Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy (Unknown)

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ABSTRACT

Background
In the 1970s a new approach to the delivery of hormonal contraception was researched and developed. It was suggested that the addition of a progestogen to a non-medicated contraceptive device improved its contraceptive action. An advantage of these hormonally impregnated intrauterine systems (IUS) is that they are relatively maintenance free, with users having to consciously discontinue using them to become pregnant rather than taking a proactive daily decision to avoid conception.

Objectives
To assess the contraceptive efficacy, tolerability and acceptability of hormonally impregnated intrauterine systems (IUSs) in comparison to other reversible contraceptive methods.

Search strategy
Literature was identified through database searches, reference lists and individuals/organisations working in the field. Searches covered the period from 1972 to July 1998.

Selection criteria
All randomised controlled trials comparing IUSs with other forms of reversible contraceptives and reporting on pre-determined outcomes in women of reproductive years. The primary outcomes were pregnancy due to method/user failure and continuation rate.

Data collection and analysis
The quality assessment of studies and data extraction were completed independently by two blinded reviewers. A quality checklist was designed to identify general methodological and contraceptive specific factors which could bias results. Events per women months and single decrement life table rates were extracted where possible for pregnancy, continuation, adverse events and reasons for discontinuation. Events per total number of women at follow up were collected for hormonal side effects and menstrual disturbance.

When appropriate, data were pooled at the same points of follow up to calculate rate ratios in order to determine the relative effectiveness of one method compared to another. For the single decrement life table rates, the rate differences were pooled to determine the absolute difference in effectiveness of one method compared to another. Interventions were only combined if the contraceptive methods were similar. Non-hormonal IUDs were divided into three categories for the purpose of comparison with IUSs: IUDs >250mm2 (i.e. CuT 380A IUD and CuT 380 Ag IUD), IUDs <=250mm2 (i.e. Nova-T, Multiload, CuT 200 and CuT 220 IUDs) and non-medicated IUDs.

Main results
Nineteen RCTs comparing hormonally impregnated IUSs to a reversible contraceptive method met the inclusion criteria and it was possible to include eight of these in the meta-analyses, four comparing LNG-20 IUSs with non-hormonal IUDs, one comparing the LNG-20 IUS with Norplant-2 and three comparing Progestasert with non-hormonal IUDs.

No significant difference was observed between the pregnancy rates for the LNG-20 users and those for the IUD >250mm2 users. However, women using the LNG-20 IUS were significantly less likely to become pregnant than those using the IUD <=250mm2. Women using the LNG-20 IUS were more likely to experience amenorrhoea and device expulsion than women using IUDs >250mm2. LNG-20 users were significantly more likely than all the IUD users to discontinue because of hormonal side effects and menstrual disturbance, which on further breakdown of the data was due to amenorrhoea. When the LNG-20 IUS was compared to Norplant-2, the LNG-20 users were significantly more likely to experience amenorrhoea and oligomenorrhoea, but significantly less likely to experience prolonged bleeding and spotting. No other significant differences were observed.

Progestasert users were significantly less likely to become pregnant and less likely to continue on the method than non-medicated IUD users after one year, but no significant difference was noted for these two outcomes when Progestasert users were compared to IUD<=250mm2 users. The only other significant differences found in the meta-analyses were that Progestasert users were less likely to expel the device and more likely to discontinue the method because of menstrual bleeding and pain than users of IUDs <=250mm2.

Reviewers' conclusions
Current evidence suggests LNG-20 IUS users are no more or less likely to have unwanted pregnancies than IUD >250mm2 and Norplant-2 users. The LNG-20 IUS was more effective in preventing either intrauterine or extrauterine pregnancies than IUDs <=250mm2. The contraceptive effectiveness of Progestasert was significantly better than non-medicated IUDs, but no difference was observed when compared to IUDs<=250mm2. Continuation of LNG-20 IUS use was similar to continuation of the non-hormonal IUDs and Norplant-2. Amenorrhoea was the main reason for the discontinuation for the LNG-20 IUS and women should be informed of this prior to starting this method.

SYNOPSIS

No difference found in pregnancy rates for women using either the LNG-20 intrauterine system (IUS) ot intra-uterine device (IUD) for contraception

Reversible methods of contraception include the use of a system or device placed inside the uterus. The IUD is a copper device inserted into the uterus to prevent pregnancy. The intrauterine system (IUS) contains hormones that will be gradually released and change the environment inside the uterus to provide effective contraception until removed.
The review of trials compared IUDs to IUSs and found there was no difference in the rate of unplanned pregnancies. The review found that amenorrhoea (no menstrual period) is more likely with IUS use and that IUD use is more likely to cause heavy menstrual bleeding and pain.

BACKGROUND

In the 1970s a new approach to the delivery of hormonal contraception was researched and developed. It was suggested that the addition of a progestogen to a non-medicated contraceptive device improved its contraceptive action. An advantage of these hormonally impregnated intrauterine systems (IUS) is that they are relatively maintenance free, with users having to consciously discontinue using them to become pregnant rather than taking a proactive daily decision to avoid conception.

Progestasert
The first IUS to be marketed was Progestasert. It has a plastic T shaped frame with a 32 mm horizontal cross bar and a 36 mm vertical stem. The vertical stem holds 38 mg of progesterone within a silicone base and when it is placed within the uterus will release 65 mcg of progesterone per day. Its contraceptive action lasts for 12-18 months (Barnhart 1985) and is achieved by the endometrial suppression preventing implantation. A second mechanism involves the thickening of the cervical mucus preventing sperm penetration. Ovulation, however, is not affected with normal hormonal cyclical patterns demonstrated in users.

The license has been not renewed by the company in some countries in light of its reported disadvantages. These included:-

- yearly reinsertions with the associated risk of pelvic inflammatory disease;
- increased ectopic pregnancy rate when compared to copper bearing devices;
- some women experiencing persistent menstrual spotting.

Levonorgestrel Intrauterine System
The levonorgestrel intrauterine system (LNG-IUS), Mirena, is licensed for contraceptive use in 25 countries (Schering 1999). It has a T shaped plastic frame 32 mm long with a reservoir on the vertical stem of the IUS containing 52 mg of levonorgestrel mixed with polydimethylsiloxane. This allows a steady, local release of 20µg levonorgestrel per day. Insertion of the LNG-20 IUS may require local anaesthesia and dilatation of the cervical canal in nulliparous or peri-menopausal woman. The net ingredient cost of the LNG-20 IUS is more expensive than copper bearing IUDs, however it offers non-contraceptive benefits particularly in women with heavy periods and may offer an alternative to hysterectomy (Barrington 1997; Irvine 1998).

Measuring contraceptive effectiveness
Extensive reviews have helped to provide greater clarity in the understanding of the various methods and terminologies employed to measure contraceptive effectiveness and have examined their relative advantages and disadvantages (Trussell 1991;Farley 1986). In brief, there are generally two methods which have been adopted, the Pearl Index (PI) and life-tables. The PI, the older method (Pearl 1933), provides a rate per women years and is calculated by dividing the number of events (such as the number of women who discontinue using a contraceptive method) by the total number of women months and multiplying by 1200 (or 1300 if measurement is calculated by menstrual cycle). This method has been criticised because it does not account for the variation in risk of outcomes over time, nor does it account for the variation in loss to follow up (Potter 1966; Higgins 1985). Life tables do account for these factors and are therefore the most appropriate way to report contraceptive data. Confusion arises because inconsistent methods are used to define and calculate these probabilities. In brief, multiple-decrement life table probabilities (also known as net, competing or crude rates) are calculated by working out the monthly probability of reasons for discontinuation, such as pregnancy or hormonal side effects, and multiplying these to establish the probability of discontinuation over a fixed period of time, i.e. at six months follow up, a year follow up, etc. However, single decrement life table probabilities (also known as gross, noncompeting or net rates) are recommended. They are calculated the same way but only for a single reason i.e. they censor women who discontinue a method for reasons other than the one being measured. Unfortunately, it is often impossible to distinguish which method has been used if it is not clearly stated by the authors as 'net' can be refering to single or multiple decrement probabilities.

OBJECTIVES

To determine the effectiveness, acceptability and tolerability of IUSs. In order to do this the following questions were asked:

1. What is the relative effectiveness of IUSs in comparison to other reversible contraceptive methods?
2. What is the relative acceptability of IUSs in comparison to other reversible contraceptive methods?
3. What is the relative tolerability of IUSs in comparison to other reversible contraceptive methods?
4. What is the relative effectiveness of different types of IUS?
5. What is the relative acceptability of different types of IUS?
6. What is the relative tolerability of different types of IUS?

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trial and controlled clinical (i.e. quasi-randomised) trial comparisons of hormonally impregnated IUSs with other forms of reversible contraceptives.

