (pelvic inflammatory disease) often limits use of the IUD, a highly effective contraceptive. Prophylactic antibiotic administration around the time of induced abortion significantly reduces the risk of postoperative endometritis (Sawaya 1996) Since the risk of IUD-related infection is largely limited to the first few weeks to months after insertion (Lee 1983; Farley 1992) contamination of the endometrial cavity at the time of insertion (Mishell 1966) appears to be the mechanism, rather than the IUD or string itself. Thus, antibiotic administration before IUD insertion might reduce the risk of upper genital tract infection from passive introduction of bacteria at insertion.

OBJECTIVES

To determine the effectiveness of oral antibiotics before IUD insertion in reducing the risk of IUD complications. In four reports, pelvic inflammatory disease (salpingitis) within 90 days was the principal outcome measure, and in two reports it was removal of the IUD for any reason other than partial expulsion within 90 days.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We included only randomized controlled trials in this review. Two cohort studies (Jovanovic 1988; Rogovskaya 1998) have also addressed this question, but we did not include them.

Types of participants

Women requesting IUD insertion who met local guidelines for IUD use. Specific inclusion and exclusion criteria appear in the table of trial characteristics. The African and Turkish trials specified admission criteria; in the Los Angeles trial, this decision was left to clinicians at the participating clinical sites. These varied by site but reflected package labeling of U.S. IUDs, which limits their use to low-risk women.

Types of intervention

Doxycycline 200 mg by mouth one hour before insertion (four reports), doxycycline 200 mg by mouth one hour before insertion followed by 200 mg daily for two days (one report), or azithromycin 500 mg by mouth one hour before insertion (one report).

Types of outcome measures

Three principal outcomes measures were pelvic inflammatory disease, unscheduled visits to the clinic, and removal of the IUD within three months of insertion. One study (Zorlu 1993) reported febrile morbidity without a clinical diagnosis of pelvic inflammatory disease. Because of the infrequency of upper genital tract infection, the trial by Walsh et al. (Walsh 1994; Walsh 1998) used premature IUD discontinuation as the primary outcome measure.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We conducted searches of MEDLINE using PubMed, POPLINE, and EMBASE. The latter identified no additional trials over those found in MEDLINE. We used the MeSH terms

'intrauterine devices,' 'antibiotics,' and 'infection' and the text words 'intrauterine device,' 'IUD,' 'antibiotics,' and 'infection.' 'Prophylactic' [all fields] and 'complications' [subheading] were additional search terms. We reviewed the reference lists of identified articles and wrote to IUD experts on several continents to seek trials we might have missed. The pilot study for the Los Angeles trial (Walsh 1998) was published separately as Walsh 1994. We contacted these investigators to get the number of women who made one or more unscheduled visits, but this information had not been collected in the pilot phase. Since the pilot study (Sinei 1985) for the main Kenya trial (Sinei 1990) was not published, we contacted the investigators to get these data. We attempted to contact one author (Zorlu 1993) by mail but without success.

METHODS OF THE REVIEW

Both authors screened potentially relevant trials. Agreement occurred on trial identification and data abstraction. This review presents only the Peto odds ratios. We assessed clinical heterogeneity by reviewing characteristics of participants in these trials, which were conducted on three continents. Statistical heterogeneity was evaluated by using a chi-squared test.

DESCRIPTION OF STUDIES

Women enrolling in the four different trials met local criteria for IUD insertion. In the African trials (Sinei 1990; Ladipo 1991), IUD was less restrictive than in the other trials (see Characteristics of included studies table). The prevalence of cervical infections with Neisseria gonorrhoeae among participants in the Kenya trial (Sinei 1990) was 3%, while that in the Nigerian trial (Ladipo 1991) was 1%. The prevalence of Chlamydia trachomatis in the cervix was higher (11% and 7%, respectively).

METHODOLOGICAL QUALITY

Several of the trials were of high quality. The Kenyan trial (Sinei 1985; Sinei 1990), Nigerian trial (Ladipo 1991), and Los Angeles trial (Walsh 1994; Walsh 1998) featured adequate allocation concealment, double blinding of treatment, and intention-to-treat analysis. However, the Nigerian trial stopped prematurely, and the incidence of pelvic inflammatory disease is higher than that of unscheduled visits to the clinic, a doubtful occurrence. The Turkish trial (Zorlu 1993) did not describe its method of randomization. No placebo was provided, and blinding was not maintained. No sample size calculation is available.

RESULTS

We found four randomized controlled trials; two had pilot study data available. The primary outcomes studied were pelvic inflammatory disease (four reports), unscheduled visits back to the clinic (four reports), or early removals of the device (two reports).

