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Krashin J, Tang JH, Mody S, Lopez LM

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# 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 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

To compare the contraceptive failure (pregnancy) rates and to examine the continuation rates for hormonal and intrauterine contraception among young women aged 25 years and younger.

### Search methods

We searched until 4 August 2015 for randomized controlled trials (RCTs) that compared hormonal or intrauterine methods of contraception in women aged 25 years and younger. Computerized databases included the Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, POPLINE, CINAHL, and LILACS. We also searched for current trials via ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP).

### Selection criteria

We considered RCTs in any language that reported the contraceptive failure rates for hormonal or intrauterine contraceptive methods, when compared with another contraceptive method, for women aged 25 years and younger. The other contraceptive method could have been another intrauterine contraceptive, another hormonal contraceptive or different dose of the same method, or a non-hormonal contraceptive. Treatment duration must have been at least three months. Eligible trials had to include the primary outcome of contraceptive failure rate (pregnancy). The secondary outcome was contraceptive continuation rate.

### Data collection and analysis

One author conducted the primary data extraction and entered the information into Review Manager. Another author performed an independent data extraction and verified the initial entry. For dichotomous outcomes, we computed the Mantel-Haenszel odds ratio (OR) with 95% confidence interval (CI). Because of disparate interventions and outcome measures, we did not conduct meta-analysis.

## Main results

Five trials met the inclusion criteria. The studies included a total of 1503 women, with a mean of 301 participants. The trials compared the following contraceptives: combined oral contraceptive (COC) versus transdermal contraceptive patch, vaginal contraceptive ring, or levonorgestrel intrauterine system 20 µg/day (LNG-IUS 20); LNG-IUS 12 µg/day (LNG-IUS 12) versus LNG-IUS 16 µg/day (LNG-IUS 16); and LNG-IUS 20 versus the copper T380A intrauterine device (IUD). In the trials comparing two different types of methods, the study arms did not differ significantly for contraceptive efficacy or continuation. The sample sizes were small for two of those studies. The only significant outcome was that a COC group had a higher proportion of women who discontinued for 'other personal reasons' compared with the group assigned to the LNG-IUS 20 (OR 0.27, 95% CI 0.09 to 0.85), which may have little clinic relevance. The trial comparing LNG-IUS 12 versus LNG-IUS 16 showed similar efficacy over one and three years. In three trials that examined different LNG-IUS, continuation was at least 75% at 6 to 36 months.

## Authors' conclusions

We considered the overall quality of evidence to be moderate to low. Limitations were due to trial design or limited reporting. Different doses in the LNG-IUS did not appear to influence efficacy over three years. In another study, continuation of the LNG-IUS appeared at least as high as that for the COC. The current evidence was insufficient to compare efficacy and continuation rates for hormonal and intrauterine contraceptive methods in women aged 25 years and younger.

## PLAIN LANGUAGE SUMMARY

### Hormonal and intrauterine methods for birth control in women age 25 years or younger

#### Background

Women aged 25 years and younger are more likely to stop using birth control than women over 25 years of age. They are also more likely to get pregnant while using birth control compared with older women. We do not know which birth control methods have the lowest pregnancy rates and the highest continued use in young women.

#### Study characteristics

We searched for randomized trials of birth control methods until August 2015. Randomized trials are clinical studies in which people are randomly put into one of two or more treatment groups. Women in these studies were 25 years old or younger. The birth control methods could be either hormonal or a non-hormonal device placed in the uterus. The hormonal methods included pills, vaginal rings, or implants. The methods that are placed in the uterus include the intrauterine device (IUD) without hormones and the intrauterine system that has the hormone levonorgestrel (LNG-IUS). IUDs and the LNG-IUS are sometimes called intrauterine contraception (IUC).

#### Key results and quality of the evidence

We found five trials that enrolled had a total of 1503 women. Some studies looked at different types of IUC, while others compared pills versus a vaginal ring, skin patch, or IUC. No study showed any major difference between the groups in pregnancy or continued use. Some of the trials were too small to find a difference. Women kept using IUC at least as long as pills in one study. IUC may be useful for women in this age group. Studies of different birth control with more women would help determine which methods work the best for young women. Overall, the quality of the results was moderate to low.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [\[Explanation\]](#)

Contraceptive failure rate (pregnancy)				
<b>Patient or population:</b> women aged $\leq 25$ years with desire for contraception <b>Settings:</b> clinic or community <b>Intervention:</b> hormonal or intrauterine method <b>Comparison:</b> other hormonal or intrauterine method				
Outcomes	Relative effect (95% CI)	Participants (study)	Quality of the evidence (GRADE)	Interventions
Pregnancy (12 months)	Not estimable (none)	193 ( <a href="#">Suhonen 2004</a> )	⊕○○○ <b>very low</b>	LNG-IUS 20 vs. COC (EE 30 µg + desogestrel 150 µg)
Estimated cumulative failure rate (3 years)	<i>Reported Kaplan-Meier:</i> 0.010 (0.004 to 0.027) vs. 0.005 (0.001 to 0.019)	1130 ( <a href="#">Kaunitz 2013</a> )	⊕⊕○○ <b>low</b>	LNG-IUS 12 vs. LNG-IUS 16
Pregnancy (6 months)	OR 1.00 (0.05 to 18.57)	20 ( <a href="#">Stuart 2005</a> )	⊕⊕⊕○ <b>moderate</b>	COC (EE 30 µg + norgestimate 250 µg) vs. transdermal contraceptive patch
GRADE Working Group grades of evidence <b>High quality:</b> Further research is very unlikely to change our confidence in the estimate of effect. <b>Moderate quality:</b> Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. <b>Low quality:</b> Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. <b>Very low quality:</b> We are very uncertain about the estimate.				

CI: confidence interval; LNG-IUS 20: levonorgestrel-releasing intrauterine system (20 µg/day); COC: combined oral contraceptive; EE = ethinyl estradiol; OR: odds ratio

## BACKGROUND

### Description of the condition

Women between the ages of 15 and 24 years have a high demand for contraception, and Millennium Development Goal 5 includes increased access to contraception among young women ([United Nations 2013](#)). In sub-Saharan Africa, south central Asia, and Southeast Asia, 68% of women between the ages of 15 and 19

years, and 51% of women between 20 and 24 years old want to avoid pregnancy ([Darroch 2011](#)). However, in low-income countries, approximately 33 million women aged 15 to 24 years old have an unmet need for contraception ([MacQuarrie 2014](#)). Unmet need in these age groups is not limited to low-income countries. In the United States (US), over half of the pregnancies among women under age 25 years are unintended ([Finer 2014](#)). In the US, 30% of women 15 to 19 years old use contraception, and the percentage increases as women age and use female sterilization as

a permanent method of contraception (Jones 2012).

