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Authors
Lopez, Laureen M
Newmann, Sara J
Grimes, David A
et al.

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[Intervention Review]

Immediate start of hormonal contraceptives for contraception

Laureen M Lopez[1], Sara J Newmann[2], David A Grimes[3], Kavita Nanda[4], Kenneth F Schulz[5]

[1]Clinical Sciences, FHI 360, Research Triangle Park, North Carolina, USA. [2]Obstetrics and Gynecology and Reproductive Sciences, University of California, San Francisco General Hospital, San Francisco, California, USA. [3]Obstetrics and Gynecology, University of North Carolina, School of Medicine, Chapel Hill, North Carolina, USA. [4]Clinical Sciences, FHI, Research Triangle Park, North Carolina, USA. [5]Quantitative Sciences, FHI 360 and UNC School of Medicine, Research Triangle Park, North Carolina, USA

Contact address: Laureen M Lopez, Clinical Sciences, FHI 360, P.O. Box 13950, Research Triangle Park, North Carolina, 27709, USA. llopez@fhi360.org.

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ABSTRACT

Background

Health care providers often tell women to wait until the next menses to begin hormonal contraception. The intent is to avoid contraceptive use during an undetected pregnancy. An alternative is to start hormonal contraception immediately with back-up birth control for the first seven days. Immediate initiation was introduced with combined oral contraceptives (COCs), and has expanded to other hormonal contraceptives. At the time of the initial review, how immediate start compared to conventional menses-dependent start was unclear regarding effectiveness, continuation, and acceptability. The immediate-start approach may improve women's access to, and continuation of, hormonal contraception.

Objectives

This review examined randomized controlled trials (RCTs) of immediate-start hormonal contraception for differences in effectiveness, continuation, and acceptability.

Search methods

In August 2012, we searched MEDLINE, CENTRAL, POPLINE, LILACS, ClinicalTrials.gov, and ICTRP for trials of immediate-start hormonal contraceptives. We contacted researchers to find other studies. Earlier searches also included EMBASE.

Selection criteria

We included RCTs that compared immediate start to conventional start of hormonal contraception. Also included were trials that compared immediate start of different hormonal contraceptive methods with each other.

Data collection and analysis

Data were abstracted by two authors and entered into RevMan. The Peto odds ratio (OR) with 95% confidence interval (CI) was calculated.

Main results

Five studies were included. No new eligible studies have been found since the review was initially conducted. Method discontinuation was similar between groups in all trials. Bleeding patterns and side effects were similar in trials that compared immediate with conventional start. In a study of depot medroxyprogesterone acetate (DMPA), immediate start of DMPA showed fewer pregnancies than a 'bridge' method before DMPA (OR 0.36; 95% CI 0.16 to 0.84). Further, more women in the immediate-DMPA group were very satisfied versus those with a 'bridge' method (OR 1.99; 95% CI 1.05 to 3.77). A trial of two immediate-start methods showed the vaginal ring group had less prolonged

bleeding (OR 0.42; 95% CI 0.20 to 0.89) and less frequent bleeding (OR 0.23; 95% CI 0.05 to 1.03) than COC users. The ring group also reported fewer side effects. Also, more immediate ring users were very satisfied than immediate COC users (OR 2.88; 95% CI 1.59 to 5.22).

Authors' conclusions

We found limited evidence that immediate start of hormonal contraception reduces unintended pregnancies or increases method continuation. However, the pregnancy rate was lower with immediate start of DMPA versus another method. Some differences were associated with contraceptive type rather than initiation method, i.e., immediate ring versus immediate COC. More studies are needed of immediate versus conventional start of the same hormonal contraceptive.

PLAIN LANGUAGE SUMMARY

Immediate start of hormonal birth control

Health care providers often tell women to wait until their next menstrual cycle to begin birth control pills. The main reason is to avoid using birth control during an undetected pregnancy. Another method involves starting the pills right away ('immediate start' or 'quick start'). Another birth control method should be used as back-up for the first seven days. Unclear issues were whether quick start of hormonal birth control works as well as the usual start and whether women like it. The quick start method might improve women's use of hormonal birth control.

In August 2012, did computer searches for randomized controlled trials of the quick-start method for pills and other hormonal birth control. We contacted researchers to find other studies. We included trials that compared quick start to the usual start of birth control. Also included were studies that compared quick start of different types of hormonal birth control with each other. Birth control methods could have the hormones estrogen and progestin (combined hormonal birth control) or just the progestin.

Five studies were included. In a study of 'depo,' which is given as a shot, fewer women with quick start of depo became pregnant than those who used another method for 21 days before depo. In this review, the numbers of women who stopped using their birth control method early were similar between groups in all trials. In the depo trial, more women with quick start of depo were very satisfied.

A trial of two quick-start methods showed women with the vaginal ring had less long-term bleeding and less frequent bleeding than those with pills. For six side effects, including changes in breasts, mood, and nausea, quick start of the ring showed fewer problems than quick start of pills. For satisfaction in that trial, more women in the ring group were very satisfied with their method of birth control.

We found little evidence that quick start leads to fewer pregnancies or fewer women stopping early. However, fewer women on quick start of depo became pregnant than the women who started with another method. Other differences were between types of birth control rather than start times. Women using the vaginal ring had fewer problems than women using birth control pills. More studies are needed comparing quick start versus usual start of the same hormonal birth control method.

BACKGROUND

The optimal time to start hormonal contraception remains unknown. Worldwide, nearly 104 million women use contraceptive pills and nearly 45 million use injectable contraceptives or implants (UNDP 2011). Traditionally, women have been instructed to start combined oral contraceptives (COCs) in relation to their menstrual cycle: either on day one or within the first five to seven days of their menses (Kubba 1993) or on the Sunday after their menses began (Williams-Deane 1992). Many health care providers and pharmaceutical companies suggest multiple options for starting oral contraceptives (OCs), which are timed in relation to menses (Williams-Deane 1992). These multiple options can create confusion regarding when to start the pill. Furthermore, menstruation requirements for initiation of contraception impede access to contraception for non-menstruating women, i.e., those who present for family planning services between two bleeding periods or during postpartum amenorrhea. Prospective studies in four developing countries showed service denial rates ranging from 5% to 47% among new family planning clients if they were not menstruating at the time of their visit (Stanback 2005; Stanback 2007). Only 16% of providers in Kenya felt safe in giving women OCs to start taking later (Stanback 2003). In Ghana and Senegal, less than 5% of providers reported they gave pills to non-menstruating women for later use at the onset of menses (Stanback 2003).

The recommendation for women to wait until the next menses to begin hormonal contraception is intended to avoid contraceptive use during an undetected pregnancy. During this delay in contraceptive initiation, unintended pregnancies can occur, women may choose a less effective method or forget instruction (FSRH 2010), and fears of side effects increase (Westhoff 2002). This medically-imposed delay in starting contraception may increase the cost of family planning due to more repeat or return clinic visits. Worldwide, unintended pregnancies are associated with preventable morbidity and mortality. In contrast, reviews of epidemiological data and prospective studies have indicated that exogenous hormones during pregnancy did not increase risk of developing abnormalities in non-genital organs (Wilson 1981); oral contraceptives were not associated with congenital malformations (Bracken 1990).

An alternative is to start hormonal contraceptives immediately with back-up birth control for the first seven days (Lara-Torre 2004). This 'immediate-start' or 'quick-start' method may improve initiation and continuation of hormonal contraceptives, among both adolescents and adults, compared to conventional start methods (Lara-Torre 2002; Westhoff 2002). Immediate start of birth control was introduced with combined oral contraceptives, which have both progestin and estrogen, and has been expanded to other hormonal contraceptives (WHO 2004; Murthy 2005; Westhoff 2005). When we conducted this initial review, how immediate start of hormonal contraception compared to conventional menses-dependent start was unclear regarding effectiveness, continuation, and acceptability. The practice of 'quick start' for hormonal contraceptives has since become accepted by professional organizations (FSRH 2010; ARHP 2011).

OBJECTIVES

This review examined randomized controlled trials (RCTs) of immediate-start hormonal contraception for differences in effectiveness, continuation, and acceptability.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs) in any language that compared immediate start of hormonal contraceptives to conventional start. We also included RCTs that compared immediate start of different hormonal contraceptive methods with each other. Treatment duration had to be at least three cycles or 84 days.

Types of participants

All women with data in the eligible trials were included in this review.

Types of interventions

We included any contraception initiation method: immediate start and start in relation to timing of menses. We also included any type of hormonal contraception: oral, intramuscular, transdermal, and transvaginal.

Types of outcome measures

Contraceptive effectiveness, continuation rates, bleeding patterns, acceptability, and side effects.

Search methods for identification of studies

Electronic searches

In August 2012, we searched the computerized databases MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), POPLINE, and LILACS for studies of immediate-start hormonal contraceptives. We also searched for trials via ClinicalTrials.gov and the search portal of the International Clinical Trials Registry Platform (ICTRP). The search strategy is shown in Appendix 1. The earlier strategy, which also included EMBASE, can be found in Appendix 2.

Searching other resources

We examined reference lists of relevant articles. We also wrote to known investigators for information about other published or unpublished trials not discovered in our search.

Data collection and analysis

Selection of studies

We assessed for inclusion the titles and abstracts identified during the literature searches.

Data extraction and management

One author reviewed the search results and identified reports for inclusion or exclusion. Another author also examined the reports identified for appropriate categorization. Similarly, one author abstracted the data and entered the information into RevMan. Another author conducted a second data abstraction and verified correct data entry. Any discrepancies were resolved by discussion.

Assessment of risk of bias in included studies

Studies were examined for methodological quality, according to the principles recommended in Higgins 2005. Factors

considered were study design, randomization method, allocation concealment, blinding, and losses to follow-up and early discontinuation. Adequate methods for allocation concealment include a centralized telephone system and the use of sequentially-numbered, opaque, sealed envelopes (Schulz 2002a). Pharmacy distribution of pill bottles is another good method. Excluding randomized persons is not consistent with an intent-to-treat analysis and can bias the results (Schulz 2002b). High losses to follow-up threaten validity (Strauss 2005). Limitations in design are presented in Risk of bias in included studies and were considered when interpreting the results.

Data synthesis

For dichotomous outcomes, the Peto odds ratio (OR) with 95% Confidence Interval (CI) was calculated. Examples are the proportion of women who became pregnant or who discontinued contraception early. The Peto OR is useful when treatment effects are small and when events are not very common (Higgins 2005). This approach performs well under many circumstances, except when the study arm sizes are severely unbalanced, which rarely occurs in RCTs (Deeks 2001). A fixed-effect model does not require the assumption of normal distribution for the effects (Deeks 2001; Higgins 2005). Fixed effect and random effects will give the same result if no heterogeneity exists, which is also the case if a comparison includes a single study. There is no consensus regarding the use of either model. We had planned to test for statistical heterogeneity. However, we did not combine data from any studies in meta-analysis due to differences in interventions.

For analysis, we used intent to treat or per protocol as data were available in the reports. Outcome data are described in Characteristics of included studies, along with any exceptions due to reporting. Exclusions by the trial authors are described in the Risk of bias tables.

RESULTS

Description of studies

Results of the search

In 2012, the searches produced 170 unduplicated references. This included 147 citations from the electronic databases and 23 from other sources (ClinicialTrials.gov, ICTRP, and communication from a researcher). We did not identify any new eligible trials. When the review was updated in 2010, we did not find any new trials to include either.

Included studies

Five randomized controlled trials met the eligibility criteria. All trials were conducted in the USA and published from 2003 to 2007. Four trials were related, having been conducted by members of the same research group (Westhoff 2003; Westhoff 2005; Rickert 2007; Westhoff 2007).