The Kenyan trial (Sinei 1990) found a significant reduction in unscheduled visits, and the meta-analysis had an odds ratio of 0.82 (95% CI 0.70 to 0.98). No other significant benefit emerged when the trials were combined.

The Kenyan trial (Sinei 1990) found that doxycycline reduced the risk of pelvic inflammatory disease by about one-third, which was not statistically significant (Relative risk (RR) 0.69; 95% CI 0.32 to 1.47). PID was diagnosed with the Hager 1983 criteria. A similar reduction in unscheduled return visits because of an IUD-related problem was statistically significant (RR 0.69; 95% CI 0.52 to 0.91). The Nigerian trial (Ladipo 1991), which attempted to replicate the Kenyan trial, found no benefit of prophylaxis in reducing either salpingitis or unscheduled visits.

The Los Angeles trial (Walsh 1998), which focused on premature IUD discontinuation, found no overall benefit of prophylactic azithromycin (RR 1.13; 95% CI 0.70 to 1.81). Only one case of pelvic inflammatory disease occurred in each treatment group. Similarly, the rate of unscheduled visits to the provider did not differ significantly.

The Turkish trial (Zorlu 1993) found no significant difference in rates of pelvic inflammatory disease.

No statistically significant heterogeneity was detected between studies' results. Nevertheless, important clinical differences existed between women in these four countries, notably the high prevalence of sexually transmitted diseases among women enrolled in the African studies.

We performed a sensitivity analysis by including only the four trials with rigorous methods (Sinei 1985; Sinei 1990; Walsh 1994; Walsh 1998). This allowed a reassessment of two outcome measures: pelvic inflammatory disease and unscheduled visits back to the clinic. For pelvic inflammatory disease, the odds ratio from this meta-analysis was 0.70 (95% CI 0.36 to 1.38). The odds ratio for unscheduled visits from the meta-analysis was unchanged (0.82; 95% CI 0.70 to 0.98).

DISCUSSION

Use of prophylactic antibiotics before IUD insertion reduced the likelihood of an unscheduled visit to provider by 18%, which was marginally statistically significant. No other important benefits were observed, specifically reduction in upper genital tract infection or improvement in IUD continuation rates.

In Kenya, where the prevalence of gonorrhea and chlamydial infection was high, doxycycline was associated with a reduction in both upper genital tract infection and unscheduled visits. This was not seen in Nigeria, where the prevalence of these two infections was not as high. Nevertheless, the discrepancy between rates of salpingitis and unscheduled visits in the Nigerian trial remains unexplained after discussions with the investigators. In populations with a high prevalence of sexually transmitted diseases, such as Kenya (Sinei 1990), prophylaxis may offer modest protection against both pelvic inflammatory disease and unscheduled visits to the clinic.

The trial from Los Angeles found little effect with either doxycycline (Walsh 1994) or azithromycin (Walsh 1998). The latter drug has the appeal of a very long half-life and low incidence of gastrointestinal side effects. Nevertheless, the cost of the 500 mg dose is higher than that of doxycycline 200 mg.

The sensitivity analysis using only rigorous trials showed more protection (OR 0.70) against pelvic inflammatory disease than did the overall meta-analysis (OR 0.89). Nevertheless, this difference was not statistically significant. Excluding the Ladipo 1991 study from the meta-analysis of unscheduled visits had no effect.

AUTHORS' CONCLUSIONS

Implications for practice

The overriding message from these four trials is that contemporary IUD use is safe, with or without use of prophylactic antibiotics. This holds true for populations with a high prevalence of sexually transmitted diseases, as is the case in much of Africa. The concern about high rates of upper genital tract infection, even in the critical early months of use, (Lee 1983; Farley 1992) appears unwarranted. As noted by the World Health Organization, contemporary copper IUDs are among the safest and most effective reversible methods of contraception available today.

Use of prophylactic antibiotics may reduce the likelihood of an unscheduled visit back to the clinic. Authors (Sinei 1990) have suggested that complaints of pain and bleeding associated with IUD use may represent subclinical endometritis. Antibiotic administration may reduce this risk and thus lead to fewer problem visits. While fewer problem-related visits will save money and reduce inconvenience, prophylaxis would probably only be cost-effective where sexually transmitted diseases are common, as observed in the study from Kenya (Sinei 1990).

Implications for research

The low rate of infection or premature removals of IUDs is important clinical news. On the other hand, the low incidence of IUD-related problems poses difficult challenges for researchers. The Kenyan trial, which enrolled over 1800 women, had insufficient power to identify the anticipated treatment effect. In the Los Angeles trial, the investigators anticipated the low incidence of pelvic inflammatory disease and focused instead on premature IUD discontinuation as the primary outcome measure. In the main trial with over 1800 participants, only two cases of salpingitis occurred.