Women under the age of 25 account for a large proportion of maternal mortality worldwide. Maternal sepsis and hemorrhage are major causes of death among women under 25 years of age in low-income countries (Patton 2009). Over eight million unsafe abortions, which are the third major cause of maternal mortality, occurred in women aged 15 to 24 years in 2008 (Shah 2012). Third-quarters of these unsafe abortions, as well as other causes of maternal mortality, could be prevented by improved access to modern contraception (WHO 2014).

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; UNPF 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, the contraceptive implant and intrauterine contraception 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.

Among women using modern contraceptives, those under the age of 25 years have higher typical contraceptive failure rates within the first 12 months compared with women aged 25 years and older. For example, the first-year contraceptive failure rates are 13% for women younger than 20 years, 14% for women aged 20 to 24 years and 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 (Guttmacher 2010). Data from 2006 to 2008 indicated that typical discontinuation rates at 12 months were 30% for oral contraceptives, 43% for the contraceptive injection, and 50% for the contraceptive patch (Mosher 2010). A 12-month cohort study of 1387 US women aged 15 to 24 years showed that continuation rates were lower for the contraceptive patch (10.9 per 100 person-years) and injection (12.1 per 100

person-years) when compared with the contraceptive ring (29.4 per 100 person-years) and pills (32.7 per 100 person-years). Discontinuation was independently associated with the method initiated and younger age (Raine 2011). In one prospective study that emphasized counseling, free devices, and immediate access, age less than 20 years was associated with higher discontinuation of contraception over 24 months compared with that among older women. However, young women were less likely to discontinue long-acting reversible methods of contraception (i.e. intrauterine contraception and implants) compared with other types of contraception (O'Neil-Callahan 2013).

## 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. When we conducted the initial review, a systematic review had not been done with randomized controlled trials (RCTs) on hormonal and intrauterine contraception in this population. The findings of this update 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

To compare the contraceptive failure (pregnancy) rates and to examine the continuation rates for hormonal and intrauterine contraception among women aged 25 years and younger.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We considered RCTs that reported the contraceptive failure rates for hormonal and intrauterine contraceptives when compared with another contraceptive method. The other contraceptive could be another intrauterine contraceptive, another hormonal contraceptive or different dose of the same method, 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, or anorexia.

## Types of interventions

Any hormonal or intrauterine contraceptive was examined, such as the combined oral contraceptive (COC), progestin-only pill, transdermal patch, vaginal ring, contraceptive injection (both the combined injectable and the progestin-only injectable), contraceptive implant, copper intrauterine device (IUD), or levonorgestrel intrauterine system (LNG-IUS). The comparison group could be another intrauterine contraceptive, another hormonal contraceptive or different dose of the same method, 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 (pregnancy)

### Secondary outcomes

Contraceptive continuation rate

## Search methods for identification of studies

### Electronic searches

We searched Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, POPLINE, and LILACS until 4 August 2015. We also searched for ongoing trials via [ClinicalTrials.gov](http://ClinicalTrials.gov) and the search portal of the International Clinical Trials Registry Platform (ICTRP). Appendix 1 shows the search strategies. Appendix 2 has the strategies for the initial review.

### 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.

### Data extraction and management

Two authors conducted the data extraction. One author entered the data into Review Manager 5 ([RevMan 2014](#)), and a second author checked accuracy ([Contributions of authors](#)). These data included the study characteristics, risk of bias, and outcome data. We resolved any discrepancies by discussion.

### Assessment of risk of bias in included studies

We examined the RCTs for methodological quality according to recommended principles in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). The methodology considered included randomization sequence generation, allocation concealment, blinding, loss 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](#)). We presented limitations in design in the [Risk of bias in included studies](#) and considered these when interpreting the results.

### Measures of treatment effect

For dichotomous outcomes, we computed the Mantel-Haenszel odds ratio (OR) with 95% confidence interval (CI). For the contraceptive failure rate, we compared the proportions of women who became pregnant in each study arm at the reported time intervals. For the continuation rate, we compared the proportions of women who were using the hormonal or intrauterine contraceptive at the reported time intervals. We also compared the proportion of women who discontinued by specific reason (if available). When data were not available for analysis, we presented the results as reported by the investigators. This includes the Pearl Index with 95% CI. We could not perform life-table analysis.

### Dealing with missing data

We contacted four investigators to obtain supplemental data ([Suhonen 2004](#); [Stuart 2005](#); [Stewart 2007](#); [Kaunitz 2013](#)). We obtained additional information for three trials ([Stuart 2005](#); [Stewart 2007](#); [Kaunitz 2013](#)).

## Assessment of heterogeneity

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

## Data synthesis

We applied principles from GRADE to assess the quality of evidence and address confidence in the effect estimates (Balslem 2011; Higgins 2011). Our assessment of the body of evidence was based on the quality of evidence from the studies. When a meta-analysis is not viable because of varied interventions or outcome measures, a formal GRADE assessment is not feasible, that is, with an evidence profile and 'Summary of findings' table (Guyatt 2011). However, we did provide 'Summary of findings' tables.

To assess the quality of evidence from each trial, we used a rating system. We considered RCTs to be high quality then downgraded for the following: each risk of bias criteria judged as 'high'; risk of bias 'unclear' for two or more criteria due to missing or incomplete information.

# RESULTS

## Description of studies

### Results of the search

For the initial review in 2012, two authors independently reviewed 786 abstracts. We considered 15 studies 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 US. All trials were published within the previous 10 years and included contraceptive methods currently available.

For the 2015 update, the database searches produced 342 citations. After we removed 73 duplicates electronically or by hand, we had 269 unduplicated references. We considered 17 studies for inclusion. One trial met our eligibility criteria and 16 were excluded.

Searches of clinical trials databases yielded 17 unduplicated listings. We listed one as excluded; the others did not appear to be eligible for this review. In most of those trials with young women, the interventions were educational rather than clinical.

### Included studies

Five trials met our eligibility criteria (see [Characteristics of included studies](#)). The studies included a total of 1503 women,

ranging from 20 to 1130; the mean was 301. Two studies compared different methods of intrauterine contraception.