Types of participants

women of reproductive years

Types of intervention

Hormonally impregnated IUSs versus:
non-hormonal IUDs
barrier contraceptives
oral contraceptives
injectable contraceptives
subdermal implants

Comparisons of different IUSs

Types of outcome measures

Primary outcome measures
Pregnancy due to method/user failure at 1, 2, 3, 4 and 5 years after starting contraceptive method
Continuation of contraceptive method after 1, 2, 3, 4 and 5 years

Not enough evidence about hormonal contraceptive use during breastfeedingBreastfeeding provides some protection against another pregnancy, but the return of fertility is unpredictable. Which contraceptive method to use while breastfeeding, and when to start using it, are complicated decisions. Choices of contraception may be limited due to concerns about the effects of hormonal contraceptives such as the Pill on the quality and quantity of breastmilk, and the effects on the baby. The review found there is not enough evidence from trials to show the effects of hormonal contraceptives during breastfeeding.Secondary outcome measures
Planned pregnancy after discontinuation of contraceptive method at 1 and 2 years

Failed removal

Hormonal side effects:
Headaches
Pelvic pain
Breast tenderness
Acne
Weight gain
Nausea/vomiting
Dizziness/vertigo
Hair growth
Hair loss
Ovarian cysts
Uterine cramps
Mood changes
Loss of libido

Menstrual changes:
Dysmenorrhoea
Spotting
Oligomenorrhoea
Amenorrhoea
Menorrhagia
Prolonged bleeding
Irregular bleeding

Local device problems:
Malposition
Translocation
Expulsion

Adverse clinical events:
Ectopic pregnancy
Pelvic inflammatory disease
Sexually transmitted infections
Anaemia
Breast cancer
Fibroids
Vaginitis
Urinary tract infection
Cervical intraepithelial neoplasia I
Cervical intraepithelial neoplasia II
Cervical intraepithelial neoplasia III
Invasive cervical cancer
Myocardial infarction
Stroke
Pulmonary Embolism/thrombophlebitis
Gall bladder disease
Death

Reason for discontinuation:
Hormonal side effects
Menstrual disturbance
Adverse clinical event
Local device problem
Planning pregnancy
Patient choice - other

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: search strategy

The following search strategy was used:
#1 "INTRAUTERINE-DEVICES,-MEDICATED" / all subheadings
#2 INTRAUTERINE SYSTEM* or IUS*
#3 explode "NORGESTREL" / all subheadings
#4 "LEVONORGESTREL"/all subheadings
#5 NORGESTREL
#6 LEVONORGESTREL
#7 KETO near DESOGESTREL
#8 ETONORGESTREL
#9 PROGESTASERT
#10 MIRENA
#11 LEVONOVA
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Computerised databases The Cochrane Controlled Trials Register, MEDLINE, EMBASE, POPLINE, the Science Citation Index and Psych. Lit. were searched (from 1972 to July, 1998) to identify publications describing randomised and controlled clinical trials of IUSs. The reference lists of all identified publications were searched for previously unidentified articles.

The relevant pharmaceutical companies were contacted and asked to release results of any relevant unpublished studies for inclusion in the review. Individuals and organisations with an interest in IUS research were contacted to identify unpublished and ongoing studies relevant to the review.

METHODS OF THE REVIEW

The selection of studies for inclusion and their methodological quality were independently assessed and reported by reviewers (RF and FC). Quality assessment forms were designed, and included general methodological factors, as well as some of contraceptive specific factors recommended by Trussell 1991.The following quality factors were included on the checklist:
- method of randomisation described,
- allocation concealment,
- blinded assessment of outcomes,
- groups treated identically other than named intervention,
- description of women who withdrew or were lost to follow up provided,

- description of hormonal contraceptive method or pregnancy immediately prior to study enrolment,
- statistical method (with reference) used to analyse pregnancy and continuation of methods,
- description of contraceptive failure provided (i.e. user or method failure or both),
- active follow up conducted (i.e. analysis of follow up delayed a few months to allow inclusion of undetected pregnancies)

Single-decrement life table probabilities with their standard errors (SEs), and events per women months, akin to the Pearl Index rate, were collected for each outcome at specific follow up points (at one, two, three, four and five years). It was decided to collect both ways of reporting event rates as, although single-decrement rates are the ideal, they are not commonly employed and there was usually sufficient information in the papers to collect events per women months. Of those papers which had reported single decrement probabilities, only a few had given SEs, a necessity for meta-analysis. Authors who had used single decrement probabilities but had not given their SEs were contacted and asked to provide them where possible. Unless otherwise stated, in the rest of the text life table probabilities refers to single decrement life tables for any discontinuation outcomes.

Menstrual disturbance outcomes were only collected if investigators had stipulated that they had been measured over 90 day intervals as recommended by Rodriguez 1976. Number of events and total number of women at each 90 day interval were collected to calculate risk ratios for menstrual disturbance outcomes.

Data on hormonal side effects and planned pregnancy (after discontinuation of contraceptive method) were collected at yearly time intervals. Data on these outcomes were only collected if the investigators provided number of events and total number of women at follow up, so that risk ratios for each of the side effects identified in the protocol could be determined. Data on weight change were collected by extracting the mean weight difference, with its standard deviation, between the contraceptive methods under investigation.

A description of the demographic characteristics of the study participants, the interventions, environmental and geographical factors which may influence findings, quality and the measured outcomes were collected, so that a decision could be made about the results of individual studies and whether it was feasible to combine the data.

Studies were only combined when the comparative interventions were similar, such as IUSs versus subdermal implants or IUSs versus non-hormonal IUDs contraceptives. Non-hormonal IUDs were divided into three categories for the purpose of data synthesis. The first, defined as IUDs >250mm2, included CuT 380A and CuT 380Ag IUDs; the second, defined as IUDs <=250mm2, included the Nova-T, Multiload, CuT 200 and CuT 220 IUDs; and the third were non-medicated IUDs. The first two categories were based on the surface area of the copper wire. In situations where it was not possible or appropriate to synthesise data, a narrative description is provided.

In order to obtain a summary effect size of an event per women months the rate ratios of the case and control events were combined. This method gave a relative measure of 'treatment' effect, that is how much more or less likely IUS users experienced an event in comparison to users of other contraceptive methods. The log rate ratios and their variances for events were calculated for each study (Hasselblad 1995). It was then possible to calculate the inverse weighted average of the log rate ratios. Events were only combined if they were measured over the same time period (i.e. one year, two years and so on) because of their variability over time. For the purpose of data synthesis, in situations where there were no events in one arm of the trial a continuity correction was implemented by adding a half to each cell.

In order to synthesis life table probabilities, it was necessary to calculate the absolute measurement of 'treatment' effect. This was done by subtracting the control group probability from the intervention group probability. The SE for the measurement of true effect was then calculated by obtaining the square root of sum of the squared SE of the intervention group probability and the squared SE of the control group probability. If there was a probability of zero in one of the groups, its SE was assumed to be the same as the SE of the probability in the comparison group. The inverse weighted average of the rate differences was then calculated. It was thus possible to obtain an absolute difference in percentage terms of 'treatment' effect, that is the attributable risk, between IUS users and users of other contraceptive methods.

To order to obtain pooled estimates for risk ratios and mean differences, the inverse variance weighted average was used with the sample log risk ratio and the sample mean difference, respectively, calculated from each study (Petitti 1994). A continuity correction was performed when necessary as described above for the calculated rate ratios.

Microsoft Excel was used to calculate the pooled effect sizes as it was not possible to calculate rate ratios or life table differences in RevMan.

The degree of heterogeneity was investigated and reported. A random effects approach was used for the meta-analysis (Dersimonian 1986). In the absence of heterogeneity this coincides with a fixed effect analysis. No statistical heterogeneity was identified in the analyses unless explicitly stated in the results below.

An economic evaluation was conducted using the results of the systematic review and meta-analysis, and this has been published elsewhere (French 2000)

DESCRIPTION OF STUDIES

Nineteen RCTs, identified from 38 publications, comparing hormonally impregnated IUSs to a reversible contraceptive method met the inclusion criteria (See Table of Included Studies). Seven trials were conducted in developing or transitional countries (Affandi 1980; Andrade 1988; Baveja 1989; el Mahgoub 1982; Lavin 1983; Piazarro 1979; Wang 1992) six in developed countries (Andersson 1994; Fylling 1979; Heikkila 1982; Larsen 1981; Pakarinen 1996; Rybo 1983) and five were international multicentre studies conducted in both developed and developing countries (Luukkainen 1986; Sivin 1994; WHO 1983; WHO 1987; WHO 1997). In one publication it was not possible to determine the study setting (Newton 1979). The majority of trials (10) were set in community-based family planning clinics.

The age range of participants varied from 15 - 44 years. None of the studies confined entry to specific age requirements, other than ensuring the recruited women were of reproductive age. Thirteen of the 19 trials limited recruitment to women with proven fertility (Andersson 1994; Andrade 1988; Baveja 1989; Heikkila 1982; Lavin 1983; Luukkainen 1986; Piazarro 1979; Rybo 1983; Sivin 1994; WHO 1987; Wang 1992; el Mahgoub 1982). Three studies recruited women immediately post partum or post abortion (Heikkila 1982; Lavin 1983; el Mahgoub 1982). One study restricted recruitment to women who were breast feeding (Heikkila 1982). Three studies stated that they only included women with regular menstrual cycles (Baveja 1989; Pakarinen 1996; Piazarro 1979).

Nearly all of the interventions were either comparisons of IUSs with different hormonal release rates or of IUSs versus non-hormonal IUDs. The one exception was a comparison of LNG-20 IUS with Norplant-2 (Wang 1992).

It was documented in two of the 19 trials that contraceptive counselling had been provided (Andersson 1994; Wang 1992). None of the studies mentioned any specific training for those inserting the devices.

METHODOLOGICAL QUALITY

Details of the methodological quality of each of the studies are provided in the Characteristics of Included Studies Table. It was documented that allocation of contraceptive method was concealed to the investigator in eight trials (Andersson 1994; Baveja 1989; Newton 1979; Pakarinen 1996; Sivin 1994; Wang 1992; WHO 1997; WHO 1983). It was reported that investigators were blind to contraceptive method when assessing outcomes in only three of the trials (Luukkainen 1986; Newton 1979; Piazarro 1979). Women were blind to allocated method in an additional two studies (Andersson 1994; Larsen 1981).