Additional studies of prophylactic antibiotics in low-risk populations appear unjustified. In women at higher risk, further research may be considered. However, because of the low incidence of PID even in these settings, the number of women needed to treat to avert a single case of infection will be large.

POTENTIAL CONFLICT OF INTEREST

Dr. Grimes has consulted with or served on a speakers bureau for Schmid, ALZA, Ortho, GynoPharma, and Searle, all of which have sold IUDs. He served as a court-appointed expert to the Claimants' Committee in the A. H. Robins (distributor of the Dalkon Shield IUD) bankruptcy proceedings. Drs. Grimes and Schulz were investigators in the Kenya trial (Sinei 1985; Sinei 1990) and Dr. Grimes in the Los Angeles trial (Walsh 1994; Walsh 1998) included in this review.

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Sinei 1985 *{unpublished data only}*
> Sinei SKA, Schulz KF, Lamptey PR, Grimes DA, Mati JKG, Rosenthal SM, et al. Kenya, January 14, 1985 - February 7, 1985. Consultation regarding the analysis of the pilot phase and the initiation of the full-scale phase of the randomized clinical trial of prophylactic doxycycline at the time of IUCD insertion to prevent pelvic inflammatory disease. Schulz KF: Foreign trip report (AID/RSSA); 1985 Feb.

Sinei 1990 *{published data only}*
> Sinei SKA, Schulz KF, Lamptey PR, Grimes DA, Mati JKG, Rosenthal SM, et al. Preventing IUCD-related pelvic infection: the efficacy of prophylactic doxycycline at insertion. *British Journal of Obstetrics and Gynaecology* 1990;**97**:412–9. [MedLine: 1990321890].

Walsh 1994 *{published data only}*
> Walsh TL, Bernstein GS, Grimes DA, Frezieres R, Bernstein L, Coulson AH. Effect of prophylactic antibiotics on morbidity associated with IUD insertion: results of a pilot randomized controlled trial. IUD Study Group. *Contraception* 1994;**50**:319–27. [MedLine: 1995112564].

Walsh 1998 *{published and unpublished data}*
> Walsh T, Grimes D, Frezieres R, Nelson A, Bernstein L, Coulson A, et al. Randomised controlled trial of prophylactic antibiotics before insertion of intrauterine devices. *Lancet* 1998;**351**:1005–8. [MedLine: 1998206581].

Zorlu 1993 *{published data only}*
> Zorlu CG, Aral K, Cobanoglu O, Gurler S, Gokmen O. Pelvic inflammatory disease and intrauterine devices: prophylactic antibiotics to reduce febrile complications. *Advances in Contraception* 1993;**9**:299–302. [MedLine: 1994197034].

References to studies excluded from this review

Jovanovic 1988
> Jovanovic R, Barone CM, Van Natta FC, Congema E. Preventing infection related to insertion of an intrauterine device. *Journal of Reproductive Medicine* 1988;**33**:347–52.

Rogovskaya 1998
> Rogovskaya SI. *Prophylaxis of complications connected with intrauterine contraception [dissertation]*. Moscow (Russia): Research Centre of Ob/Gyn and Perinatology, 1998.

Additional references

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Hager 1983
> Hager WD, Eschenbach DA, Spence MR, Sweet RL. Criteria for diagnosis and grading of salpingitis. *Obstetrics and Gynecology* 1983;**61**:113–4. [MedLine: 1983116011].

Lee 1983
> Lee NC, Rubin GL, Ory HW, Burkman RT. Type of intrauterine device and the risk of pelvic inflammatory disease. *Obstetrics and Gynecology* 1983;**62**:1–6. [MedLine: 1983220071].

Mishell 1966
> Mishell DR Jr, Bell JH, Good RG, Moyer DL. The intrauterine device: a bacteriologic study of the endometrial cavity. *American Journal of Obstetrics and Gynecology* 1966;**96**:119–26. [MedLine: 1967007916].

Sawaya 1996
> Sawaya GF, Grady D, Kerlikowske K, Grimes DA. Antibiotics at the time of induced abortion: the case for universal prophylaxis based on a meta-analysis. *Obstetrics and Gynecology* 1996;**87**:884–90. [MedLine: 1996200660].

TABLES

Characteristics of included studies

Study	Ladipo 1991
Methods	Computer-generated randomization; allocation concealment by prepackaged pill bottles with drug or identical-appearing placebo.
Participants	1485 women requesting IUDs from University College Hospital, Ibaden, Nigeria. Inclusion criteria: age 20-44 yr and current menstruation. Exclusion criteria: history of ectopic pregnancy, pregnancy within 42 days, leiomyomata uteri, current salpingitis, uterine malignancy, sensitivity to tetracyclines, antibiotic administration within 14 days, impaired immune response, residence outside of Ibaden, or poor likelihood of follow up. All women were screened for gonorrhea and chlamydial infection.
Interventions	Doxycycline 200 mg by mouth one hour before IUD insertion or an identical-appearing placebo.