- [Godfrey 2010](#) was a multicenter pilot study of 23 women, aged 14 to 18 years, assigned to either the copper T380A IUD or the levonorgestrel intrauterine system with 20 µg/day initial release (LNG-IUS 20). 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.

- [Kaunitz 2013](#) is a subanalysis from a multicenter Phase III study of 2884 women, aged 18 to 35 years, which had a full report ([Nelson 2013](#)). [Kaunitz 2013](#) was an abstract from a conference poster. Women were assigned to one of two LNG-IUS: 12 µg/day initial release (LNG-IUS 12) or 16 µg/day initial release (LNG-IUS 16). Most women were parous. Of the 2884 original participants, 1130 were included in a sub-analysis of women aged 18 to 25 years. The study was completed in 138 centers in 11 countries. The Phase III study compared the rates of pregnancy at one and three years, bleeding over three years, ectopic pregnancies, and bone mineral density. The primary report described side effects and continuation over three years ([Nelson 2013](#)). This abstract provides rates of pregnancy and ectopic pregnancy over one and three years according to the women's ages. The abstract also describes discontinuation because of side effects for both groups combined. The LNG-IUS 12 is approved by the US Food and Drug Administration (FDA) for use over three years. The investigators provided additional data on the number of women aged 18 to 25 years who were randomized to each arm.

Three trials compared a COC with another hormonal method: vaginal ring, transdermal patch, or LNG-IUS 20.

- [Suhonen 2004](#) was a multicenter trial of 200 women, aged 18 to 25 years. Women were assigned to either COC (ethinyl estradiol 30 µg plus desogestrel 150 µg) or the LNG-IUS 20. The study was completed in urban family planning clinics located in the cities of Linköping, Sweden and Helsinki, Finland. All women except one were white, and all women were nulliparous. The primary outcome was the continuation rate, but the study also assessed pregnancy, infection, patterns of bleeding, and acceptability. In the LNG-IUS group, evaluation by both the women and the doctors of the insertion as well as perforation and expulsion rates were recorded and analyzed. Three-month packages of the COCs were given at each three-month visit.

- [Stuart 2005](#) was a pilot study of 20 women, aged 15 to 19 years. [Stuart 2005](#) was an abstract from a conference poster; no full report was published. An author of this review (JT) was involved in the study and provided data for the outcome analyses. Women were assigned to either COC (ethinyl estradiol



30 µg plus norgestimate 250 µg) or the transdermal contraceptive patch (daily dose of ethinyl estradiol 20 µg plus norelgestromin 150 µg). 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 women was not reported, although less than half had previously had an abortion. The primary outcome was 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. Women were allowed to switch methods at the three-month visit and were considered to have discontinued their assigned method if they switched.

- [Stewart 2007](#) was a cross-over pilot study of 130 women, aged 15 to 21 years. The women were assigned to either COC (ethinyl estradiol 35 µg plus norgestimate 250 µg) or the vaginal contraceptive ring (daily dose of ethinyl estradiol 15 µg and etonogestrel 120 µg) for three cycles, followed by three cycles 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 women were either African-American or Latina and had not completed high school. Only 6% had previously given birth. The primary outcome was acceptability of the two methods, but also reported were rates of compliance, side effects, continuation, and pregnancy for each three-cycle period. A co-investigator shared the database with a review author (JT) for use in the initial review.

### Excluded studies

We excluded 28 studies. The reasons included contraceptive method not used primarily for pregnancy prevention in all women, different contraceptive methods not compared, participants not limited to women aged 25 years or younger, no hormonal or intrauterine method used for comparison, or continuation measured for less than three months. In addition, the full text for one study indicated it was not an RCT and several studies included special populations of women. See [Characteristics of excluded studies](#) for more details.

### Risk of bias in included studies

#### Allocation

Two studies had adequate information on the randomization sequence generation and allocation concealment. [Stuart 2005](#) had blocks of four and six. [Godfrey 2010](#) had a computer-generated random number sequence with block sizes of six. Both studies used sequentially numbered, sealed, opaque envelopes to conceal allocation.

Three studies had adequate information on the sequence generation but no mention of allocation concealment. [Suhonen 2004](#) randomized into two equal-sized groups in blocks of eight prior to study initiation and carried out separately in both centers. [Stewart 2007](#) used a random number generator in blocks (size unspecified). In the main study from which [Kaunitz 2013](#) was derived, the randomization sequence was developed using cards in ascending order and lists were prepared for each study site ([Nelson 2013](#)).

#### Blinding

In [Godfrey 2010](#) and [Kaunitz 2013](#), the women were blinded to which intrauterine method was inserted until the study ended ([Godfrey 2010](#)) or three years ([Kaunitz 2013](#)). None of the studies used 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 IUD versus the LNG-IUS 20 and different reservoir sizes for the LNG-IUS 12 versus LNG-IUS 16).

#### Incomplete outcome data

Losses greater than 20% threaten trial validity ([Strauss 2005](#)). In three studies, the information on loss to follow-up was incomplete ([Suhonen 2004](#); [Stewart 2007](#); [Kaunitz 2013](#)).

- [Suhonen 2004](#) had overall discontinuation greater than 20% (LNG-IUS 20%; COC 27%). Loss to follow-up was not specified by method. The investigators excluded from the outcome analyses seven randomized women who never began the study intervention. They excluded five women randomized to the LNG-IUS 20 for the following reasons: uterus too small at insertion, chlamydia infection detected at randomization, genital infection, and lost to follow-up. Two women randomized to the COC were excluded because the participant moved abroad or never started the study medication. However, the investigators did include two women in the COC group who had a positive chlamydia test but entered the study after receiving treatment. [Suhonen 2004](#) listed loss to follow-up as one of the 'personal reasons' for discontinuation of the assigned method. COC users had a higher proportion of women reporting 'personal reasons' for discontinuation ( $P = 0.02$ ). They may have had pregnancies not identified in the study.

- [Stewart 2007](#) included all randomized women in the analysis for continuation at three months. The discontinuation rate at three months was high (25% for the COC, 24% for the vaginal contraceptive ring). Only 51% of women completed the six months of the study. The reasons for discontinuation, including loss to follow-up, were not available by assigned method. An attrition analysis showed no difference between women lost to follow-up and women who completed the six-month study visit for age, race or ethnicity, previous pregnancy,

prior use of hormones, condoms use at last intercourse, or age of sexual debut.