The trials included a total of 2427 women. Sample sizes ranged from 60 to 1720 with an average of 485. Sample sizes were 113 in Westhoff 2003, 60 in the pilot study of Murthy 2005, 201 in Westhoff 2005, 333 for Rickert 2007, and 1720 in Westhoff 2007. All studies reported an a priori sample size determination: three focused on discontinuation rates (Murthy 2005; Rickert 2007; Westhoff 2007) and two were based on bleeding and spotting days (Westhoff 2003; Westhoff 2005).

Treatment duration was three cycles or 84 to 90 days in Westhoff 2003, Murthy 2005, and Westhoff 2005 and six months in Rickert 2007 and Westhoff 2007.

The comparisons differed across trials. Immediate start refers to initiating contraception during the first visit. Conventional start of contraception included instruction to start during the next menses. Only Rickert 2007 excluded women who were currently menstruating. Two studies compared immediate versus conventional start of OCs; Westhoff 2003 used a COC (norethindrone 1 mg plus ethinyl estradiol (EE) 35 µg), while in Westhoff 2007 the type of OC depended on the clinician's preference. Murthy 2005 examined immediate versus conventional start of the contraceptive patch (containing norelgestromin 6 mg plus EE 75 µg (Ortho-McNeil 2007)). Rickert 2007 examined immediate injection of depot medroxyprogesterone acetate (DMPA) versus a contraceptive 'bridge' to DMPA. 'Bridge' participants could choose pills, patch, or ring before DMPA and were given a 21-day supply; their first DMPA injection was administered 21 to 28 days later. The trial of Westhoff 2005 differed in that immediate use of the vaginal contraceptive ring (daily release: etonogestrel 120 µg plus EE 15 µg) was compared with immediate COC (norgestimate (NGM) 180/215/250 µg plus EE 30 µg).

In four trials, participants in both groups were instructed to use condoms as a backup (or abstain) for the first seven days or until they started their contraceptive method (Westhoff 2003; Westhoff 2005; Rickert 2007; Westhoff 2007). Women in Westhoff 2005 were also given emergency contraception. In Murthy 2005, reportedly just the immediate-start group was instructed to use a back-up method like condoms for seven days; however, all participants were given a prescription for emergency contraception.

The outcomes included pregnancy data for all but Murthy 2005, discontinuation of method for four trials, bleeding or cycle control data for all but Rickert 2007, and satisfaction with method in three trials (Westhoff 2003; Westhoff 2005; Rickert 2007). Data on side effects or adverse events were varied. For examples, Murthy 2005 only reported on nausea, and Westhoff 2007 reported just the serious adverse events. The Schafer 2006 report from the Westhoff 2005 trial assessed the women for 10 potential side effects; participants could report no change, good change, or bad change.

Excluded studies

Two older trials were brought to our attention by a colleague. Earlier, we determined that Bednarek 2008 was not relevant based on the abstract. We have now added it to 'excluded studies' with the reason that the outcome measure of bleeding was not relevant. Martin 1998 was also identified; it was not found in earlier searches because the title and abstract did not indicate quick or immediate start. We added it to 'excluded studies' because it was not a contraception trial.

Also excluded was a trial listed earlier as ongoing (Karjane 2011). It has since been terminated due to recruitment problems. Lastly, we examined the full text of Madden 2011 and found that it was not an RCT.

Risk of bias in included studies

Allocation

The quality of reporting was uneven for some design issues. Randomization in four trials was described as generated with random numbers table or random numbers generator. One trial did not provide information on how the randomization sequence was generated and did not specify if the allocation was concealed before assignment (Murthy 2005). Two studies had adequate allocation concealment with sequentially-numbered, opaque, sealed envelopes (Westhoff 2003; Westhoff 2005). Two trials had some concealment, as they reported using sequential sealed envelopes (Rickert 2007) or numbered opaque envelopes (Westhoff 2007).

Blinding

All appeared to be open-label, most likely due to the differences in the interventions. However, Westhoff 2003 noted that the person who abstracted the diary information was blinded to group assignment.

Incomplete outcome data

Three studies appeared to use intent-to-treat analysis, in which all the women who were randomized and had follow-up data were included in the analysis (Murthy 2005; Westhoff 2005; Rickert 2007). Two studies excluded women from the study who had been randomized but then were found to have been ineligible due to pregnancy (Westhoff 2003; Westhoff 2007).

Losses to follow-up also varied. Westhoff 2003 and Murthy 2005 had losses around 2%, while Westhoff 2005 lost 13% and Westhoff 2007 lost about 16%. The DMPA study of Rickert 2007 had high losses of 32% for each group. High losses to follow-up threaten validity (Strauss 2005), and many methodologists would question whether Rickert 2007 should still be considered 'randomized' given the losses.

Effects of interventions

The trials examined here included several different types of comparisons. Three trials compared immediate versus conventional start of the same contraceptive method: a specific COC (Westhoff 2003), various types of OCs (Westhoff 2007), and the contraceptive patch (Murthy 2005). Rickert 2007 compared immediate start of DMPA to a 'bridge' to DMPA (using pills, transdermal patch, or vaginal ring for 21 days before the first DMPA injection). Westhoff 2005 compared two immediate-start methods (vaginal ring versus COC). Most differences were found between types of contraceptives rather than between immediate and conventional initiation. No trials were combined in meta-analysis due to the differences in interventions.

Effectiveness

Four studies reported the proportions of women who became pregnant during the study. In Rickert 2007, the immediate DMPA group was less likely to become pregnant than the bridge group (OR 0.36; 95% CI 0.16 to 0.84). The groups were similar in contraceptive effectiveness in Westhoff 2003 and Westhoff 2007, which compared immediate to conventional start of OCs. When the pregnancies estimated to have occurred prior to enrollment were included in the analysis, the groups were still similar in Westhoff 2003 and Westhoff 2007. A secondary publication of Westhoff 2007 included analysis of the subset younger than 18 years. The immediate start and conventional start groups in that subset were also similar for pregnancy.

Westhoff 2005 compared two immediate-start methods (ring and COC); no difference in pregnancy rates was evident in that study, either.

Contraceptive method discontinuation

Method discontinuation was similar across groups in the studies with such data. Murthy 2005 compared immediate to conventional start of the patch, Rickert 2007 examined immediate DMPA and a bridge to DMPA, and Westhoff 2003 studied immediate versus conventional start of the same COC. For method discontinuation, Westhoff 2007 provided percentages for the groups combined; the immediate and conventional start groups were reportedly similar. Westhoff 2007 included various OCs, according to the clinician's preference.

No difference in discontinuation was noted in the Schafer 2006 report from Westhoff 2005, which compared two immediate-start methods (ring versus COC).

Cycle control

Four trials reported bleeding data. The study groups had similar bleeding profiles in three trials that compared immediate with conventional start: Murthy 2005 (patch); Westhoff 2003 (same COC); and Westhoff 2007 (various OCs).

In Westhoff 2005, which compared two immediate start methods, prolonged bleeding (bleeding or spotting episode lasting at least 10 days) was lower for the group with the ring compared to those with COCs (OR 0.42; 95% CI 0.20 to 0.89). Frequent bleeding, defined as more than four episodes of bleeding or spotting, also differed in favor of the vaginal ring group (OR 0.23; 95% CI 0.05 to 1.03) (Westhoff 2005).

Adverse events

Information on side effects varied.

- Murthy 2005 reported on nausea, for which the immediate and conventional start of the patch groups were similar.
- Rickert 2007 reported no adverse events with either the immediate start of DMPA or the group with a bridge to DMPA.
- Westhoff 2007 only reported serious adverse events (SAEs), for which the immediate and conventional start groups were similar; various OCs were included. Examples of SAEs were cholecystectomy, pyelonephritis, and pelvic inflammatory disease (Westhoff 2007); the authors did not specify whether any SAEs were considered related to the intervention.

For the Westhoff 2005 trial, the later report of Schafer 2006 showed that 6 of 10 side effects were less common for the immediate use of the vaginal ring versus immediate start of COCs. The vaginal ring group less frequently reported a "bad change" for weight (OR 0.42; 95% CI 0.21 to 0.87), bleeding (OR 0.28; 95% CI 0.14 to 0.55), breasts (OR 0.36; 95% CI 0.18 to 0.73), mood (OR 0.36; 95% CI 0.19 to 0.69), appetite (OR 0.44; 95% CI 0.21 to 0.95), or nausea (OR 0.30; 95% CI 0.14 to 0.62) (Westhoff 2005).

Satisfaction and future use

Three trials provided data on method satisfaction (Westhoff 2003; Westhoff 2005; Rickert 2007). In Rickert 2007, women in the immediate start of DMPA group were more likely to be very satisfied with their method at six months compared to those with use of a bridge method (OR 1.99; 95% CI 1.05 to 3.77). Westhoff 2003 showed no differences between the immediate and conventional start of the COC.

In Westhoff 2005, which studied two immediate-start methods, more women with the vaginal ring reported being very satisfied with their method compared to the group with COCs (OR 2.88; 95% CI 1.59 to 5.22). Similarly, more women with immediate start of the vaginal ring planned to use the method after the study (OR 2.51; 95% CI 1.32 to 4.77).

DISCUSSION

One of the purposes of immediate start of contraception is to improve initiation and continuation rates and thus decrease unintended pregnancies. In this review, pregnancy differed in one study that compared immediate start of DMPA to using a bridge to DMPA. Compared to many other contraceptive methods, DMPA is long-acting and less user-dependent. While the 'immediate-DMPA' group had proportionately fewer pregnancies, losses were high in that trial. Some of the studies were underpowered to detect differences in pregnancies. However, method discontinuation was similar between study groups in this review.

Cycle control, from bleeding diaries, only differed in a study of two immediate methods. The vaginal ring group had fewer bleeding problems than the COC group (Westhoff 2005). The same trial solicited side effect information and showed differences between the vaginal ring and COC groups. Westhoff 2005 did not provide criteria or details for reporting side effects. Other trials showed the comparison groups to be similar for adverse events. The trials did not have consistent recording or reporting of side effects, which complicates interpretation. Furthermore, side effects may dissipate over time and these trials were relatively short-term.

For satisfaction, two trials showed some differences. In the DMPA trial, the group with immediate use of DMPA was more satisfied than those with a bridge method first. In the trial of two immediate methods, the vaginal ring group was more satisfied than the COC group. However, these studies were only three or six months in duration and satisfaction may vary over time.

All of the trials were relatively recent, yet they did not follow CONSORT guidelines for reporting (Moher 2001; CONSORT 2010). Design details were sometimes lacking. In addition, CONSORT recommends the reporting of outcome data in absolute numbers, rather than percentages. For outcomes reported as means, a measure of variation is needed to interpret the results. Two trials did not follow those guidelines, which prevented the inclusion of some data in the review.

This review was limited due to having only five trials and to great variation in the comparisons. One study compared two immediate-start methods. Of the four trials comparing immediate start with conventional start, one focused on the skin patch and another on DMPA (with or without a bridge method). The remaining two trials studied OCs, but one examined the same COC with different initiation methods, while the other left the OC choice to clinicians. In addition, no study was adequately powered for contraceptive effectiveness (pregnancy), a primary outcome for this review. Trials were generally powered to detect differences in continuation or bleeding patterns.

AUTHORS' CONCLUSIONS

Implications for practice

We found little evidence that immediate start of hormonal contraceptives reduces unintended pregnancies or increases continuation. Bleeding patterns and side effects were similar in trials that compared immediate start with conventional start. Immediate start is one of several acceptable options for starting COCs although more data are needed. One trial showed a lower risk of pregnancy with immediate start of DMPA versus bridging to DMPA with another method. High losses in that trial could have biased the results.