Characteristics of included studies (*Continued*)

Outcomes	Pelvic inflammatory disease diagnosed by Hager et al. criteria; unscheduled visits back to the clinic.
Notes	Rates of pelvic inflammatory disease exceeded rates of unscheduled visits; study did not reach intended sample size (1800)
Allocation concealment	A – Adequate

Study	Sinei 1985
Methods	See Sinei 1990
Participants	180 women (see Sinei 1990)
Interventions	See Sinei 1990
Outcomes	Pelvic inflammatory disease diagnosed by Hager 1983 criteria
Notes	Pilot study for Sinei 1990
Allocation concealment	A – Adequate

Study	Sinei 1990
Methods	Computer random number generator with blocked randomization, randomly varied block lengths. Allocation concealment by pre-labeled pill bottles with drug or identical-appearing placebo.
Participants	1813 women requesting IUDs in family planning clinic at Kenyatta National Hospital, Nairobi, Kenya. Inclusion criteria: 20-44 years old with regular menses. Exclusion criteria: history of ectopic pregnancy, pregnancy within 42 days, leiomyomata uteri, active salpingitis, uterine malignancy, hypersensitivity to tetracyclines, antibiotic administration within 14 days, impaired immune response, residence outside Nairobi or low likelihood of follow up. All patients were screened for gonorrhea and chlamydial infection.
Interventions	Doxycycline 200 mg by mouth one hour before IUD insertion or identical-appearing placebo.
Outcomes	Pelvic inflammatory disease diagnosed by Hager 1983 criteria; unscheduled visits back to the clinic.
Notes	High follow rates; rigorous methods.
Allocation concealment	A – Adequate

Study	Walsh 1994
Methods	See Walsh 1998.
Participants	447 women (See Walsh 1998).
Interventions	Doxycycline 200 mg by mouth one hour before IUD insertion or an identical-appearing placebo.
Outcomes	IUD removal for medical reasons, including pelvic inflammatory disease, within three months of insertion.
Notes	Pilot study for Walsh 1998.
Allocation concealment	A – Adequate

Study	Walsh 1998
Methods	Computer-generated randomization with block size of ten at each site; allocation concealment by prepackaged pill bottles that were identical, opaque, and sealed. Bottles contained drug or identical-appearing placebo.
Participants	1867 women requesting IUDs from 11 clinical sites in Los Angeles County, California. Inclusion and exclusion criteria determined locally at each site. All participants were screened for gonorrhea and chlamydial infection; 70% had screening done before insertion and 30% at the time of insertion.
Interventions	Azithromycin 500 mg by mouth one hour before insertion or an identical-appearing placebo.
Outcomes	IUD removal for medical reasons, including pelvic inflammatory disease, within 90 days of insertion.

Notes	Table includes total number of follow-up visits, not patients with one or more visits. Supplemental information obtained from investigator.
Allocation concealment	A – Adequate

Study	Zorlu 1993
Methods	Method of randomization not specified. Method of allocation concealment not stated. No blinding or placebo.
Participants	Women requesting IUDs in the family planning clinic in Dr. Zekai Tahir Burak Women's Hospital, Ankara, Turkey. Exclusion criteria: previous ectopic pregnancy, pregnancy within 3 months, active salpingitis, dysfunctional uterine bleeding, diagnosed or suspected genital malignancy, antibiotic administration within one month, and any organic pelvic disease.
Interventions	Doxycycline 200 mg by mouth one hour before IUD insertion, followed by 200 mg daily for two days versus no treatment.
Outcomes	Pelvic inflammatory disease (requiring fever plus other criteria) and febrile morbidity without a diagnosis of pelvic inflammatory disease.
Notes	Antibiotic prophylaxis regimen lasted three days.
Allocation concealment	B – Unclear

Characteristics of excluded studies

Study	Reason for exclusion
Jovanovic 1988	Not a randomized controlled trial.
Rogovskaya 1998	Not a randomized controlled trial.