- [Kaunitz 2013](#) included all randomized women in the analysis for pregnancy and continuation rates. However, the report did not specify whether discontinued women requested device removal or were lost to follow-up.

Two trials had low losses to follow-up. [Godfrey 2010](#) included all randomized women in the pregnancy and continuation rates. The six-month loss to follow-up was 9% for the copper T380A IUD and 18% for the LNG-IUS 20. [Stuart 2005](#) included all randomized women in the pregnancy and continuation rates. The six-month loss to follow-up was 10% for the COC and 20% for the transdermal contraceptive patch.

### Selective reporting

Four trials did not have complete reporting for all outcomes. Two studies did not report how pregnancy was assessed at the study visits ([Suhonen 2004](#); [Godfrey 2010](#)). [Kaunitz 2013](#) used pregnancy tests at screening, baseline, the three-year study visit, and when clinically indicated. Three studies did not include information on how continuation was determined ([Suhonen 2004](#); [Stuart 2005](#); [Stewart 2007](#)). [Stewart 2007](#) did not include reasons for discontinuation and loss to follow-up by assigned method.

### Effects of interventions

See: [Summary of findings for the main comparison Contraceptive failure \(pregnancy\)](#); [Summary of findings 2 Continuation of contraceptive method](#)

[Godfrey 2010](#) compared the copper T380A IUD with the LNG-IUS 20. Only one pregnancy occurred among 23 women. This small trial was not informative regarding contraceptive efficacy. The one pregnancy was diagnosed 37 days after copper T380A IUD removal for prolonged bleeding. One-month continuation rates were 92% (11 of 12) for the LNG-IUS 20 and 82% (9 of 11) for the copper T380A IUD (OR 2.44, 95% CI 0.19 to 31.53; Analysis 1.1). Six-month continuation rates were 75% (9 of 12) for the LNG-IUS 20 and 45% (5 of 11) for the copper T380A IUD (OR 3.60, 95% CI 0.62 to 21.03; Analysis 1.2). Bleeding problems were mentioned as the reason for discontinuation by one woman in each group. In the copper T380A IUD group, three additional women reported reasons for discontinuation: one reported excessive cramping and two had expulsion.

[Kaunitz 2013](#) compared LNG-IUS with two different dosages: 12 µg/day (LNG-IUS 12) versus 16 µg/day (LNG-IUS 16). Unadjusted Pearl Indices were similar for the two interventions: 0.22 (95% CI 0.01 to 1.22) for LNG-IUS 12 and 0.21 (95% CI 0.01 to 1.18) for LNG-IUS 16 at one year (Analysis 5.1). At three years, the unadjusted Pearl Indices were 0.36 (0.10 to 0.92) for

the LNG-IUS 12 and 0.17 (0.02 to 0.60) for the LNG-IUS 16 (Analysis 5.2). Of four ectopic pregnancies, two occurred with each device over three years: 0.17 per 100 women-years for the LNG-IUS 12; 0.18 per 100 women-years for the LNG-IUS 16. The risk of expulsion was 4.78% overall, and two cases (0.2%) of pelvic inflammatory disease were reported overall. Twenty-two percent of women discontinued an IUS due to adverse events; however, overall continuation was not stated.

The cross-over trial of [Stewart 2007](#) compared the COC with the vaginal contraceptive ring. Overall, 13 pregnancies occurred: four were associated with an interval of vaginal contraceptive ring use and nine related to an interval of COC use. Because the report did not specify whether the pregnancies occurred with cycles one to three or with cycles four to six, we could not calculate contraceptive efficacy rates. However, continuation rates did not differ significantly between the intervention groups for the first three months (OR 1.09, 95% CI 0.49 to 2.42) or the second three months (OR 0.61, 95% CI 0.26 to 1.43) (Analysis 2.1). For the COC, 50 of 67 (75%) women completed three cycles compared with 48 of 63 (76%) women for the vaginal contraceptive ring. Reasons for study discontinuation 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). A co-investigator provided additional data for this review.

[Stuart 2005](#) compared the COC with the transdermal contraceptive patch. The trial was underpowered to show important differences in pregnancy or continuation rates. One of 10 women in each intervention group became pregnant during the study (OR 1.00, 95% CI 0.05 to 18.57; Analysis 3.1). Eight of 10 women continued the COC at six months, whereas six women continued the transdermal contraceptive patch at six months (OR 0.38, 95% CI 0.05, 2.77; Analysis 3.2). Reasons for discontinuation for the COC 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).

Finally, [Suhonen 2004](#) compared the LNG-IUS 20 versus the COC. This trial also showed no important differences in pregnancy rates or continuation rates. No pregnancies occurred in either intervention group over 12 months (Analysis 4.1). Twelve-month continuation rates were 80% (75 of 94) in the LNG-IUS group and 73% (72 of 99) in the COC group (OR 1.48, 95% CI 0.76 to 2.89; Analysis 4.2). Women in the LNG-IUS 20 group were more likely than women in the COC group to discontinue their method because of pain (OR 14.62, 95% CI 0.81 to 263.16) and less likely to discontinue because of personal reasons (OR 0.27, 95% CI 0.09 to 0.85; Analysis 4.3). In the LNG-IUS 20 group, four out of six discontinuations because of pain occurred within the first three months after insertion. For discontinuation due to pain, the study arms differed somewhat but the confidence interval was wide (Analysis 4.3).

## ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Continuation or discontinuation of contraceptive method				
<b>Patient or population:</b> women aged $\leq 25$ years with desire for contraception <b>Settings:</b> clinic or community <b>Intervention:</b> hormonal or intrauterine method <b>Comparison:</b> other hormonal or intrauterine method				
Outcomes	Relative effect (95% CI)	Participants (study)	Quality of the evidence (GRADE)	Interventions
<b>Continuation</b> (12 months)	OR 1.48 (0.76 to 2.89)	193 (Suhonen 2004)	⊕○○○ <b>very low</b>	LNG-IUS 20 vs. COC (EE 30 µg + desogestrel 150 µg)
<b>Continuation</b> (1 month; 6 months)	OR 2.44 (0.19 to 31.53); OR 3.60 (0.62 to 21.03)	23 (Godfrey 2010)	⊕⊕⊕○ <b>moderate</b>	Cu T380A IUD vs. LNG-IUS 20
<b>Continuation</b> (cycles 1 to 3; cycles 4 to 6)	OR 1.09 (0.49 to 2.42); OR 0.61 (0.26 to 1.43)	130 (Stewart 2007)	⊕⊕⊕○ <b>moderate</b>	COC (EE 35 µg + norgestimate 250 µg) vs. vaginal contraceptive ring
<b>Continuation</b> (6 months)	OR 0.38 (0.05 to 2.77)	20 (Stuart 2005)	⊕⊕⊕○ <b>moderate</b>	COC (EE 30 µg + norgestimate 250 µg) vs. transdermal contraceptive patch
<b>Discontinuation: other personal reasons</b> (12 months)	OR 0.27 (0.09 to 0.85)	193 (Suhonen 2004)	⊕○○○ <b>very low</b>	LNG-IUS 20 vs. COC (EE 30 µg + desogestrel 150 µg)
<b>Discontinuation: pain, hormonal, bleeding, spotting, other medical, or planning pregnancy</b> (12 months)	No significant difference	193 (Suhonen 2004)	⊕○○○ <b>very low</b>	LNG-IUS 20 vs. COC (EE 30 µg + desogestrel 150 µg)
GRADE Working Group grades of evidence <b>High quality:</b> Further research is very unlikely to change our confidence in the estimate of effect. <b>Moderate quality:</b> Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. <b>Low quality:</b> Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. <b>Very low quality:</b> We are very uncertain about the estimate.				

CI: confidence interval; OR: Odds ratio; LNG-IUS: levonorgestrel-releasing intrauterine system; COC: combined oral contraceptive; EE = ethinyl estradiol

## DISCUSSION

### Summary of main results

Four studies compared different contraceptive methods and one trial compared two levonorgestrel-releasing intrauterine systems (LNG-IUS). Of those comparing different methods, two were pilot studies and, therefore, were underpowered to find important differences (Stuart 2005; Godfrey 2010). The other two did not provide a power calculation (Suhonen 2004; Stewart 2007). However, Suhonen 2004 noted the sample size was based on 80% continuation in the LNG-IUS group, and for Stewart 2007 the primary outcome of the trial (acceptability) differed from the outcomes for this review.

The trials that assessed pregnancy did not show any significant difference between study groups (Summary of findings for the main comparison). In addition, the study groups did not differ significantly for method continuation (Summary of findings 2). Among reasons for discontinuation, one study showed a significant difference between the study arms for 'other personal reasons' but not for the various other reasons. Kaunitz 2013 compared two LNG-IUS doses in a secondary analysis from a larger trial. The study arms did not differ significantly in contraceptive effectiveness, and the overall incidence of adverse events in either group was rare. High loss to follow-up or discontinuation may have played a role in the studies. None of the trials reported loss to follow-up by assigned method; we obtained additional data for three studies (Stuart 2005; Stewart 2007; Kaunitz 2013).

### Overall completeness and applicability of evidence

Four studies reported pregnancy and continuation data for the interventions in the study (Suhonen 2004; Stuart 2005; Stewart 2007; Godfrey 2010). One study reported pregnancy data (Kaunitz 2013). None of the studies assessed the same comparisons, precluding meta-analysis. In addition, we did not find any trials of other commonly used contraceptives in this age group, such as the contraceptive injection or the contraceptive implant. Four studies were completed in urban settings, although they had very different participant populations (Suhonen 2004; Stuart 2005; Stewart 2007; Godfrey 2010). One study in Europe enrolled only white

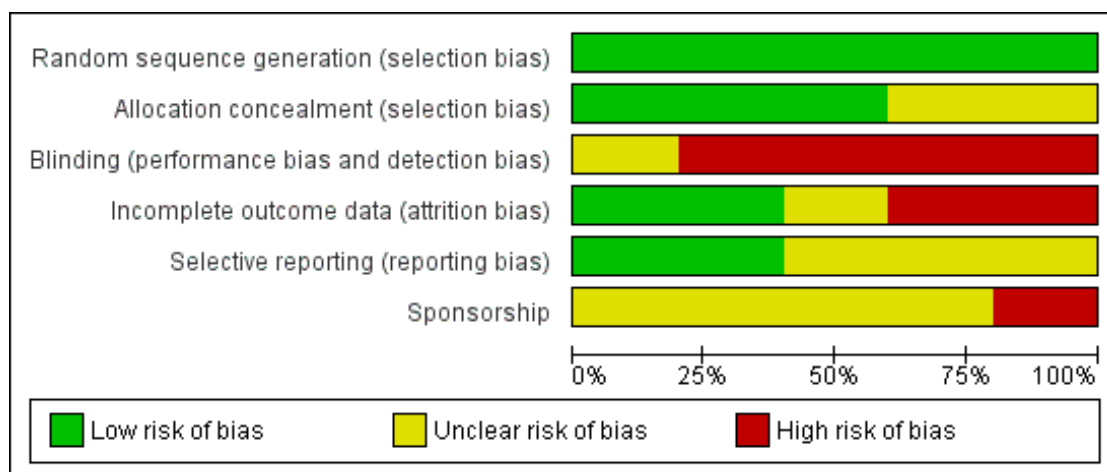
or Asian women (Suhonen 2004), whereas three other studies enrolled mostly low-income Latina or African-American women in the US (Stuart 2005; Stewart 2007; Godfrey 2010). These studies may not be applicable to populations with different racial and socioeconomic characteristics. The fifth study was conducted across Europe and the Americas (Kaunitz 2013). While that trial may have had a diverse participant population, neither the abstract nor the main report had demographic details.

Three of the five studies noted enrollment difficulties, which decreased the generalizability of the studies. Godfrey 2010 approached 37 women but randomized only 62% of these women. Stewart 2007 screened 230 women but only enrolled and randomized 56% of screened women. The most common reasons for not enrolling in the study were recent use of hormonal contraceptives, lack of interest in potential participants after receiving study information, ineligible age, and not sexually active. Stuart 2005 screened 72 women but only randomized 20% of those screened. The most common 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. Suhonen 2004 did not report how many women were screened to recruit 200 women for the study. The main trial that served as the source for Kaunitz 2013 randomized 79% of screened women in all age groups, but the percentage of screened women who were randomized in the 18- to 25-year-old group is unknown.