Implications for research

More trials are needed of immediate versus conventional start of the same (rather than a different) hormonal contraceptive method. The primary analysis should be done by intent-to-treat; that is, all enrolled participants should be included. Consistent recording and reporting of bleeding and other side effects would aid interpretation across trials. Improved follow-up is critical to interpretation of trial results, as high losses threaten validity. Sackett suggested that trials with greater than 20% loss to follow-up after randomization should not be considered valid (Strauss 2005); Schulz suggested that the frequency of loss to follow-up should not exceed the frequency of the outcome event, e.g., pregnancy (Schulz 2002b).

In general, we endorse planning for adequate power (Schulz 2005). However, if the scientific world insisted exclusively on large trials, many questions in medicine would languish unanswered. 'Underpowered' trials can be acceptable because they could be combined in a meta-analysis. Our suggestion has three caveats. First, the trial should be methodologically strong, thus eliminating bias. If designed and implemented properly, the trial would yield an unbiased estimate of effect even if it has low power (and precision). The results could then be combined with similar unbiased trials in a meta-analysis. Second, to avoid misinterpretation, authors should report their methods and results properly. If trial results were reported using interval estimation, the wide confidence intervals around the estimated treatment effect would depict the low power. Third, low-powered trials should be published regardless of their results so they can be used in meta-analysis.

Finally, authors should adhere to the internationally accepted guidelines for reporting randomized controlled trials (CONSORT 2010).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Murthy 2005

Methods	Randomized controlled trial ("pilot investigation") conducted at a university hospital in Pittsburgh (USA). Sample size calculation based on ability to detect difference in continuation rates for immediate start (87%) versus traditional start (60%).
Participants	60 women recruited via newspaper advertisements and flyers. Inclusion criteria: 18 to 45 years old, request transdermal delivery for contraception, willing to comply with protocol and visit schedule, willing to answer questionnaires. Exclusion criteria: contraindication to combined contraceptive hormones, unprotected sex since last menstrual period > 120 hours before enrollment, recent abortion without a subsequent period, and weight > 90 kg.
Interventions	Immediate initiation (N=30) versus traditional start (N=30) of contraceptive patch (norelgestromin 150 µg + EE 20 µg); treatment duration 3 cycles. For traditional start, participants were to start on the first day on their next menses.
Outcomes	Continuation rates, side effects, breakthrough bleeding. Analysis was done by intent-to-treat.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention of method for generating randomization sequence.
Allocation concealment (selection bias)	Unclear risk	No information
Blinding (performance bias and detection bias) All outcomes	High risk	Open-label
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up: 2%; by group, quick start zero and traditional start 1/30 = 3%.

Rickert 2007

Methods	Randomized controlled trial at a family planning clinic in New York City (USA). Sample size calculation based on ability to detect difference in continuation rates of 17%.

Rickert 2007 *(Continued)*

Participants	333 women (age 14 to 26 years) who sought care at a family planning clinic and were interested in using DMPA. Exclusion criteria: currently menstruating, pregnant, or breastfeeding; contraindication to hormonal contraception; using DMPA (within past 14 weeks); consistently used birth control pills, patch, ring, or other prescription contraception method in past 30 days; history of serious mental illness.
Interventions	Immediate DMPA (depot medroxyprogesterone acetate) (N=101) versus 'bridge' method (choice of pills, patch, or ring with a 21-day supply prior to first DMPA injection) (N=232); treatment duration 6 months.
Outcomes	Pregnancy, continuation, satisfaction, adverse events. Analysis was by intent-to-treat, except for satisfaction, which only included those who completed the visit interview.
Notes	Women who discontinued their method were followed for discontinuation interview by phone or face-to-face. Interview addressed sexual behaviors, current contraception, and reasons for discontinuing method. Women who completed the interview are not included in the losses to follow-up.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization sequence developed from a random number table.
Allocation concealment (selection bias)	Low risk	Sequential sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow: 32% overall; by group, Depo Now 32/101 = 32%; bridge method 74/232 = 32%.

Westhoff 2003

Methods	Randomized controlled trial at a university medical center in New York City (USA). Sample size calculation was based on detecting difference of 3 or more bleeding or spotting days during 90-day reference period.
Participants	113 women recruited by local advertisements. Inclusion criteria: 18 to 35 years old, English- or Spanish-speaking, regular menstrual cycles of 21 to 35 days in past 12 months, no contraindication to OC use, no hormonal contraception for > 2 menses (or > 6 menses for injectables), > 2 menses since last pregnancy, no emergency contraception in current cycle. Exclusion criteria: positive pregnancy test or unprotected sex 10 days before screening.
Interventions	Immediate (N=67) versus conventional start (N=46) of oral contraceptives (norethindrone 1 mg + EE 35 µg). Immediate: took first pill with direct observation. Conventional: instructed to take first pill on first Sunday after menses onset. Reference period of 90 days from treatment start.
Outcomes	Bleeding patterns, discontinuation, satisfaction. Analysis was by intent-to-treat for pregnancy and discontinuation. For other outcomes, the authors reported those who had data collected (were not lost to follow-up and did not discontinue method).

Westhoff 2003 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization sequence was generated with random numbers table prior to study recruitment. Participants had 60% chance of allocation to quick start and 40% chance of allocation to conventional start.
Allocation concealment (selection bias)	Low risk	Sequentially-numbered opaque sealed envelopes
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Abstractor of diary data was blinded to group assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up: 1.5% overall; by group, immediate start zero; conventional start 1/46 = 2% One woman was excluded (prior to receiving study product) due to not having met the inclusion criteria.

Westhoff 2005

Methods	Open-label randomized trial in metropolitan university-affiliated clinic in New York City (USA). Report provided information on a priori power calculation - based on detecting difference of 4 or more bleeding or spotting days during 84-day reference period.
Participants	201 women recruited through flyers and internet postings. Inclusion criteria: English-speaking, 18 to 40 years old, regular menstrual cycles, no contraindication to hormonal contraception, no hormonal contraceptive use in past 2 menses (or 6 menses for injectables), > 2 menses since pregnancy, no recent use of emergency contraception, and no unprotected sex in past 10 days.
Interventions	Immediate start: vaginal ring releasing etonogestrel 120 µg + EE 15 µg daily (N=101) versus triphasic COC containing norgestimate 180/215/250 µg + EE 25 µg (N=100); treatment duration 84 days.
Outcomes	Pregnancy, continuation, cycle control, satisfaction, side effects. Analysis was by intent-to-treat for pregnancy. For other outcomes, the authors reported those who completed follow-up and had bleeding diaries, which they referred to as ITT.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Researcher not involved in study generated assignments with random number table and simple randomization.
Allocation concealment (selection bias)	Low risk	Sequentially-numbered opaque sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No mention of blinding other than 'Study coordinator and interviewers were blinded to assignment before opening the envelope.'

Westhoff 2005 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up: overall 27/201 = 13%; ring 12/101 = 12% and COC 15/100 = 15%.

Westhoff 2007

Methods	Randomized controlled trial in family planning clinics - 3 university sites in the USA. Sample size calculation based on detecting continuation increase from 50% to 60% at 6 months. Power was 63% to detect pregnancy decrease from 11% to 7%.
Participants	1720 young women requesting OCs. Inclusion criteria: < 25 years old, not pregnant, sexually active, no OC in past 7 days or DMPA in 6 months, no desire for pregnancy in next 6 months, no lactational amenorrhea. Exclusion criteria (IRB required): postpartum or postabortion if less than 18 years old.
Interventions	Immediate start (N=856) versus conventional initiation (N=864) of OC. Immediate: first pill was taken under direct observation. Conventional: instructed to take first pill during next period. Clinician preference determined OC brand and number of pill packs or prescriptions provided. Study duration 6 months.
Outcomes	Pregnancy and serious adverse events. Insufficient data were reported for calculating method discontinuation. Analysis for pregnancy included those who "had well-dated pregnancies that began during the study." The denominator for SAEs did not include the women that the researchers excluded due to pregnancy prior to baseline and those who had other violations of inclusion criteria.
Notes	Medical records were used to identify pregnancy in 96 women who missed both follow-ups.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization via random number generator; coordinating center generated allocation schedule.
Allocation concealment (selection bias)	Low risk	Numbered opaque envelopes
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up: 16% overall by group, immediate start 128/846 = 15%; conventional initiation 135/837 = 16%. Excluded 4 women due to not having met the inclusion criteria and 33 women who initially had a negative pregnancy test but whose estimated conception date (based on ultrasound) preceded enrollment.

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

Study	Reason for exclusion
Bednarek 2008	Bleeding assessed from first dose of medication for abortion until all bleeding stopped (not related to cycle control). Contraception continuation assessed at 6 weeks after abortion. Results grouped for contraceptive pill, patch, or ring (women chose method). Offered participation in sub-study (of medical abortion RCT) at first follow-up, 6 to 8 days after abortion. Observed start during that visit. Comparison group to begin the first Sunday following visit (not menses-dependent).
Karjane 2011	Study was terminated due to recruitment problems (ClinicalTrials.gov last updated 20 Oct 2011)
Madden 2011	Women were not randomized to immediate and delayed start groups.
Martin 1998	This trial studied four different approaches to decreasing bleeding after medical abortion and was not a contraception trial.
Paseková 2003	Non-comparative study of oral contraceptive start based on menses
Sitavarin 2003	Oral contraceptive start at two different times (both based on menses)
Were 1997	Oral contraceptive start based on length of time postpartum or return of menses
Yeshaya 1998	Oral contraceptive start based on menses

Characteristics of studies awaiting assessment *[ordered by study ID]*

Nanda 2006

Methods	Randomized controlled trial conducted in Nicaragua; designed to have 85% power to detect 20% difference in COC continuation and 3-day difference in bleeding and spotting days per trimester.
Participants	232 women. Inclusion criteria: regular menses; not in first 7 days of cycle
Interventions	30 µg COC: quick start (N=116) or advance provision (N=116)
Outcomes	Primary: pill continuation at 6 months Secondary: bleeding patterns and 6-month pregnancy rates
Notes	30 Aug 2012: Researcher communicated that report was drafted but not peer-reviewed Contact: K Nanda, FHI 360, Research Triangle Park, NC; knanda@fhi360.org

Steinauer 2012a

Methods	RCT, open label
Participants	300 women. Inclusion Criteria: woman aged 13 to 45 who presents to Women's Options Clinic and desires to use patch for post-abortion contraception Exclusion Criteria: gestational age above 23 weeks and 1 day; contraindication for patch use (smoking > 20 cigarettes a day over age 35, history of venous thromboembolic event or pulmonary embolism, ischemic heart disease, stroke; vascular disease, complicated valvular heart disease [pulmonary hypertension, atrial fibrillation, history of subacute bacterial endocarditis], blood pressure >160/100, migraines with focal neurologic symptoms, current breast cancer, active viral hepatitis,

Steinauer 2012a *(Continued)*

	severe cirrhosis, or liver tumor); speak language other than English or Spanish; no phone or have phone where contact might compromise confidentiality of the abortion
Interventions	All receive a month's worth of patch and one-year prescription Immediate start: place first patch in the clinic, observed by clinic staff, before leaving. Control: instructed to place first patch on first Sunday following abortion; follow-up by telephone interview at 2 and 6 months after abortion
Outcomes	Primary: continuation of patch after abortion Secondary: compliance with patch after abortion, bleeding patterns on [patch] after abortion, satisfaction with patch after abortion
Notes	Start date: Aug 2005. 11 Oct 2012: JE Steinauer corresponded that they recently submitted a draft manuscript for publication consideration.