A N A L Y S E S

Comparison 01. Antibiotic versus placebo or no treatment

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pelvic inflammatory disease (OR)	6	5797	Peto Odds Ratio 95% CI	0.89 [0.53, 1.51]
02 Pelvic inflammatory disease (RR)	6	5797	Relative Risk (Fixed) 95% CI	0.89 [0.53, 1.50]
03 Unscheduled visits to the clinic (OR)	3	4917	Peto Odds Ratio 95% CI	0.82 [0.70, 0.98]
04 Unscheduled visits to the clinic (RR)	3	4917	Relative Risk (Fixed) 95% CI	0.86 [0.75, 0.98]
05 Removal of the IUD within 90 days (OR)	2	2275	Peto Odds Ratio 95% CI	1.05 [0.68, 1.63]
06 Removal of the IUD within 90 days (RR)	2	2275	Relative Risk (Fixed) 95% CI	1.05 [0.69, 1.60]
07 Fever without PID diagnosis	1	277	Peto Odds Ratio 95% CI	0.65 [0.11, 3.81]

I N D E X   T E R M S

Medical Subject Headings (MeSH)

*Antibiotic Prophylaxis; Bacterial Infections [etiology; *prevention & control]; Genital Diseases, Female [etiology; *prevention & control]; *Intrauterine Devices [adverse effects]; Pelvic Inflammatory Disease [prevention & control]; Randomized Controlled Trials

MeSH check words

Female; Humans

C O V E R   S H E E T

Title	Antibiotic prophylaxis for intrauterine contraceptive device insertion
Authors	Grimes DA, Schulz FK
Contribution of author(s)	Both authors developed the proposal, conducted the literature search, abstracted the data, performed the analysis, and wrote the review.
Issue protocol first published	1998/4
Review first published	1999/3
Date of most recent amendment	21 February 2007
Date of most recent SUBSTANTIVE amendment	08 March 1999
What's New	The review was updated in February 2002. No new trials were found. Review was updated in May 2004. No new trials were found. Review was updated in February 2007. No new trials were found. Plain Language Summary was added, and the text was updated for Cochrane style issues.
Date new studies sought but none found	08 February 2007
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	Dr David Grimes Vice President of Biomedical Affairs Clinical Research Family Health International Post Office Box 13950 Research Triangle Park North Carolina 27709 USA E-mail: dgrimes@fhi.org Tel: +1 919 544 7040 Fax: +1 919 544 7261
DOI	10.1002/14651858.CD001327
Cochrane Library number	CD001327
Editorial group	Cochrane Fertility Regulation Group
Editorial group code	HM-FERTILREG

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Antibiotic versus placebo or no treatment, Outcome 01 Pelvic inflammatory disease (OR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 01 Pelvic inflammatory disease (OR)

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Ladipo 1991	12/721	9/708		36.8	1.31 [0.55, 3.10]
Sinei 1985	1/81	2/80		5.3	0.50 [0.05, 4.90]
Sinei 1990	11/827	16/828		47.3	0.69 [0.32, 1.47]
Walsh 1994	1/219	1/223		3.5	1.02 [0.06, 16.33]
Walsh 1998	1/918	1/915		3.6	1.00 [0.06, 15.95]
Zorlu 1993	1/140	1/137		3.5	0.98 [0.06, 15.73]
Total (95% CI)	2906	2891		100.0	0.89 [0.53, 1.51]

Total events: 27 (Treatment), 30 (Control)

Test for heterogeneity chi-square=1.48 df=5 p=0.91 I² =0.0%

Test for overall effect z=0.43 p=0.7

0.1 0.2 0.5 1 2 5 10

Favors Treatment   Favors Control
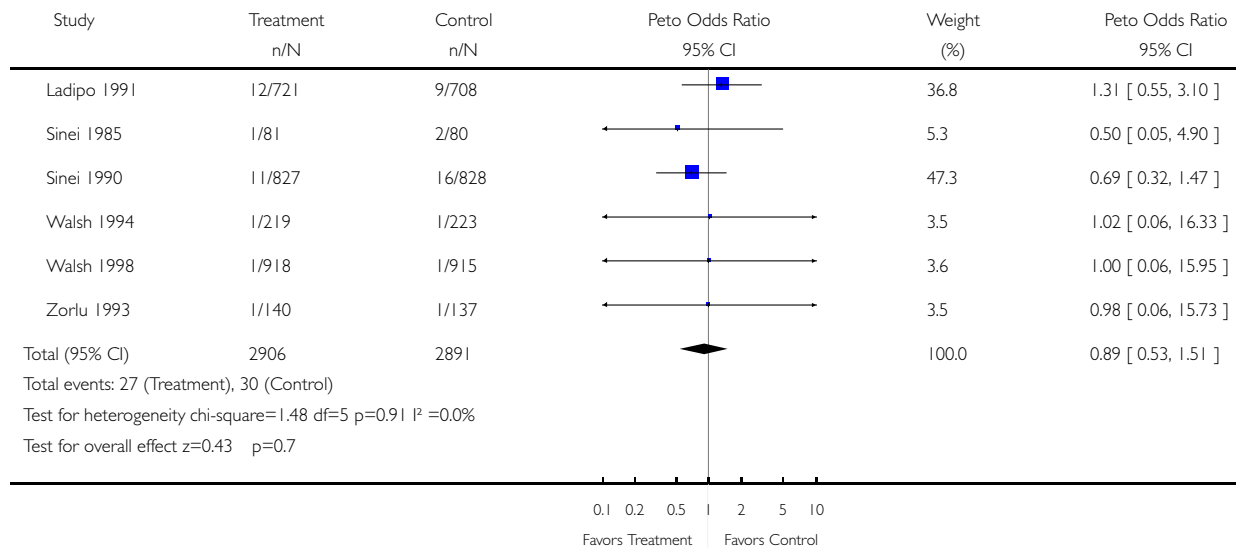
Analysis 01.02.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 02 Pelvic inflammatory disease (RR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 02 Pelvic inflammatory disease (RR)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Ladipo 1991	12/721	9/708		30.2	1.31 [0.56, 3.09]
Sinei 1985	1/81	2/80		6.7	0.49 [0.05, 5.34]
Sinei 1990	11/827	16/828		53.1	0.69 [0.32, 1.47]
Walsh 1994	1/219	1/223		3.3	1.02 [0.06, 16.18]
Walsh 1998	1/918	1/915		3.3	1.00 [0.06, 15.91]
Zorlu 1993	1/140	1/137		3.4	0.98 [0.06, 15.49]
Total (95% CI)	2906	2891		100.0	0.89 [0.53, 1.50]

