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Hormonal and intrauterine methods for contraception for women aged 25 years and younger (Review)

Tang JH, Lopez LM, Mody S, Grimes DA

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[Intervention Review]

Hormonal and intrauterine methods for contraception for women aged 25 years and younger

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ABSTRACT

Background

Women between the ages of 15 and 24 years have high rates of unintended pregnancy; over half of women in this age group want to avoid pregnancy. However, women under age 25 years have been found to have higher typical contraceptive failure rates within the first 12 months of use than older women. High discontinuation rates may also be a problem in this population. Concern that adolescents and young women will not find hormonal or intrauterine contraceptives acceptable or effective might deter healthcare providers from recommending these contraceptive methods.

Objectives

This review examined randomized controlled trials of hormonal or intrauterine methods used for contraception in women aged 25 years and younger.

Search methods

In February 2012, we searched the computerized databases Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, POPLINE, CINAHL, and LILACS for randomized controlled trials that compared hormonal or intrauterine methods used for contraception in women aged 25 years and younger. We also searched for current trials via ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (ICTRP).

Selection criteria

We considered all randomized controlled trials in any language that reported the contraceptive failure rates for hormonal or intrauterine contraceptive methods, when compared to another contraceptive method, for women aged 25 years and younger. The other contraceptive method could be another intrauterine method, another hormonal method, or a non-hormonal method. Treatment duration must have been at least three months.

Data collection and analysis

The first author extracted the data and entered the information into RevMan. Another author performed an independent data extraction and verified the initial entry. Because of disparate contraceptive exposures, we were not able to combine the studies in meta-analysis.

Main results

Four trials met the inclusion criteria. The trials compared the combined oral contraceptive versus the transdermal contraceptive patch, the combined oral contraceptive versus the vaginal contraceptive ring, the combined oral contraceptive versus the levonorgestrel intrauterine system, and the levonorgestrel intrauterine system versus the copper T380A intrauterine device. Because of small numbers of participants, the trials were not informative regarding contraceptive efficacy. Data on continuation rates were also limited. In one of these trials, the levonorgestrel intrauterine system was found to have a similar 12-month continuation rate as the combined oral contraceptive (odds ratio (OR) 1.48; 95% CI 0.76 to 2.89). In that trial, a higher proportion of women discontinued the levonorgestrel intrauterine system because of pain (OR 14.62; 95% CI 0.81 to 263.16), whereas a higher proportion of women discontinued the combined oral contraceptive for personal reasons (OR 0.27; 95% CI 0.09 to 0.85).

Authors' conclusions

Current evidence is insufficient to compare contraceptive efficacy and continuation rates for hormonal and intrauterine methods in women aged 25 years and younger. Limited data suggests that the levonorgestrel intrauterine system may be an acceptable alternative to the combined oral contraceptive in this population.

PLAIN LANGUAGE SUMMARY

Hormonal and intrauterine methods for contraception in women aged 25 years and younger

Women aged 25 years and younger are more likely to stop using birth control methods. They are also more likely to get pregnant while using birth control than older women are. We do not know which birth control methods have the lowest pregnancy rates and the highest continuation rates in this group of women. In February 2012, we did a computer search to find randomized trials that included birth control methods with hormones or intrauterine devices (IUDs) in women aged 25 years and younger. We found four trials. All had too few women to find a difference in pregnancy or continuation rates. Women kept using the birth control pill and the intrauterine device at similar rates. Therefore, the IUD may be an acceptable to women in this age group. Studies with larger numbers of participants would help determine which birth control methods work the best in these women.

BACKGROUND

Description of the condition

In sub-Saharan Africa, south central Asia, and southeast Asia, women between the ages of 15 and 24 years have the greatest unmet need for contraception. In these regions, 68% of women between the ages of 15 and 19 years, and 51% of women between the ages of 20 and 24 years want to avoid pregnancy (Darroch 2011). Unmet need for contraception in these age groups is not limited to developing countries; in the United States, over half of the pregnancies among women under age 25 years are unintended (Finer 2006). Even among married women, unmet need for contraception is highest among women between the ages of 15 and 24 years. This unmet need then tends to decline as women become older and start using female sterilization as a permanent method of contraception (Guttmacher 2010).

Women under the age of 25 years also account for nearly 60% of all unsafe abortions in sub-Saharan Africa. Complications from these unsafe abortions contribute to maternal mortality and morbidity and could be prevented by meeting the contraceptive needs of women (WHO 2004).

Even among women who are using modern contraceptives, women under the age of 25 years have higher typical contraceptive failure rates within the first 12 months of use than women aged 25 years and older. For example, women younger than 20 years and women aged 20 to 24 years were found to have first-year failure rates of 13% and 14%, respectively, compared to 8% for women aged 30 years and older. These findings were particularly pronounced for women who were using condoms or oral contraceptives (Kost 2008). In addition, high discontinuation rates may be a problem in this population. Among married women aged 15 to 24 years with an unmet need for contraception, only 8% cited lack of access or high cost as the reason for not using a method, but 15% to 19% reported concern about health or side effects as their reason (Guttmacher 2010). Typical discontinuation rates at 12 months are 30% for oral contraceptives, 43% for the contraceptive injection, and 50% for the contraceptive patch (Mosher 2010). A 12-month prospective cohort study of 1387 UnitedStates women aged 15 to 24 years showed that continuation rates were lower for the contraceptive patch and injection (10.9 and 12.1 per 100 person-years, respectively) when compared to the contraceptive ring and pills (29.4 and 32.7 per 100 person-years, respectively). Discontinuation was independently associated with the method initiated and younger age (Raine 2011).

The age range for the transition from adolescence to young adulthood is poorly defined in the scientific literature and among policymakers. Healthcare policy organizations have defined the lower age cutoff for adolescence as 10 to 15 years of age and the upper limit as 18 to 24 years of age (DHHS 2008; Gavin 2009; UNFPA 2010; WHO 2011). Given the inconsistency of definitions for adolescence, this review will focus on women aged 25 years and younger.

Description of the intervention

Among reversible forms of contraception, hormonal and intrauterine contraceptives have the lowest contraceptive failure rates and the highest continuation rates in the general population. These forms of contraception are also likely to have the highest continuation rates and lowest pregnancy rates for women aged 25 years and younger. First-year pregnancy rates for typical use range from 9% for oral contraceptives, the patch, and the ring to less than 1% with the contraceptive implant and intrauterine contraception (Trussell 2011). Many factors may contribute to the gap between perfect use and typical use, including missed doses and discontinuation due to inconvenience, forgetfulness, or side effects.

Why it is important to do this review

The comparative efficacy and acceptability of contraceptive methods for adolescents and young women are important public health issues. Concern that adolescents and young women will not find hormonal or intrauterine contraceptives acceptable or effective might deter healthcare providers from recommending them. A systematic review of randomized controlled trials on hormonal and intrauterine contraception has not yet been conducted in this population. The findings of this review could help clinicians and policymakers improve their recommendations for contraceptive counseling and use, and decrease the high unintended pregnancy rate in this age group.

OBJECTIVES

The primary objective is to compare the contraceptive failure (pregnancy) rates for various methods of hormonal and intrauterine contraception among young women aged 25 years and younger. A secondary objective is to compare the continuation rates.