In 14 studies, the compared groups were treated identically in terms of measurement of outcomes (Andersson 1994; Baveja 1989; Fylling 1979; Larsen 1981; Lavin 1983; Luukkainen 1986; Newton 1979; Pakarinen 1996; Piazarro 1979; Rybo 1983; Sivin 1994; Wang 1992; WHO 1983; WHO 1987). A description of the characteristics of women lost to follow up or who withdrew from the study was not provided in any of the publications.

Twelve studies used life table analysis to determine pregnancy and continuation rates (Andersson 1994; Baveja 1989; el Mahgoub 1982; Larsen 1981; Luukkainen 1986; Newton 1979; Pakarinen 1996; Piazarro 1979; Sivin 1994; Wang 1992; WHO 1983; WHO 1987). It was possible to determine whether single or multiple decrement probabilities had been reported in nine of these studies (Andersson 1994; Baveja 1989; Larsen 1981; Luukkainen 1986; Pakarinen 1996; Sivin 1994; Wang 1992; WHO 1983; WHO 1987) and all but one provided single decrement probabilities (Larsen 1981).

Less than half of all studies provided information of contraceptive methods used (or pregnancy) immediately prior to enrolment (Andersson 1994; Andrade 1988; el Mahgoub 1982; Heikkila 1982; Lavin 1983; Luukkainen 1986; Piazarro 1979; Wang 1992). In the 15 studies where pregnancy occurred, nine distinguished between user or method failure (or both) (Andersson 1994; Baveja 1989; Luukkainen 1986; Pakarinen 1996; Piazarro 1979; Sivin 1994; Wang 1992; WHO 1983; WHO 1987). Active follow up was conducted in three trials (Sivin 1994; WHO 1983; WHO 1987).

RESULTS

Some studies which would have met the inclusion criteria but examined prototype contraceptive methods or methods that are not longer available were excluded from the meta-analyses (el Mahgoub 1982; Heikkila 1982; Pakarinen 1996; WHO 1983; WHO 1987).

Three studies compared the LNG-20 IUS with the non-hormonal IUD >250mm2 (Baveja 1989; Sivin 1994; WHO 1997). It was possible to extract data from two of these studies (Baveja 1989; Sivin 1994). The other study was still in progress at the time of this review. Rate ratios and single decrement life table differences derived from the two studies are presented in Table 01 and Table 02, respectively (for the following outcomes: pregnancy, continuation, expulsion, embedded device, ectopic pregnancy, PID, and discontiniation due to hormonal side effects, menstrual side effects, adverse events, planning a pregnancy and/or personal choice). The relative risk for planned pregnancy after removal of the LNG-20 IUS compared to CuT 380 Ag IUD was 1.05 (95% CI 0.83 to 1.33) at one year (Sivin 1994). It was possible to extract data on menstrual disturbance outcomes from one study only (Sivin 1994). Data from this study indicated that women using LNG-20

IUSs were more likely to experience amenorrhoea than women using CuT 380Ag IUDs and this risk increased over time, at three months the risk ratio was 2.25 [95% CI 1.36 to 3.56] which increased to 7.24 [95% CI 4.14 - 12.55] at three years follow up. No significant differences were noticed between LNG-20 IUS and CuT 380Ag IUDs in terms of prolonged bleeding, with risk ratios of 0.90 [95% CI 0.62 to 1.30] at three months and 0.1 [95% CI 0.01 to 2.06] at three years. It was not possible to extract data for any other menstrual disturbance outcomes, but Sivin et al (1994) reported that LNG-20 IUS users were significantly less likely to experience dysmenorrhoea. No data were collected for hormonal side effects.

Three included studies compared the LNG-20 IUS with non-hormonal <=250mm2 IUDs (Andersson 1994; Baveja 1989; Luukkainen 1986). Data could be extracted from each of these studies. The calculated rate ratios and single decrement life table differences are shown in Table 03 and Table 04, respectively, for the following outcomes: unplanned pregnancy, continuation of method, adverse event outcomes and reasons for discontinuation. Unpublished data on discontinuation of the LNG-20 IUS compared to the Nova-T because of amenorrhoea from Andersson 1994 (provided by Leiras Ltd 1999) demonstrated a huge variation between the participating centres, ranging from a multiple decrement probability of 2.7% in Finland to 19.6% in Hungary. No significant differences were observed in the rate ratios for planned pregnancy after discontinuation of the LNG-20 IUS and the Nova-T IUD (Andersson 1994). The rate ratios at one and two years were 1.07 (95% CI 0.88 to 1.32) and 1.07 (95% CI 0.9 to 1.28), respectively. It was not possible to extract any data on menstrual disturbance outcomes that did not result in discontinuation. The Andersson 1994 study was the only one where it was possible to extract any data on hormonal side effects. No significant differences were observed between the risk of hormonal side effects for women using the LNG-20 IUS compared to women using the Nova-T IUD. These data were collected at five year follow up. The reported side effects and their risk ratios were as follows: acne, 5.56 [95% CI 0.73 to 42.35]; headaches, 1.71 [95% CI 0.49 to 6.02]; breast tenderness, 1.50 [95% CI 0.31 to 7.17; ovarian cysts 1.50 [95% CI 0.51 to 4.40] and nausea, 4.99 [95% CI 0.24 to 103.86]. Luukkainen 1986 observed that women using the LNG-20 IUS were more likely to report an increase in headaches and acne than women using the Nova-T IUD, but it was not possible to extract these data for the meta-analysis. The life table differences indicate there were no significant differences between the expulsion rates of these two methods (Table 04). However, the rate ratios suggest that women using the LNG-20 IUS are significantly less likely to have an expulsion after two years of follow up (Table 03). As it is data from one study used to calculate the life table differences (Baveja 1989) and data from two other studies used to calculate the summary rate ratios (Andersson 1994, Luukkainen 1986), it is impossible to ascertain what effect the different methods of analysis have had on the results or whether it is in fact caused by differences in the shape of the different IUDs. Andersson 1994 found that LNG-20 IUS users were significantly less likely to experience PID, in particular younger women, but we were unable to use the data in the meta-analysis. No other data on adverse outcomes were collected.

Seven trials comparing Progestasert with non-hormonal IUDs <=250mm2 were were identified (Affandi 1980; Andrade 1988; Fylling 1979; Larsen 1981; Lavin 1983; Piazarro 1979; Rybo 1983) and two of these provided data that could be included in the meta-analysis, one comparing Progestasert with the Nova-T IUD (Fylling 1979) and other with the CuT 200 IUD (Larsen 1981). The reasons for exclusion of data from the meta-analyses was either because Progestaert was compared to methods that are no longer or have never been licensed (Affandi 1980; Andrade 1988; Piazarro 1979) or it was not possible to extract data (Lavin 1983; Rybo 1983) Both included trials ran for one year. The rate ratios for pregnancy, continuation of method, expulsion and ectopic pregnancy calculated for these studies are presented in Table 05. No data for any of these outcomes were included in the meta-analysis. Lavin 1983 reported that Progestasert users were significantly more likely to experience intermenstrual spotting, but significantly less likely to experience dysmenorrhoea.

One comparison of Progestasert and non-medicated IUDs was included (Newton 1979) and women were followed up for one year. Rate ratios for pregnancy, expulsion, ectopic pregnancy, and discontinuation for a planned pregnancy or personal reasons calculated from this study are presented in Table 06. No data were included in the meta-analysis on menstrual disturbance or hormonal side effect outcomes.

One study which compared users of the LNG-20 IUS with users of subdermal implants, Norplant-2, was identified (Wang 1992). The rate ratios calculated for pregnancy, continuation, expulsion, ovarian cysts, breast cancer, and discontinuation due to hormonal side effects, menstrual side effects, device problems and/or adverse events are presented in Table 07. There were significant differences found in the rates of reported menstrual disturbance. LNG-20 IUS users were significantly more likely to experience amenorrhoea compared to Norplant-2 users. The risk ratios were 2.27 [95% CI 1.03 to 4.99] at one year follow up, 42.46 [95% CI 2.62 to 689.20] at two years' follow up and 2.65 [95% CI 0.53 to 13.20] at three years' follow up. They were also significantly more likely to experience oligomenorrhoea, risk ratio 6.17 [95% CI 2.76 to 13.78] at two year follow up, although significant differences were not found at years' one and three follow up. LNG-20 IUS users were significantly less likely to experience spotting than Norplant-2 users, risk ratios 0.33 [95% CI 0.18 to 0.60] at one year, 0.18 [95% CI 0.07 to 0.5] at two years and 0.17 [95% CI 0.05 to 0.57] at three years, and significantly less likely to have prolonged bleeding, risk ratios 0.13 [95% CI 0.05 to 0.35] at one year, 0.17 [95% CI 0.06 to 0.46] at two years and 0.15 [95% CI 0.04 to 0.64] at three years.

There were no RCTs identified that compared IUSs with barrier, oral or injectable contraceptive methods.

DISCUSSION

There was insufficient evidence to suggest a difference in the pregnancy rates between LNG-20 IUS users and IUD >250mm2 users. The rate of pregnancy in LNG-20 IUS users was significantly lower than the rate in the IUD <=250mm2 users. Progestasert was significantly better at preventing pregnancy than the non-medicated IUD after one year, but not when compared to copper IUDs <=250mm2.

When interpreting these findings on contraceptive effectiveness consideration must be paid to the limitations of the data. First, in the main, comparisons were of contraceptive methods with similar default states rather than comparisons of IUSs with methods where user adherence is likely to be a factor in effectiveness. Therefore, this review is unable to look at the relative advantages and disadvantages of contraceptive methods which rely on differing default states, such as comparing the LNG-20 IUS to oral contraceptives or to DMPA injections. Second, very large numbers of women would need to be recruited into these trials where in general the contraceptive methods being compared are highly effective in preventing unwanted pregnancy. Failure to detect a significant difference in contraceptive effectiveness between methods may be due to the small number of women enrolled and followed up in the included studies. Third, although life tables have been recommended as the most appropriate way to analyse contraceptive effectiveness data, and many of the included studies employed this method, confusion arose because of the inconsistent way these methods were defined and calculated. This resulted in some studies being excluded. It was much easier to extract data on number of events and women months or years from papers to provide an estimate akin to the Pearl Index.