Total events: 27 (Treatment), 30 (Control)

Test for heterogeneity chi-square=1.47 df=5 p=0.92 I² =0.0%

Test for overall effect z=0.43   p=0.7

```
          0.1  0.2   0.5   1    2    5   10
          Favors Treatment    Favors Control
```

Analysis 01.03.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 03 Unscheduled visits to the clinic (OR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 03 Unscheduled visits to the clinic (OR)

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Ladipo 1991	4/721	5/708		1.7	0.79 [0.21, 2.91]
Sinei 1990	74/827	108/828		30.3	0.66 [0.48, 0.90]
Walsh 1998	242/918	258/915		68.0	0.91 [0.74, 1.12]
Total (95% CI)	2466	2451		100.0	0.82 [0.70, 0.98]

Total events: 320 (Treatment), 371 (Control)

Test for heterogeneity chi-square=2.98 df=2 p=0.23 I² =32.9%

Test for overall effect z=2.24   p=0.03

```
          0.1  0.2   0.5   1    2    5   10
          Favors Treatment    Favors Control
```

Analysis 01.04.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 04 Unscheduled visits to the clinic (RR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 04 Unscheduled visits to the clinic (RR)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Ladipo 1991	4/721	5/708		1.4	0.79 [0.21, 2.91]
Sinei 1990	74/827	108/828		29.1	0.69 [0.52, 0.91]
Walsh 1998	242/918	258/915		69.6	0.93 [0.81, 1.09]
Total (95% CI)	2466	2451		100.0	0.86 [0.75, 0.98]

Total events: 320 (Treatment), 371 (Control)

Test for heterogeneity chi-square=3.72 df=2 p=0.16 I² =46.3%

Test for overall effect z=2.24   p=0.03

```
        0.1  0.2   0.5   I   2   5   10
       Favors Treatment    Favors Control
```