METHODS

Criteria for considering studies for this review

Types of studies

We considered randomized controlled trials that reported the contraceptive failure rates for hormonal and intrauterine contraceptives when compared to another contraceptive method. The other contraceptive could be another intrauterine contraceptive, another hormonal contraceptive, or a non-hormonal contraceptive.

Types of participants

We only included studies that specified that their primary study population was adolescents or young women and in which data were presented for women aged 25 years or younger. We excluded studies that focused on special populations of young women, such as women with diabetes, polycystic ovarian syndrome, and anorexia.

Types of interventions

Any hormonal or intrauterine contraceptive was examined, such as the combined oral contraceptive, the progestin-only pill, the transdermal patch, the vaginal ring, the contraceptive injection (both the combined injectable and the progestin-only injectable), the subdermal implant, the copper intrauterine device, or the levonorgestrel intrauterine system. The comparison group could be another intrauterine contraceptive, another hormonal contraceptive, or a non-hormonal contraceptive. Treatment duration must have been at least three months. The contraceptive method must have been used primarily for pregnancy prevention in all participants.

Types of outcome measures

Primary outcomes

Contraceptive failure rate

Secondary outcomes

Contraceptive continuation rate

Search methods for identification of studies

We searched Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, POPLINE, and LILACS. We also searched for ongoing trials via ClinicalTrials.gov and the search portal of the World Health Organization International Clinical Trials Registry Platform (ICTRP). The search strategies are shown below.

Electronic searches

MEDLINE via PubMed (27 February 2012)

(contraception[MESH] OR contraceptive agents[MESH] OR contraceptive devices[MESH] OR contraception[TIAB]) AND (continuation OR discontinu* OR "adverse effects" OR "patient compliance" OR "patient satisfaction")

Limits: Human, Female, Randomized Controlled Trial, Adolescent, Young Adult

EMBASE (26 February 2012)

contracept* AND ('adolescent' OR adolescents OR 'young women' OR nulliparous) AND (continu* OR discontinu* OR 'patient compliance' OR 'side effects' OR 'patient satisfaction') AND random* AND [female]/lim AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)

POPLINE (27 February 2012)

contracept* & (adolescen*/youth) & random* (adverse effect*/side effect*/continu*/discontinu*/compliance/satisfaction)

CINAHL (26 February 2012)

contracept* AND (adolescen* or young women or teen* or nulliparous) AND (adverse effect* or side effect* or continu* or discontinu* or compliance or satisfaction) AND random*

ClinicalTrials.gov (26 February 2012)

Search terms: continuation OR discontinuation OR effects OR compliance OR satisfaction

Study type: interventional studies

Condition: adolescent OR young OR nulliparous

Intervention: contraceptive OR contraception

Gender: studies with female participants

ICTRP (26 February 2012)

Title: adolescent OR young OR teen OR nulliparous

Intervention: contraception OR contraceptive

CENTRAL (27 February 2012)

(contraception or contraceptive) AND (adolescent or young or nulliparous) AND (continuation OR discontinuation OR side effects OR compliance OR satisfaction)

LILACS (27 February 2012)

(adolescen$ or young adult or adulto, joven or teen$ or youth or jovenes or menores) [Words] and (contracept$ or contraceptive agents/adverse effects or Agentes Anticonceptivos/efectos adversos or Anticoncepcionais/efeitos adversos or contraceptive devices/adverse effects or Dispositivos Anticonceptivos/efectos adversos or Dispositivos Anticoncepcionais/effeitos adversos or side effects or efectos secundarios or efeitos secundários) [Words] and (continu$ or discontinu$ or patient compliance or Cooperación del Paciente or Cooperação do Paciente or patient satisfaction or Satisfação do Paciente or Satisfacción del Paciente or contraception behavior or Conducta Anticonceptiva or Comportamento Contraceptivo) [Words]

Searching other resources

We examined the reference lists of relevant articles and contacted investigators in the field to seek additional published trials or unpublished trials.

Data collection and analysis

Selection of studies

We assessed for inclusion all titles and abstracts identified during the literature search, with no language limitations. Two authors independently reviewed the search results and identified reports for inclusion or exclusion. A third author resolved any disagreements in report selection and examined the reports identified for appropriate categorization according to the criteria for inclusion.

Data extraction and management

One author extracted the data and entered the information into RevMan. Another author conducted a second data extraction and verified correct data entry. Any discrepancies were resolved by discussion.

Assessment of risk of bias in included studies

The randomized controlled trials were examined for methodological quality according to recommended principles (Higgins 2011). The methodology considered included randomization sequence generation, allocation concealment, blinding, losses to follow-up, and early discontinuation. Adequate methods for allocation concealment included a centralized system and the use of sequentially-numbered, opaque, sealed envelopes (Schulz 2002). Limitations in design were presented in Risk of bias in included studies and were considered when interpreting the results.

Measures of treatment effect

For the contraceptive failure rate, we compared the proportions of women who became pregnant while using a hormonal or intrauterine contraceptive in the study. The contraceptive failure rate was assessed at the reported time intervals listed in the study. Life-table analysis was not possible.

For the continuation rate, we compared the proportions of women who were using the hormonal or intrauterine contraceptive at the reported time intervals listed in the study. We also compared the proportion of women who discontinued by specific reason (if available). Life-table analysis could not be done.

Dealing with missing data

We contacted three authors (Stewart 2007; Stuart 2005; Suhonen 2004) to obtain supplemental data for this review. Additional information was obtained for the Stewart 2007 and Stuart 2005 trials.

Assessment of heterogeneity

Study populations, designs, and interventions were heterogeneous. We did not pool data from studies that had different contraceptive methods or different lengths of follow-up.

Data synthesis

The Mantel-Haenszel odds ratio (OR) with 95% confidence interval (CI) was calculated using a fixed-effect model. The proportion of women who had a pregnancy or who discontinued use of a contraceptive during the study period was analyzed. We examined results by the contraceptive method studied (for example, combined oral contraceptive or transdermal contraceptive patch).

Sensitivity analysis

Not done

RESULTS

Description of studies

Results of the search

Two authors independently reviewed 786 abstracts. Fifteen studies were considered for inclusion. Four trials met our inclusion criteria. The included trials enrolled a total of 468 women, and the sample sizes ranged from 20 to 200 women. Trial locations included two European countries (Sweden and Finland) and the United States. All trials were published within the past 10 years and included contraceptive methods currently available.

Included studies

See: Characteristics of included studies.

Godfrey 2010 was a multicenter randomized controlled pilot study of 23 women aged 14 to 18 years assigned to either the copper T380A intrauterine device or the levonorgestrel intrauterine system. The study was completed in urban family planning and family medicine clinics in Chicago, Illinois and enrolled mostly African-American high school students. Eleven of the 23 women had previously given birth, although none were recently postpartum. The study compared the rates of pregnancy, expulsion, continuation, infection, side effects, bleeding, and satisfaction for the two methods at six months.

Stewart 2007 was a single-center randomized cross-over study of 130 women aged 15 to 21 years assigned to either combined oral contraception or the vaginal contraceptive ring for three months, followed by three months of the alternate method. The study was completed in an urban family planning clinic for low income young people in San Francisco, California. The majority of participants were either African-American or Latina and had not completed high school. Only 6% had previously given birth. The combined oral contraceptive contained ethinyl estradiol 35 mcg and norgestimate 250 mcg. The vaginal contraceptive ring delivered a daily dose of 15 mcg ethinyl estradiol and 120 mcg etonogestrel. The primary outcome was acceptability of the two methods, but also reported were rates of compliance, side effects, continuation, and pregnancy for the first three months.