Although it is useful to know how many unwanted pregnancies a method prevents, this information is of little value without collecting data on outcomes which reflect the acceptability of a method. A method may be efficacious in terms of preventing unwanted pregnancy, but if the method is discontinued within a short period of time its value as a method of contraception is greatly reduced. The meta-analyses conducted for continuation at yearly follow ups showed variable results between the different comparisons.

Few data could be extracted on hormonal side effects and menstrual disturbance. The one outcome that users of all types of IUSs were significantly more likely to experience was amenorrhoea. The fact that so little data were available was not necessarily because authors had not reported these outcomes, but was due to the ways these outcomes had been measured. For instance, some investigators reported a percentage of women experiencing an 'increase', 'decrease' and 'the same' as measurements for events, such as dysmenorrhoea or headaches. This does not allow baseline patterns on risk factors, such as age and parity, to be taken account of in the analysis.

The evidence on LNG-20 IUS suggested that women using this method were significantly more likely to expel the device than IUD >250mm2 users. It has been recommended that only health care workers who have received specialist training should insert and remove these methods in order to prevent local device problems. None of the studies reported whether or not health care workers had received specialist training, therefore we were not able to investigate the effect this had device expulsions.

Progestasert's license was not renewed in some countries because of concerns about increased risk of ectopic pregnancy when compared to copper bearing devices. Too few studies were eligible for inclusion in the meta-analysis for this risk to be accurately determined.

Discontinuation due menstrual changes per se is not an informative outcome as the LNG-20 and IUD >250mm2 comparison illustrates. Women using LNG-20 IUSs discontinued due to amenorrhoea, while IUD >250mm2 users discontinued because of bleeding and pain. The reporting of discontinuation due to amenorrhoea, bleeding and pain must be collected separately to provide a true picture.

An additional issue when interpreting data on discontinuation of methods due to menstrual changes is consideration of the 'cultural' setting in which the trials were conducted. For example, women from different backgrounds, as well as providers, may view menstrual change differently, as illustrated by the unpublished data from the Andersson study (Leiras Ltd 1999). Women should be informed of these potential side effects prior to starting these methods. The amenorrhoea in users of the LNG-20 IUS is benign and is due to high concentrations of levonorgestrel in the endometrium, the end organ (Scholten 1989). Therefore, if women (and providers) are informed amenorrhoea has no ill effect on their health (and for some with heavy menstrual bleeding it may have a positive effect), the acceptability of these methods may be improved.

REVIEWERS' CONCLUSIONS

Implications for practice

We found no significant difference in the risk of unwanted pregnancy between the LNG-20 IUS and IUDs >250mm2 or Norplant-2 although, given the very large numbers needed to provide adequate power to detect differences in uncommon events, this may reflect a lack of power in the included studies. We did find a lower risk of pregnancy when the LNG-20 IUS was compared to IUDs<=250mm2.

Women using the LNG-20 IUS were more likely to experience amenorrhoea and this event was a notable reason for discontinuation. The much higher net ingredient cost (i.e. the device cost) of the LNG-20 IUS when compared to IUDs, with no discernible benefit in terms of contraceptive effectiveness when compared to IUDs >250mm2, may suggest that its use should be targeted at those women who are concerned about menstrual bleeding and pain with IUD use. All women who are considering a LNG-20 IUS should be informed of the possibility of amenorrhoea.

For the most part IUS users will be parous women who require contraception for birth spacing purposes. Therefore, rather than the results being generalisable to all women seeking contraception, these findings may be applicable to this group of women.

Implications for research

This systematic review highlighted the problems which arise because of inconsistent methods used to measure and report contraceptive effectiveness. Although we were not able to assess what impact these factors had on pooled data, standardised methods need to be encouraged.

It is vital that contraceptive effectiveness research is able to answer the queries and concerns of contraceptive users. Unfortunately, this has not been the case to date. Although rates of unplanned pregnancy, continuation and reasons for discontinuation of methods do provide information on acceptability and tolerability as well as effectiveness, many studies fail to report hormonal side effects and menstrual changes. Women's choice and acceptance of different methods is likely to be affected by acceptability, tolerability and availability of alternatives and the desire not to conceive. If lay contraceptive users are involved in research development, attention can be directed to answering questions of importance to consumers.

POTENTIAL CONFLICT OF INTEREST

None

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Affandi 1980**
Methods	Setting: Indonesia 697 women randomised Follow up: 2 years
Participants	Not stated
Interventions	Progestasert [n=72] vs. CuT 200, Cu 7 and Lippes loop IUDs [n=75, 75 and 75, respectively]
Outcomes	Pregnancy Reasons for discontinuation
Notes	Abstract Quality assessment not conducted
Allocation concealment	D

Study	**Andersson 1994**
Methods	Setting: Multinational (Denmark, Finland, Hungary, Norway and Sweden), Family Planning Clinics (12) 2758 women randomised Follow up: 5 years
Participants	18-38 years Parous Not breast feeding
Interventions	LNG-20 IUS [n=1821] vs. Nova-T IUD [n=937]
Outcomes	Pregnancy

Characteristics of included studies (*Continued*)

	Continuation Reasons for discontinuation Adverse events Hormonal side effects Pregnancy after discontinuation of method
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: Centrally prepared envelopes Description of prior contraceptive method / pregnancy provided Mesurement: Groups treated identically Method of analysis: Life tables (multiple and single decrement rates) User/method failure reported
Allocation concealment	B

Study	**Andrade 1988**
Methods	Setting: Chile and Brazil (see Notes), Hospital 150 women randomised Follow up: 2 years
Participants	Parous
Interventions	Progestasert [n=49] vs. Lippes lopp and Cu 7 IUDs [n=51 and 50, respectively]
Outcomes	Menstrual blood loss Iron status
Notes	Brazil group excluded because not randomised Quality assessment: Randomisation technique: Random number table Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy provided Method of analysis: Not applicable
Allocation concealment	D

Study	**Baveja 1989**
Methods	Setting: India, Family Planning Clinics 2118 women randomised Follow up: 3 years
Participants	18-40 years Proven fertility regular menses
Interventions	LNG-20 IUS [n=475] vs. CuT 380Ag, CuT 220C and CuT 200B IUDs [n=434, 496 and 500, respectively]
Outcomes	Pregancy Continuation Reasons for discontinuation Menstrual disturbance
Notes	Quality assessment: Randomisation technique: Computed random numbers Allocation concealment technique: Sealed envelopes Measurement: Groups treated identically Method of analysis: Life tables (single decrement rates) User / method failure reported

Allocation concealment	A

Study	**Fylling 1979**
Methods	Setting: Denmark 326 women randomised Follwo up: 1 year
Participants	Mixed parity
Interventions	Progestasert [n=162] vs. Nova-T IUD [n=164]
Outcomes	Pregnancy Continuation Reasons for discontinuation Serum immunoglobin levels
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Measurement: Groups treated identically Method of analysis: Other
Allocation concealment	D

Study	**Heikkila 1982**
Methods	Setting: Finland, Maternity Unit 80 women randomised Follow up: 1 year
Participants	Postpartum Amenorrhoeic Breast feeding
Interventions	LNG-30 IUS[n=40] vs. Nova-T IUD [n=40]
Outcomes	Pregnancy Continuation Reasons for discontinuation Hormonal side effects Menstrual disturbance LNG plasma concentration
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy provided Method of analysis: Other User / method failure reported: Not applicable
Allocation concealment	D

Study	**Larsen 1981**
Methods	Setting: Denmark 382 women randomised Follow up: 1 year
Participants	15-44 years Variable parity

Characteristics of included studies (*Continued*)

Interventions	Progestasert [n=196] vs. CuT 200 IUD [n=186]
Outcomes	Pregnancy Continuation Reasons for discontinuation
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Women blinded to method Measurement: Groups treated identically Method of analysis: Life tables (multiple decrement rates)
Allocation concealment	D

Study	**Lavin 1983**
Methods	Setting: Chile, Maternity Unit 400 women randomised Follow up: 1 year
Participants	Postpartum
Interventions	Progestasert [n=200] vs. CuT 200 IUD [n=200] - 100 inserted by hand and 100 inserted an inserter in each group
Outcomes	Pregnancy Continuation Menstrual disturbance
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy provided Measurement: Groups treated identically Method of analysis: Other
Allocation concealment	D

Study	**Luukkainen 1986**
Methods	Setting: Finland and Brazil, Family Planning Clinics 484 women randomised Follow up: 2 years (Brazil and Finland) and 5 years (Finland only)
Participants	18-40 years Proven fertility Not breast feeding
Interventions	LNG-20 and LNG-30 IUSs [n=164 and 163, respectively] vs. Nova-T IUD [n=157]
Outcomes	Pregnancy Continuation Resaons for discontinuation Hormonal side effects Menstrual disturbance
Notes	Quality assessment: Randomisation technique: Random tables (permutations of nine numbers) Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy provided

	Double-blinded assessment of outcomes Measurement: Groups treated identically Method of analysis: Pearl Indices and life tables (multiple and single decrement rates) User / method failure reported
Allocation concealment	D