### Quality of the evidence

We consider the overall quality of evidence to be moderate to low. Figure 1 summarizes the risk of bias for the review overall. Figure 2 shows the risk of bias for individual trials. According to our grading system (Data synthesis), the evidence was moderate quality for three trials, low quality for one, and very low quality for one. Incomplete reporting of the methods, especially allocation concealment and loss to follow-up, were problems in three studies (Suhonen 2004; Stewart 2007; Kaunitz 2013). Two studies blinded the participants to the intervention group assignment (Godfrey 2010; Kaunitz 2013). None of the trials blinded the study staff or investigators. The trials were all published since the first CONSORT guidelines (Consolidated Standards of Reporting Trials), which have been updated (Schulz 2010), and would be expected to have adequate reporting.

**Figure 1. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.**



**Figure 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Sponsorship
Godfrey 2010	+	+	-	+	?	?
Kaunitz 2013	+	?	?	-	?	-
Stewart 2007	+	+	-	?	+	?
Stuart 2005	+	+	-	+	+	?
Suhonen 2004	+	?	-	-	?	?

## Potential biases in the review process

One author (JT) was involved in [Stuart 2005](#). JT also had access to the database for [Stewart 2007](#). Additional data and information were more easily obtained for those studies compared with the other studies.

## Agreements and disagreements with other studies or reviews

Prior 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 when using oral contraceptive pills, patch or ring, or depo-medroxyprogesterone acetate ([Kost 2008](#); [Raine 2011](#)). The two trials included in this review that addressed contraceptive pills, ring, or patch found a slightly higher proportion of contraceptive failure compared with the general population; however, they were not powered to address this outcome ([Stuart 2005](#); [Stewart 2007](#); [Trussell 2011](#)). The studies examining continuation and effectiveness of intrauterine contraception in this review showed over 75% continuation of the different doses of LNG-IUS at one year and 45% continuation of the copper IUD at one year and few pregnancies ([Suhonen 2004](#); [Godfrey 2010](#); [Kaunitz 2013](#)). The low continuation for the copper IUD occurred in a study underpowered to assess this outcome ([Godfrey 2010](#)), and was not consistent with data from other studies. In one large cohort study, over 75% of women aged 15 to 25 years continued both methods of intrauterine contraception and the contraceptive implant at one year ([Rosenstock 2012](#)). The low contraceptive failure with intrauterine contraception in this review is consistent with that reported elsewhere for young women ([Secura 2014](#)).

draw conclusions regarding the comparisons of contraceptive efficacy or continuation rates between different contraceptive methods in this review. Women aged 25 years and younger had at least as high continuation rates of the levonorgestrel intrauterine system 20 µg/day (LNG-IUS 20) as for a combined oral contraceptive (COC). A slightly higher proportion of women discontinued the LNG-IUS 20 because of pain compared with the COC group, particularly in the first three months. Healthcare providers should counsel women about the potential for increased pain during the first three months after intrauterine contraception (IUC) insertion and about strategies for reducing pain after insertion ([Grimes 2007](#)). Intrauterine contraception may provide better contraceptive effectiveness for young women. Both the LNG-IUS 12 µg and 20 µg are currently marketed; we did not find any RCTs comparing those two doses of LNG-IUS in women up to 25 years old.

## Implications for research

The quality of the evidence was moderate to low. The limitations were due to inadequate reporting, lack of blinding, or incomplete outcome data. Sample sizes were small for some trials. Randomized controlled trials of sufficient power are needed to examine the contraceptive efficacy and continuation rates of hormonal and intrauterine contraceptives in young women. Also, research should focus on the most effective and longer-acting reversible contraceptive methods, such as the contraceptive injection, contraceptive implant, and intrauterine contraception. 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 RCTs.

## AUTHORS' CONCLUSIONS

### Implications for practice

Due to inadequate sample sizes and few eligible trials, we could not

## ACKNOWLEDGEMENTS

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\* *Indicates the major publication for the study*

## 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 Conducted in Chicago, Illinois
Participants	23 women Inclusion criteria: aged 14 to 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 3 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	<ul style="list-style-type: none"> <li>• Copper T380A intrauterine device (IUD)</li> <li>• Levonorgestrel intrauterine system 20 µg/day (LNG-IUS 20)</li> </ul>
Outcomes	Pregnancy, continuation, expulsion, infection, side effects, bleeding, and satisfaction at 6 months (no primary outcome) Participants kept daily bleeding and side effect diaries and were contacted by telephone monthly Follow-up visits: 1 and 6 months after insertion
Notes	All device insertions occurred within first 5 days of menstrual cycle, at least 7 weeks after vaginal or cesarean delivery or second-trimester abortion or at least 3 weeks after first-trimester abortion Prior to randomization, all women were screened for chlamydia, gonorrhea, trichomoniasis, and pregnancy. If sexually transmitted infection detected, woman was treated and re-screened 3 weeks later

#### *Risk of bias*

#### *Risk of bias*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number sequence in 4 blocks of 6; 1:1 allocation Allocation sequence generated by a statistician unrelated to study
Allocation concealment (selection bias)	Low risk	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

**Godfrey 2010** (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included in analysis for pregnancy and continuation rates. Loss to follow-up: at 6 months, 9% for copper T380A IUD and 17% for LNG-IUS 20
Selective reporting (reporting bias)	Unclear risk	Method of pregnancy assessment not reported
Sponsorship	Unclear risk	Financial support from an anonymous foundation

**Kaunitz 2013**

Methods	Multicenter, randomized, controlled study conducted from August 2007 through July 2011 Conducted in 138 centers across 11 countries (6 Europe, 2 South America, 2 North America, 1 Mexico)	
Participants	1130 women, $\leq 25$ years old, from a trial with 2884 healthy women, nulliparous or parous Inclusion criteria: aged 18 to 35 years, regular menstrual cycles, requested contraception, healthy Exclusion criteria: contraindications for use of existing LNG-IUS in place at time of protocol development but without specific uterine dimension criteria; vaginal or cesarean delivery or abortion within past 6 weeks; known or suspected pregnancy; lactation; infected abortion or postpartum endometritis within past 3 months; distortion of uterine cavity considered likely to cause problems with placement, retention, or removal of device; unexplained abnormal uterine bleeding; history of ectopic pregnancy; genital malignancy or untreated cervical dysplasia; previous or current pelvic inflammatory disease; genital infection not yet successfully treated	
Interventions	<ul style="list-style-type: none"> <li>• LNG-IUS 12 µg/day (LNG-IUS 12)</li> <li>• LNG-IUS 12 µg/day (LNG-IUS 16)</li> </ul> Device insertions within first 7 days of menstrual cycle; up to 2 placement attempts per woman Ultrasound used to confirm correct placement Follow-up: every 3 months for 1 year, then every 6 months through 3 years	
Outcomes	Pregnancy rate, discontinuation, expulsion, perforation, pelvic inflammatory disease Pregnancy test at final 3-year visit and when clinically indicated	
Notes	Published abstract was sub-analysis of <a href="#">Nelson 2013</a> , which provided design information. Investigators provided sample sizes for women aged 18 to 25 years old randomized to each LNG-IUS	

***Risk of bias***

***Risk of bias***

Bias	Authors' judgement	Support for judgement
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**Kaunitz 2013** (Continued)

Random sequence generation (selection bias)	Low risk	Computer-generated random number sequence in blocks of 4; 1:1 allocation; balanced for sites
Allocation concealment (selection bias)	Unclear risk	Numbered randomization cards, used in ascending order, to inform investigator which device to place No mention of envelopes
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Participants blinded to device type but investigators and research assistants not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	All participants included in analysis for pregnancy and continuation rates Study completion: 57% of LNG-IUS 12; 60% of LNG-IUS 16 Unclear if discontinued women requested device removal or were lost to follow-up Discontinued due to adverse event: 23% Loss to follow-up: no mention
Selective reporting (reporting bias)	Unclear risk	Pregnancy tests at end of 3-year study and when clinically indicated; unclear if Pearl Index included self reports
Sponsorship	High risk	Source trial (Nelson 2013) was supported by Bayer HealthCare Pharmaceutical Medical. Bayer HealthCare also provided writing support

**Stewart 2007**

Methods	Single-center, randomized cross-over study conducted from April 2003 through February 2004 Conducted at an urban family planning clinic for low-income young people in San Francisco, California No mention of power calculation
Participants	130 women Inclusion criteria: aged 15 to 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 1 regular menstrual cycle preceding enrollment or within 7 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	<ul style="list-style-type: none"> <li>Combined oral contraception (ethinyl estradiol 35 µg + norgestimate 250 µg) for 3 cycles</li> <li>Vaginal contraceptive ring (daily dose of ethinyl estradiol 15 µg + etonogestrel 120 µg) for 3 cycles</li> </ul>
Outcomes	Acceptability (primary outcome), compliance, side effects, continuation, and pregnancy Follow-up: end of each 3 cycle series in this cross-over study
Notes	Co-investigator sent database to JT (review author) for analysis

<i>Risk of bias</i>		<i>Risk of bias</i>
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)	Low risk	Envelope sequence provided by separate department
Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded. Not mentioned whether investigators were blinded during analysis
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Analysis for continuation included all women randomized. Total number of pregnancies reported without any denominator Study completion: overall 51% (66/130) Loss to follow-up: 9% overall (12/130); not reported by method
Selective reporting (reporting bias)	Low risk	Pregnancy data from urine pregnancy test, 13 women: 4 during or after vaginal ring use; 9 during or after COC use
Sponsorship	Unclear risk	No mention

## Stuart 2005

Methods	Single-center randomized controlled pilot study conducted from September 2003 through May 2004 Conducted at 2 community family planning clinics in Dallas, Texas
Participants	20 women Inclusion criteria: aged 15 to 19 years, requesting hormonal contraceptive as primary method of contraception, sexually active (minimum of 2 acts per month), regular men-

	<p>strual cycles (every 21 to 35 days), at least 2 normal menses since last injection if woman received depot medroxyprogesterone acetate within 6 months, at least 1 normal menses since pregnancy if woman postpartum, and able to provide written informed consent</p> <p>Exclusion criteria: medical contraindication to hormonal contraception, pregnancy within 28 days of study admission, regular use of street drugs, more than 2 daily drinks of alcohol, history of HIV, blood pressure &gt; 140/90 mm Hg, receipt of any experimental drug or device within 30 days, history of pelvic inflammatory disease, and known history of infertility or subfertility</p>
Interventions	<ul style="list-style-type: none"> <li>• Combined oral contraception (ethinyl estradiol 30 µg + norgestimate 250 µg)</li> <li>• Transdermal contraceptive patch (daily dose of ethinyl estradiol 20 µg + norelgestromin 150 µg)</li> </ul> <p>3-month supply of contraceptive method provided at enrollment visit and after 3 cycles; women allowed to switch methods at 3-month visit</p>
Outcomes	<p>Pregnancy (primary outcome), continuation, compliance, and satisfaction with method at 3 and 6 months</p> <p>Participants considered to have discontinued method if switched to another method at 3-month visit, if pregnant, or if lost to follow-up. Reasons for switching to another method during study included fear of patch falling off (2 women)</p>
Notes	Information from conference abstract and from J Tang (review author), who worked on the study during medical school. She added design information and additional data

**Risk of bias****Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generation in blocks of 4 and 6, by statistician unrelated to study
Allocation concealment (selection bias)	Low risk	Sequentially numbered opaque sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included in analysis for pregnancy and continuation rates Loss to follow-up: 6 months, 10% COC and 20% 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)
Sponsorship	Unclear risk	No information



**Suhonen 2004**

Methods	Multicenter randomized controlled trial (study dates not specified) 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) For sample size calculation, expected continuation rate with LNG-IUS 20 was 80%. No power calculation or difference in continuation rates to be detected was specified
Participants	200 women (100 from each center) Inclusion criteria: aged 18 to 25 years, nulliparity, regular menstrual cycles (24 to 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 $\geq 32$ , acute liver disease, blood pressure $> 140/90$ mm Hg, diabetes, and coagulation disorders
Interventions	<ul style="list-style-type: none"> <li>Combined oral contraception (ethinyl estradiol 30 µg + desogestrel 150 µg); started on first day of menstrual bleeding or immediately after induced abortion; 3-month package of pills at each 3-month visit</li> <li>Levonorgestrel intrauterine system 20 µg/day; inserted within week after onset of menstrual bleeding or in conjunction with induced abortion</li> </ul>
Outcomes	Continuation (primary outcome), pregnancy, infection, patterns of bleeding, and acceptability at 6 and 12 months LNG-IUS 20 group: evaluation of insertion by both participants and doctors, perforation, and expulsion Follow-up: visits every third month; gynecologic exam at 3 and 12 months; menstrual, symptom, and sexual questionnaires at 6 and 12 months
Notes	