Stuart 2005 was a single-center randomized controlled pilot study of 20 women aged 15 to 19 years assigned to either combined oral contraception or the transdermal contraceptive patch. The study was completed in urban family planning clinics for low income people in Dallas, Texas. Seventy-five per cent of women were Latina, and 20% were African-American. Parity of the participants was not reported, although less than half had previously had an abortion. The combined oral contraceptive contained ethinyl estradiol 30 mcg and norgestimate 250 mcg. The transdermal contraceptive patch delivered a daily dose of 20 mcg ethinyl estradiol and 150 mcg norelgestromin. The primary outcome was the pregnancy rate, but the study also assessed continuation, compliance, and satisfaction for the methods at three and six months. A three-month supply of the randomized contraceptive method was provided at the enrollment visit and after three cycles. Participants were allowed to switch methods at the three-month visit and were considered to have discontinued their assigned method if they switched.

Suhonen 2004 was a multicenter randomized controlled trial of 200 women aged 18 to 25 years assigned to either combined oral contraception or the levonorgestrel intrauterine system. The study was completed in urban family planning clinics located in the cities of Linköping, Sweeden and Helsinki, Finland. All participants except for one were Caucasian, and all 200 women were nulliparous as per the inclusion criteria. The combined oral contraceptives contained ethinyl estradiol 30 mcg and desogestrel 150 mcg. The levonorgestrel intrauterine system delivered a daily dose of 20 mcg levonorgestrel. The primary outcome was the continuation rate, but pregnancy, infection, patterns of bleeding, and acceptability were also assessed. In the levonorgestrel intrauterine system group, evaluation by both the participants and the doctors of the insertion as well as perforation and expulsion rates were recorded and analyzed. Three-month packages of the combined oral contraceptives were given at each three-month visit.

Excluded studies

See: Characteristics of excluded studies.

Eleven studies were excluded. The reasons these studies were excluded were: contraceptive method not used primarily for pregnancy prevention in all participants (Briggs 1983; Cobb 2007; Davis 2005; Strokosch 2006); different contraceptive methods not compared (Rickert 2007; Thomas 2005; Westhoff 2007); participants not limited to women aged 25 years or younger (Gilliam 2010; Larsson 1979; Peterson 1991); and no hormonal or intrauterine method used for comparison (van der Straten 2010). In addition, one study was found not to be a randomized controlled trial (Larsson 1979) and two included special populations of women (Cobb 2007; Strokosch 2006). See Characteristics of excluded studies for more details.

Risk of bias in included studies

Allocation

Two studies had adequate information on allocation concealment (Godfrey 2010; Stuart 2005) and two studies had inadequate information (Stewart 2007; Suhonen 2004).

In Godfrey 2010, allocation concealment was accomplished by placing the randomization numbers in sequentially-numbered sealed, opaque envelopes. Allocation to study group was determined through a computer-generated random number sequence with block sizes of six. The allocation sequence was generated by a statistician unrelated to the study.

In Stuart 2005, the randomization sequence was developed by a statistician unrelated to the study, with blocks of four and six. Allocation concealment was achieved using sequentially-numbered sealed, opaque envelopes.

In Stewart 2007, the randomization sequence was developed using a random number generator in blocks by a statistician unrelated to the study. Information about allocation concealment and block size was not available.

Finally, in Suhonen 2004 randomization into two equal-sized groups in blocks of eight was performed prior to study initiation and was carried out separately in both centers. Information about allocation concealment was not available.

Blinding

None of the studies included blinding of the research staff or investigators since the different contraceptive methods either required different routes for use (oral, transdermal, vaginal, intrauterine) or required intrauterine insertion by a research staff member or investigator (copper T380A intrauterine device and the levonorgestrel intrauterine system). However, in Godfrey 2010 the participants were blinded as to which intrauterine method was inserted until the study ended.

Incomplete outcome data

The Godfrey 2010 study and the Stuart 2005 study both had loss to follow-up rates of 20% or less at six months for all assigned methods. For the Stewart 2007 study and the Suhonen 2004 study, the loss to follow-up information was incomplete.

In Godfrey 2010, all randomized participants were included in the analyses for pregnancy and continuation rates at six months. The six-month loss to follow-up rates were 9% for the copper T380A intrauterine device and 18% for the levonorgestrel intrauterine system.

In Stuart 2005, all randomized participants were included in the analyses for pregnancy and continuation rates at six months. The six-month loss to follow-up rates were 10% for the combined oral contraceptive and 20% for the transdermal contraceptive patch.

In Stewart 2007, all randomized participants were included in the analysis for continuation rate at three months. However, the study had a high discontinuation rate at three months (25% for the combined oral contraceptive, 24% for the vaginal contraceptive ring). The reasons for discontinuation, including loss to follow-up, were not available by assigned method.

Suhonen 2004 did not include all randomized participants in the analyses for pregnancy and continuation rates at one year. It excluded seven randomized women who never began the study intervention from the analysis. Five excluded women were randomized to the levonorgestrel intrauterine system and were excluded for the following reasons: uterus too small at insertion (n = 1), chlamydia infection detected at randomization (n = 2), genital infection (n = 1), and lost to follow-up (n = 1). Two excluded women were randomized to the combined oral contraceptive and were excluded because: the participant moved abroad (n = 1), or never started the study medication at all (n = 1). However, the authors did include in the analysis two women in the combined oral contraceptive group who had a positive chlamydia test but entered the study after receiving appropriate treatment.

The Suhonen 2004 study also did not report the loss to follow-up rate for each method and instead listed such losses as one of the 'personal reasons' for discontinuation of the assigned method. Combined oral contraceptive users were found to have a higher proportion of participants reporting 'personal reasons' for discontinuation (P = 0.02). These participants may have had pregnancies that were not identified in the study.

Selective reporting

Godfrey 2010 and Suhonen 2004 had uniform reporting of continuation rates for both assigned methods but did not report how pregnancy assessment was performed at the study visits.

Stuart 2005 had uniform reporting of pregnancy and continuation rates for both assigned groups. Pregnancy was assessed by urine pregnancy testing at study visits.

Stewart 2007 used urine pregnancy testing to assess for pregnancy in both groups. However, data for pregnancy rate, reasons for discontinuation, and losses to follow-up by the assigned method were not available.

Other potential sources of bias

None evident

Effects of interventions

The Godfrey 2010 pilot study compared the copper T380A intrauterine device to the levonorgestrel intrauterine system. Only one pregnancy occurred among 23 women. This small trial was non-informative regarding contraceptive efficacy. The one pregnancy was diagnosed 37 days after copper T380A intrauterine device removal for prolonged bleeding. One-month continuation rates were 92% (11 of 12) for the levonorgestrel intrauterine system and 82% (9 of 11) for the copper T380A intrauterine device (OR 2.44; 95% CI 0.19 to 31.53; Analysis 1.1). Six-month continuation rates were 75% (9 of 12) for the levonorgestrel intrauterine system and 45% (5 of 11) for the copper T380A intrauterine device (OR 3.60; 95% CI 0.62 to 21.03; Analysis 1.2). Bleeding problems were mentioned as the reason for discontinuation by one participant in each group. In the copper T380A intrauterine device group, three additional participants reported reasons for discontinuation: one reported excessive cramping, and two had expulsion.