Study	**Newton 1979**
Methods	Setting: Clinics (4) 676 women randomised Follow up: 1year
Participants	Various parity
Interventions	Progestasert [n=359] vs. inert IUD [n=317]
Outcomes	Pregnancy Continuation Reasons for discontinuation Menstrual disturbance
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment: 'both types of device were externally identical' Double-blinded assessment of outcomes Measurement: Groups treated identically Method of analysis: Life tables
Allocation concealment	B

Study	**Pakarinen 1996**
Methods	Setting: Finland, Family Planning Clinics 298 women randomised Follow up: 1 year
Participants	18-43 years Variable parity Regular menses
Interventions	LNG-20 IUS [n=147] vs. LNG-20 ICD [n=151]
Outcomes	Pregnancy Continuation Reasons for discontinuation Hormonal side effects
Notes	Quality assessment: Randomisation technique: Random number table with group allocation predetermined Allocation concealment technique: Consecutively numbered opaque sealed envelopes opened just before IUS insertion Measurement: Groups treated identically Method of analysis: Life tables (single decrement rates) User / method failure reported
Allocation concealment	A

Study	**Piazarro 1979**
Methods	Setting: Chile, Family Planning Clinics 295 women randomised

Characteristics of included studies (*Continued*)

	Follow up: 1 year
Participants	17-40 years Parous Regular menses
Interventions	Progesterone T IUS [n=146] vs. Cu 7 IUD [n=149]
Outcomes	Pregnancy Continuation Reasons for discontinuation Menstrual disturbance
Notes	Quality assessment: Randomisation technique: Computed tables Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy reported Blinded assessment of outcomes Measurement: Groups treated identically Method of analysis: Life tables (method not stated) User / method failure reported
Allocation concealment	D

Study	**Rybo 1983**
Methods	Setting: France Follow up: < 1 year 30 women randomised
Participants	24-42 years Multiparous
Interventions	Progestasert [n=13] vs. CuT 200 IUD [n=17]
Outcomes	Pregnancy Menstrual disturbance and blood loss
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Measurement: Groups treated identically Method of analysis: Other
Allocation concealment	D

Study	**Sivin 1994**
Methods	Setting: Multinational (Singapore, Brazil, Egypt and USA), Family Planning Clinics 2226 women randomised Follow up: 7 years
Participants	18-38 years Parous
Interventions	LNG-20 IUS [n=1125] vs. CuT 380Ag IUD [n=1121]
Outcomes	Pregnancy Continuation Reasons for discontinuation Insertion problems Hormonal side effects Menstrual disturbance

	Adverse events Pregnancy after discontinuation of method
Notes	Quality assessment: Randomisation technique: Random numbers - blocks of 50 Allocation concealment: Sealed opaque envelopes openned in ascending numerical order Women blinded to method Measurement: Groups treated identically Method of analysis: Life tables (multiple and single decrement rates) User / method failure reported Active follow up conducted
Allocation concealment	A

Study	**WHO 1983**
Methods	Multinational (13 countries), Family Planning Clinics 5542 women randomised (2514 birth spacing insertion and 3028 post abortion insertion) Follow up: 2 years
Participants	16-40 years
Interventions	1. Alza T IPCS 52 [n=1254] vs. CuT 220C IUD [n=1260] - interval insertion 2. Alza T IPCS 52 [n=985] vs. CuT 220C and Multiload IUDs [n=1032 and 1011, respectively] - post abortion insertion
Outcomes	Pregnancy Continuation Reasons for disconyinuation
Notes	Quality assessment: Randomisation technique: Computed random tables Allocation concealment technique: Sealed envelopes Measurement: Groups treated identically Method of analysis: Life tables (single decrement rates) User / method failure reported Active follow up conducted
Allocation concealment	A

Study	**WHO 1987**
Methods	Multinational (Thailand, China, India, Vietnam, Cuba, Russia, Yugloslavia and Zambia) 4182 women randomised Follow up: 2 years
Participants	16-40 years Parous
Interventions	LNG-2 IUS [n=1377] vs. CuT 220C and Nova-T IUDS [n=1412 and 1393, respectively]
Outcomes	Pregnancy Continuation Reasons fo discontinuation
Notes	Quality assessment: Randomisation technique: Computed tables Allocation concealment technique: Sealed envelopes Measurement: Groups treated identically Method of analysis: Life tables (single decrement rates) User / method failure reported Active follow up conducted
Allocation concealment	A

Study	Wang 1992
Methods	Setting: China, Family Planning Clinics 200 women randomised Follow up: 3 years
Participants	20-40 years Parous Not breast feeding
Interventions	LNG-20 IUS [n=100] vs. Norplant-2 [n=100]
Outcomes	Pregnancy Continuation Reasons for discontinuation Menstrual disturbance
Notes	Quality assessment: Randomisation technique: Sequential identication number Allocation concealment technique: Sealed envelopes Description of prior contraceptive method / pregnancy provided Meseasurement: Groups treated identically Method of analysis: Life tables (single decrement rates) User / method failure reported
Allocation concealment	A

Study	el Mahgoub 1982
Methods	Setting: Egypt, Family Planning Clinics 300 women randomised Follow up: 3 years
Participants	15-40 years Parous Hormonal contraceptive users at enrollment and immediate post partum women excluded
Interventions	LNG-10 IUS and Norgestrel T (various doses) IUSs vs. CuT 200 IUD [n=100 in each group]
Outcomes	Pregnancy Continuation Reasons for discontinuation Menstrual disturbance and blood loss Endometrial and cervical cell changes
Notes	Quality assessment: Randomisation technique: No mention Allocation concealment technique: No mention Description of prior contraceptive method / pregnancy provided Method of analysis: Life tables (method not stated)
Allocation concealment	D

Characteristics of excluded studies

Study	Reason for exclusion
Diaz 1993	Intervention: LNG-IUS vs. CuT 380Ag IUD Primary outcomes: Pregnancy, continuation and reasons for discontinuation

Characteristics of excluded studies (*Continued*)

	Only report outcomes for LNG-IUS users. Comparative results reported elsewhere (see Sivin 1994)
Faundes 1993	Intervention: LNG-IUS vs. CuT 380Ag IUD Primary outcomes: Pregnancy, continuation, reasons for discontinuation, ovarian function and LNG serum levels Only report outcomes for LNG-users. Comparative results reported elsewhere (see Sivin 1994)
Nilsson 1977	Intervention: d-norgestrel releasing IUS vs. Nova-T 200 IUD Primary outcomes: Menstrual blood loss Reported outcomes not relevant to review
Nilsson 1986	Intervention: LNg-20 IUS vs. LNG-30 IUS Primary outcomes: Plasma concentration of LNG Reported outcomes not relevant to review (other publications of study included - see Luukkainen 1986)
Pedron Neueo 1992	Intervention: Various IUSs and IUDs (11) Primary outcomes: Menstrual blood loss Reported outcomes not relevant to review
Ulstein 1987	Intervention: LNG-IUS vs. copper IUD Primary outcomes: Changes in cervical and vaginal microflora Reported outcomes not relevant to review
Yin 1993	Intervention: LNG-IUS, stainless steel ring and CuT 220 IUD Primary outcomes: Endometrial mast cell density Reported outcomes not relevant to review

Characteristics of ongoing studies

Study	**WHO 1997**
Trial name or title	
Participants	International multicentre (20) 3384 women randomised
Interventions	LNG-20 IUS (n=1693) vs. CuT 380A (N=1691)
Outcomes	Pregnancy Continuation Reseaons for discontinuation
Starting date	
Contact information	
Notes	

GRAPHS

Comparison 01. LNG-20 IUS vs. IUDs >250mm2

Outcome title	**No. of studies**	**No. of participants**	**Statistical method**	**Effect size**
Pregnancy due to method failure			Other data	No numeric data
Continuation of method			Other data	No numeric data
Planned pregnancy after discontinuation of method	1	86	Peto Odds Ratio 95% CI	1.25 [0.45, 3.48]
Amenorrhoea	2	700	Peto Odds Ratio 95% CI	5.29 [3.64, 7.68]
Prolonged bleeding	2	700	Peto Odds Ratio 95% CI	0.80 [0.51, 1.26]
Expulsion			Other data	No numeric data

Embedded	Other data	No numeric data
Ectopic pregnancy	Other data	No numeric data
Pelvic inflammatory disease	Other data	No numeric data
Hormonal reasons for discontinuation	Other data	No numeric data
Menstrual reasons for discontinuation: all	Other data	No numeric data
Menstrual reasons for discontinuation: bleeding & pain	Other data	No numeric data
Menstrual reasons for discontinuation: pain	Other data	No numeric data
Menstrual reasons for discontinuation: amenorrhoea	Other data	No numeric data
Discontinuation due to adverse event	Other data	No numeric data
Discontinuation because planning pregnancy	Other data	No numeric data
Personal reasons for discontinuation	Other data	No numeric data

Comparison 02. LNG-20 IUS vs. IUD<=250mm2

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
Pregnancy due to method failure			Other data	No numeric data
Continuation of method			Other data	No numeric data
Planned pregnancy after discontinuation of method			Peto Odds Ratio 95% CI	Totals not selected
Headaches	1	1051	Peto Odds Ratio 95% CI	1.62 [0.53, 4.92]
Breast tenderness	1	1051	Peto Odds Ratio 95% CI	1.45 [0.35, 6.07]
Acne	1	1051	Peto Odds Ratio 95% CI	3.01 [0.95, 9.51]
Nausea	1	1051	Peto Odds Ratio 95% CI	4.18 [0.20, 86.14]
Ovarian cysts			Other data	No numeric data
Expulsion			Other data	No numeric data
Ectopic pregnancy			Other data	No numeric data
Pelvic inflammatory disease			Other data	No numeric data
Hormonal reasons for discontinuation			Other data	No numeric data
Menstrual reasons for discontinuation: all			Other data	No numeric data
Menstrual reasons for discontinuation: bleeding & pain			Other data	No numeric data
Menstrual reasons for discontinuation: amenorrhoea			Other data	No numeric data
Discontinuation due to adverse event			Other data	No numeric data
Discontinuation because planning pregnancy			Other data	No numeric data