Steinauer 2012b

Methods	RCT, open label
Participants	300 women. Inclusion Criteria: woman aged 13 to 45 who presents to Women's Options Clinic and desires to use OCs for post-abortion contraception. Exclusion Criteria: gestational age above 23 weeks + 1 day; contraindication for combination OC use (smoking > 20 cigarettes a day over age 35, history of venous thromboembolic event or pulmonary embolism, ischemic heart disease, stroke; vascular disease, complicated valvular heart disease [pulmonary hypertension, atrial fibrillation, history of subacute bacterial endocarditis], blood pressure >160/100, migraines with focal neurologic symptoms, current breast cancer, active viral hepatitis, severe cirrhosis, or liver tumor); speak language other than English or Spanish; no phone or have phone where contact might compromise confidentiality of the abortion
Interventions	All receive single pack of combination OCs and one-year prescription. Immediate start: take first OC in clinic, observed by clinic staff, before leaving. Control: instructed to begin OCs on first Sunday following abortion; follow-up by telephone interview at 2 and 6 months after abortion
Outcomes	Primary: continuation of OCs after abortion Secondary: compliance with OCs after abortion, bleeding patterns on OCs after abortion, satisfaction with OCs after abortion
Notes	Start date: Aug 2005. 11 Oct 2012: JE Steinauer corresponded that they will soon submit a draft manuscript for publication consideration.

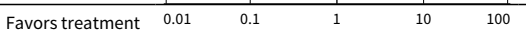
DATA AND ANALYSES

Comparison 1. Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Pregnancy per woman	1	111	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.67 [0.04, 11.47]
2 Discontinued OCs during 90-day period	1	111	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.48 [0.10, 2.28]
3 Frequent bleeding (> 4 episodes of bleeding or spotting)	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.71 [0.28, 1.79]
4 Irregular bleeding (bleeding-free interval > 17 days)	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.82 [0.34, 1.99]
5 Prolonged bleeding (bleeding or spotting episode lasting >= 10 days)	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.35, 2.24]
6 Amenorrhea (no bleeding)	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Overall satisfaction with OCs	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.76 [0.14, 4.10]
8 Would make the same decision to start OCs	1	104	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.62 [0.13, 2.94]

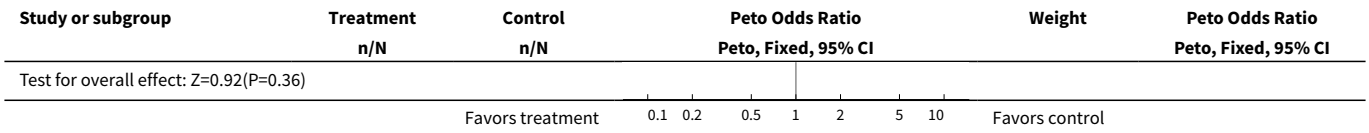
Analysis 1.1. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 1 Pregnancy per woman.

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2003	1/66	1/45		100%	0.67[0.04,11.47]
Total (95% CI)	**66**	**45**		**100%**	**0.67[0.04,11.47]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.27(P=0.78)					

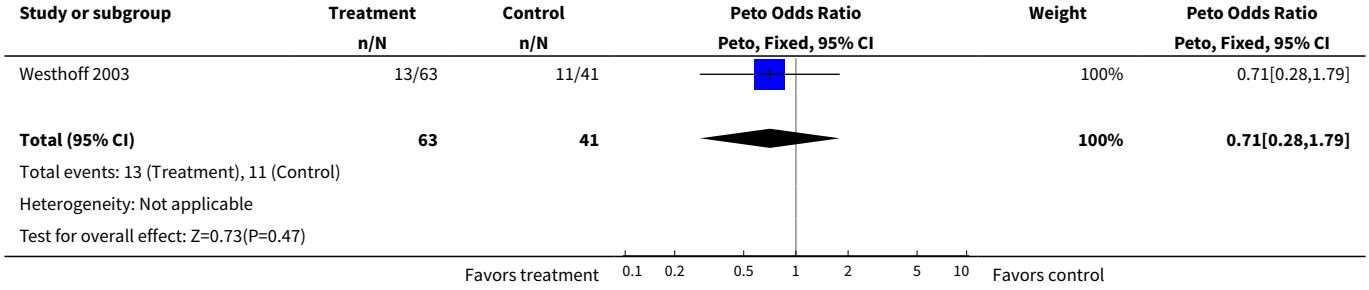


Analysis 1.2. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 2 Discontinued OCs during 90-day period.

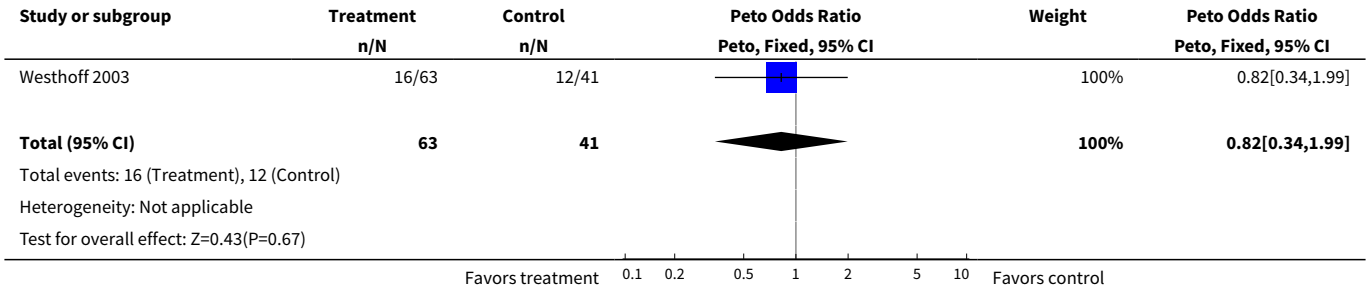
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2003	3/66	4/45		100%	0.48[0.1,2.28]
Total (95% CI)	**66**	**45**		**100%**	**0.48[0.1,2.28]**
Total events: 3 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					



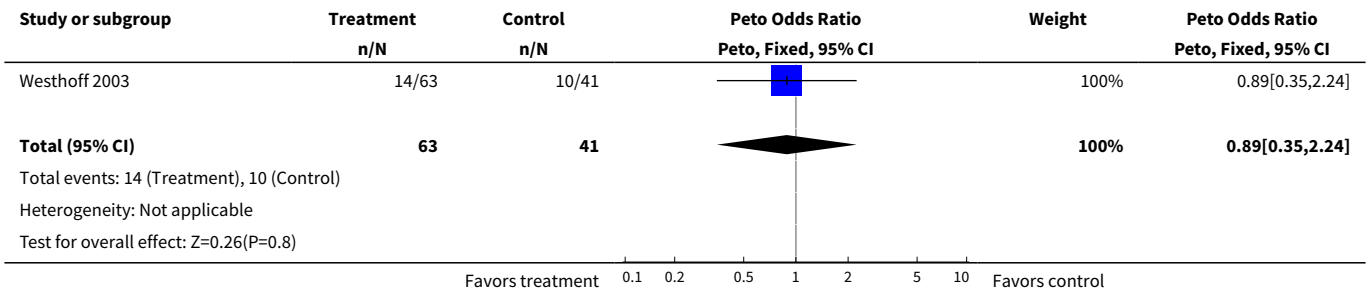
Analysis 1.3. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 3 Frequent bleeding (> 4 episodes of bleeding or spotting).



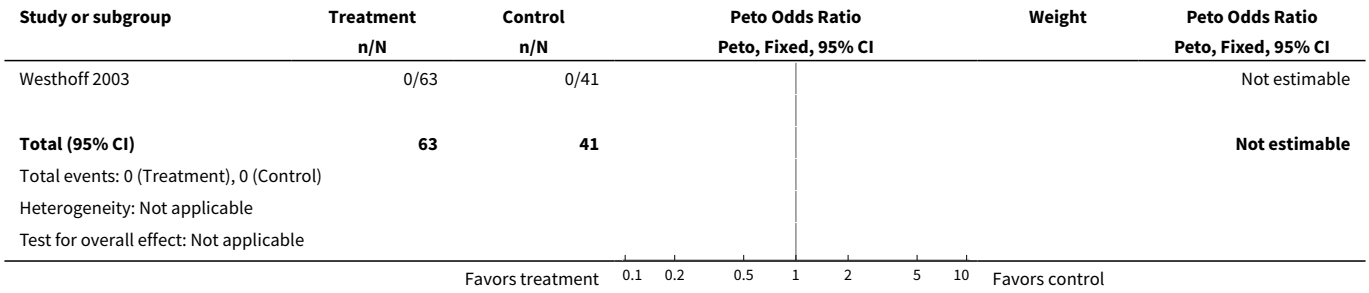
Analysis 1.4. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 4 Irregular bleeding (bleeding-free interval > 17 days).



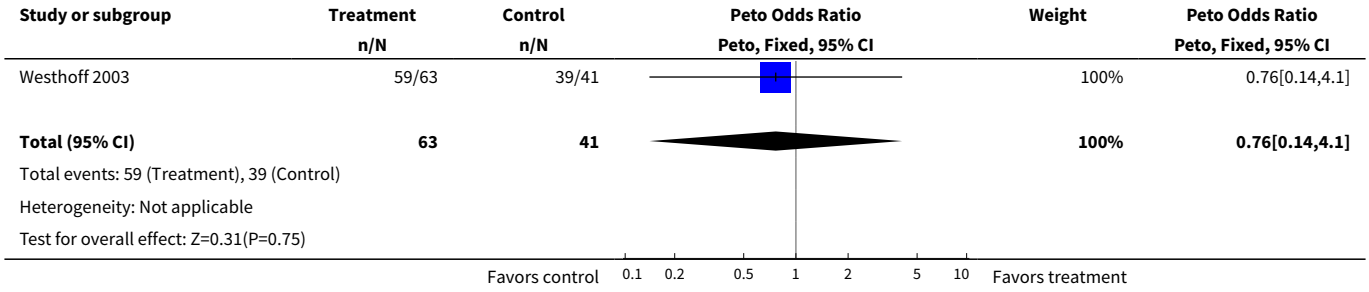
Analysis 1.5. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 5 Prolonged bleeding (bleeding or spotting episode lasting >= 10 days).



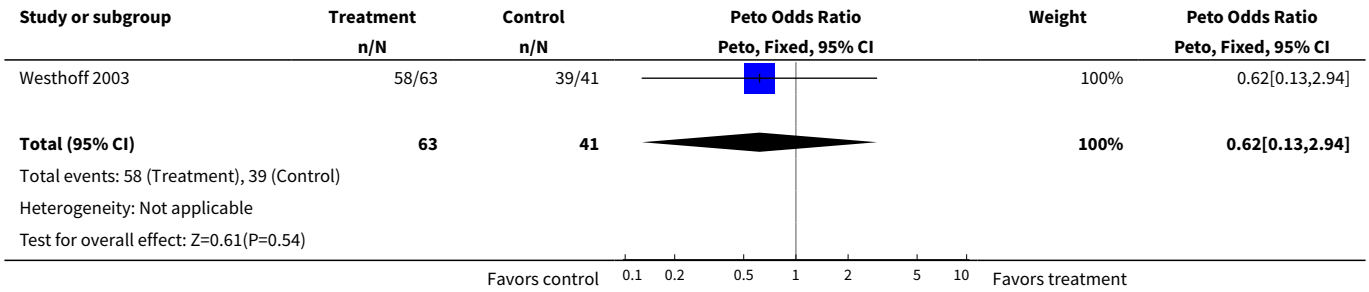
Analysis 1.6. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 6 Amenorrhea (no bleeding).



Analysis 1.7. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 7 Overall satisfaction with OCs.



Analysis 1.8. Comparison 1 Immediate versus conventional start of COC (norethindrone 1 mg + EE 35 µg), Outcome 8 Would make the same decision to start OCs.