The cross-over trial of Stewart 2007 compared the combined oral contraceptive to the vaginal contraceptive ring. During the first three months of the trial nine pregnancies occurred. Since the data did not specify how many pregnancies occurred by assigned

method, contraceptive efficacy rates could not be calculated. However, three-month continuation rates could be calculated for the first three months of the study and were similar for the two interventions (OR 1.09; 95% CI 0.49 to 2.42; Analysis 2.1). Fifty of 67 (75%) completed all three cycles of combined oral contraception compared to 48 of 63 (76%) who completed all three cycles of the vaginal ring. Reasons for discontinuation from the study included pregnancy (n = 9), side effects (n = 1), desire to switch contraceptive method (n = 1), lost to follow-up (n = 4), medical or personal reasons (n = 5), and other or unknown (n = 12).

Stuart 2005 compared the combined oral contraceptive to the transdermal contraceptive patch. The trial was underpowered to show important differences in pregnancy or continuation rates. One out of 10 participants in each intervention group became pregnant during the study (OR 1.00; 95% CI 0.05 to 18.57; Analysis 3.1). As for continuation, eight (of 10) participants were still using the combined oral contraceptive at six months, whereas six participants continued to use the transdermal contraceptive patch at six months (OR 0.38; 95% CI 0.05, 2.77; Analysis 3.2). Reasons for discontinuation for the combined oral contraceptive group included pregnancy (n=1) and loss to follow-up (n = 1), whereas reasons for discontinuation for the transdermal contraceptive patch group included loss to follow-up (n = 2) and concern about the patch falling off (n = 2, one of whom became pregnant after discontinuation).

Finally, Suhonen 2004 compared the combined oral contraceptive to the levonorgestrel intrauterine system. This trial also showed no important differences in pregnancy rates or continuation rates. No pregnancies occurred in either intervention group over 12 months (OR not estimable; Analysis 4.1). Twelve-month continuation rates were 73% (72 of 99) in the combined oral contraception group and 80% (75 of 94) in the levonorgestrel intrauterine system group (OR 1.48; 95% CI 0.76 to 2.89; Analysis 4.2). A higher proportion of levonorgestrel intrauterine system users discontinued their method because of pain (OR 14.62; 95% CI 0.81 to 263.16), while a higher proportion of combined oral contraceptive users discontinued their method because of personal reasons (OR 0.27; 95% CI 0.09 to 0.85; Analysis 4.3). In the levonorgestrel intrauterine system group, four out of six discontinuations because of pain occurred within the first three months after insertion.

DISCUSSION

Summary of main results

All four studies were underpowered to find important differences. The wide confidence intervals reflect statistical instability. Suhonen 2004 found that similar rates of women under age 25 years continued the levonorgestrel intrauterine system and the combined oral contraceptive, suggesting that intrauterine contraception is acceptable to women in this age group. High losses to follow-up may have played a role in the studies, although two of the studies did not specifically report their losses to follow-up by assigned method within their time frames (Stewart 2007; Suhonen 2004).

Overall completeness and applicability of evidence

All four studies reported pregnancy and continuation data for the interventions in the study. Only four comparisons were made in this review. None of the studies assessed the same comparisons, precluding meta-analysis. No study was adequately powered. In addition, we did not find any trials of other commonly-used contraceptives in this age group, such as the contraceptive injection and the subdermal contraceptive implant. All the studies were completed in urban settings in either Europe or the United States, although they had very different patient populations. The study in Europe enrolled only Caucasian or Asian women (Suhonen 2004) whereas the three other studies (Godfrey 2010; Stewart 2007; Stuart 2005) enrolled mostly low income Latina or African-American women in the United States. These studies may not be applicable to populations with different racial and socioeconomic characteristics.

Enrollment difficulties were noted in three out of the four studies, which decreased the generalizability of the studies. In Godfrey 2010, 37 women were approached but only 62% were randomized into the study. In Stewart 2007, 230 women were screened but only 56% were randomized. In the Stuart 2005 study, 72 women were screened but only 20% were randomized. The most commons reasons cited for non-enrollment in the three studies were ineligibility, desire by the women to choose their contraceptive method, desire to choose another contraceptive method, and disinterest in the study. The Suhonen 2004 study did not report how many women were screened to recruit 200 women for the study.

Quality of the evidence

Incomplete reporting of the methods (allocation concealment) and loss to follow-up rates were problems in two of the studies (Stewart 2007; Suhonen 2004). In addition, none of the studies blinded the study staff or investigators to the participants' assigned intervention, and only one study blinded the participants (Godfrey 2010). However, the lack of blinding is unlikely to have affected the outcomes in this review.

Potential biases in the review process

None evident

Agreements and disagreements with other studies or reviews

Both this review and other studies have found that women under the age of 25 years have high rates of contraceptive failure and discontinuation within the first year of use despite using effective methods of hormonal and intrauterine contraception (Kost 2008; Raine 2011).

AUTHORS' CONCLUSIONS

Implications for practice

Due to inadequate sample size, no conclusions can be drawn regarding the comparisons of the contraceptive efficacy or continuation rates of the contraceptive methods included in this review. Women aged 25 years and younger had similar 12-month rates of continuation for the levonorgestrel intrauterine system and the combined oral contraceptive. However, a higher proportion of women discontinued the levonorgestrel intrauterine system because of pain, particularly in the first three months. Women should be counseled about the potential for increased pain during the first three months after intrauterine device insertion and about strategies for reducing pain after insertion (Grimes 2007).

Implications for research

Larger randomized controlled trials are needed to examine the contraceptive efficacy and continuation rates of hormonal and intrauterine contraceptives in women aged 25 years and younger. Also, research should focus on the most effective and longer-acting contraceptive methods, such as the contraceptive injection, the subdermal contraceptive implant, and the intrauterine device. Young women may be less willing to be randomized in contraceptive trials than older women and follow-up can be challenging. Incentives may help encourage these women to enroll and continue to follow-up in randomized controlled trials.

ACKNOWLEDGEMENTS

Carol Manion of FHI 360 performed the literature searches.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Godfrey 2010

Methods	Multicenter, randomized, controlled pilot study conducted from December 2007 through June 2008; participant-blinded. Conducted in Chicago, Illinois.
Participants	23 women. Inclusion criteria: age 14-18 years, regular menstrual cycles, and desired long-acting reversible intrauterine contraception. Exclusion criteria: known uterine or cervical anomaly, untreated cervical infection, pelvic infection within the past three months, previous intrauterine contraception use, chronic disease (e.g., malignancy, liver or kidney disease), genital bleeding of unknown etiology, and allergy to device ingredients.
Interventions	Copper T380A intrauterine device versus levonorgestrel intrauterine system
Outcomes	Pregnancy, continuation, expulsion, infection, side effects, bleeding, and satisfaction at six months (no primary outcome)
Notes	All device insertions occurred within the first five days of the menstrual cycle at least seven weeks after a vaginal or cesarean delivery or second-trimester abortion, or at least three weeks after a first-trimester abortion. Prior to randomization, all participants underwent a screening visit. Tests for chlamydia, gonorrhea, trichomoniasis, and pregnancy were done at the screening visit; if sexually transmitted infection detected, the participant was treated and re-screened three weeks later prior to randomization. Follow-up visits were done at one and six months after insertion. Participants kept daily bleeding and side effect diaries and were called monthly.