Discontinuation for personal reasons	Other data	No numeric data

Comparison 03. LNG-20 IUS vs. Norplant-2

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
Pregnancy			Other data	No numeric data
Continuation of method			Other data	No numeric data
Expulsion			Other data	No numeric data
Breast cancer			Other data	No numeric data
Ovarian cysts			Other data	No numeric data
Spotting			Peto Odds Ratio 95% CI	Subtotals only
Oligomenorrhoea			Peto Odds Ratio 95% CI	Subtotals only
Amenorrhoea			Peto Odds Ratio 95% CI	Subtotals only
Prolonged bleeding			Peto Odds Ratio 95% CI	Subtotals only

Comparison 04. Progestasert vs. IUDs <=250mm2

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
Pregnancy			Other data	No numeric data
Continuation of method			Other data	No numeric data
Expulsion			Other data	No numeric data
Ectopic pregnancy			Other data	No numeric data
Menstrual reasons for discontinuation: bleeding & pain			Other data	No numeric data

Comparison 05. Progestasert vs. non-medicated IUD

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
Pregnancy			Other data	No numeric data
Continuation of method			Other data	No numeric data
Expulsion			Other data	No numeric data
Ectopic pregnancy			Other data	No numeric data
Menstrual reasons for discontinuation: all			Other data	No numeric data
Discontinuation because planning pregnancy			Other data	No numeric data
Discontinuation for personal reasons			Other data	No numeric data

COVER SHEET

Title Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

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Comparison 05. Pregnancy due to method failure

GRAPHS AND OTHER TABLES

At 1 year

Study	
Baveja 1989	Single decrement life table probabilities (SE) = 0.0 (0.4) vs. 0.8 (0.4)
Sivin 1994	2/7680 women months vs. 2/7740 women months Single decrement life table probabilities (SE) = 0.3 (0.2) vs. 0.3 (0.2)

At 2 years

Study	
Baveja 1989	Single decrement life table probabilities (SE) = 0.0 (0.5) vs. 1.0 (0.5)
Sivin 1994	2/19644 women months vs. 7/20436 women months

At 3 years

Study	
Baveja 1989	0/10589 women months vs. 4/10869 women months Single decrement life table probabilities (SE) = 0.0 (0.5) vs. 1.0 (0.5)

At 5 years

Study	
Sivin 1994	6/34944 women months vs. 10/38268 women months Single decrement life table probabilities (SE) = 1.1 (0.5) vs. 1.4 (0.4)

Comparison 05. Continuation of method

At 1 year
Study

Baveja 1989	339/4809 women months vs. 350/4599 women months
Sivin 1994	743/11892 women months vs. 791/12084 women months Life table probabilities (SE) = 73.5 (1.4) vs. 79.8 (1.3)

At 2 years
Study

Baveja 1989	257/8321 women months vs. 276/8333
Sivin 1994	548/19644 women months vs. 605/20436 women months Life table probabilities (SE) = 59.4 (1.6) vs. 67.5 (1.5)

At 3 years
Study

Baveja 1989	150/10589 women months vs. 170/10869 women months

At 5 years
Study

Sivin 1994	298/34944 women months vs. 335/38268 women months Life table probabilities (SE) = 33 (1.5) vs. 40.6 (1.6)

Comparison 05. Planned pregnancy after discontinuation of method

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy
Comparison: 01 LNG-20 IUS vs. IUDs >250mm2
Outcome: 03 Planned pregnancy after discontinuation of method

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 1 year					
Sivin 1994	39/49	28/37		100.0	1.25 [0.45, 3.48]
Total (95% CI)	49	37		100.0	1.25 [0.45, 3.48]
Total events: 39 (Treatment), 28 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.43 p=0.7					

Comparison 05. Amenorrhoea

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 01 LNG-20 IUS vs. IUDs >250mm2

Outcome: 04 Amenorrhoea

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 3 months					
Sivin 1994	41/215	20/226		47.7	2.35 [1.37, 4.04]
Subtotal (95% CI)	215	226		47.7	2.35 [1.37, 4.04]
Total events: 41 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.10 p=0.002					
02 At 3 years					
Sivin 1994	75/120	12/139		52.3	11.08 [6.61, 18.57]
Subtotal (95% CI)	120	139		52.3	11.08 [6.61, 18.57]
Total events: 75 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=9.13 p<0.00001					
Total (95% CI)	335	365		100.0	5.29 [3.64, 7.68]
Total events: 116 (Treatment), 32 (Control)					
Test for heterogeneity chi-square=16.53 df=1 p=<0.00011 =94.0%					
Test for overall effect z=8.75 p<0.00001					

Comparison 05. Prolonged bleeding

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 01 LNG-20 IUS vs. IUDs >250mm2

Outcome: 05 Prolonged bleeding

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 3 months					
Sivin 1994	42/215	49/226		94.8	0.88 [0.55, 1.39]
Subtotal (95% CI)	215	226		94.8	0.88 [0.55, 1.39]
Total events: 42 (Treatment), 49 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.56 p=0.6					
02 At 3 years					
Sivin 1994	0/120	4/139		5.2	0.15 [0.02, 1.10]
Subtotal (95% CI)	120	139		5.2	0.15 [0.02, 1.10]
Total events: 0 (Treatment), 4 (Control)					

(*Continued . . .*)

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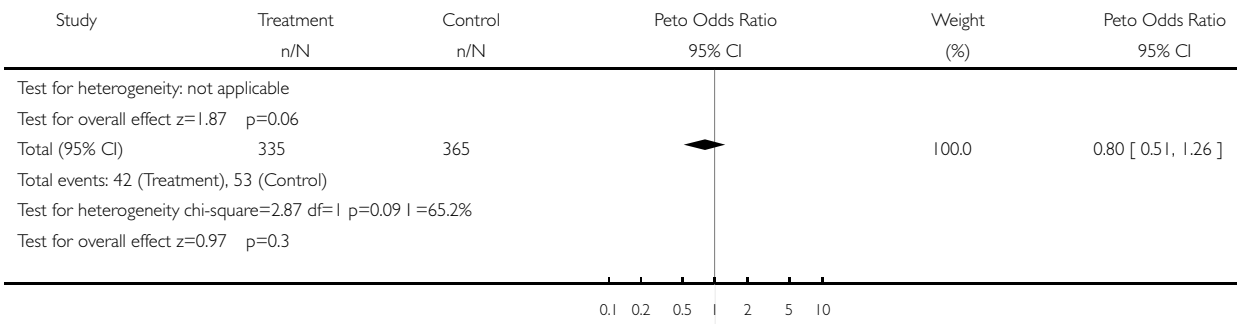


Comparison 05. Expulsion

At 1 year
Study

Baveja 1989 — Single decrement life table probabilities (SE) = 6.5 (1.2) vs. 5.3 (1.1)

Sivin 1994 — 43/7680 women months vs. 39/7740 women months
Single decrement life table probabilities (SE) = 6.4 (1.0) vs. 5.8 (1.9)

At 2 years
Study

Baveja 1989 — Single decrement life table probabilities (SE) = 9.2 (1.4) vs. 7.1 (1.3)

At 3 years
Study

Baveja 1989 — Single decrement life table probabilities (SE) = 10.6 (1.6) vs. 7.6 (1.4)

At 5 years
Study

Sivin 1994 — 99/34944 women months vs. 71/38268 women months
Single decrement life table probabilities (SE) = 11.8 (1.2) vs. 7.4 (0.9)

Comparison 05. Embedded

At 5 years
Study

Sivin 1994 — 3/34944 women months vs. 0/38268 women months

Comparison 05. Ectopic pregnancy

At 1 year
Study

Sivin 1994	0/7680 women months vs. 0/7740 women months

At 2 years
Study

Sivin 1994	0/19644 women months vs. 0/20436 women months

At 5 years
Study

Sivin 1994	0/34944 women months vs. 2/38268 women months

Comparison 05. Pelvic inflammatory disease

At 1 year
Study

Sivin 1994	10/7680 women months vs. 8/7740 women months Single decrement life table probabilities (SE) = 1.6 (0.5) vs. 1.3 (0.4)

Comparison 05. Hormonal reasons for discontinuation

At 1 year
Study

Sivin 1994	4/7680 women months vs. 5/7740 women months Single decrement life table probabilities (SE) = 0.7 (0.4) vs. 0.8 (0.4)

At 3 years
Study

Baveja 1989	10/10589 women months vs. 6/10869 women months

At 5 years
Study

Sivin 1994	31/34994 women months vs. 8/38268 women months

Comparison 05. Menstrual reasons for discontinuation: all

At 1 year
Study

Baveja 1989	Single decrement life table probabilities (SE) = 13.8 (1.7) vs. 7.1 (1.3)
Sivin 1994	69/7680 women months vs. 47/7740 women months Single decremt life table probabilities (SE) = 11.1 (7.5) vs. 1.6 (1.1)

At 2 years
Study

Baveja 1989 — Single decrement life table probabilities (SE) = 21.9 (2.1) vs. 10.8 (1.3)

At 3 years
Study

Baveja 1989 — Single decrement life table probabilities (SE) = 27.9 (2.3) vs. 13.4 (1.8)