Analysis 01.05.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 05 Removal of the IUD within 90 days (OR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 05 Removal of the IUD within 90 days (OR)
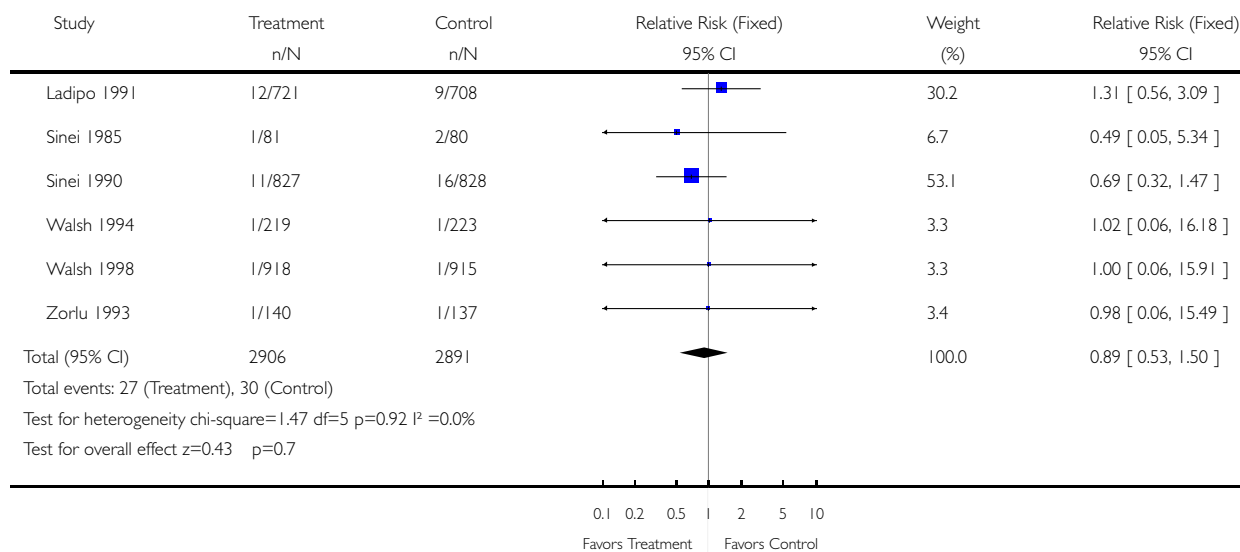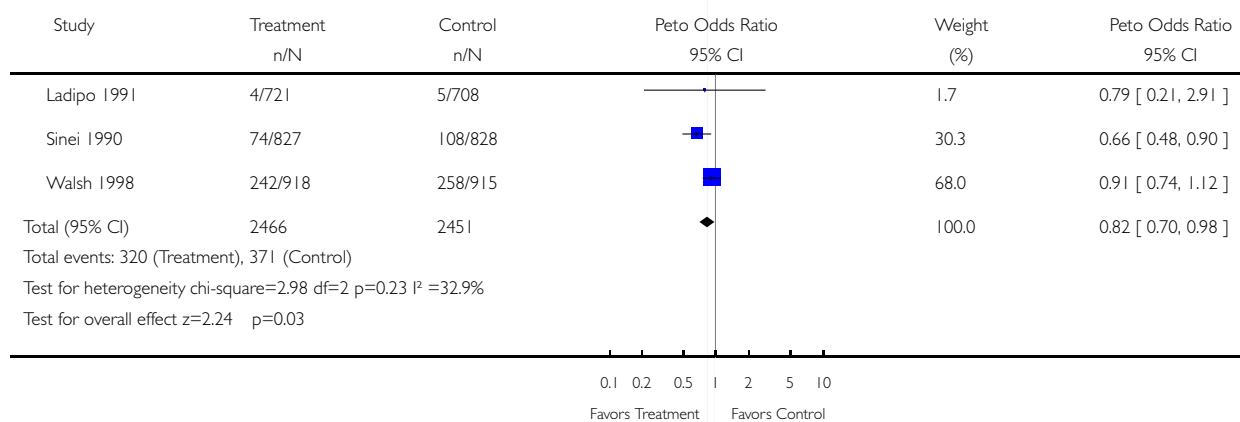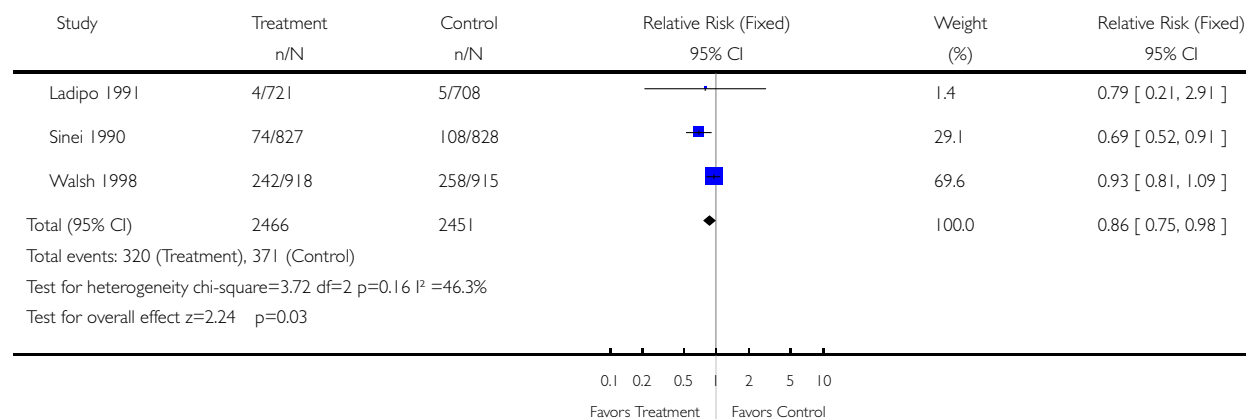
Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Walsh 1994	8/219	10/223		21.4	0.81 [0.32, 2.08]
Walsh 1998	35/918	31/915		78.6	1.13 [0.69, 1.85]
Total (95% CI)	1137	1138		100.0	1.05 [0.68, 1.63]

Total events: 43 (Treatment), 41 (Control)