Godfrey 2010 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Allocation to study group determined through a computer-generated random number sequence in blocks of six. Allocation sequence generated by a statistician unrelated to study.
Allocation concealment (selection bias)	Low risk	Allocation concealed in sequentially-numbered opaque sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Participants blinded to the device type but investigators and research assistants not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included in analysis for pregnancy and continuation rates. Six-month loss to follow-up rates were 9% for copper T380A intrauterine device and 18% for levonorgestrel intrauterine system.
Selective reporting (reporting bias)	Unclear risk	Method of pregnancy assessment not reported

Stewart 2007

Methods	Single-center, randomized cross-over study conducted from April 2003 through February 2004; non-blinded. Conducted at an urban family planning clinic for low income young people in San Francisco, California.
Participants	130 women. Inclusion criteria: age 15-21 years, requested contraception, medically appropriate for use of hormonal contraception, wanted to use hormonal contraceptive, wanted to participate in study, consented to participate in study, and at least one regular menstrual cycle preceding enrollment or within seven days post induced abortion, English or Spanish speaking. Exclusion criteria: use of hormonal contraception during month preceding enrollment, and contraindications to use of combined hormonal contraception.
Interventions	Combined oral contraception (ethinyl estradiol 35 mcg and norgestimate 250 mcg) versus vaginal contraceptive ring (daily dose of 15 mcg ethinyl estradiol and 120 mcg etonogestrel)
Outcomes	Acceptability (primary outcome), compliance, side effects, continuation, and pregnancy at three and six months
Notes	No mention of power calculation for the study. Reasons for discontinuation in study included: pregnancy, desire to switch contraceptive method, loss to follow-up (failure to return for follow-up interviews within four weeks from scheduled date), medical/personal reasons, and unknown. However, the reasons for discontinuation, including the loss to follow-up rates, were not available by assigned method.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization sequence developed using random number generator in blocks
Allocation concealment (selection bias)	Unclear risk	Information not available

Stewart 2007 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	All participants included in analysis for pregnancy and continuation rates; however, high discontinuation rate at three months (75% total).
Selective reporting (reporting bias)	High risk	Urine pregnancy test used to confirm pregnancy in both groups. Data for pregnancy rate, reasons for discontinuation, and loss to follow-up rates at three months by assigned method not available.

Stuart 2005

Methods	Single-center randomized controlled pilot study conducted from September 2003 to May 2004; non-blinded. Conducted at two community family planning clinics in Dallas, Texas.
Participants	20 women. Inclusion criteria: age 15-19 years, requesting hormonal contraceptive as primary method of contraception, sexually active (minimum of two acts per month), regular menstrual cycles (every 21-35 days), at least two normal menses since last injection if participant received depot medroxyprogesterone acetate within six months, at least one normal menses since pregnancy if patient postpartum, and able to provide written informed consent. Exclusion criteria: medical contraindication to hormonal contraception, pregnancy within 28 days of study admission, regular use of street drugs, more than two daily drinks of alcohol, history of HIV, blood pressure >140/90, receipt of any experimental drug or device within 30 days, history of pelvic inflammatory disease, and known history of infertility or subfertility.
Interventions	Combined oral contraception (ethinyl estradiol 30 mcg and norgestimate 250 mcg) versus transdermal contraceptive patch (daily dose of 20 mcg ethinyl estradiol and 150 mcg norelgestromin)
Outcomes	Pregnancy (primary outcome), continuation, compliance, and satisfaction for the methods at three and six months
Notes	A three-month supply of the randomized contraceptive method was provided at the enrollment visit and after three cycles, although participants were allowed to switch methods at the three-month visit. For this analysis, participants were considered to have discontinued their method if they reported switching to another method at the three-month visit, if they were pregnant, or if they were lost to follow-up. Reasons for switching to another method during the study included fear of the patch falling off (n=2).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random sequence generation in blocks of four and six by statistician unrelated to study
Allocation concealment (selection bias)	Low risk	Allocation concealed in sequentially-numbered opaque sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded

Stuart 2005 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included in analysis for pregnancy and continuation rates. Six month loss to follow-up rates were 10% for combined oral contraception and 20% for the transdermal contraceptive patch.
Selective reporting (reporting bias)	Low risk	Uniform determination of pregnancy and compliance rates for both groups (urine pregnancy test used to confirm pregnancy)

Suhonen 2004

Methods	Multicenter randomized controlled trial (study dates not specified); non-blinded. Conducted at family planning clinics of the Departments of Obstetrics and Gynecology at Linköping University Hospital (Linköping, Sweden) and Helsinki University Central Hospital (Helsinki, Finland).
Participants	200 women (100 from each center). Inclusion criteria: age 18-25 years, nulliparity or nulligravidity, regular menstrual cycles (24-35 days), estimated normal size of uterus, and normal cervical smear. Exclusion criteria: known or suspected pregnancy, congenital or acquired uterine abnormalities, gynecological or breast malignancy, estrogen-dependent tumors, current genital infection, history of pelvic inflammatory disease, history of ectopic pregnancy, body mass index greater or equal to 32, acute liver disease, blood pressure >140/90, diabetes, and coagulation disorders.
Interventions	Combined oral contraception (30 mcg ethinyl estradiol and 150 mcg desogestrel) and levonorgestrel intrauterine system (20 mcg levonorgestrel/day)
Outcomes	Continuation (primary outcome), pregnancy, infection, patterns of bleeding, and acceptability at 6 and 12 months. In the levonorgestrel intrauterine system group, evaluation of insertion by both the participants and doctors, as well as perforation and expulsion rates, were recorded and analyzed.
Notes	The levonorgestrel intrauterine system was inserted within a week after the onset of menstrual bleeding or in conjunction with induced abortion. Combined oral contraception was started on the first day of menstrual bleeding or immediately after induced abortion. Follow-up visits were scheduled every third month. Participants randomized to combined oral contraception received three-month packages of the pills at each three-month visit. Gynecological exam was performed at 3 and 12 months. Menstrual, symptom, and sexual questionnaires were completed at 6 and 12 months. In determining the sample size, the expected continuation rate with the levonorgestrel intrauterine system was 80%. However, neither an actual power calculation nor a prespecified difference in continuation rates to be detected was mentioned. Two hundred women were randomized, but seven women did not initiate their randomized method (five in the levonorgestrel intrauterine system group and two in the combined oral contraception group). These women were not followed up and therefore were not included in the analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization into two equal-sized groups in blocks of eight. Randomization performed prior to study initiation and carried out separately in both centers.
Allocation concealment (selection bias)	Unclear risk	Information not available
Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded

Suhonen 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Not all enrolled participants were included in analysis for pregnancy and continuation rates. Loss to follow-up rates not specifically mentioned and were included as part of the discontinuation rates.
Selective reporting (reporting bias)	Unclear risk	Method of pregnancy assessment not reported