At 5 years
Study

Sivin 1994 — 252/34944 women months vs. 186/38268 women months

Comparison 05. Menstrual reasons for discontinuation: bleeding & pain

At 5 years
Study

Sivin 1994 — 118/34944 women months vs. 183/38268 women months
Single decrement life table probabilities (SE) = 15.4 (1.4) vs. 23.3 (0.6)

Comparison 05. Menstrual reasons for discontinuation: pain

At 1 year
Study

Sivin 1994 — Single decrement life table probabilities (SE) = 2.5 (0.6) vs. 3.4 (0.8)

At 5 years
Study

Sivin 1994 — 15/7680 women months vs. 47/7740 women months
Single decrement life table probabilities (SE) = 19.7 (1.6) vs. 0.4 (0.2)

Comparison 05. Menstrual reasons for discontinuation: amenorrhoea

At 1 year
Study

Sivin 1994 — 32/7680 women months vs. 0/7740 women months
Single decrement life table probabilities (SE) = 5.6 (1.0) vs. 0.0

At 5 years
Study

Sivin 1994 — 134/34944 women months vs. 3/38268 women months

Comparison 05. Discontinuation due to adverse event

At 3 years

Study	
Baveja 1989	2/10589 women months vs. 2/10869 women months

Comparison 05. Discontinuation because planning pregnancy

At 1 year

Study	
Sivin 1994	15/7680 women months vs. 16/7740 women months Single decrement life table probabilities (SE) = 2.8 (0.7) vs. 2.9 (0.7)

At 5 years

Study	
Sivin 1994	155/34944 women months vs. 153/38268 women months Single decrement life table probabilities (SE) = 25.0 (1.9) vs. 23.5 (1.7)

Comparison 05. Personal reasons for discontinuation

At 1 year

Study	
Sivin 1994	18/7680 women months vs. 13/7740 women months Single decrement life table probabilities (SE) = 3.0 (0.7) vs. 2.2 (0.6)

At 5 years

Study	
Sivin 1994	56/34944 women months vs. 55/38268 women months Single decrement life table probabilities (SE) = 9.5 (1.3) vs. 9.4 (1.3)

Comparison 05. Pregnancy due to method failure

At 1 year

Study	
Andersson 1994	1/18664 women months vs. 8/9326 women months
Baveja 1989	Single decrement life table probabilities (SE) = 0.0 vs. CuT 220C 0.0 and vs. CuT 200B 0.9 (0.4)
Luukkainen 1986	1/1654 women months vs. 4/1708 women months

At 2 years

Study	
Baveja 1989	Single decrement life table probabilities (SE) = 0.0 vs. CuT 220C 0.0 and vs. CuT 200B 0.9 (0.4)

At 3 years
Study

Andersson 1994	3/46200 women months vs. 24/23568 women months
Baveja 1989	0/10589 women months vs. 7/24225 women months (vs. CuT 220C 1/12076 women months and vs. CuT 220B 6/12149 women months) Single decrement life table probabilities (SE) = 0.0 vs. CuT 220C 0.3 (0.3) and vs. CuT 200B 1.6 (0.6)

At 5 years
Study

Andersson 1994	5/67380 women months vs. 35/33312 women months
Luukkainen 1986	1/5495 women months vs. 7/5176 women months

Comparison 05. Continuation of method

At 1 year
Study

Andersson 1994	1362/18664 women months vs. 680/9326 women months
Baveja 1989	339/4809 women months vs. 791/9814 women months

At 2 years
Study

Baveja 1989	257/8321 women months vs. 617/18819 women months

At 3 years
Study

Andersson 1994	902/46200 women months vs. 435/23568 women months
Baveja 1989	150/10589 women months vs. 344/24255 women months

At 5 years
Study

Andersson 1994	67/5495 women months vs. 53/5176 women months
Luukkainen 1986	736/67380 women months vs. 315/33312 women months

Comparison 05. Planned pregnancy after discontinuation of method

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 02 LNG-20 IUS vs. IUD<=250mm2

Outcome: 03 Planned pregnancy after discontinuation of method

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Peto Odds Ratio 95% CI
01 At 1 year				
Andersson 1994	96/138	46/71		1.24 [0.67, 2.29]
02 At 2 years				
Andersson 1994	104/138	50/71		1.29 [0.67, 2.46]

Comparison 05. Headaches

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 02 LNG-20 IUS vs. IUD<=250mm2

Outcome: 04 Headaches

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 5 years					
Andersson 1994	12/736	3/315		100.0	1.62 [0.53, 4.92]
Total (95% CI)	736	315		100.0	1.62 [0.53, 4.92]
Total events: 12 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.85 p=0.4					

Comparison 05. Breast tenderness

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 02 LNG-20 IUS vs. IUD<=250mm2

Outcome: 05 Breast tenderness

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 5 years					
Andersson 1994	7/736	2/315		100.0	1.45 [0.35, 6.07]
Total (95% CI)	736	315		100.0	1.45 [0.35, 6.07]
Total events: 7 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.51 p=0.6					

Comparison 05. Acne

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 02 LNG-20 IUS vs. IUD<=250mm2

Outcome: 06 Acne

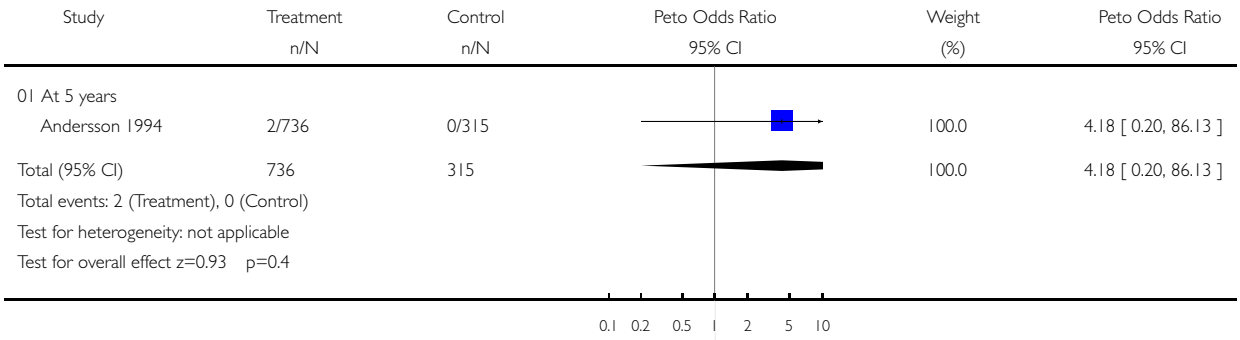
Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 5 years					
Andersson 1994	13/736	1/315		100.0	3.01 [0.95, 9.51]
Total (95% CI)	736	315		100.0	3.01 [0.95, 9.51]
Total events: 13 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.88 p=0.06					

Comparison 05. Nausea

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 02 LNG-20 IUS vs. IUD<=250mm2

Outcome: 07 Nausea



Comparison 05. Ovarian cysts

At 1 year
Study

Andersson 1994 12/18664 women months vs. 4/9326 women months

Comparison 05. Expulsion

At 1 year
Study

Andersson 1994 62/18664 women months vs. 32/9326 women months

Baveja 1989 Single decrement life table probabilities (SE) = 6.5 (1.2) vs. CuT 220C 4.8 (1.0) and vs. CuT 200B 4.9 (1.0)

At 2 years
Study

Baveja 1989 Single decrement life table probabilities (SE) = 9.2 (1.4) vs. CuT 220C 7.1 (1.2) and vs. CuT 200B 7.7 (1.3)

Luukkainen 1986 1/3083 women months vs. 9/2989 women montths

At 5 years
Study

Luukkainen 1986 2/5495 women months vs. 7/5176 women months

Comparison 05. Ectopic pregnancy

At 1 year
Study

Andersson 1994	0/18664 women months vs. 1/9326 women months
Luukkainen 1986	1/1654 women months vs. 0/1708 women months

At 3 years
Study

Andersson 1994	1/46200 women months vs. 5/23568 women months

At 5 years
Study

Andersson 1994	1/67380 women months vs. 7/33312 women months

Comparison 05. Pelvic inflammatory disease

At 1 year
Study

Luukkainen 1986	0/1654 women months vs. 0/1708 women months

At 2 years
Study

Luukkainen 1986	0/3083 women months vs. 3/2989 women months

Comparison 05. Hormonal reasons for discontinuation

At 1 year
Study

Andersson 1994	54/18664 women months vs. 5/9326 women months

At 3 years
Study

Andersson 1994	110/46200 women months vs. 5/23568 women months
Baveja 1989	Total: 10/10589 women months vs. 27/24225 women months (vs. CuT220C 13/12076 women months and vs. CuT200B 14/12149 women months)

At 5 years
Study

Luukkainen 1986	11/5495 women months vs. 2/5176 women months

Comparison 05. Menstrual reasons for discontinuation: all

At 1 year
Study

Andersson 1994 153/18664 women months vs. 65/9326 women months

Baveja 1989 Single decrement life table probabilities (SE) = 13.8 (1.7) vs. CuT 220C 6.0 (1.1) and vs. CuT 200B 5.7 (1.1)

At 2 years
Study

Baveja 1989 Single decrement life table probabilities (SE) = 21.9 (2.1) vs. CuT 220C 9.9 (1.4) and vs. CuT 200B 8.8 (1.4)

At 3 years
Study

Baveja 1989 Single decrement life table probabilities (SE) = 27.9 (2.3) vs. CuT 220C 15.4 (1.9) and vs. CuT 200B 14.6 (1.9)