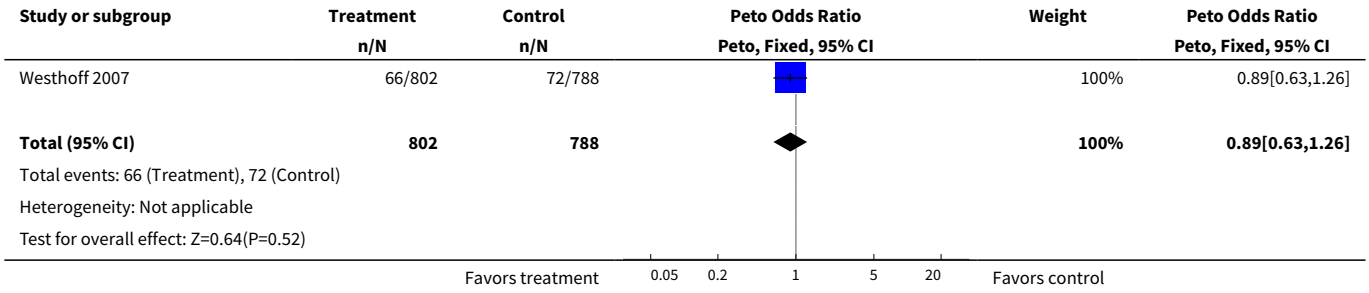


Comparison 2. Immediate versus conventional start of OCs

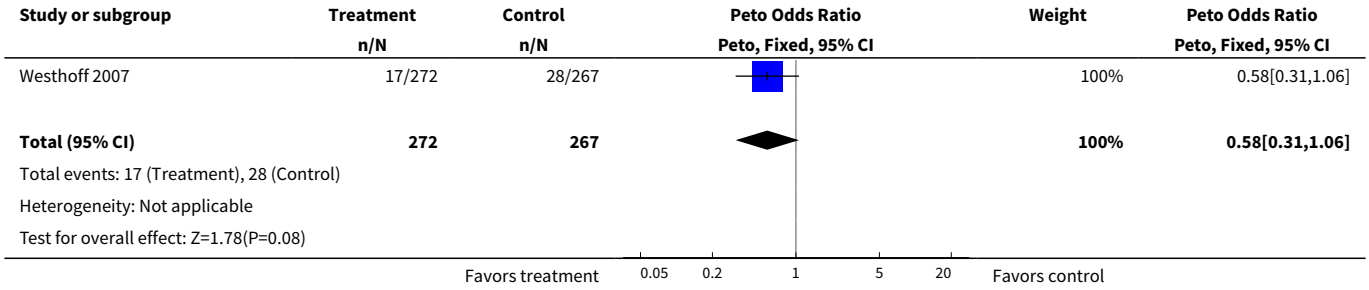
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman	1	1590	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.63, 1.26]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Pregnancy per young woman (<18 years old)	1	539	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.58 [0.31, 1.06]
3 Serious adverse events	1	1683	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.38 [0.64, 3.00]

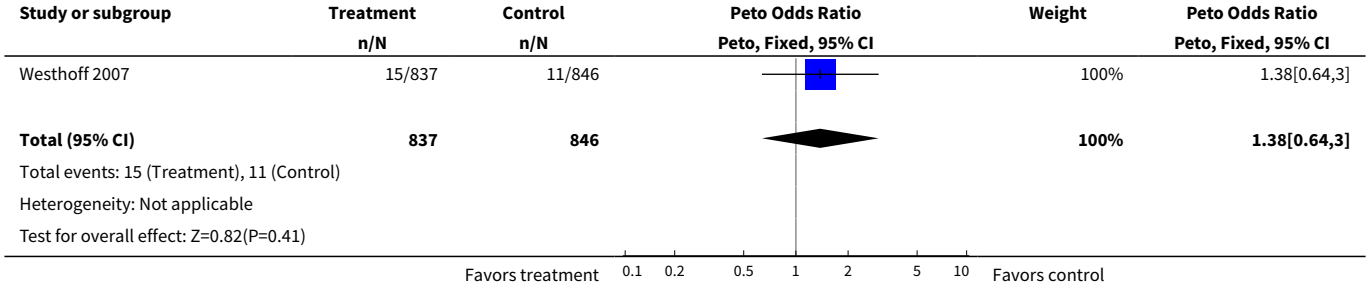
Analysis 2.1. Comparison 2 Immediate versus conventional start of OCs, Outcome 1 Pregnancy per woman.



Analysis 2.2. Comparison 2 Immediate versus conventional start of OCs, Outcome 2 Pregnancy per young woman (<18 years old).



Analysis 2.3. Comparison 2 Immediate versus conventional start of OCs, Outcome 3 Serious adverse events.

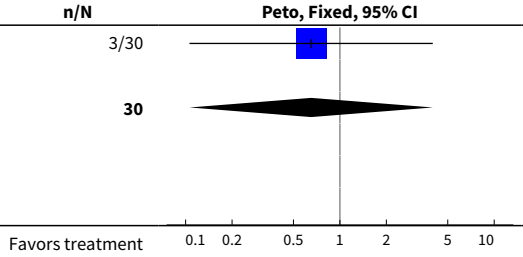


Comparison 3. Immediate versus conventional start of contraceptive patch (norelgestromin 150 µg + EE 20 µg)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Discontinuation of patch by cycle 3	1	60	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.65 [0.11, 4.00]
2 Breakthrough bleeding	1	60	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.65 [0.11, 4.00]
3 Nausea	1	60	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.40 [0.75, 7.64]

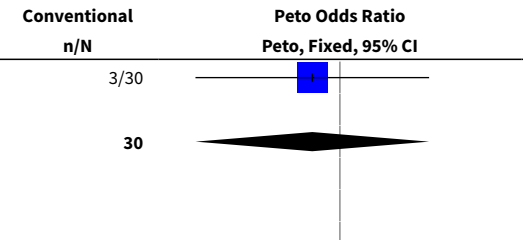
Analysis 3.1. Comparison 3 Immediate versus conventional start of contraceptive patch (norelgestromin 150 µg + EE 20 µg), Outcome 1 Discontinuation of patch by cycle 3.

Study or subgroup	Immediate n/N	Conventional n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Murthy 2005	2/30	3/30		100%	0.65[0.11,4]
Total (95% CI)	**30**	**30**		**100%**	**0.65[0.11,4]**
Total events: 2 (Immediate), 3 (Conventional)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					



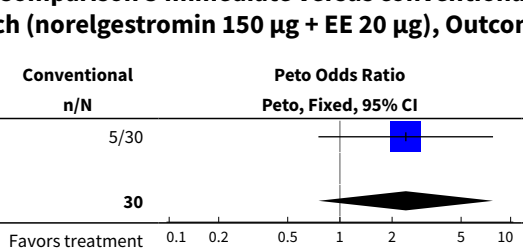
Analysis 3.2. Comparison 3 Immediate versus conventional start of contraceptive patch (norelgestromin 150 µg + EE 20 µg), Outcome 2 Breakthrough bleeding.

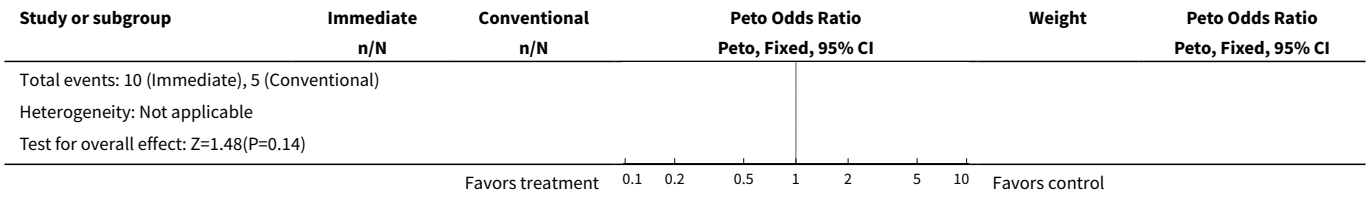
Study or subgroup	Immediate n/N	Conventional n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Murthy 2005	2/30	3/30		100%	0.65[0.11,4]
Total (95% CI)	**30**	**30**		**100%**	**0.65[0.11,4]**
Total events: 2 (Immediate), 3 (Conventional)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					



Analysis 3.3. Comparison 3 Immediate versus conventional start of contraceptive patch (norelgestromin 150 µg + EE 20 µg), Outcome 3 Nausea.

Study or subgroup	Immediate n/N	Conventional n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Murthy 2005	10/30	5/30		100%	2.4[0.75,7.64]
Total (95% CI)	**30**	**30**		**100%**	**2.4[0.75,7.64]**





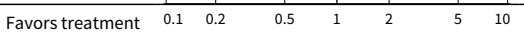
Comparison 4. Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Pregnancy per woman	1	201	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Discontinued method in 84-day period	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.84 [0.33, 2.18]
3 Frequent bleeding (> 4 episodes of bleeding or spotting)	1	156	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.23 [0.05, 1.03]
4 Irregular bleeding (bleeding-free interval > 17 days)	1	156	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.77 [0.33, 1.75]
5 Prolonged bleeding (bleeding or spotting episode lasting >= 10 days)	1	156	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.42 [0.20, 0.89]
6 Amenorrhea	1	156	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Very satisfied with method	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.88 [1.59, 5.22]
8 Planned to use method	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.51 [1.32, 4.77]
9 Reported bad change in weight	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.42 [0.21, 0.87]
10 Reported bad change in bleeding	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.14, 0.55]
11 Reported bad change in headache	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.53 [0.24, 1.18]
12 Reported bad change in breasts	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.18, 0.73]
13 Reported bad change in mood	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.19, 0.69]
14 Reported bad change in acne	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.39 [0.59, 3.29]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
15 Reported bad change in appetite	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.44 [0.21, 0.95]
16 Reported bad change in nausea	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.30 [0.14, 0.62]
17 Reported bad change in cramps	1	145	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.79 [0.37, 1.67]
18 Reported bad change in hair	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.05, 1.65]
19 Serious adverse events (total)	1	174	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

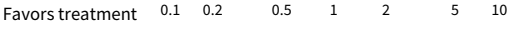
Analysis 4.1. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 1 Pregnancy per woman.

Study or subgroup	Ring n/N	COC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2005	0/101	0/100			Not estimable
Total (95% CI)	**101**	**100**			**Not estimable**
Total events: 0 (Ring), 0 (COC)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

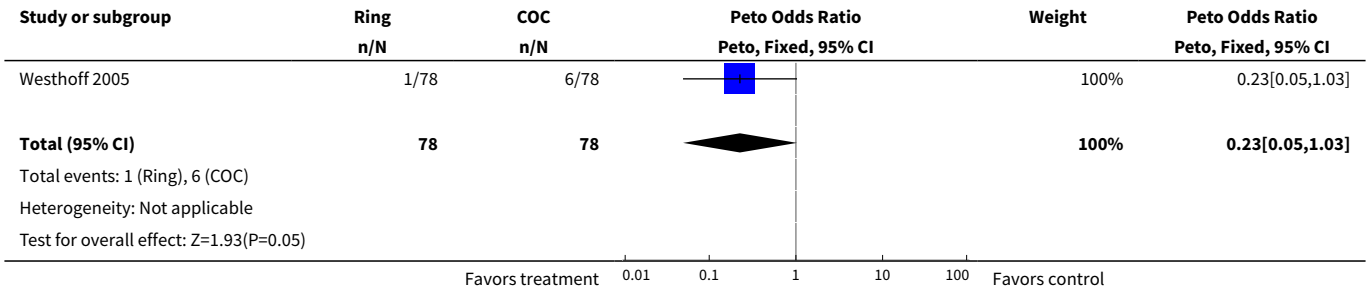


Analysis 4.2. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 2 Discontinued method in 84-day period.