Characteristics of excluded studies *[ordered by study ID]*

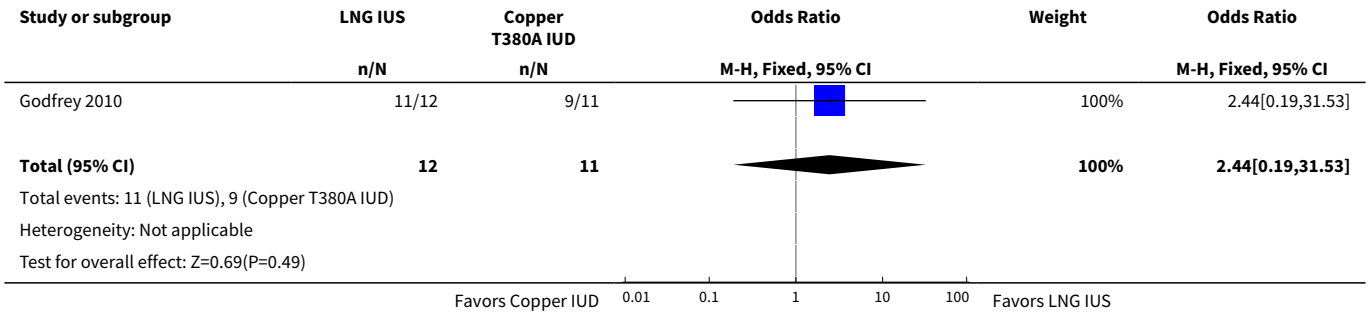
Study	Reason for exclusion
Briggs 1983	Combined oral contraception not used for pregnancy prevention in all participants; used to evaluate metabolic effects of different progestins. Did not assess pregnancy rate.
Cobb 2007	Combined oral contraception not used for pregnancy prevention in all participants; used to assess effect on bone mineral density and stress fractures. Did not use another contraceptive method for comparison. Did not assess pregnancy rate. Included special population (female runners).
Davis 2005	Combined oral contraception not used for pregnancy prevention method in all participants; used to treat dysmenorrhea. Did not use another contraceptive method for comparison.
Gilliam 2010	Not limited to women aged 25 years and younger.
Larsson 1979	Not limited to women aged 25 years and younger. Not a randomized controlled trial; women 'randomly' assigned to Gravigard intrauterine device or copper 7 intrauterine device, but no attempt was made to control the allocation.
Peterson 1991	Not limited to women aged 25 years and younger.
Rickert 2007	Did not compare different contraceptive methods (compared different timing for initiation of same contraceptive method).
Strokosch 2006	Combined oral contraception not used for pregnancy prevention in all participants; used to evaluate effect on bone mineral density. Did not use another contraceptive method for comparison. Did not include pregnancy rate. Includes special population (anorexic women).
Thomas 2005	Did not compare different contraceptive methods (compared different concentrations for administering the same dose of depot medroxyprogesterone acetate).
van der Straten 2010	No hormonal or intrauterine method used as contraceptive method.
Westhoff 2007	Did not compare different contraceptive methods (compared different timing for initiation of same contraceptive method).

DATA AND ANALYSES

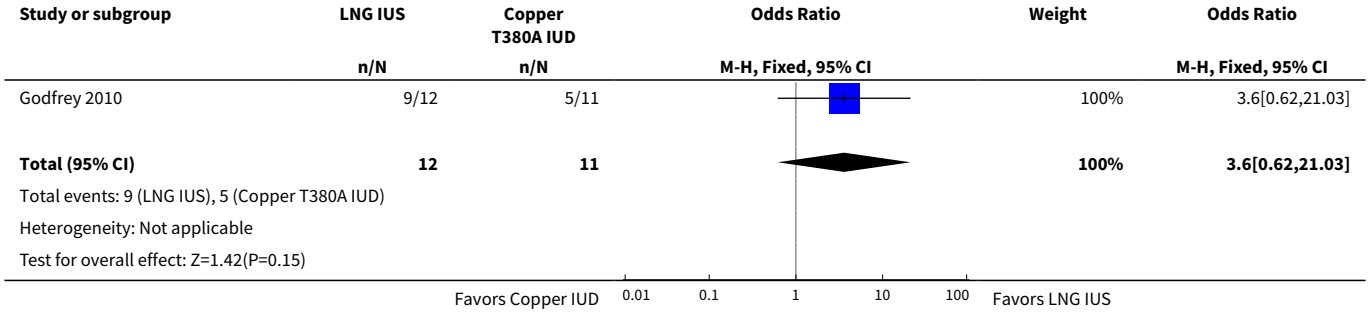
Comparison 1. Copper T380A IUD versus levonorgestrel IUS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Continuation at one month	1	23	Odds Ratio (M-H, Fixed, 95% CI)	2.44 [0.19, 31.53]
2 Continuation at six months	1	23	Odds Ratio (M-H, Fixed, 95% CI)	3.6 [0.62, 21.03]

Analysis 1.1. Comparison 1 Copper T380A IUD versus levonorgestrel IUS, Outcome 1 Continuation at one month.



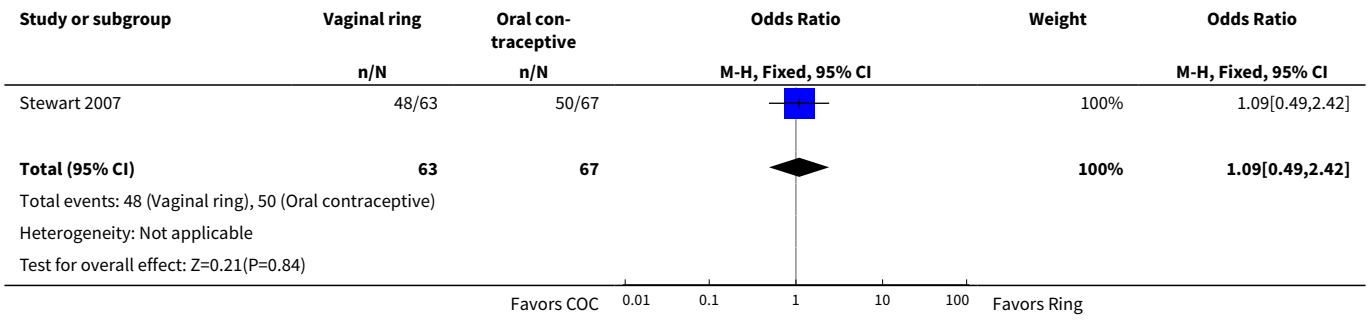
Analysis 1.2. Comparison 1 Copper T380A IUD versus levonorgestrel IUS, Outcome 2 Continuation at six months.