At 5 year
Study

Luukkainen 1986 26/5495 women months vs. 21/5176 women months

Comparison 05. Menstrual reasons for discontinuation: bleeding & pain

At 5 years
Study

Luukkainen 1986 11/5495 women months vs. 21/5176 women months

Comparison 05. Menstrual reasons for discontinuation: amenorrhoea

At 5 years
Study

Luukkainen 1986 15/5495 womenmonths vs. 0/5176 women months

Comparison 05. Discontinuation due to adverse event

At 1 year
Study

Andersson 1994 42/18664 women months vs. 21/9326 women months

At 3 years
Study

Baveja 1989 Total: 2/10589 women months vs. 4/24225 women months (vs. CuT220C 0/12076 women months and vs. CuT200B 4/12149 women months)

At 5 years
Study

Luukkainen 1986 5/5495 women months vs. 6/5176 women months

Comparison 05. Discontinuation because planning pregnancy

At 5 years
Study

Luukkainen 1986 10/5495 women months vs. 16/5176 women months

Comparison 05. Discontinuation for personal reasons

At 5 years
Study

Luukkainen 1986 6/5495 women months vs. 3/5176 women months

Comparison 05. Pregnancy

At 1 year
Study

Wang 1992 1/1157 women months vs. 0/1187 women months

At 2 years
Study

Wang 1992 1/2171 women months vs. 0/2218 women months

At 3 years
Study

Wang 1992 1/3098 women months vs. 0/3093 women months

Comparison 05. Continuation of method

At 1 year
Study

Wang 1992 81/1157 women months vs. 93/1187 women months

Comparison 05. Expulsion

At 1 year
Study

Wang 1992 3/1157 women months vs. 0/1187 women months

Comparison 05. Breast cancer

At 1 year
Study

Wang 1992 0/1157 women months vs. 0/1187 women months

Comparison 05. Ovarian cysts

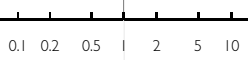
At 1 year
Study

Wang 1992 4/1157 women months vs. 1/1187 women months

Comparison 05. Spotting

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy
Comparison: 03 LNG-20 IUS vs. Norplant-2
Outcome: 06 Spotting

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 1 year					
Wang 1992	11/90	36/96		100.0	0.26 [0.14, 0.51]
Subtotal (95% CI)	90	96		100.0	0.26 [0.14, 0.51]
Total events: 11 (Treatment), 36 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.95 p=0.00008					
02 At 2 years					
Wang 1992	4/79	22/79		100.0	0.19 [0.08, 0.45]
Subtotal (95% CI)	79	79		100.0	0.19 [0.08, 0.45]
Total events: 4 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.85 p=0.0001					
03 At 3 years					
Wang 1992	3/65	18/69		100.0	0.20 [0.08, 0.50]
Subtotal (95% CI)	65	69		100.0	0.20 [0.08, 0.50]
Total events: 3 (Treatment), 18 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.40 p=0.0007					

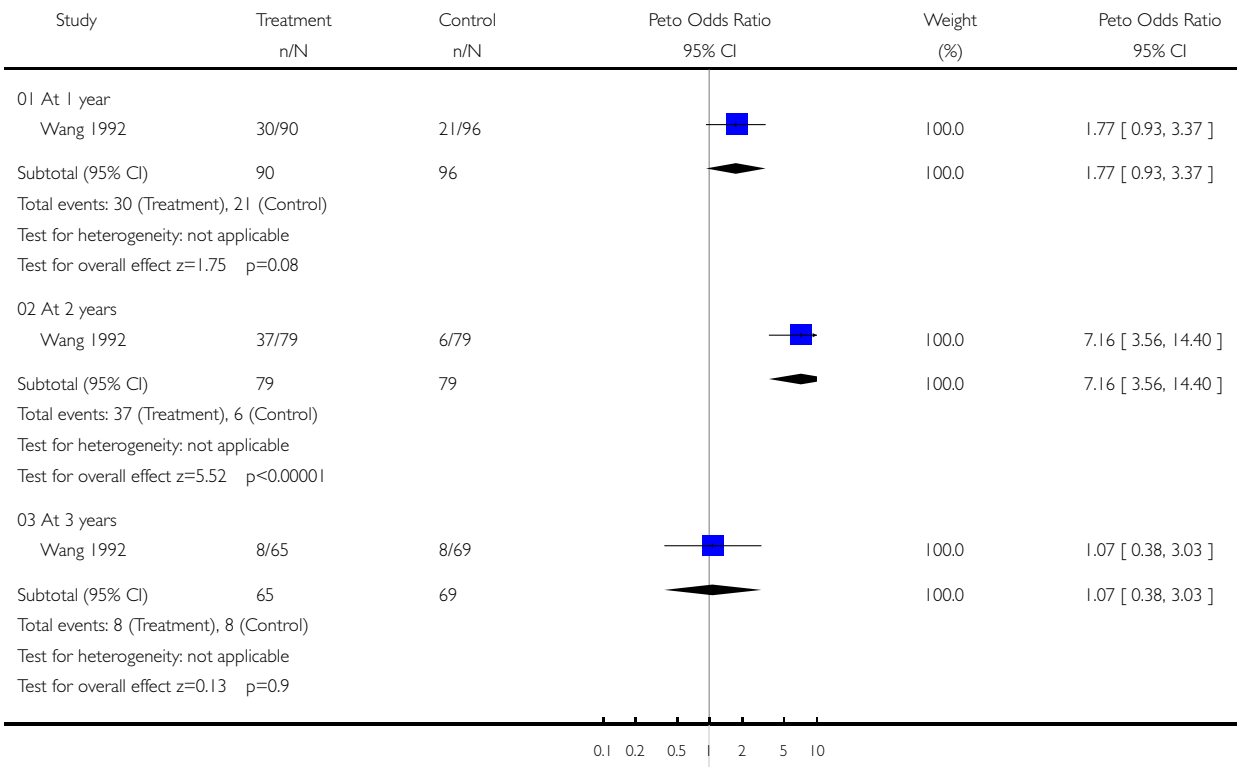


Comparison 05. Oligomenorrhoea

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 03 LNG-20 IUS vs. Norplant-2

Outcome: 07 Oligomenorrhoea



Comparison 05. Amenorrhoea

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 03 LNG-20 IUS vs. Norplant-2

Outcome: 08 Amenorrhoea

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 1 year					
Wang 1992	17/90	8/96		100.0	2.47 [1.06, 5.72]
Subtotal (95% CI)	90	96		100.0	2.47 [1.06, 5.72]
Total events: 17 (Treatment), 8 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.10 p=0.04					
02 At 2 years					
Wang 1992	21/79	0/79		100.0	9.89 [3.96, 24.72]
Subtotal (95% CI)	79	79		100.0	9.89 [3.96, 24.72]
Total events: 21 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.91 p<0.00001					
03 At 3 years					
Wang 1992	5/65	2/69		100.0	2.61 [0.57, 11.92]
Subtotal (95% CI)	65	69		100.0	2.61 [0.57, 11.92]
Total events: 5 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.24 p=0.2					

Comparison 05. Prolonged bleeding

Review: Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy

Comparison: 03 LNG-20 IUS vs. Norplant-2

Outcome: 09 Prolonged bleeding

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 At 1 year					
Wang 1992	4/90	33/96		100.0	0.15 [0.08, 0.32]
Subtotal (95% CI)	90	96		100.0	0.15 [0.08, 0.32]
Total events: 4 (Treatment), 33 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.10 p<0.00001					
02 At 2 years					
Wang 1992	4/79	24/79		100.0	0.18 [0.08, 0.40]
Subtotal (95% CI)	79	79		100.0	0.18 [0.08, 0.40]
Total events: 4 (Treatment), 24 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.15 p=0.00003					
03 At 3 years					
Wang 1992	2/65	14/69		100.0	0.20 [0.07, 0.56]
Subtotal (95% CI)	65	69		100.0	0.20 [0.07, 0.56]
Total events: 2 (Treatment), 14 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.06 p=0.002					

Comparison 05. Pregnancy

At 1 year

Study	
Fylling 1979	7/1729 women months vs. 3/1483 women months
Larsen 1981	4/1996 women months vs. 4/1943 women months

Comparison 05. Continuation of method

At 1 year

Study	
Larsen 1981	150/1996 women months vs. 142/1943 women months Life table probabilities (SE) = 76.2 (3.1) vs. 76 (3.2)

Comparison 05. Expulsion

At 1 year
Study

Fylling 1979	2/1729 women months vs. 15/1483 women months

Comparison 05. Ectopic pregnancy

At 1 year
Study

Fylling 1979	2/1729 women moths vs. 0/1483 women months
Larsen 1981	1/1996 women months vs. 0/1934 women months

Comparison 05. Menstrual reasons for discontinuation: bleeding & pain

At 1 year
Study

Fylling 1979	35/1729 women months vs. 10/1483 women months

Comparison 05. Pregnancy

At 1 year
Study

Newton 1979	3/3389 women months vs. 28/2953 women months

Comparison 05. Continuation of method

At 1 year
Study

Newton 1979	Life table probabilities (SE) = 74.4 (2.4) vs. 65.8 (2.8)

Comparison 05. Expulsion

At 1 year
Study

Newton 1979	25/3389 women months vs. 23/2953 women months

Comparison 05. Ectopic pregnancy

At 1 year
Study

Newton 1979 0/3389 women months vs. 1/2953 women months

Comparison 05. Menstrual reasons for discontinuation: all

At 1 year
Study

Newton 1979 29/3389 women months vs. 22/2953 women months

Comparison 05. Discontinuation because planning pregnancy

At 1 year
Study

Newton 1979 10/3389 women months vs. 6/2953 women months

Comparison 05. Discontinuation for personal reasons

At 1 year
Study

Newton 1979 8/3389 women months vs. 15/2953 women months