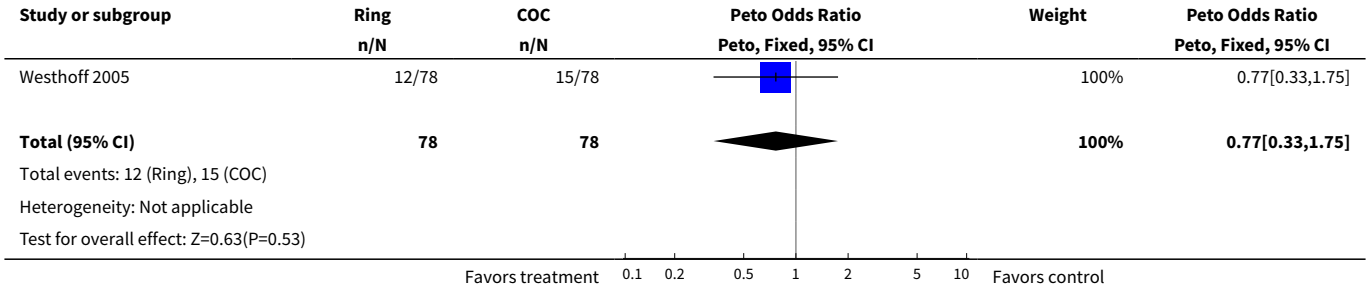
Study or subgroup	Ring n/N	COC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2005	9/89	10/85		100%	0.84[0.33,2.18]
Total (95% CI)	**89**	**85**		**100%**	**0.84[0.33,2.18]**
Total events: 9 (Ring), 10 (COC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.35(P=0.73)					



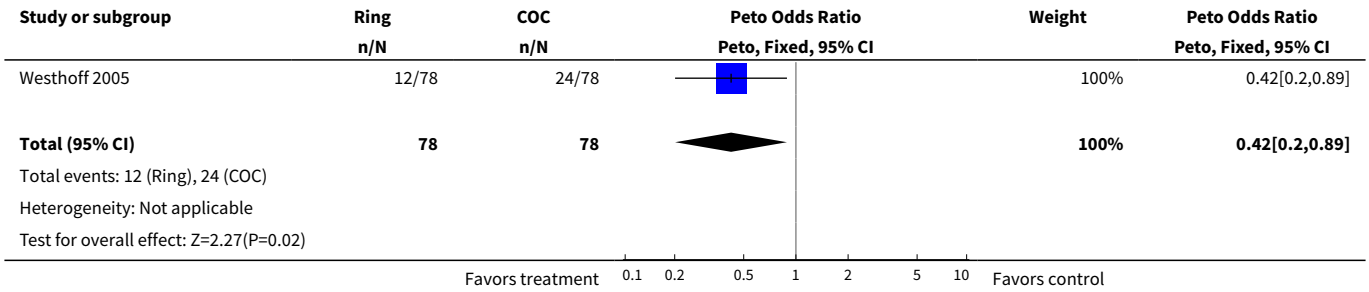
Analysis 4.3. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 3 Frequent bleeding (> 4 episodes of bleeding or spotting).



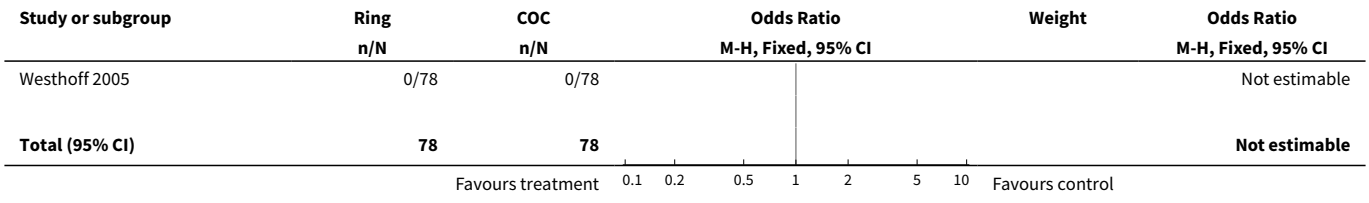
Analysis 4.4. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 4 Irregular bleeding (bleeding-free interval > 17 days).

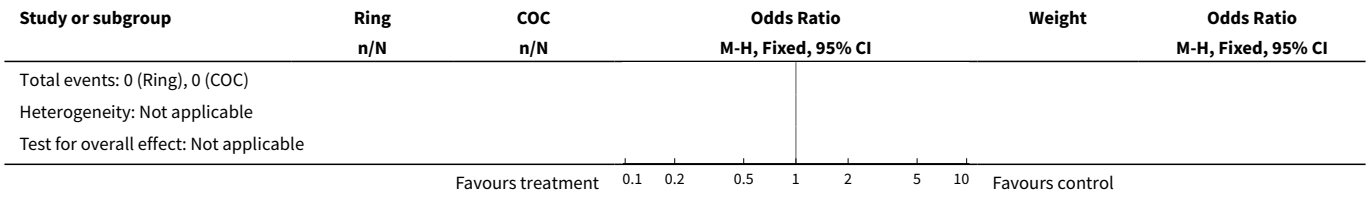


Analysis 4.5. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 5 Prolonged bleeding (bleeding or spotting episode lasting >= 10 days).

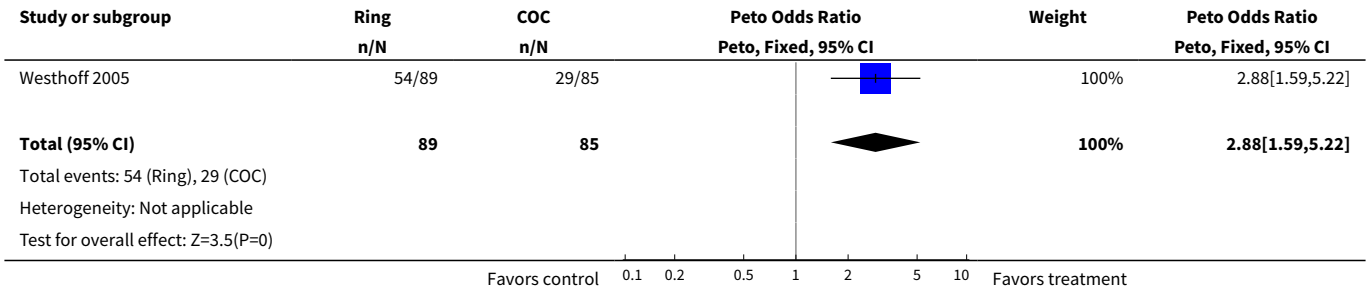


Analysis 4.6. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 6 Amenorrhea.

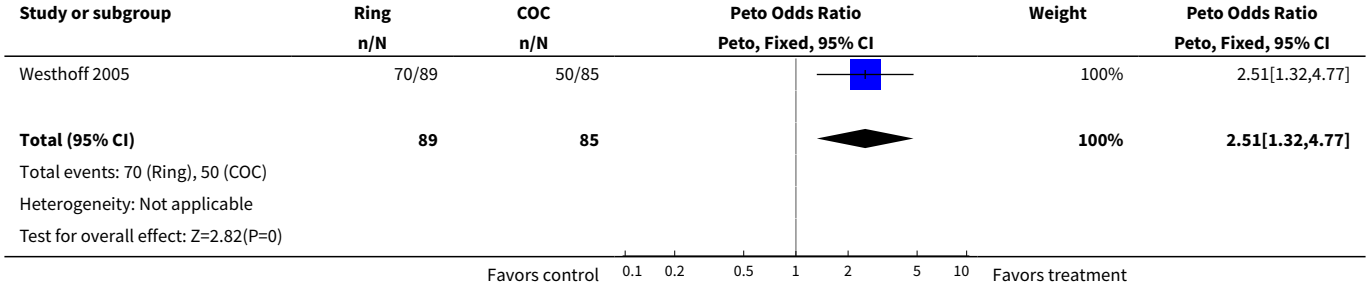




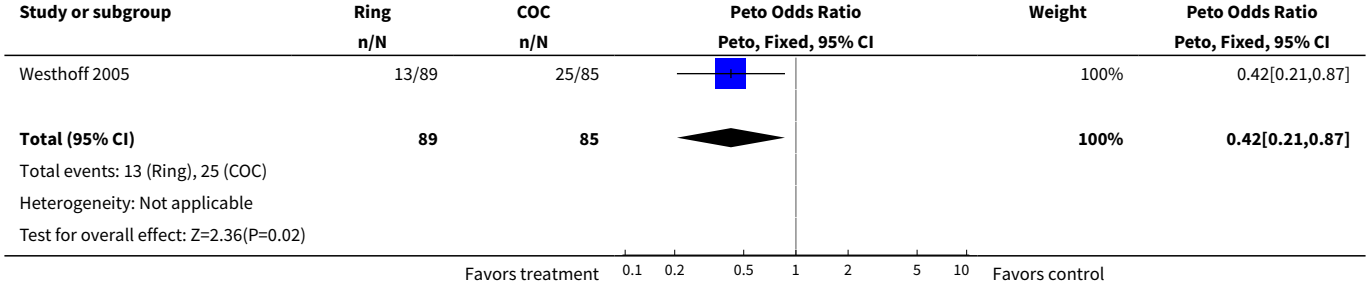
Analysis 4.7. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 7 Very satisfied with method.



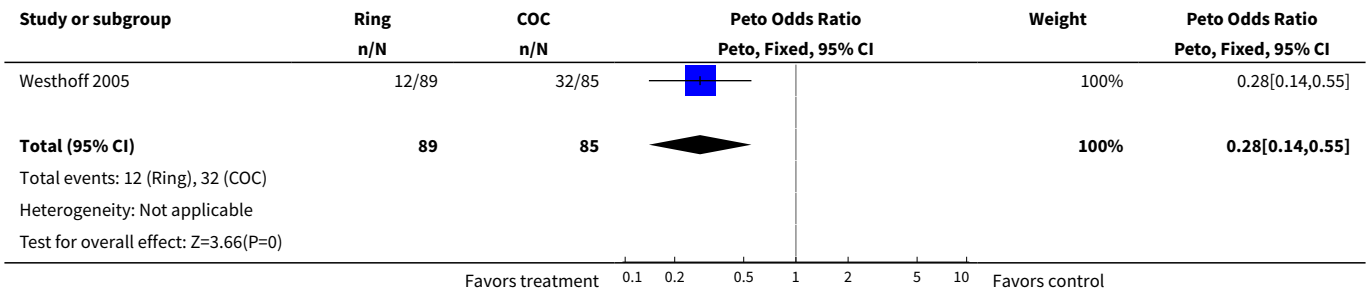
Analysis 4.8. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 8 Planned to use method.



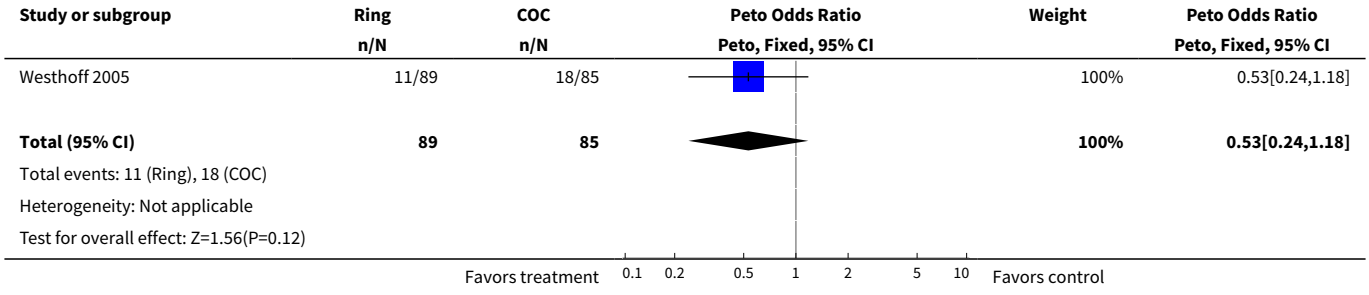
Analysis 4.9. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 9 Reported bad change in weight.