Comparison 2. Combined oral contraception versus vaginal contraceptive ring

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Continuation at three months	1	130	Odds Ratio (M-H, Fixed, 95% CI)	1.09 [0.49, 2.42]

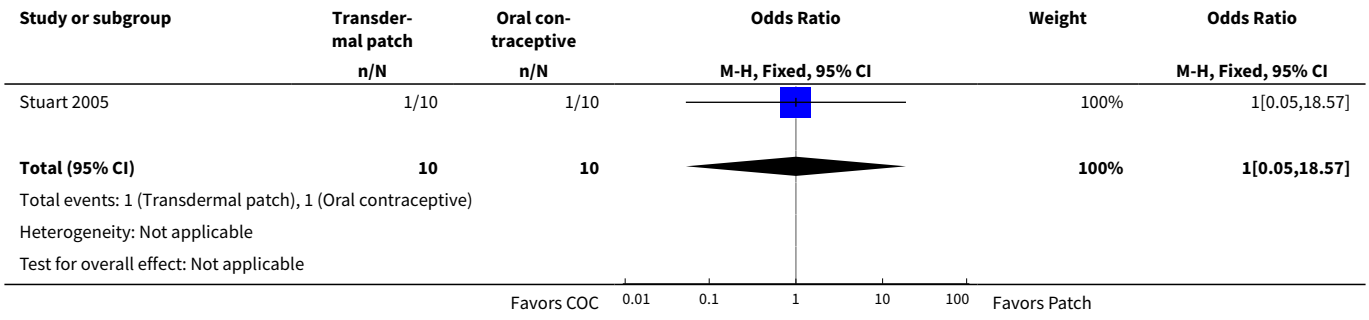
Analysis 2.1. Comparison 2 Combined oral contraception versus vaginal contraceptive ring, Outcome 1 Continuation at three months.



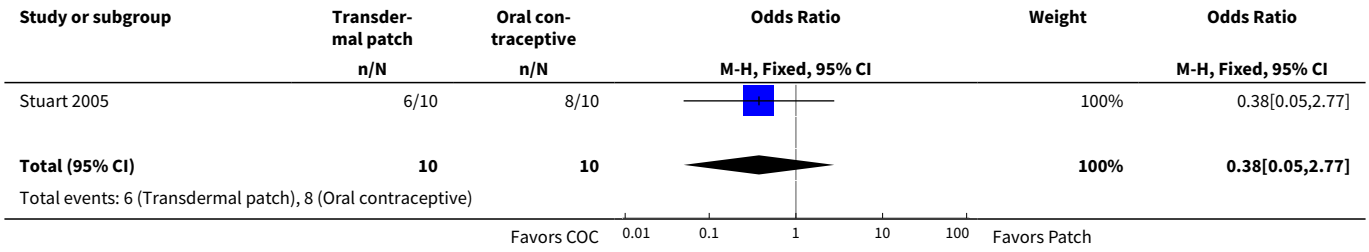
Comparison 3. Combined oral contraception versus transdermal contraceptive patch

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy at six months	1	20	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.05, 18.57]
2 Continuation at six months	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.05, 2.77]

Analysis 3.1. Comparison 3 Combined oral contraception versus transdermal contraceptive patch, Outcome 1 Pregnancy at six months.



Analysis 3.2. Comparison 3 Combined oral contraception versus transdermal contraceptive patch, Outcome 2 Continuation at six months.



Study or subgroup	Transder-mal patch n/N	Oral con-traceptive n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%					
Test for overall effect: Z=0.96(P=0.34)					

Favors COC 0.01 0.1 1 10 100 Favors Patch

Comparison 4. Combined oral contraception versus levonorgestrel IUS

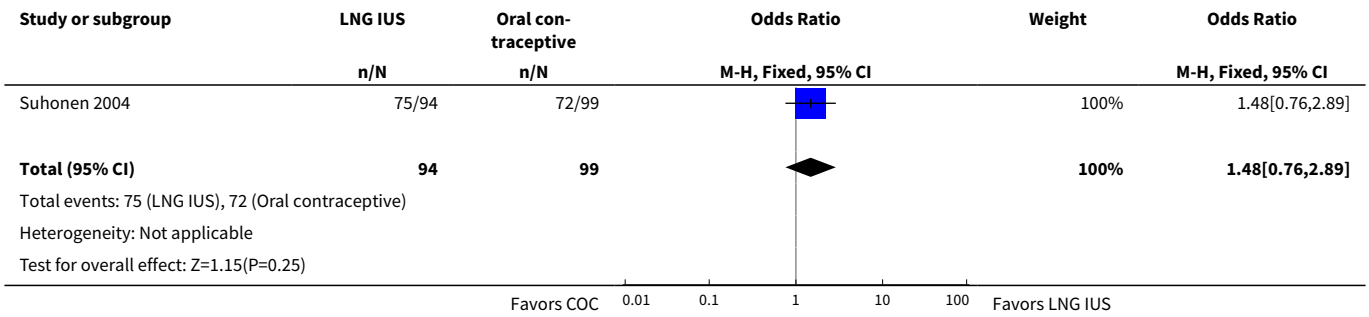
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Pregnancy at 12 months	1	193	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Continuation at 12 months	1	193	Odds Ratio (M-H, Fixed, 95% CI)	1.48 [0.76, 2.89]
3 Discontinuation at 12 months by reason	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Pain	1	193	Odds Ratio (M-H, Fixed, 95% CI)	14.62 [0.81, 263.16]
3.2 Hormonal	1	193	Odds Ratio (M-H, Fixed, 95% CI)	0.44 [0.13, 1.50]
3.3 Bleeding	1	193	Odds Ratio (M-H, Fixed, 95% CI)	5.38 [0.25, 113.51]
3.4 Spotting	1	193	Odds Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.64]
3.5 Other medical	1	193	Odds Ratio (M-H, Fixed, 95% CI)	2.13 [0.19, 23.89]
3.6 Plannng pregnancy	1	193	Odds Ratio (M-H, Fixed, 95% CI)	0.21 [0.01, 4.36]
3.7 Other personal	1	193	Odds Ratio (M-H, Fixed, 95% CI)	0.27 [0.09, 0.85]

Analysis 4.1. Comparison 4 Combined oral contraception versus levonorgestrel IUS, Outcome 1 Pregnancy at 12 months.