**Risk of bias**
**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization into 2 equal-sized groups in blocks of 8. Performed prior to study initiation and carried out separately in each center
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) All outcomes	High risk	Method use unable to be blinded. Not mentioned whether investigators were blinded during analysis
Incomplete outcome data (attrition bias) All outcomes	High risk	Loss to follow-up: no mention Discontinuation: 20% LNG-IUS 20 (19/94); 27% COC (27/99)

		Of 200 randomized women, 7 did not initiate method (5 LNG-IUS 20 group; 2 COC group). These women were not followed and not included in analysis
Selective reporting (reporting bias)	Unclear risk	Method of pregnancy assessment not reported
Sponsorship	Unclear risk	No mention

COC: combined oral contraceptive

HIV: human immunodeficiency virus

IUD: intrauterine device

LNG-IUS 12: levonorgestrel intrauterine system 12 µg/day

LNG-IUS 16: levonorgestrel intrauterine system 16 µg/day

LNG-IUS 20: levonorgestrel intrauterine system 20 µg/day

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

Study	Reason for exclusion
Berenson 2012	Did not compare different contraceptive methods (compared monthly phone calls to standard on contraceptive continuation)
Borgatta 2014	Not limited to women aged $\leq 25$ years
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
Bryant 2015	Did not compare different contraceptive methods (compared timing of postpartum implant placement)
Castaño 2012	Did not compare different contraceptive methods (compared text messaging intervention on contraceptive continuation)
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 (women runners)
Creinin 2008	Not limited to women aged $\leq 25$ years
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 $\leq 25$ years

(Continued)

Jensen 2012	Did not compare different contraceptive methods (compared flexible versus traditional use of the same oral contraceptive)
Kaunitz 2014	Not limited to women aged $\leq 25$ years
Larsson 1979	Not limited to women aged $\leq 25$ years. Not a randomized controlled trial; women 'randomly' assigned to Gravigard IUD or copper 7 IUD, but no attempt was made to control the allocation
Li 2011	Not limited to women aged $\leq 25$ years
Mansour 2011	Not limited to women aged $\leq 25$ years
Meirik 2013	Not limited to women aged $\leq 25$ years
Nanda 2014	Original study did not compare different contraceptive methods (compared counseling intervention)
Peterson 1991	Not limited to women aged $\leq 25$ years
Rickert 2007	Did not compare different contraceptive methods (compared different timing for initiation of same contraceptive method)
Stephenson 2013	Did not compare different contraceptive methods (compared tailored versus standard use of the same oral contraceptive)
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. Included special population (women with anorexia)
Tang 2012	Not limited to women aged $\leq 25$ years. Included special population (women with prior cesarean delivery)
Thomas 2005	Did not compare different contraceptive methods (compared different concentrations for administering the same dose of depot medroxyprogesterone acetate)
Tuppurainen 2014	Not limited to women aged $\leq 25$ years
van der Straten 2010	No hormonal or intrauterine method used as contraceptive method
Wang 2013	Not limited to women aged $\leq 25$ years
Westhoff 2007	Did not compare different contraceptive methods (compared different timing for initiation of same contraceptive method)
Westhoff 2012	Not limited to women aged $\leq 25$ years
Williams 2013	Unable to compare continuation for at least 3 months. Participants in randomized intramuscular injection arm required only 1 injection over 3-month period

IUD: intrauterine device

## DATA AND ANALYSES

### Comparison 1. Copper T380A IUD versus LNG-IUS 20 µg/day)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Continuation at 1 month	1	23	Odds Ratio (M-H, Fixed, 95% CI)	2.44 [0.19, 31.53]
2 Continuation at 6 months	1	23	Odds Ratio (M-H, Fixed, 95% CI)	3.6 [0.62, 21.03]

### 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	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Cycles 1 to 3	1	130	Odds Ratio (M-H, Fixed, 95% CI)	1.09 [0.49, 2.42]
1.2 Cycles 4 to 6 (cross-over)	1	98	Odds Ratio (M-H, Fixed, 95% CI)	0.61 [0.26, 1.43]

### 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 6 months	1	20	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.05, 18.57]
2 Continuation at 6 months	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.05, 2.77]

### Comparison 4. LNG-IUS 20 µg/day versus combined oral contraception

Outcome or subgroup title	No. of studies	No. of participants	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	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
by reason				
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 Planning 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]
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### Comparison 5. LNG-IUS 12 µg/day versus LNG-IUS 16 µg/day

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Reported unadjusted Pearl Index at year 1			Other data	No numeric data
2 Reported unadjusted Pearl Index at year 3			Other data	No numeric data
3 Reported 3-year Kaplan-Meier estimated cumulative failure rates			Other data	No numeric data

## WHAT'S NEW

Last assessed as up-to-date: 4 August 2015.

Date	Event	Description
4 August 2015	New search has been performed	Searches updated
5 May 2015	New citation required but conclusions have not changed	One new trial
11 February 2015	Amended	New trial included ( <a href="#">Kaunitz 2013</a> )

## CONTRIBUTIONS OF AUTHORS

### 2015 (update)

JK reviewed the search results, conducted the primary data extraction, and drafted the update to the review. LL examined search results, conducted the second data extraction, and helped revise the review. All authors reviewed and commented on the manuscript.

## 2012 (initial review)

JT developed the idea, reviewed the search results, conducted the primary data extraction, and drafted the review. Former author David A Grimes (FHI 360) reviewed the search results and conducted the second data extraction. LL and SM provided guidance on development of the protocol and the review. All authors reviewed and commented on the manuscript.

## DECLARATIONS OF INTEREST

J Tang conducted the initial 2012 review and J Krashin conducted the 2015 update as fellows working under the mentorship of G Stuart, the principal investigator for [Stuart 2005](#).

S Mody is a MERCK Nexplanon Trainer.

## SOURCES OF SUPPORT

### Internal sources

- No sources of support supplied

### External sources

- Family Planning Fellowship, USA.

Support for conducting the review and update at University of North Carolina: 2011 to 2012 (JHT) and 2014 to 2015 (JWK)

- National Institute of Child Health and Human Development, USA.

2011 to 2015: Support for conducting the review and update at FHI 360

- United States Agency for International Development, USA.

2011 to 2012: Support for conducting the review at FHI 360

## 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