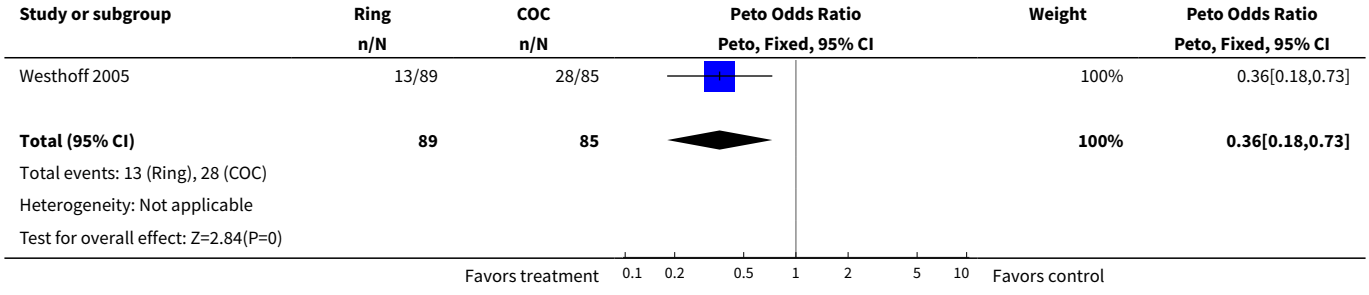
Analysis 4.10. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 10 Reported bad change in bleeding.



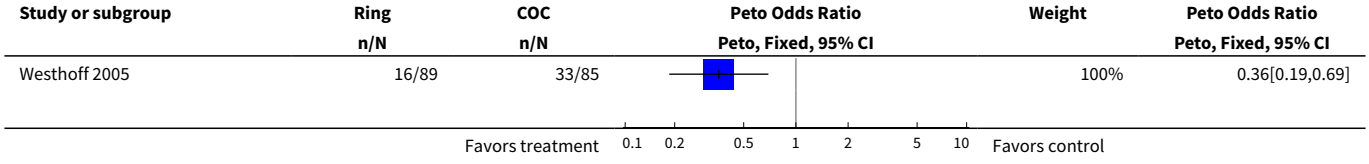
Analysis 4.11. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 11 Reported bad change in headache.

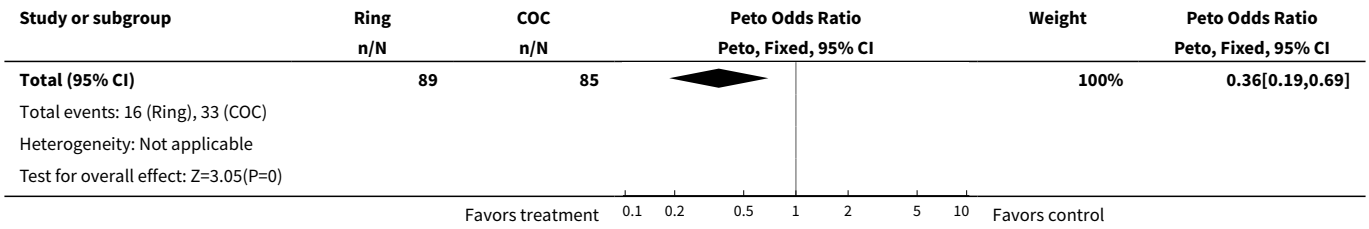


Analysis 4.12. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 12 Reported bad change in breasts.

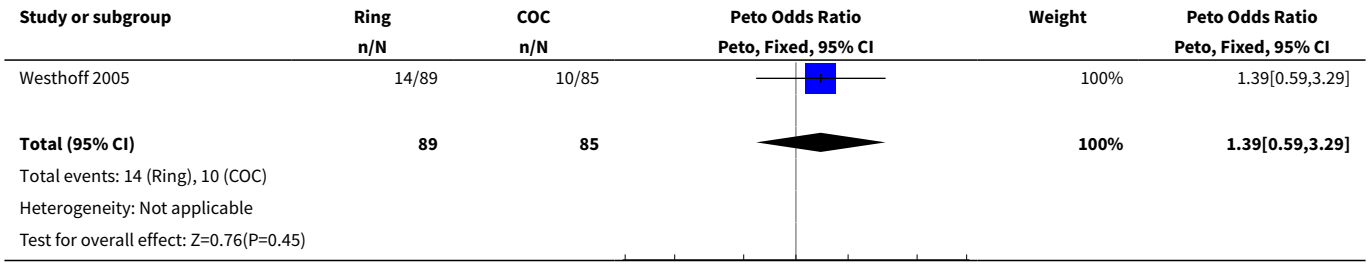


Analysis 4.13. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 13 Reported bad change in mood.

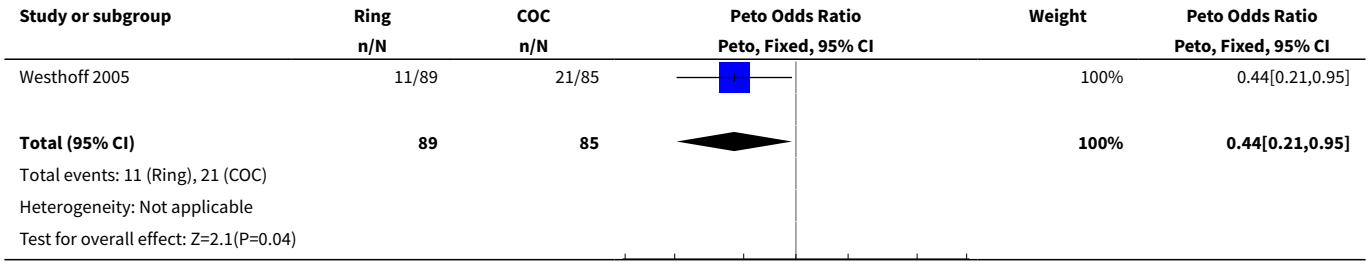




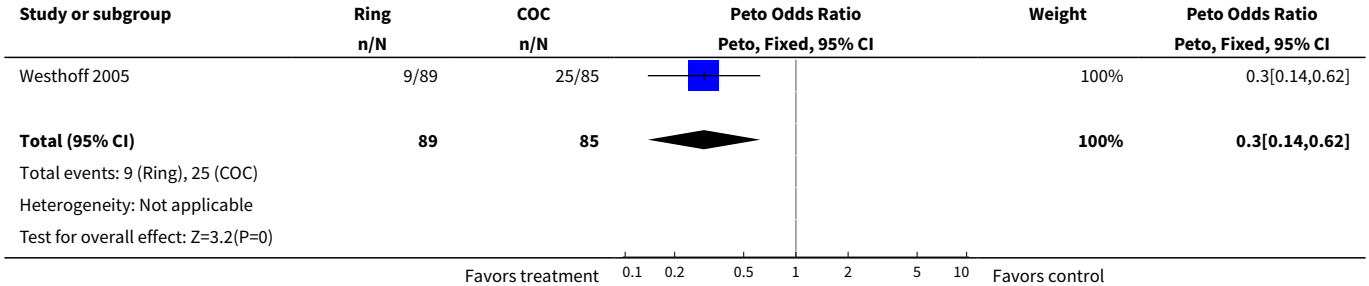
Analysis 4.14. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 14 Reported bad change in acne.



Analysis 4.15. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 15 Reported bad change in appetite.

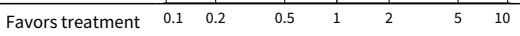


Analysis 4.16. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 16 Reported bad change in nausea.



Analysis 4.17. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 17 Reported bad change in cramps.

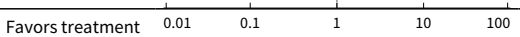
Study or subgroup	Ring n/N	COC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2005	17/75	19/70		100%	0.79[0.37,1.67]
Total (95% CI)	**75**	**70**		**100%**	**0.79[0.37,1.67]**
Total events: 17 (Ring), 19 (COC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.62(P=0.53)					



Favors treatment — Favors control

Analysis 4.18. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 18 Reported bad change in hair.

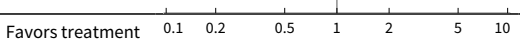
Study or subgroup	Ring n/N	COC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2005	1/89	4/85		100%	0.28[0.05,1.65]
Total (95% CI)	**89**	**85**		**100%**	**0.28[0.05,1.65]**
Total events: 1 (Ring), 4 (COC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.41(P=0.16)					



Favors treatment — Favors control

Analysis 4.19. Comparison 4 Immediate ring (etonogestrel 120 µg + EE 15 µg) versus immediate COC (NGM 180/215/250 µg + EE 30 µg), Outcome 19 Serious adverse events (total).

Study or subgroup	Ring n/N	COC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Westhoff 2005	0/89	0/85			Not estimable
Total (95% CI)	**89**	**85**			**Not estimable**
Total events: 0 (Ring), 0 (COC)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



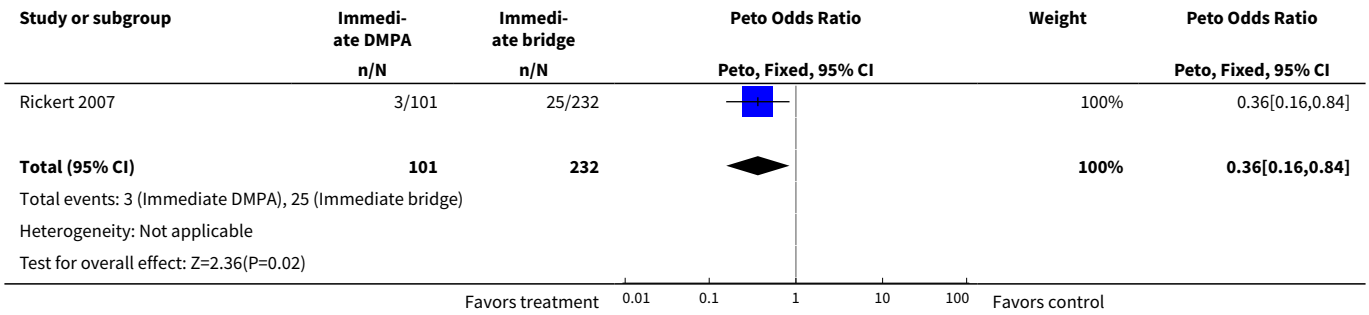
Favors treatment — Favors control

Comparison 5. Immediate DMPA versus contraceptive bridge to DMPA

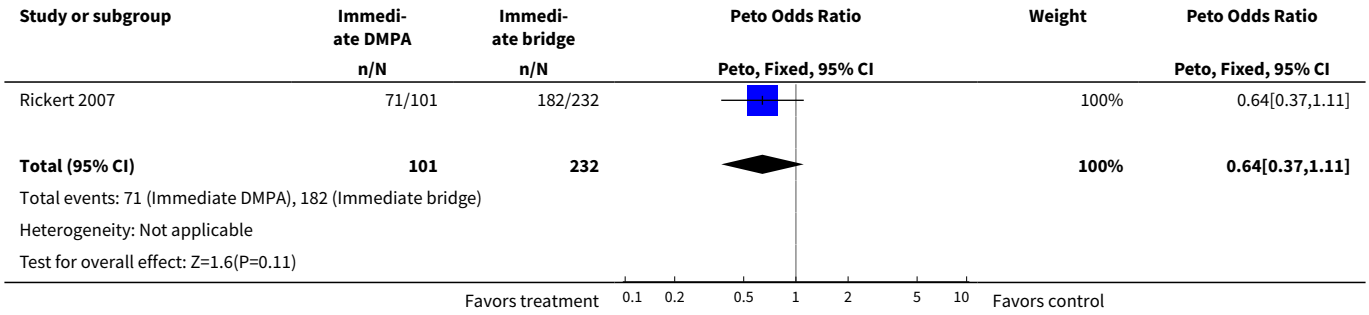
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman	1	333	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.16, 0.84]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Discontinued method before 6 months	1	333	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.64 [0.37, 1.11]
3 Very satisfied with method at 6 months	1	227	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.99 [1.05, 3.77]
4 Adverse events	1	333	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

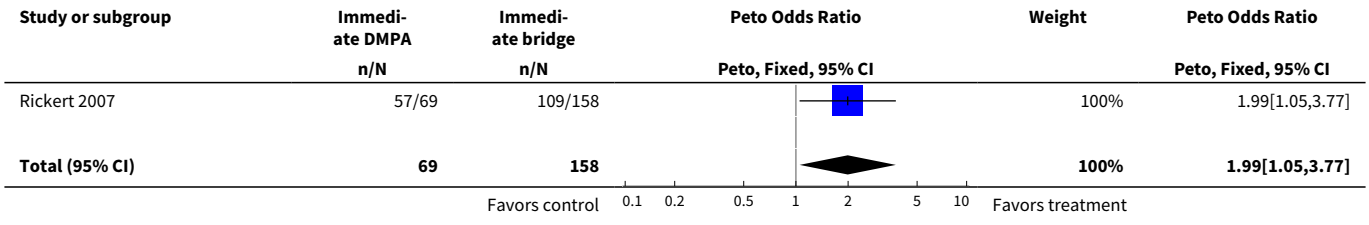
Analysis 5.1. Comparison 5 Immediate DMPA versus contraceptive bridge to DMPA, Outcome 1 Pregnancy per woman.