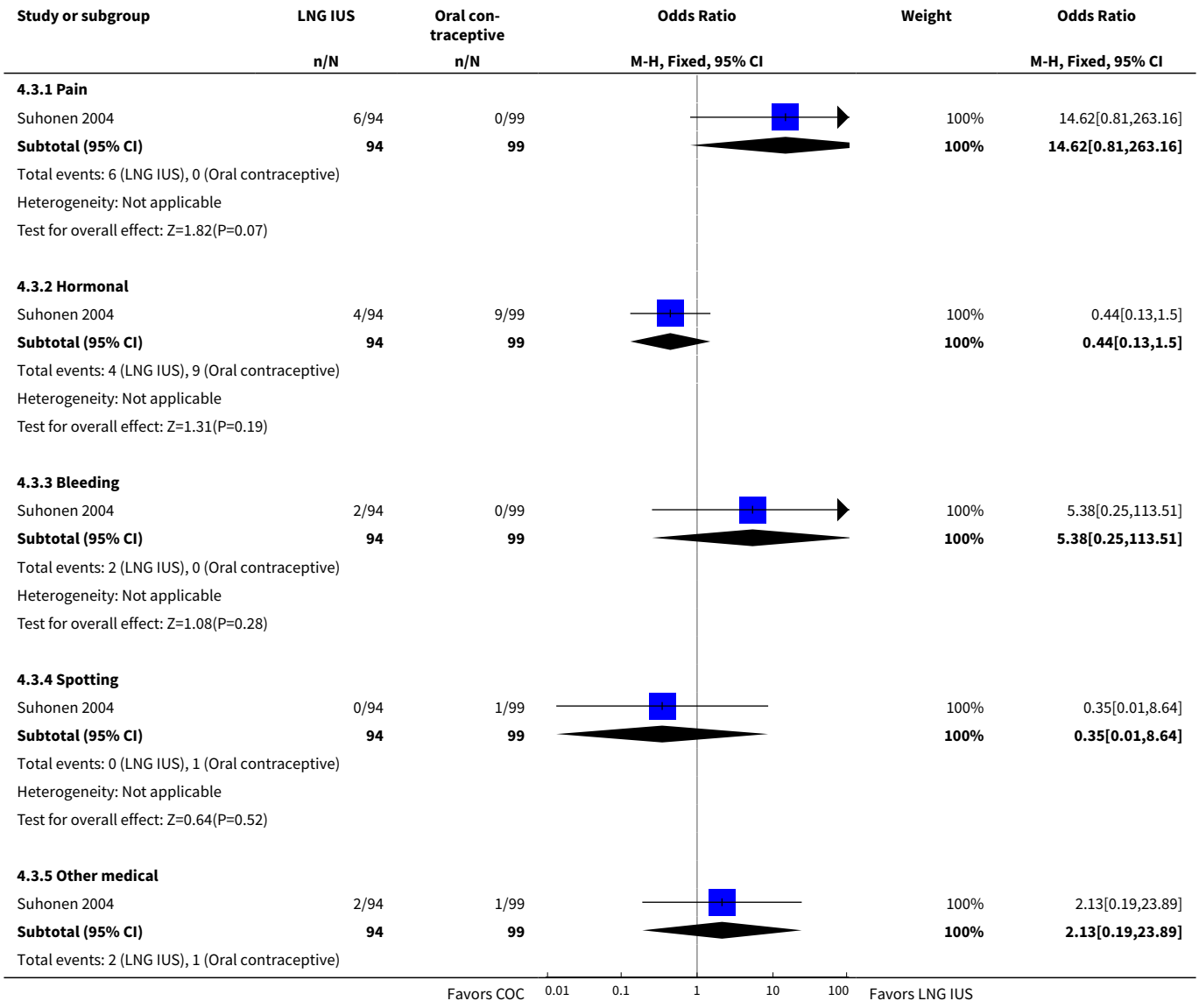
Study or subgroup	LNG IUS n/N	Oral con-traceptive n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Suhonen 2004	0/94	0/99			Not estimable
Total (95% CI)	**94**	**99**			**Not estimable**
Total events: 0 (LNG IUS), 0 (Oral contraceptive)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

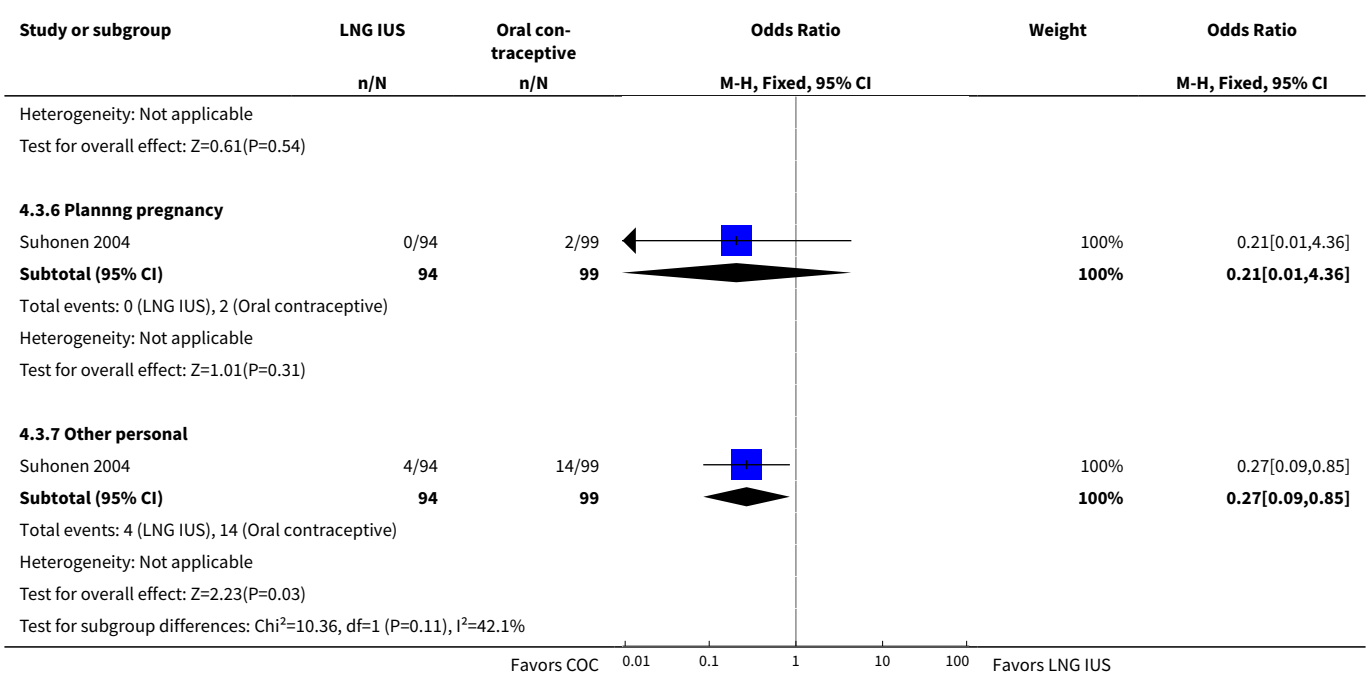
Favors COC 0.01 0.1 1 10 100 Favors LNG IUS

Analysis 4.2. Comparison 4 Combined oral contraception versus levonorgestrel IUS, Outcome 2 Continuation at 12 months.



Analysis 4.3. Comparison 4 Combined oral contraception versus levonorgestrel IUS, Outcome 3 Discontinuation at 12 months by reason.





CONTRIBUTIONS OF AUTHORS

J Tang developed the idea, reviewed the search results, conducted the primary data extraction, and drafted the review. D Grimes also reviewed the search results and conducted the second data extraction. L Lopez and S Mody provided guidance on development of the protocol and the review. All authors reviewed and commented on the manuscript.

DECLARATIONS OF INTEREST

Dr Grimes is a consultant to Bayer and Merck.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The following sentence was added to Types of participants: 'We will exclude studies that focus on special populations of young women, such as women with diabetes, polycystic ovarian syndrome, and anorexia'. This clarification was added so that the studies would be more generalizable and applicable to adolescents with unimpaired fertility.

The following sentence was added to Types of interventions: 'The contraceptive method must be used primarily for pregnancy prevention in all participants'. This clarification was added to ensure that the hormonal and intrauterine contraceptives in the study were being used for contraception rather than for other medical uses.

INDEX TERMS

Medical Subject Headings (MeSH)

*Contraceptives, Oral, Combined; *Intrauterine Devices; Administration, Topical; Contraception [*methods]; Contraceptive Agents, Female; Intrauterine Devices, Copper; Levonorgestrel; Randomized Controlled Trials as Topic; Time Factors

MeSH check words

Adolescent; Adult; Female; Humans; Young Adult