Test for heterogeneity chi-square=0.38 df=1 p=0.54 I² =0.0%

Test for overall effect z=0.23   p=0.8

```
        0.1  0.2   0.5   I   2   5   10
       Favors Treatment    Favors Control
```
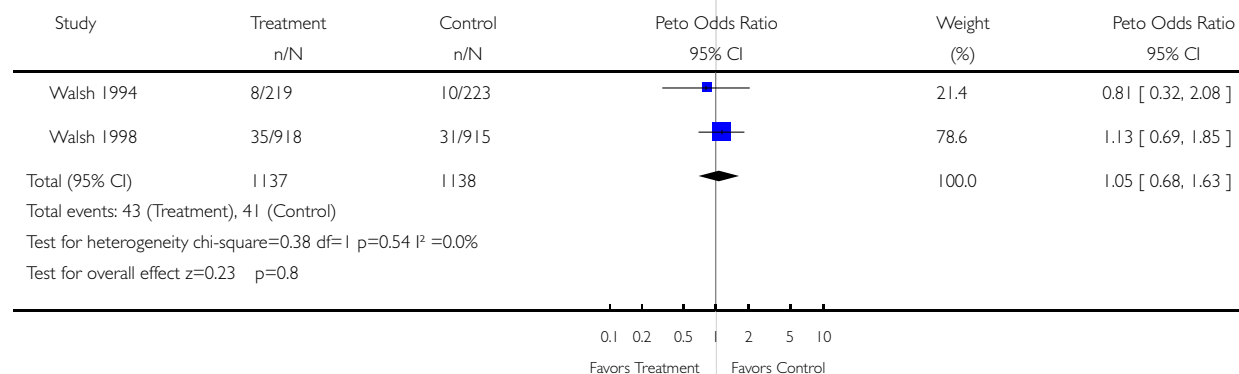
Analysis 01.06.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 06 Removal of the IUD within 90 days (RR)

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

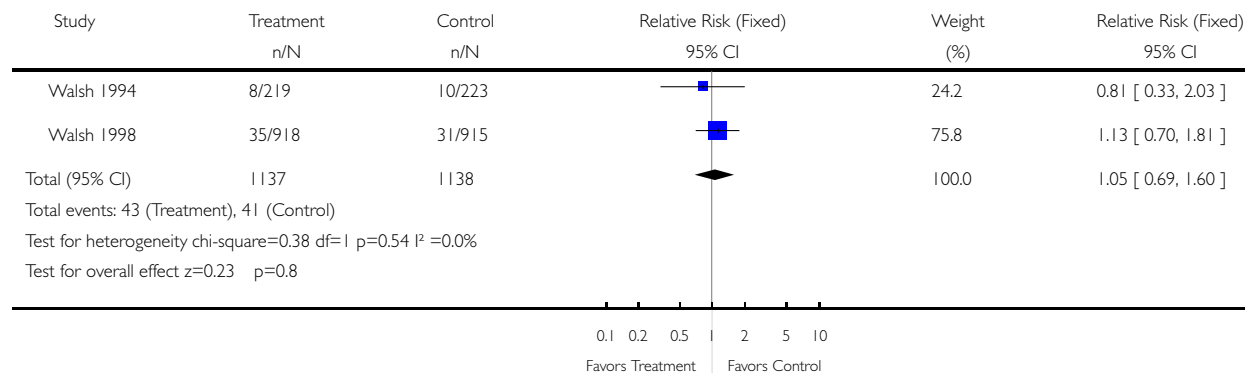Outcome: 06 Removal of the IUD within 90 days (RR)

Study	Treatment	Control	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Walsh 1994	8/219	10/223		24.2	0.81 [0.33, 2.03]
Walsh 1998	35/918	31/915		75.8	1.13 [0.70, 1.81]
Total (95% CI)	1137	1138		100.0	1.05 [0.69, 1.60]

Total events: 43 (Treatment), 41 (Control)

Test for heterogeneity chi-square=0.38 df=1 p=0.54 I² =0.0%

Test for overall effect z=0.23   p=0.8

```
0.1  0.2   0.5   I   2   5   I0
Favors Treatment    Favors Control
```

Analysis 01.07.   Comparison 01 Antibiotic versus placebo or no treatment, Outcome 07 Fever without PID diagnosis

Review: Antibiotic prophylaxis for intrauterine contraceptive device insertion

Comparison: 01 Antibiotic versus placebo or no treatment

Outcome: 07 Fever without PID diagnosis

Study	Treatment	Control	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Zorlu 1993	2/140	3/137		100.0	0.65 [0.11, 3.81]
Total (95% CI)	140	137		100.0	0.65 [0.11, 3.81]

Total events: 2 (Treatment), 3 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=0.47   p=0.6

```
0.1  0.2   0.5   I   2   5   I0
Favors Treatment    Favors Control
```