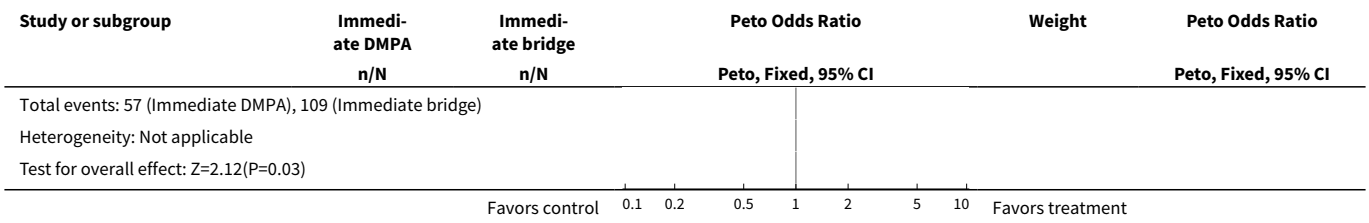


Analysis 5.2. Comparison 5 Immediate DMPA versus contraceptive bridge to DMPA, Outcome 2 Discontinued method before 6 months.

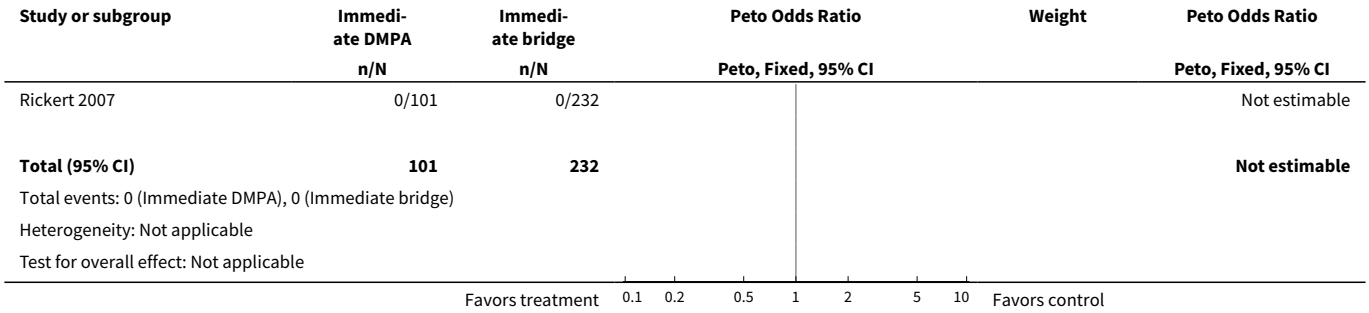


Analysis 5.3. Comparison 5 Immediate DMPA versus contraceptive bridge to DMPA, Outcome 3 Very satisfied with method at 6 months.





Analysis 5.4. Comparison 5 Immediate DMPA versus contraceptive bridge to DMPA, Outcome 4 Adverse events.



APPENDICES

Appendix 1. Search strategy, 2012

MEDLINE via PubMed (01 Jan 2010 to 12 Sep 2012)

contraceptive agents, female OR (steroid* AND contracept*) OR orthoevra OR "ortho evra" OR "norelgestromin" OR (contraceptive devices, female and ring) OR NuvaRing OR cyclofem OR lunelle OR mesigyna OR cycloprovera OR (medroxyprogesterone 17-acetate AND (contracept* OR inject* OR depo OR depot)) OR depot medroxyprogesterone OR depo medroxyprogesterone OR depotmedroxyprogesterone OR depomedroxyprogesterone OR dmpa OR "net en" OR norethisterone enantate OR norplant OR uniplant OR jadelle OR implanon OR ((levonorgestrel OR etonogestrel) AND implant) OR (levonorgestrel AND intrauterine devices) OR mirena OR ((progestational hormones OR progestin) AND (contracept* AND (oral OR pill* OR tablet*))) AND (((time factors OR immediate OR timing) AND (start* OR begin* OR initiat*)) OR "quick start" OR starting day OR drug administration schedule OR (observed AND start) OR “Sunday start”) AND Clinical Trial[ptyp]

CENTRAL (2010 to 28 Aug 2012)

contracept* in Title, Abstract or Keywords
AND initiat* OR start* OR begin* OR quick start OR drug administration schedule in Title, Abstract or Keywords
NOT IVF OR cancer OR PCOS OR HIV OR emergency OR migraine in Record Title

POPLINE (2010 to 29 Aug 2012)

Global: (contraceptive agents, female) OR (contraceptive methods) OR (contraceptive implants)
AND (start AND (quick OR immediate OR time OR timing)) OR "quick start"
Filter by keywords: Research report

LILACS (2010 to 12 Sep 2012)

contraceptive agents, female or agentes anticonceptivos femeninos or anticoncepcionais femeninos or contraceptives, oral or anticonceptivos orales or anticoncepcionais orais [Words]
AND start or initiator or inciador or begin or beginning or comienzo or incio or initiation or quick start or starting day or drug administration schedule [Words]

ClinicalTrials.gov (01 Jan 2010 to 28 Aug 2012)

Search terms: (((time factors OR immediate OR timing) AND (start* OR begin* OR initiat*)) OR "quick start" OR starting day OR drug administration schedule)
Condition: NOT (in vitro OR IVF OR cataract)
Intervention: contraceptive OR contraception
Study type: interventional studies
Gender: studies with female participants

ICTRP (01 Jan 2010 to 29 Aug 2012)

Title: immediate OR timing OR start OR starting OR begin OR initiate OR initiation OR quick
Condition: contraceptive OR contraception

Appendix 2. Search strategy, 2008 and 2010

MEDLINE via PubMed (through 28 Aug 2010)

(contraceptive agents, female OR (steroid* AND contracept*) OR orthoevra OR "ortho evra" OR "norelgestromin" OR (contraceptive devices, female and ring) OR NuvaRing OR cyclofem OR lunelle OR mesigyna OR cycloprovera OR (medroxyprogesterone 17-acetate AND (contracept* OR inject* OR depo OR depot)) OR depot medroxyprogesterone OR depo medroxyprogesterone OR depotmedroxyprogesterone OR depomedroxyprogesterone OR dmpa OR "net en" OR norethisterone enantate OR norplant OR uniplant OR jadelle OR implanon OR ((levonorgestrel OR etonogestrel) AND implant) OR (levonorgestrel AND intrauterine devices) OR mirena OR ((progestational hormones OR progestin) AND contracept* AND (oral OR pill* OR tablet*))) AND (((time factors OR immediate OR timing) AND (start* OR begin* OR initiat*)) OR "quick start" OR starting day OR drug administration schedule)

CENTRAL (through 28 Aug 2010)

contracept* and (initiat* or start* or begin* or quick start or drug administration schedule) in Title, Abstract, or Keywords

POPLINE (through 30 Aug 2010)

(Contraceptive Agents Female/depo provera/dmpa/medroxyprogesterone/(steroid* & contracept*) /orthoevra/ortho evra / norelgestromin/(contraceptive devices, female and ring)/ NuvaRing /cyclofem /lunelle/ mesigyna/ cycloprovera/ (medroxyprogesterone 17-acetate & (contracept* /inject*/depo/depot))/ depot medroxyprogesterone/ depo medroxyprogesterone/ depot medroxyprogesterone/ depo medroxyprogesterone/dmpa/ net en/ norethisterone-enantate/norplant/uniplant/jadelle/implanon/((levonorgestrel/ etonogestrel) & implant)/(levonorgestrel & intrauterine devices)/mirena /((progestational hormones/progestin) & contracept* & (oral/pill*/tablet*))) & (start & (quick/immediate/time/timing))/"quick start"

LILACS (01 Sep 2010)

contraceptive agents, female or agentes anticonceptivos femeninos or anticoncepcionais femeninos or contraceptives, oral or anticonceptivos orales or anticoncepcionais orais [Words] and start or initiator or inciador or begin or beginning or comienzo or incio or initiation or quick start or starting day or drug administation schedule [Words]

EMBASE (through 03 Sep 2010)

CONTRACEPTIVE AGENT? OR STEROID?(W)CONTRACEPT?
AND DRUG ADMINISTRATION AND (QUICK(W)START OR START? OR INITIAT?OR BEGIN?).

ClinicalTrials.gov (through 30 Aug 2010)

Search terms: (((time factors OR immediate OR timing) AND (start* OR begin* OR initiat*)) OR "quick start" OR starting day OR drug administration schedule)
Intervention: contraceptive OR contraception
Study type: interventional studies
Gender: studies with female participants

ICTRP (through 31 Aug 2010)

Title: immediate OR timing OR start OR starting OR begin OR initiate OR initiation OR quick
Condition: contraceptive OR contraception

WHAT'S NEW

Date	Event	Description
29 October 2012	New citation required but conclusions have not changed	No new trials included. Excluded 3 published trials (Bednarek 2008; Madden 2011; Martin 1998) and one that was discontinued (Karjane 2011).
26 October 2012	Amended	Added to Types of studies: Treatment duration had to be at least three cycles or 84 days.
12 September 2012	New search has been performed	Searches updated

HISTORY

Protocol first published: Issue 4, 2006
Review first published: Issue 2, 2008

Date	Event	Description
17 September 2010	New search has been performed	We updated the searches and added searches of ClinicalTrials.gov and ICTRP. A secondary report of Westhoff 2007 was located, but no new trials were found.
15 April 2008	Amended	Converted to new review format.
15 January 2008	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

S Newmann and D Grimes developed the concept. S Newmann drafted the protocol, reviewed the initial searches, and began data abstraction. L Lopez completed the searches for the review, did the primary data abstraction, and drafted the review; she also updated the review in 2010 and 2012. D Grimes did the second data extraction and edited and advised on the review. K Nanda edited and advised on the review. K Schulz provided statistical expertise and edited the review.

DECLARATIONS OF INTEREST

DA Grimes has consulted with the pharmaceutical companies Bayer Healthcare Pharmaceuticals and Merck & Co, Inc.

K Nanda is the principal investigator of a trial on this subject; the results may be included in an update.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- US Agency for International Development, USA.
- National Institute of Child Health and Human Development, USA.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In 2012, we added to Types of studies: Treatment duration had to be at least three cycles or 84 days.

INDEX TERMS

Medical Subject Headings (MeSH)

*Drug Chronotherapy; *Menstruation; *Pregnancy, Unplanned; Contraception [*methods]; Contraceptives, Oral, Hormonal [*administration & dosage]; Intrauterine Devices; Medroxyprogesterone Acetate [administration & dosage]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy