Triphasic versus monophasic oral contraceptives for contraception (Review)

Grimes DA, Lopez LM, Schulz KF, Van Vliet HAAM, Helmerhorst FM

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[Intervention Review]

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ABSTRACT

Background

Side effects of oral contraceptive (OC) pills discourage adherence to and continuation of OC regimens. Strategies to decrease adverse effects led to the introduction of the triphasic OC in the 1980s. Whether triphasic OCs have higher accidental pregnancy rates than monophasic pills is unknown. Nor is it known if triphasic pills give better cycle control and fewer side effects than the monophasic pills.

Objectives

To compare triphasic OCs with monophasic OCs in terms of efficacy, cycle control, and discontinuation due to side effects.

Search strategy

We searched the computerized databases of MEDLINE, EMBASE, POPLINE, LILACS and CENTRAL, as well as clinical trials databases (ClinicalTrials.gov and ICTRP). Additionally, we searched the reference lists of relevant articles and book chapters. We also contacted researchers and pharmaceutical companies to identify other trials not found in our search.

Selection criteria

We included randomized controlled trials (RCTs) comparing any triphasic OC with any monophasic pill used to prevent pregnancy. Interventions had to include at least three treatment cycles.

Data collection and analysis

We assessed the studies found in the literature searches for possible inclusion and for their methodological quality. We contacted the authors of all included studies and of possibly randomized trials for supplemental information about the methods and outcomes studied. We entered the data into RevMan 4.2 and calculated odds ratios for the outcome measures of efficacy, breakthrough bleeding, spotting, withdrawal bleeding and discontinuation.

Main results

Of 21 trials included, 18 examined contraceptive effectiveness: the triphasic and monophasic preparations did not differ significantly. Several trials reported favorable bleeding patterns, i.e. less spotting, breakthrough bleeding or amenorrhea, in triphasic versus monophasic OC users. However, meta-analysis was generally not possible due to differences in measuring and reporting the cycle disturbance data as well as differences in progestogen type and hormone dosages. No significant differences were found in the numbers of women who discontinued due to medical reasons, cycle disturbances, intermenstrual bleeding or adverse events.

Authors' conclusions

The available evidence is insufficient to determine whether triphasic OCs differ from monophasic OCs in effectiveness, bleeding patterns or discontinuation rates. Therefore, we recommend monophasic pills as a first choice for women starting OC use. Large, high-quality RCTs that compare triphasic and monophasic OCs with identical progestogens are needed to determine whether triphasic pills differ from monophasic OCs. Future studies should follow the WHO recommendations on recording menstrual bleeding patterns and the CONSORT reporting guidelines.

PLAIN LANGUAGE SUMMARY

Birth control pills with three phases versus one phase

Side effects of birth control pills may keep women from using them as planned. Attempts to decrease side effects led to the three-phase pill in the 1980s. Pills with three phases provide different amounts of hormones over three weeks. One-phase pills have the same amount of hormone for three weeks. Whether three-phase pills lead to fewer pregnancies is unknown. Nor is it known if the pills give better cycle control or fewer side effects. This review looked at whether three-phase pills worked as well as one-phase pills. It also studied whether women had fewer side effects with these pills.

We did a computer search for studies of pills with three phases versus pills with one phase. We also wrote to researchers and manufacturers to find other trials. We included randomized trials in any language. The studies had to have at least three treatment cycles.

We found 21 trials that looked at three-phase versus one-phase birth control pills. Many studies did not have good methods and the authors did not always report all their methods. The two types of pills did not differ in the numbers of women who got pregnant. Some trials found better bleeding patterns with the three-phase pill. The numbers of women who stopped using the pills were about the same for both types of pills.

The evidence was not strong enough to say whether the three-phase pill was better than the one-phase pill for pregnancy prevention, bleeding patterns, or continued use. Therefore, we recommend one-phase pills for women starting to use birth control pills. Large trials of good quality are needed to see if pills with three phases work better than those with one phase.

BACKGROUND

Side effects of oral contraceptive pills discourage adherence to and continuation of oral contraceptive regimens (Rosenberg 1995; Rosenberg 1998). Three approaches have been used to decrease these adverse effects: (a) reduction of the steroid dose; (b) development of new steroids; and (c) new formulas and schedules of administration. These strategies led to the introduction of the triphasic oral contraceptive pill in the 1980s.

Triphasic oral contraceptives allegedly attempt to 'mimic' the rising and falling of estrogen and progesterone during the normal menstrual cycle (Upton 1983). This purportedly results in a more 'physiologic' approach and, with some pills, a lower total monthly steroid dosage compared to the older monophasic oral contraceptives. Possible benefits of the triphasic approach are better cycle control and fewer side effects (Guillebaud 1993; Hale 1987). In a cohort study conducted in France, women using 30 to 40 μg pills had similar reports of menstrual symptoms regardless of whether the pills were monophasic, biphasic, or triphasic (Moreau 2007). However, potential disadvantages include an increased risk of pill-taking errors caused by the array of different color pills, the higher price of the pills and the possible higher incidence of accidental pregnancy (Guillebaud 1993).

Soon after the introduction in Britain of Logynon, a triphasic

preparation of levonorgestrel and ethinylestradiol, two case reports described a probable method failure of the pill (Fay 1982; Graham 1982). Studies at abortion clinics in Australia and the Netherlands demonstrated a significant over-representation of triphasic oral contraceptives used by women with an unplanned pregnancy (Ketting 1988; Kovacs 1989). Whether triphasic oral contraceptives have higher accidental pregnancy rates than monophasic oral contraceptives is unknown. Nor is it known if triphasic contraceptive pills give better cycle control and fewer side effects than the monophasic pills.

OBJECTIVES

The aim of this review was to compare triphasic oral contraceptive pills with monophasic oral contraceptive pills. Based on observational studies (Ketting 1988; Kovacs 1989), the a priori hypotheses were: (a) triphasic oral contraceptives are less effective in preventing pregnancy compared to monophasic oral contraceptives; (b) triphasic oral contraceptives are similar to monophasic pills in terms of cycle control and continuation rates.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomized controlled trials in this review. No language restrictions were placed on the reporting of the trials.

Types of participants

Healthy women of reproductive age were included if they had no contraindications for oral contraceptive use and desired to use oral contraceptives for preventing pregnancy. Women starting oral contraceptives as well as women switching oral contraceptives were included.

Types of interventions

We included any triphasic oral contraceptive pill (OC) compared to any monophasic oral contraceptive pill when used to prevent pregnancy. Both 21-pill and 28-pill packages were included. We excluded studies comparing triphasic pills with monophasic pills when the pills were used as a treatment (e.g. for acne, dysmenorrhea or menorrhagia) and not as a contraceptive. Interventions had to be applied for a minimum of three consecutive cycles to be eligible for inclusion.

Types of outcome measures

We focused on clinically relevant outcome measures. Studies were not included if they primarily looked at metabolic outcome measures or follicular growth. Principal outcomes were contraceptive efficacy, bleeding patterns and trial discontinuation. To be eligible, studies had to report results in a format that could be converted to outcomes as follows:

Contraceptive efficacy

- Proportion of women pregnant.

Cycle control

We used the definitions of spotting and breakthrough bleeding as specified by the authors.

- Proportion of cycles with spotting or breakthrough bleeding or intermenstrual bleeding within 3 cycles, 6 cycles and 12 cycles of pill use.
- Proportion of cycles with spotting or breakthrough bleeding or intermenstrual bleeding during the third cycle, the sixth cycle and the twelfth cycle of pill use.
- Proportion of women with spotting or breakthrough bleeding or intermenstrual bleeding within 3 cycles, 6 cycles and 12 cycles of pill use.
- Proportion of women with spotting or breakthrough bleeding or intermenstrual bleeding during the third cycle, the sixth cycle and the twelfth of pill use.
- Proportion of cycles with absence of withdrawal bleeding within 3, 6 and 12 cycles of pill use.
- Proportion of women with absence of withdrawal bleeding within 3, 6 and 12 cycles of pill use.
- Proportion of women with absence of withdrawal bleeding during the third, the sixth and the twelfth cycles of pill use.

Discontinuation

- Proportion of women that discontinued within 3, 6 and 12 cycles of pill use.
- Proportion of women that discontinued due to bleeding disturbances or adverse events within 3, 6 and 12 cycles of pill use.

Search methods for identification of studies

Electronic searches

We searched the computerized databases of MEDLINE using PubMed, EMBASE, POPLINE, LILACS and Cochrane Central Register of Controlled Trials (CENTRAL) for publications comparing monophasic, biphasic or triphasic oral contraceptives. In addition, we searched for recent clinical trials through ClinicalTrials.gov (NIH 2008) and the International Clinical Trials Registry Platform (ICTRP) (ICTRP 2008). The search strategies are shown below.

MEDLINE via PubMed
((“contraceptives, oral”[MeSH Terms]
AND
(((monophasic[ALL] OR biphasic[ALL]) OR triphasic[ALL]) OR multiphasic[ALL]))
AND
((((((((((“clinical
trials”[MeSH Terms] OR comparative stud*[ALL]) OR (“random allocation”[MeSH Terms] OR random allocation[Text Word])) OR compar*[ALL]) OR clinical trial*[ALL]) OR controlled clinical trial*[ALL]) OR multicenter stud*[ALL]) OR randomized controlled trial*[All]) OR random[ALL]) OR (“double-blind method”[MeSH Terms] OR double-blind method[Text Word])) OR (“single-blind method”[MeSH Terms] OR single-blind method[Text Word])))
POPLINE
(kw) oral contraceptives
AND
(tw) (monophasic OR biphasic OR triphasic OR multiphasic)
AND
(tw) (compar* OR clinical trials OR comparative studies OR random OR double blind studies)
EMBASE
1. oral contraceptive agent
2. biphasic
3. triphasic
4. multiphasic
5. 2 OR 3 OR 4
6. 1 AND 5
7. monophasic
8. 6 AND 7
LILACS
((((“contraceptives, oral”) or “contraceptive”)) or “contraceptives”) or “contraception” [Words]
and
(((“monophasic”) or “biphasic”) or “triphasic”) or “multiphasic” [Words]
CENTRAL
1. (contraceptives and oral)
2. monophasic
3. biphasic
4. triphasic
5. multiphasic
6. (((#2 or #3) or #4) or #5)
7. (#1 and #6)
ClinicalTrials.gov
Search terms: monophasic OR biphasic OR triphasic OR multiphasic
Condition: oral contraceptive
ICTRP
Title: monophasic OR biphasic OR triphasic OR multiphasic
Intervention or condition: contraception OR contraceptive

We searched the holdings of the Family Health International library for relevant trials, book chapters and review articles.

Searching other resources

We reviewed the reference lists of identified studies for additional trials. We examined the references lists from relevant book chapters and review articles identified with the search strategies. In addition, we attempted to contact the authors of all included trials. We also wrote a letter to pharmaceutical companies in the USA and Europe marketing oral contraceptives. In the contact letters, we provided a list of studies identified and asked if they knew of unpublished or published trials we had missed.

Data collection and analysis

Selection of studies

Two authors independently evaluated the titles and abstracts identified during the literature searches under unblinded conditions, and all potentially relevant articles were photocopied (Berlin 1997). Family Health International employees translated Russian, Chinese, Norwegian and German articles into English (Chen 1987; Dubnitskaia 1988; Engebretsen 1987; Lachnit-Fixson (1979) of Zador 1979; Lachnit-Fixson 1984). Then the authors independently examined the retrieved studies for possible inclusion. We excluded studies that were clearly not randomized, were quasi-randomized controlled trials, or did not focus on interventions included in this review. Discrepancies were resolved through consensus.

Data extraction and management

One author extracted the data from the included studies under unblinded conditions and entered the data into RevMan 4.2 (Berlin 1997). In addition to the outcome measures and methodological quality of the study, we extracted data on participants, inclusion and exclusion criteria, study sites, duration of study, study medication, method of collecting the data and funding. Correct entry of the data was verified by a second author. No disagreements about the extracted and entered data occurred.
We wrote a letter to the authors of the included trials and to the authors of possibly randomized studies. In the letter we asked for additional information about the study methods and the various outcome measures.

Assessment of risk of bias in included studies

The validity of trials was critically appraised by assessing the potential risk for bias (Higgins 2005). We did not calculate summary quality scores but focused on the method of generating the allocation sequence, the use and method of allocation concealment,

the use and method of blinding, exclusion of participants after randomization and loss to follow up (Juni 1999).

Assessment of heterogeneity

Most of the meta-analyses combined a small number of trials. However, when substantial heterogeneity was evident (I^2 > 50%), we examined the studies separately and discussed the results in Effects of interventions.

Data synthesis

The review was limited to the analytic method used in the paper (e.g. intent-to-treat or per-protocol).

Contraceptive efficacy

All studies that included contraceptive failure data reported the number of women who became pregnant. We used these proportions of women to calculate the odds ratio (OR) and 95% confidence interval (CI) with the random effects model.

Cycle control

Due to the possible relationship between (a) progestogen type and (b) dosage of estrogen and progestogen and bleeding patterns, we only combined trials that compared pills with identical contents (Maitra 2004; Rosenberg 1992) as was done in Gallo 2008. Most trials did not report bleeding pattern data according to the World Health Organization (WHO) recommendations (Belsey 1986). They generally reported the proportion of women or cycles with spotting, breakthrough bleeding or amenorrhea within 3, 6 or 12 cycles or at the third, sixth or twelfth cycle. We used these proportions to calculate the OR and 95% CI with the random effects model. Narrative summaries were provided when the reported bleeding data were not compatible with RevMan.

Discontinuation

We used the proportion of women discontinuing, discontinuing due to adverse events and discontinuing due to cycle disturbances within 3, 6 and 12 cycles to calculate the OR and 95% CI with the random effects model.

Sensitivity analysis

We did not conduct a sensitivity analysis based on the methodological quality of the trials.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Included studies

We included 21 studies comparing triphasic oral contraceptives and monophasic oral contraceptives in this review. Six studies were published in duplicate (Carlborg 1983; Dieben 1984; Lachnit-Fixson 1984; Saxena 1992; Sulak 1999). Detailed information regarding participants, inclusion and exclusion criteria, study sites, duration of study, study medication and outcome measures is presented in the Characteristics of included studies table. Six trials included more than two intervention groups.

Triphasic levonorgestrel oral contraceptives versus monophasic oral contraceptives

Seven studies compared a triphasic OC composed of 50-75-125 μg levonorgestrel (LNG) and 30-40-30 μg ethinylestradiol (EE) with a monophasic pill composed of 150 μg levonorgestrel and 30 μg ethinylestradiol (Carlborg 1983; Chen 1987; Dunson 1993; Engebretsen 1987; Ramos 1989; Saxena 1992; Zador 1979). Pharmaceutical companies market the triphasic preparation under the brand names Logynon, Trionetta 21 and 28, Triquilar, Trinordiol, and Triphasil. The monophasic preparation is marketed under the names Microgynon 30, Stediril, Neovletta, Rigevidon, Lo-Femenal, Follimin, and Nordette. Chen 1987 evaluated a third preparation, which was composed of 600 μg norethindrone and 35 μg ethinylestradiol. Ramos 1989 also examined a third preparation, i.e. 400 μg norethindrone and 35 μg ethinylestradiol (Micropil). The triphasic pill of 50-75-125 μg levonorgestrel and 30-40-30 μg ethinylestradiol was compared with a monophasic pill containing 150 μg desogestrel and 30 μg ethinylestradiol (Marvelon) in three studies (Dieben 1984; Ismail 1991; Lachnit-Fixson 1984).

Percival-Smith 1990 compared the triphasic 50-75-125 μg levonorgestrel and 30-40-30 μg ethinylestradiol pill, a triphasic pill containing 500-750-1000 μg norethindrone and 35 μg ethinylestradiol, and a monophasic pill of 1500 μg norethindrone acetate and 30 μg ethinylestradiol (Percival-Smith 1990). Brand names of the triphasic norethindrone oral contraceptive are Ortho Novum 7/7/7 and Trinovum. The monophasic norethindrone pill is Loestrin. Percival-Smith 1990 also examined a biphasic pill of 500-1000 μg norethindrone and 35 μg ethinylestradiol, but those data were not part of this review. The biphasic pill is known as Ortho 10/11.

One study compared 1) the 50-75-125 μg levonorgestrel and 30-40-30 μg ethinylestradiol triphasic OC and 2) the 500-750-1000 μg norethindrone and 35 μg ethinylestradiol triphasic OC with a monophasic OC containing 1000 μg norethindrone and 35 μg ethinylestradiol (Reiter 1990). The monophasic pill is marketed as Ortho-Novum 1/35.

Triphasic norethindrone oral contraceptives versus

monophasic oral contraceptives

Two studies compared a triphasic formulation containing 500-750-1000 μg norethindrone (NET) and 35 μg ethinylestradiol with a monophasic formulation containing 100 μg levonorgestrel and 20 μg ethinylestradiol (Chavez 1999; Reisman 1999). The monophasic formulation is marketed as Alesse and Loette.
We also included a study which compared an 'estrophasic' 1000 μg norethindrone acetate (NETA) and 20-30-35 μg ethinylestradiol combination with a monophasic 1500 μg norethindrone acetate and 30 μg ethinylestradiol combination (Rowan 1999).

Triphasic gestodene oral contraceptives versus monophasic oral contraceptives

Two trials compared a triphasic formulation composed of 50-70-100 μg gestodene (GTD) and 30-40-30 μg ethinylestradiol with a monophasic pill of 150 μg desogestrel (DSG) and 30 μg ethinylestradiol (Agoestina 1987; Andrade 1993). Brand names of the triphasic preparation are Trimulet and Triodeen.
The triphasic 50-70-100 μg gestodene and 30-40-30 μg ethinylestradiol oral contraceptive pill was also compared with 1) a monophasic 75 μg gestodene and 30 μg ethinylestradiol pill and 2) a monophasic 150 μg desogestrel and 20 μg ethinylestradiol pill (Bruni 2000). Companies market the monophasic gestodene and ethinylestradiol OC under the name Minulet and the monophasic desogestrel and ethinylestradiol pill under the name Mercilon.

Triphasic norgestimate oral contraceptives versus monophasic oral contraceptives

Sulak 1999 compared a triphasic formulation composed of 180-215-250 μg norgestimate (NGM) and 35 μg ethinylestradiol with a monophasic formulation of 1000 μg norethindrone acetate and 20 μg ethinylestradiol (Sulak 1999). Companies market the triphasic pill under the name Ortho Tri-Cyclen and the monophasic pill under the name Loestrin Fe 1/20.
In Rosenberg 1999, the triphasic formulation of 180-215-250 μg norgestimate and 35 μg ethinylestradiol was compared with 1) a formulation of 100 μg levonorgestrel and 20 μg ethinylestradiol (mentioned above for Chavez 1999 and Reisman 1999) and 2) a monophasic formulation of 150 μg desogestrel and 20 μg ethinylestradiol for 21 days and 10 μg ethinylestradiol for 5 days (Rosenberg 1999). The brand name of the desogestrel containing monophasic preparation is Mircette.
A triphasic preparation of 180-215-250 μg norgestimate and 25 μg ethinylestradiol was compared with a monophasic preparation of 1000 μg norethindrone acetate and 20 μg ethinylestradiol (Hampton 2001). The triphasic oral contraceptive is marketed as Ortho Tri-Cyclen Lo. Hampton 2001 also compared the triphasic to two 'cyclophasic' preparations, but those data were not part of this review. Neither 'cyclophasic' regimen has been put on the market yet. The 'cyclophasic' pills had a fixed daily dose of EE and a dose of NGM that alternated every other day.

Excluded studies

We excluded one study described as a randomized controlled trial that proved to be a matched cohort study (Dubnitskaia 1988). Seven studies did not report the method used to generate the allocation sequence. After communication with the author, we excluded Grace 1994 because the allocation sequence was not randomized. We excluded the remaining six studies because we were unable to contact the authors (Christie 1989; Dik 1984; Matsumoto 1988; Otolorin 1989; Perrone 1987; Rubio-Lotvin 1992). We did not include Bancroft 1987 due to the lack of relevant outcomes for this review.

Risk of bias in included studies

Overall, the description of the study methods was poor (DerSimonian 1982; Moher 2001).

Allocation

Only 2 of the 21 included trials reported the method of generating the allocation sequence (Agoestina 1987; Chen 1987). In addition, only four studies reported the use and method of concealing the treatment allocation sequence (Agoestina 1987; Ismail 1991; Ramos 1989; Reisman 1999). Communication with the authors provided the method of generating the allocation sequence for seven trials (Carlborg 1983; Dunson 1993; Hampton 2001; Ismail 1991; Reiter 1990; Rosenberg 1999; Saxena 1992). Nine authors informed us on whether allocation concealment was done, and if so, what method was used (Carlborg 1983; Chavez 1999; Dieben 1984; Dunson 1993; Hampton 2001; Reiter 1990; Rosenberg 1999; Rowan 1999; Saxena 1992).
Seven studies featured adequate randomization and concealment of treatment allocation (Schulz 2002c). Randomization was done by a computer (Carlborg 1983; Dunson 1993; Hampton 2001; Ismail 1991; Rosenberg 1999; Saxena 1992) or a random number table (Agoestina 1987). The methods used to conceal the allocation sequence included numbered pharmacy packages (Carlborg 1983); numbered containers (Agoestina 1987); sequentially-numbered, sealed envelopes opened at the time of admission (Dunson 1993; Ismail 1991; Saxena 1992); sequentially-numbered randomization cards with a opaque scratch-off dot (Rosenberg 1999); and a centralized voice-activated randomization system (Hampton 2001). Only Dunson 1993 mentioned that the envelopes were opaque. Chen 1987 randomized using a random number table but did mention the method used to conceal the allocation sequence. Reiter 1990 generated the allocation sequence by a random number table but did not conceal the allocation sequence. We could not find out the method of randomization in four studies, but the studies appeared to use a proper method to conceal

the treatment allocation sequence. Acceptable methods include numbered pharmacy packages (Ramos 1989; Rowan 1999) and sequentially-numbered, opaque, sealed envelopes (Chavez 1999; Reisman 1999). However, Chavez 1999 did not mention whether the envelopes were sealed and Reisman 1999 did not note if the envelopes were opaque. In Dieben 1984, the method of randomization was unclear and the study featured inadequate concealment of allocation. The remaining seven trials did not mention the method used to generate the allocation sequence or the method used to conceal the allocation sequence (Andrade 1993; Bruni 2000; Engebretsen 1987; Lachnit-Fixson 1984; Percival-Smith 1990; Sulak 1999; Zador 1979). Either we could not reach the researchers or the researchers could not elucidate the study methods.

Blinding

Blinding was not mentioned in four trials (Agoestina 1987; Carlborg 1983; Lachnit-Fixson 1984; Saxena 1992). None of the studies provided information regarding successful implementation of blinding (Schulz 2002b). Additionally, two of the studies (Hampton 2001; Ramos 1989) reported information to judge the adequacy of the blinding methods (DerSimonian 1982; Schulz 2002b). We obtained details on the use of blinding of three trials from the researchers (Carlborg 1983; Rowan 1999; Saxena 1992). Two trials blinded investigators and participants (Carlborg 1983; Ramos 1989). Furthermore, two trials reported that the study was double-blinded without specifying who was kept unaware of the oral contraceptives assigned (Chen 1987; Rowan 1999) (DerSimonian 1982; Schulz 2002b). One trial was blinded for the outcome assessor (Percival-Smith 1990). Fourteen trials were open (Andrade 1993; Bruni 2000; Chavez 1999; Dieben 1984; Dunson 1993; Engebretsen 1987; Hampton 2001; Ismail 1991; Reisman 1999; Reiter 1990; Rosenberg 1999; Saxena 1992; Sulak 1999; Zador 1979). The remaining two trials did not mention the use of blinding; we were unable to contact one researchers (Agoestina 1987), and another investigator could not provide additional information (Lachnit-Fixson 1984).

Follow up and exclusions

Eight trials described detailed information on number and reasons for discontinuation (Andrade 1993; Bruni 2000; Chavez 1999; Chen 1987; Ismail 1991; Ramos 1989; Reisman 1999; Saxena 1992). We acquired information on number and reasons for discontinuation from the authors of two studies (Dieben 1984; Rosenberg 1999).The other trials provided insufficient or no information on withdrawal.

Study discontinuation ranged from 4% to 77%. Eleven trials included data on loss to follow up. Loss to follow up varied from zero to 39%. In the Dunson 1993 trial, more than 20% of the participants were lost to follow up. Loss to follow-up rates greater than 20% may threaten validity of trials (Strauss 2005).

Fifteen of the 21 included studies excluded participants after randomization for reasons like failure to start oral contraceptives, failure to appear at the first follow-up visit, incorrect administration of oral contraceptives, protocol violations such as incorrect pill-taking or skipping the pill-free interval, inaccurate recording of data, loss to follow up or cycle disturbances (Andrade 1993; Bruni 2000; Carlborg 1983; Chavez 1999; Chen 1987; Dieben 1984; Engebretsen 1987; Hampton 2001; Ismail 1991; Percival-Smith 1990; Ramos 1989; Reisman 1999; Reiter 1990; Saxena 1992; Sulak 1999). Exclusion of participants after randomization may lead to bias (Schulz 2002a).

Two trials reported an analysis based on the intent-to-treat principle (Dunson 1993; Hampton 2001). Sulak 1999 stated that the analysis was carried out on the intent-to-treat population. However, the population included only participants who had started oral contraceptives and who had at least one cycle control measurement after the baseline (Sulak 1999). In addition, cycles were considered invalid and excluded if they had incorrect pill-taking or were without a pill-free interval, lasted longer than 31 days or had inaccurate recording of bleeding data. Fourteen trials did not perform an intent-to-treat analysis (Agoestina 1987; Andrade 1993; Bruni 2000; Carlborg 1983; Chavez 1999; Chen 1987; Dieben 1984; Engebretsen 1987; Ismail 1991; Percival-Smith 1990; Ramos 1989; Reisman 1999; Reiter 1990; Saxena 1992). In four studies, it was unclear whether an analysis based on the intent-to-treat approach was performed (Lachnit-Fixson 1984; Rosenberg 1999; Rowan 1999; Zador 1979).

Four studies continued with a proportion of the participants after six cycles of pill use. In Hampton 2001, women were enrolled for 6 cycles or 12 cycles of pill use at admittance. In Andrade 1993, Carlborg 1983 and Dieben 1984, we could not find out whether the continuation was decided previously or during the study. The latter may result in selection bias.

Other potential sources of bias

A priori hypothesis and sample size calculation

An a priori hypothesis and sample size calculation were provided in two studies (Percival-Smith 1990; Reisman 1999) (DerSimonian 1982). Another study stated that the sample size was developed to meet the US regulatory requirements to evaluate the safety and efficacy of oral contraceptives and provided the power (Hampton 2001). One study reported a sample size without explanation (Lachnit-Fixson 1984).

Funding

Five of the 21 included trials have been conducted or supported by independent organizations: World Health Organization (Chen 1987); Family Health International (Dunson 1993; Ismail 1991); Planned Parenthood Federation (Reiter 1990); and Indian Council of Medical Research (Saxena 1992). Thirteen

trials were conducted or sponsored by pharmaceutical companies (Agoestina 1987; Bruni 2000; Carlborg 1983; Chavez 1999; Dieben 1984; Hampton 2001; Lachnit-Fixson 1984; Percival-Smith 1990; Reisman 1999; Rosenberg 1999; Rowan 1999; Sulak 1999; Zador 1979). One study was supported by an international organization (United Nations Population Fund) in combination with a pharmaceutical company (Ramos 1989). We could not identify any assistance for two trials (Andrade 1993; Engebretsen 1987). Studies sponsored by pharmaceutical companies are more likely to have outcomes favoring the sponsor than studies funded by other sources (Als-Nielsen 2003; Lexchin 2003).

Effects of interventions

Contraceptive effectiveness

Eighteen studies comparing a triphasic formulation with a monophasic formulation assessed contraceptive effectiveness (Agoestina 1987; Andrade 1993; Bruni 2000; Carlborg 1983; Chavez 1999; Chen 1987; Dieben 1984; Dunson 1993; Hampton 2001; Engebretsen 1987; Ismail 1991; Lachnit-Fixson 1984; Ramos 1989; Reisman 1999; Rosenberg 1999; Saxena 1992; Sulak 1999; Zador 1979). Three studies did not report data regarding pregnancy (Percival-Smith 1990; Reiter 1990; Rowan 1999). Most studies included pregnancies caused by inadequacy of the method as well as imperfect use in the reported number of pregnancies (Trussell 1991). However, in two reports we could not figure out whether the pregnancies were caused by method failures solely or by both method and user failures (Engebretsen 1987; Saxena 1992). In the analyses, we considered the number of pregnancies reported in these two studies as method and user failures. There was a discrepancy in the described numbers of pregnancies between Cullberg et al (1982) from Dieben 1984 and the later report of Dieben 1984. The Dieben 1984 paper mentions two pregnancies, and the paper by Cullberg et al (1982) noted three pregnancies. Communication with the author revealed that three pregnancies occurred in the study period.

No significant differences were found between the various pills in contraceptive effectiveness (Analysis 1.1, Analysis 1.2, Analysis 2.1, Analysis 3.1, Analysis 4.1, Analysis 4.2, Analysis 9.1, Analysis 11.1, Analysis 11.2, Analysis 12.1, Analysis 13.1, Analysis 14.1, Analysis 15.1, Analysis 16.1, Analysis 17.1, Table 1).

Table 1. Pregnancies and total study cycles for triphasic and monophasic formulations

Study	Pregnancies (triphasic)	Total cycles (triphasic)	Pregnancies (monophasic)	Total cycles (monophasic)
Agoestina 1987	1	915	1	903
Andrade 1993	1	1398	0	1245
Carlborg 1983	1	1574	0	3275
	0	1623		
Chavez 1999	2	400	1	384
Chen 1987	2	492	3	478
			2	474
Dieben 1984	3	2709	0	2771
Engebretsen 1987	1	1442	1	1416
Hampton 2001	20	11003	19	7497

Table 1. Pregnancies and total study cycles for triphasic and monophasic formulations (*Continued*)

Ismail 1991	3	741	0	811
Lachnit-Fixson 1984	1	1536	0	1524
Reisman 1999	2	506	1	453
Rosenberg 1999	3	831	1	819
			0	848
Saxena 1992	0	3319	0	2949
Zador 1979	0	1440	0	1343

Cycle control

50-75-125 μg LNG/ 30-40-30 μg EE versus 150 μg LNG/30 μg EE (Comparison 1)

Four studies provided data on intermenstrual bleeding that fulfilled the inclusion criteria (Carlborg 1983; Dunson 1993; Ramos 1989; Zador 1979). In Carlborg 1983 and Zador 1979, users of monophasic LNG oral contraceptives reported more cycles with spotting and breakthrough bleeding within 3, 6 and 12 cycles of pill use compared to users of triphasic LNG oral contraceptives (Analyses 1.03 to 1.08). For the two studies combined, the OR was 0.57 (95% CI 0.48 to 0.67) for the proportion of cycles with spotting within 6 cycles (Analysis 1.05). For the proportion of cycles with breakthrough bleeding by 6 cycles, the OR was 0.63 (95% CI 0.50 to 0.80) for the two studies combined (Analysis 1.06). In Dunson 1993, which reported the proportion of women with intermenstrual bleeding within 12 cycles, the two formulations did not differ (Analysis 1.14). The sample size of the Ramos 1989 study was too small to assess differences in the number of women with spotting or breakthrough bleeding during cycle 6 or 12 (Analyses 1.10 to 1.13).

Saxena 1992 found no bleeding pattern differences between triphasic LNG and monophasic LNG oral contraceptives (Table 2). Chen 1987 observed less spotting in the participants using triphasic pills (Table 2). Engebretsen 1987 reported that triphasic LNG OC and the monophasic LNG OC were similar in the incidence of spotting and breakthrough bleeding.

Table 2. Bleeding pattern 50-75-125 μg LNG plus 30-40-30 μg EE versus 150 μg LNG plus 30 μg EE

Study and COC	Reference period	Number	Acceptable pattern	Infrequent bleeding	Frequent/ prolonged bleeding	No. of bleeding runs	Total bleeding days	Total spotting days
Saxena 1992								
Triphasic LNG	1	289	82.7	11.8	5.5	2.9 ± 0.6	9.9 ± 3.5	2.8 ± 3.6
	2	250	84.4	10.4	5.2	3.1 ± 0.6	9.8 ± 3.5	2.5 ± 2.8
	3	195	90.3	8.2	1.5	3.0 ± 0.5	9.4 ± 3.1	2.7 ± 2.9
	4	123	83.7	10.6	5.7	3.1 ± 0.6	9.0 ± 2.6	3.0 ± 3.1
Monophasic LNG	1	248	80.2	15.7	4.0	2.8 ± 0.8	8.9 ± 2.9	3.3 ± 4.1
	2	207	85.0	12.1	2.9	3.0 ± 0.6	9.2 ± 2.7	2.7 ± 3.1
	3	183	85.2	13.7	1.1	3.0 ± 0.6	8.8 ± 2.8	2.8 ± 2.9
	4	129	89.1	10.1	0.8	2.9 ± 0.5	8.5 ± 2.5	3.5 ± 3.5
Chen 1987								
Triphasic LNG	1						16.0 ± 4.1	5.6 ± 4.8
	1+2						26.2 ± 5.8	8.7 ± 7.5
Monophasic LNG	1						15.1 ± 4.3	8.0 ± 7.1
	1+2						25.0 ± 7.0	11.2 ± 8.4
Monophasic NET	1						14.8 ± 5.0	9.4 ± 6.3
	1+2						25.8 ± 8.2	14.2 ± 8.9

Three studies reported data on absence of withdrawal bleeding (Carlborg 1983; Dunson 1993; Zador 1979). Users of triphasic LNG OC were less likely to experience amenorrhea than users of monophasic LNG OC within 12 cycles (OR 0.27; 95% CI 0.17 to 0.45) (Analysis 1.16) (Carlborg 1983). However, the Dunson 1993 and Zador 1979 studies did not find a difference between the two groups in the proportion of cycles with amenorrhea within 6 cycles and the proportion of women with amenorrhea within 12 cycles (Analyses 1.15 and 1.24). Ramos 1989 also did not observe a difference between the two groups in the incidence of amenorrhea (Table 3).

50-75-125 μg LNG and 30-40-30 μg EE versus 600 μg NET and 35 μg EE (Comparison 2)

This comparison is based on a single trial (Chen 1987). Triphasic LNG oral contraceptive users reported less spotting compared to

monophasic NET oral contraceptive users (Table 2).

Table 3. Withdrawal bleeding 50-75-125 μg LNG plus 30-40-30 μg EE versus 150 μg LNG plus 30 μg EE (Ramos 1989)

Months	Triphasic LNG	Monophasic LNG	Monophasic NET
0 to 3	39.4	42.6	45.9
4 to 6	88.1	89.7	89.7
7 to 9	95.2	96.0	94.4
10 to 12	93.9	93.7	94.2

50-75-125 μg LNG and 30-40-30 μg EE versus 400 μg NET and 35 μg EE (Comparison 3)

One trial was included for this comparison (Ramos 1989). During the sixth cycle, spotting and breakthrough bleeding were less common in women taking triphasic LNG contraceptive pills in comparison with women taking monophasic NET pills. For spotting, the OR was 0.12 (95% CI 0.01 to 0.94) (Analysis 3.02). For breakthrough bleeding, the OR was 0.31 (95% CI 0.11 to 0.86) (Analysis 3.03). This difference did not remain at the twelfth cycle (Analyses 3.04 and 3.05).

50-75-125 μg LNG and 30-40-30 μg EE versus 150 μg DSG and 30 μg EE (Comparison 4)

Three studies reported data on intermenstrual bleeding consistent with the inclusion criteria (Dieben 1984; Ismail 1991; Lachnit-Fixson 1984). Dieben 1984 provided data regarding intermenstrual bleeding not described in the paper. Overall, the incidence of spotting or breakthrough bleeding did not differ between women using triphasic LNG OC and monophasic DSG oral contraceptives (Analyses 4.03 to 4.07 and 4.09 to 4.22). Significant heterogeneity was present in Analysis 4.6 and Analysis 4.7. By study, the effects were in different directions. When the studies were examined separately, Lachnit-Fixson 1984 showed the triphasic group had fewer cycles with spotting (Analysis 4.6) and with breakthrough bleeding (Analysis 4.7) than the monophasic group. In the Dieben 1984 and Lachnit-Fixson 1984 trials combined, users of triphasic LNG oral contraceptives reported fewer cycles in which breakthrough bleeding and spotting occurred in the same cycle compared to users of monophasic DSG OC during the first six months (OR 0.50; 95% CI 0.29 to 0.86) (Analysis 4.08).

These three studies also described data on withdrawal bleeding. No significant differences between the two preparations were found regarding the outcome of amenorrhea (Analyses 4.23 to 4.29). However, significant heterogeneity was present in Analysis 4.24. When the studies were examined separately, Lachnit-Fixson 1984 showed the triphasic group had fewer cycles with amenorrhea than the monophasic group within six cycles.

50-75-125 μg LNG and 30-40-30 μg EE versus 1500 μg NETA and 30 μg EE (Comparison 5)

One trial is included in this comparison (Percival-Smith 1990). Users of triphasic LNG oral contraceptives were somewhat less likely to experience intermenstrual bleeding and amenorrhea within six cycles of pill use than were users of the monophasic NETA OC. The OR for intermenstrual bleeding was 0.76 (95% CI 0.56 to 1.01) (Analysis 5.01). For amenorrhea, the OR was 0.02 (95% CI 0.00 to 0.18) (Analysis 5.02).

500-750-1000 μg NET and 35 μg EE versus 1500 μg NETA and 30 μg EE (Comparison 6)

This comparison is based on a single trial (Percival-Smith 1990). Users of triphasic NET oral contraceptives were more likely to experience intermenstrual bleeding (OR 1.37; 95% CI 1.05 to 1.80) (Analysis 6.01) and less likely to experience amenorrhea (OR 0.59; 95% CI 0.35 to 1.01) (Analysis 6.02) compared to users of the monophasic NETA OCs.

50-75-125 μg LNG and 30-40-30 μg EE versus 1000 μg NET and 35 μg EE (Comparison 7)

One study provided data for this comparison (Reiter 1990). The numbers of women having intermenstrual bleeding within 12 cycles were similar for the triphasic LNG OC and the monophasic NET OC groups (Analysis 7.01). In the group of triphasic LNG pill users, the incidence of amenorrhea was lower than in the group of monophasic NET pill users (OR 0.03; 95% CI 0.00 to 0.43) (Analysis 7.02).

500-750-1000 μg NET and 35 μg EE versus 1000 μg NET and 35 μg EE (Comparison 8)

This comparison is based on a single trial (Reiter 1990). The occurrence of intermenstrual bleeding did not differ between triphasic NET and monophasic NET OCs (Analysis 8.01). Women receiving triphasic NET pills experienced amenorrhea less frequently

than women using monophasic NET pills (OR 0.25; 95% CI 0.08 to 0.76) (Analysis 8.02).

500-750-1000 μg NET and 35 μg EE versus 100 μg LNG and 20 μg EE (Comparison 9)

Data on intermenstrual bleeding and amenorrhea was described in two trials (Chavez 1999; Reisman 1999). Reisman 1999 provided us with the number of women that had spotting/breakthrough bleeding/amenorrhea at each treatment cycle. No difference was found in the occurrence of intermenstrual bleeding and amenorrhea between triphasic NET OC and monophasic LNG oral contraceptives (Analyses 9.02 to 9.11).

1000 μg NETA and 20-30-35 μg EE versus 1500 μg NETA and 30 μg EE (Comparison 10)

One trial is included in this comparison. Rowan 1999 notes that 'estrophasic' NETA pills and monophasic NETA pills had a similar incidence of breakthrough bleeding, but the report does not provide the proportion of women or cycles with breakthrough bleeding. No data regarding the incidence of amenorrhea is provided.

50-70-100 μg GTD and 30-40-30 μg EE versus 150 μg DSG and 30 μg EE (Comparison 11)

This comparison is based on two studies (Agoestina 1987; Andrade 1993). Andrade 1993 observed in the group of women using triphasic GTD OC less cycles with breakthrough plus spotting within 6 cycles compared to the group of women using monophasic DSG oral contraceptives (OR 0.49; 95% CI 0.33 to 0.73) (Analysis 11.05). Overall, the two preparations did not differ regarding the outcomes spotting, breakthrough bleeding and amenorrhea (11.03 to 11.18).

50-70-100 μg GTD and 30-40-30 μg EE versus 150 μg DSG and 20 μg EE (Comparison 12)

One trial provided data for this comparison. Bruni 2000 states that the proportion of women with spotting or breakthrough bleeding was generally lower in the group of women using triphasic GTD pills compared to women using monophasic DSG oral contraceptives. However, the numbers of women with spotting or breakthrough bleeding are not provided in the paper. Triphasic pills were reportedly associated with significantly less spotting than monophasic pills at cycles 1, 2, 4 to 7, 9 and 11 and with significantly less breakthrough bleeding at cycles 1, 3, 4, 6, 9 and 11. From 1% to 6% of the triphasic pill users and 3% to 6% of the monophasic pill users experienced amenorrhea.

50-70-100 μg GTD and 30-40-30 μg EE versus 75 μg GTD and 30 μg EE (Comparison 13)

This comparison is based on a single study. Bruni 2000 reported that triphasic and monophasic GTD preparations produced similar patterns of cycle control, but the report does not provide the proportion of women with intermenstrual bleeding/amenorrhea.

180-215-250 μg NGM and 35 μg EE versus monophasic 1000 μg NETA and 20 μg EE (Comparison 14)

One study provided data on this comparison (Sulak 1999). During all six treatment cycles, the incidence of spotting or breakthrough bleeding was significantly lower among triphasic NGM preparation users compared with monophasic NETA preparation users. However, except for the sixth cycle, the report does not provide the proportion of women or cycles with spotting or breakthrough bleeding. The percentage of cycles with spotting or breakthrough bleeding within the treatment period was 9.6% for the triphasic group and 32.6% for the monophasic group. During the sixth cycle, significantly fewer participants using triphasic NGM contraceptive pills did experience spotting and breakthrough bleeding than participants using monophasic NETA pills (OR 0.26; 95% CI 0.14 to 0.51) (Analysis 14.02).

Further, the report mentions that amenorrhea was significantly less common in the triphasic group compared to the monophasic group during the second to sixth cycles (Sulak 1999). However, except for the sixth cycle, the number of women cycles with amenorrhea is not provided. Analysis 14.03 displays the difference in number of women with amenorrhea at cycle six (OR 0.17; 95% CI 0.06 to 0.45).

180-215-250 μg NGM and 35 μg EE versus 100 μg LNG and 20 μg EE (Comparison 15)

The comparison is based on one study. Rosenberg 1999 provided us with the number of cycles with spotting, breakthrough bleeding, and amenorrhea in the total treatment period. The incidence of spotting was lower among users of triphasic NGM OC compared to users of the monophasic LNG oral contraceptive (OR 0.59; 95% CI 0.42 to 0.81) (Analysis 15.02). The incidence of breakthrough bleeding was similar for the two preparations (Analysis 15.03). Women receiving triphasic NGM pills experienced less amenorrhea than women receiving monophasic LNG pills (OR 0.57; 95% CI 0.34 to 0.96) (Analysis 15.05).

180-215-250 μg NGM and 35 μg EE versus 150 μg DSG and 20 μg EE + 5 days of 10 μg EE (Comparison 16)

One study is included in this comparison. Rosenberg 1999 provided the number of cycles with spotting, breakthrough bleeding, and amenorrhea within the treatment period. Spotting was less common in the group of triphasic NGM oral contraceptives users as compared to monophasic DSG OC users (OR 0.65; 95% CI 0.47 to 0.91) (Analysis 16.02). No difference was found in the occurrence of breakthrough bleeding (Analysis 16.03). The incidence of amenorrhea was lower among women receiving triphasic NGM pills than women receiving monophasic DSG pills (OR 0.37; 95% CI 0.23 to 0.60) (Analysis 16.04).

180-215-250 μg NGM and 25 μg EE versus 1000 μg NETA and 20 μg EE (Comparison 17)

This comparison includes one study. Hampton 2001 observed that users of triphasic NGM oral contraceptives were less likely to experience intermenstrual bleeding and amenorrhea than users of monophasic NETA OC (Analyses 17.02 to 17.11, 17.13 and 17.14). For the proportion of cycles with breakthrough bleeding or spotting within 12 cycles, the OR was 0.45 (95% CI 0.41 to 0.49) (Analysis 17.07). The OR for amenorrhea within 13 cycles was 0.05 (95% CI 0.04 to 0.07) (Analysis 17.14).

Discontinuation

Nineteen studies provided data regarding discontinuation of participants. No significant differences were found in the number of women who discontinued or who discontinued due to medical reasons, cycle disturbances, intermenstrual bleeding or adverse events (Analyses 1.17 to 1.23, 2.02 to 2.04, 3.06 to 3.08, 4.30 to 4.38, 5.03, 6.03, 9.12, 9.13, 10.01, 11.19 to 11.23, 12.02, 12.03, 13.02, 13.03, 14.04, 14.05, 15.06, 15.07, 16.05, 16.06, 17.15 and 17.16). However, significant heterogeneity was present in Analysis 4.34 and Analysis 9.13. When the studies were examined individually, the triphasic group had fewer discontinuations due to medical reasons than the monophasic group in Lachnit-Fixson 1984 (Analysis 4.34) and in Reisman 1999 (Analysis 9.13).

DISCUSSION

Summary of main results

Contraceptive effectiveness

The 21 comparative trials included in this systematic review provided insufficient evidence to assess whether the contraceptive effectiveness of triphasic oral contraceptives differs from that of monophasic oral contraceptives. Pooling of the data on contraceptive effectiveness in a meta-analysis was generally not possible due differences in (a) progestogen type and (b) dosage of estrogen or progestogen of the studied oral contraceptives. The sample sizes of the individual trials were too small to detect differences in contraceptive effectiveness.

Cycle control

Several trials included in this review reported favorable bleeding patterns, i.e. less spotting, breakthrough bleeding or amenorrhea, in triphasic oral contraceptive users compared to monophasic OC users (Andrade 1993; Bruni 2000; Carlborg 1983; Chen 1987; Hampton 2001; Percival-Smith 1990; Reiter 1990; Rosenberg 1999; Sulak 1999; Zador 1979). Combining menstrual bleeding data in a meta-analysis was generally not possible due to (a) differences between the trials in measuring, analyzing and reporting the data on cycle disturbances and (b) differences in progestogen type, progestogen dosage and estrogen dosage of the studied contraceptive pills. When interpreting the findings on menstrual bleeding, consideration should be paid to the limitations of the studies. In most trials that reported favorable bleeding patterns in triphasic pill users compared to monophasic pill users, the progestogen type differed between the studied triphasic and monophasic oral contraceptive (Andrade 1993; Bruni 2000; Chen 1987; Hampton 2001; Percival-Smith 1990; Reiter 1990; Rosenberg 1999; Sulak 1999). The progestogen type is thought to affect cycle control, so the differences in bleeding pattern might be partially explained by the differences in progestogen content (Maitra 2004; Rosenberg 1992). Further, several trials used the proportion of all cycles with spotting, breakthrough bleeding or amenorrhea as effect measure (Andrade 1993; Carlborg 1983; Hampton 2001; Percival-Smith 1990; Rosenberg 1999; Zador 1979). This measure might give a distorted impression as one do not know whether a few women had all the cycles with bleeding problems or lots of women had a few cycles with bleeding problems.

The proportion of women that discontinued due to bleeding problems is as an indicator of how women tolerated the bleeding pattern. No significant differences were found in the number of women who discontinued due to intermenstrual bleeding and cycle disturbances.

Other adverse events

This review did not focus on the incidence of minor adverse events of oral contraceptives like headache, nausea, breast pain and acne. Women may vary in their acceptability of the various minor side effects, so the clinical importance of incidence differences is difficult to assess. We considered discontinuation from the trial as a 'surrogate' outcome for the acceptability of the contraceptive method. No significant differences were observed in the number of women who discontinued due to side effects. The findings on discontinuation may not reflect usage of oral contraceptives in the 'real world'. Participants of prospective comparative trials are not likely to represent the general population of contraceptive users. Free provision of contraceptive methods, financial allowance, and regular follow-up visits all may encourage continuation of the method.

The risk of serious adverse events of oral contraceptives like venous thromboembolism or myocardial infarction was not a subject of our review. Due to the low incidence of these adverse events, the randomized controlled trial does not suit evaluation of the absolute or relative risks. Observational studies, e.g. case-control studies and cohort studies, are more appropriate to assess these risks. Preliminary results of a case-control study by van Hylckama 2003 showed a comparable risk of venous thrombosis for triphasic and monophasic oral contraceptives.

Quality of the evidence

Overall, the reporting of the study methods and the methodological quality of the studies were poor (DerSimonian 1982; Moher 2001). Only 2 of the 21 trials reported the method of generating the allocation sequence, and only 4 described the use and method of concealing the treatment allocation sequence. After communication with the researchers, we learned that seven of the included studies featured adequate randomization and allocation concealment. Fourteen of the 21 trials were unblinded, and 15 studies excluded participants after randomization. Several excluded participants because of incorrect pill intake. Bias may result from nonrandom methods of generating the allocation sequence, inadequate allocation concealment, not blinding the participants or outcome assessors and exclusion of participants after randomization (DerSimonian 1982; Schulz 1995; Schulz 2002c; Schulz 2002d; Schulz 2002e). Further, 13 trials were conducted or funded by pharmaceutical companies. Studies sponsored by pharmaceutical companies are more likely to have outcomes favoring the sponsor than studies funded by other sources (Als-Nielsen 2003; Lexchin 2003).

Implications for research

Large, adequately reported, high-quality, randomized controlled trials comparing triphasic and monophasic oral contraceptives with identical progestogens are needed to determine whether triphasic pills differ from monophasic pills in contraceptive effectiveness, menstrual bleeding pattern and continuation rates. Combining the data on menstrual bleeding was complicated by the lack of uniformity in measuring, analyzing and reporting menstrual patterns. Future studies should follow the WHO recommendations by Belsey 1986 on recording menstrual bleeding patterns. Further, reporting of the study methods and the methodological quality of the studies was poor. Future studies should adhere to the CONSORT guidelines on reporting of randomized controlled trials (Moher 2001).

AUTHORS' CONCLUSIONS

Implications for practice

The available evidence is insufficient to determine whether triphasic oral contraceptives differ from monophasic oral contraceptives in important ways, such as efficacy, bleeding patterns, and continuation rates. This reflects the generally poor quality of comparative trials to date. Given the often higher cost and greater complexity of triphasic-pill regimens, monophasic pills should be the first choice in oral contraceptives. According to guidelines of the International Planned Parenthood Federation (IPPF), women should start on a monophasic pill containing 30 to 35 μg of estrogen (IPPF 2004). Pills with 20 μg estrogen cause more breakthrough bleeding and discontinuation because of bleeding than do pills with more estrogen (Gallo 2008).

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REFERENCES

References to studies included in this review

Agoestina 1987 *{published data only}*

Agoestina T, Sulaeman M, Rarung M, Sabarudin U. Clinical evaluation of low dose pill triphasic (EE + estoden) versus monophasic (EE + desogestrel). Presented at the XIth Asian and Oceanic Congress of Obstetrics and Gynecology; 1987 Dec 6-12; Hongkong.

Andrade 1993 *{published data only}*

* Andrade RP. Clinical comparison of a triphasic gestodene preparation and a monophasic desogestrel preparation. *Gynecological Endocrinology* 1993;**7**(Suppl):33–41.

Bruni 2000 *{published data only}*

* Bruni V, Croxatto H, De La Cruz J, Dhont M, Durlot F, Fernandes MT, et al.A comparison of cycle control and effect on well-being of monophasic gestodene-, triphasic gestodene- and monophasic desogestrel-containing oral contraceptives. *Gynecological Endocrinology* 2000;**14**:90–8.

Lacante P. A comparison of cycle control and effect on well-being of monophasic gestodene-, triphasic gestodene- and monophasic desogestrel-containing oral contraceptives. *Gynecological Endocrinology* 1996;**10**(Suppl 2):33–41.

Carlborg 1983 *{published and unpublished data}*

Carlborg L. Acceptability of low-dose oral contraceptives: results of a randomized Swedish multicenter study comparing a triphasic (Trionetta) and a fixed-dose combination (Neovletta). Benefits and risk of hormonal contraception: Proceedings of an International Symposium; 1982 March 19; Amsterdam. Boston (MA): MTP Press, 1982:78–92.

* Carlborg L. Comparison of contraceptive acceptability of levonorgestrel and ethinyl oestradiol administered in one three-phasic (Trionetta) and one monophasic (Neovletta) version. *Contraception* 1983;**27**:439–52.

Chavez 1999 *{published and unpublished data}*

Chavez A, DelConte A. A comparison of cycle control with monophasic levonorgestrel/ethinylestradiol 100 micrograms/20 micrograms versus triphasic norethindrone/ethinylestradiol 500-750-1000 micrograms/35 micrograms: a multicenter, randomized, open-label study. *European Journal of Contraception & Reproductive Health Care* 1999;**4**:75–83.

Chen 1987 *{published data only}*

* Chen JK. A comparative clinical study of the effects of three types of low dose estrogen/progestogen oral contraceptives. *Reproduction and Contraception* 1987;**7**:11–6.

Chen JK. A comparative clinical study of the effects of three types of low-dose estrogen/progestogen oral contraceptives. *Shengzhi Yu Biyun* 1987;**7**:11–6.

Dieben 1984 *{published and unpublished data}*

Cullberg G. A comparative multicentre study on a triphasic, and a fixed low-dose oral contraceptive combination. *Acta Obstetricia et Gynecologica Scandinavica* 1983;**Suppl 116**:97.

Cullberg G, Samsioe G, Andersen RF, Bredesgaard P, Andersen NB, Ernerot H, et al. Two oral contraceptives, efficacy, serum proteins, and lipid metabolism. A comparative multicentre study on a triphasic and a fixed dose combination. *Contraception* 1982;**26**:229–43.

* Dieben T. A comparative study of the clinical efficacy of Marvelon and a triphasic combination. *Organorama* 1984;**21**:16–8.

Mattsson LA, Cullberg G. Clinical and metabolic effects of Marvelon: Scandinavian experience. *British Journal of Family Planning* 1984; **10**:43–8.

Dunson 1993 *{published and unpublished data}*

Dunson TR, McLaurin VL, Aguayo EL, de Silva P, Calventi V, Gerais AS, et al. A multicenter comparative trial of triphasic and monophasic, low dose combined oral contraceptives. *Contraception* 1993;**47**:515–25.

Engebretsen 1987 *{published data only}*

Engebretsen T, Thorsen E, Smith CC, Bull-Njaa T, Christensen A. Triphasic versus monophasic p-pill. A comparative multicenter study [Trefasisk versus monofasisk p–pille: en sammenlignende multisenterstudie]. *Tidsskrift for den Norske Laegeforening* 1987;**107**:941–3.

Hampton 2001 *{published and unpublished data}*

* Hampton RM, Short M, Bieber E, Bouchard C, Ayotte N, et al. Comparison of a novel norgestimate/ethinyl estradiol oral contraceptive (Ortho Tri-Cyclen Lo) with the oral contraceptive Loestrin Fe 1/20. *Contraception* 2001;**63**:289–95.

Hampton RM, Zhang HF, Barnowski C, Wan GJ. Bleeding patterns with monophasic and triphasic low-dose ethinyl estradiol combined oral contraceptives. *Contraception* 2008;**77**:415–9.

Ismail 1991 *{published and unpublished data}*

Ismail MTM. A randomised comparative study of Triquilar versus Marvelon: the Malaysian experience. *Malaysian Journal of Reproductive Health* 1991;**9**:9–17.

Lachnit-Fixson 1984 *{published data only}*

Lachnit-Fixson U. Progress in oral contraception. Advantages of a levonorgestrel-containing 3-stage preparation over low-dose levonorgestrel and desogestrel containing monophasic combination preparations [Fortschritte in der oralen kontrazeption: vorteille eines levonorgestrel–haltigen dreistufenpraparates gegenuber niedrigdosierten levonorgestrel– und desogestrel–haltigen monophasischen kombinationspraparaten]. *Fortschritte der Medizin* 1984;**102**:825–30.

* Lachnit-Fixson U, Aydinlik S, Lehnert J. Clinical comparison between a monophasic preparation and a triphasic preparation. In: Rolland R, Harrison RF, Bonnar J, Thompson W editor(s). *Advances in fertility control and the treatment of sterility. Proceedings of a special symposium held at the XIth world congress on fertility and sterility; 1983 June; Dublin*. Lancaster: MTP Press, 1984:71–9.

Percival-Smith 1990 *{published data only}*

Percival-Smith RK, Yuzpe AA, Desrosiers JA, Rioux JE, Guilbert E. Cycle control on low-dose oral contraceptives: a comparative trial. *Contraception* 1990;**42**:253–62.

Ramos 1989 *{published data only}*

Ramos R, Apelo R, Osteria T, Vilar E. A comparative analysis of three different dose combinations of oral contraceptives. *Contraception* 1989;**39**:165–77.

Reisman 1999 *{published and unpublished data}*

Reisman H, Martin D, Gast MJ. A multicenter randomized comparison of cycle control and laboratory findings with oral contraceptive agents containing 100 μg levonorgestrel with 20 μg ethinyl estradiol or triphasic norethindrone with ethinyl estradiol. *American Journal of Obstetrics and Gynecology* 1999;**181**:45–52.

Reiter 1990 *{published and unpublished data}*

Reiter SL, Baer LJ. Initial selection of oral contraceptives. *Journal of Reproductive Medicine* 1990;**35**:547–8.

Rosenberg 1999 *{published and unpublished data}*

Rosenberg MJ, Meyers A, Roy V. Efficacy, cycle control, and side effects of low- and lower-dose oral contraceptives: a randomized trial of 20 μg and 35 μg estrogen preperations. *Contraception* 1999;**60**: 321–9.

Rowan 1999 *{published and unpublished data}*

Rowan JP. "Estrophasic" dosing: A new concept in oral contraceptive therapy. *American Journal of Obstetrics and Gynecology* 1999;**180**: 302–6.

Saxena 1992 *{published and unpublished data}*

Datey S, Gaur LN, Saxena BN. Vaginal bleeding patterns of women using different contraceptive methods (implants, injectables, IUDs, oral pills)-an Indian experience. *Contraception* 1995;**51**:155–65.

* Saxena B. Randomised clinical trial with Triquilar-ED and low-dose combination pill. *Journal of Obstetrics and Gynaecology of India* 1992;**42**:71–7.

Sulak 1999 *{published data only}*

Lippman J, Siu C, Godwin A, Massaro J. A clinical comparison of two oral contraceptives: triphasic norgestimate/35 μg ethinylestradiol versus monophasic norethindrone acetate/20 μg ethinylestradiol. *Obstetrics and Gynecology* 1999;**93**(Suppl):37S.

* Sulak P, Lippman J, Siu C, Massaro J, Godwin A. Clinical comparison of triphasic norgestimate/35 μg ethinyl estradiol and monophasic norethindrone acetate/20 μg ethinyl estradiol: cycle control, lipid effects, and user satisfaction. *Contraception* 1999;**59**:161–6.

Zador 1979 *{published data only}*

Lachnit-Fixson U. Clinical investigation with a new triphasic oral contraceptive. In: Greenblatt RB editor(s). *The development of a new triphasic oral contraceptive. Proceedings of a Special Symposium held at*

the 10th World Congress on Fertility and Sterility; 1980 July; Madrid. Lancaster: MTP Press Limited, 1980:99–107.

Lachnit-Fixson U. Progress in oral contraception. Advantages of a levonorgestrel-containing 3-stage preparation over low-dose levonorgestrel and desogestrel containing monophasic combination preparations [Fortschritte in der oralen kontrazeption: vorteille eines levonorgestrel–haltigen dreistufenpraparates gegenuber niedrigdosierten levonorgestrel– und desogestrel–haltigen monophasischen kombinationspraparaten]. *Fortschritte der Medizin* 1984;**102**:825–30.

Lachnit-Fixson U. The first three-stage preparation for hormonal contraception. Clinical results [Erstes dreistufenpraeparat zur hormonalen konzeptionsverhutung: klinische ergebnisse]. *Munchener Medizinische Wochenschrift* 1979;**121**:1421–6.

Zador G. Clinical performance of a triphasic administration of ethinyl estradiol and levonorgestrel in comparison with the 30 + 150 μg fixed-dose regimen. In: Haspels AA, Rolland R editor(s). *Benefits and risk of hormonal contraception. Proceedings of an international symposium; 1982 March 19; Amsterdam*. Boston (Massachusetts): MTP Press, 1982:43–55.

* Zador G. Fertility regulation using "triphasic" administration of ethinyl estradiol and levonorgestrel in comparison with the 30 plus 150 μg fixed dose regime. *Acta Obstetricia et Gynecologica Scandinavica. Supplement* 1979;**88**:43–8.

References to studies excluded from this review

Bancroft 1987 ***{published data only}***

Bancroft J, Sanders D, Warner P, Loudon N. The effects of oral contraceptives on mood and sexuality: A comparison of triphasic and combined preparations. *Journal of Psychosomatic Obstetrics and Gynaecology* 1987;**7**:1–8.

Christie 1989 ***{published data only}***

Christie T. A clinical overview of a new triphasic contraceptive containing gestodene. *International Journal of Fertility* 1989;**34**(Suppl): 40–9.

Dik 1984 ***{published data only}***

Dik M, Eckert H, Hones S, Schindler AE. Comparison of a 2-phase preparation (Oviol 22) with a low-dose 1-phase preparation (Ovoresta M) [Vergleich eines zweiphasenpraparates (Oviol 22) mit einem niedrig dosierten Einphasenpraparat (Ovoresta M)]. *Geburtshilfe und Frauenheilkunde* 1984;**44**:808–12.

Dubnitskaia 1988 ***{published data only}***

Dubnitskaia LV. Acceptability of hormonal contraceptives with a low steroid content. *Akusherstvo I Ginekologiia* 1988;**8**:47–50.

Grace 1994 ***{published data only}***

Grace E, Emans SJ, Havens KK, Merola JL, Woods ER. Contraceptive compliance with a triphasic and a monophasic norethindrone-containing oral contraceptive pill in a private adolescent practice. *Adolescent and Pediatric Gynecology* 1994;**7**:29–33.

Kuhl 1985 ***{published data only}***

Kuhl H, Gahn G, Romberg G, Marz W, Taubert H-D. A randomized cross-over comparison of two low-dose oral contraceptives upon hormonal and metabolic parameters: 1. Effects upon sexual hormone levels. *Contraception* 1985;**31**:583–93.

Matsumoto 1988 ***{published data only}***

Matsumoto S, Sato T, Matsuyama E, Tamada T, Wagatsuma T, Honda H. Results of a clinical study with low-dose oral contraceptives: investigation with triphasic and monophasic preparations containing levonorgestrel and ethinylestradiol. *Current Therapeutic Research, Clinical and Experimental* 1988;**44**:165–77.

Otolorin 1989 ***{published data only}***

Otolorin EO. Clinical experience with a triphasic oral contraceptive containing ethinyloestradiol and levonorgestrel in Nigerian women. *West African Journal of Medicine* 1989;**8**:116–21.

Perrone 1987 ***{published data only}***

Perrone G, Calzolari E, Mancone M, Masci A, Steffe M, Tesseri E. Oral contraceptives and their minor side effects: comparison of three low-dose estroprogestinic combinations [Contraccettivi orali ed effetti collaterali minori: confronto fra tre estroprogestinici a basso dosaggio]. *Patologia e Clinica Ostetrica e Ginecologica* 1987;**15**:6–11.

Rubio-Lotvin 1992 ***{published data only}***

Rubio-Lotvin B, Ruiz-Moreno JA, Gonzalez-Ansorena R. Desogestrel-ethinylestradiol, an oral monophasic contraceptive. Clinical and lipid metabolic effects: a 5 year experience. *Advances in Contraceptive Delivery Systems* 1992;**8**:75–88.

References to ongoing studies

Bayer 2008 ***{unpublished data only}***

Bayer Schering Pharma AG. Cycle Control and Safety of E2-DRSP. Available from: http://clinicaltrials.gov/ct2/home (accessed 21 Nov 2008).

Additional references

Als-Nielsen 2003

Als-Nielsen B, Chen W, Gluud C, Kjaergard LL. Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events?. *Journal of the American Medical Association* 2003;**290**:921–8.

Belsey 1986

Belsey EM, Machin D, d' Arcangues C. The analysis of vaginal bleeding patterns induced by fertility regulating methods. World Health Organization Special Programme of Research, Development and Research Training in Human Reproduction. *Contraception* 1986;**34**: 253–61.

Berlin 1997

Berlin JA. Does blinding of readers affect the results of meta-analyses?. *Lancet* 1997;**350**:185–6.

DerSimonian 1982

DerSimonian R, Charette LJ, McPeek B, Mosteller F. Reporting on methods in clinical trials. *New England Journal of Medicine* 1982; **306**:1332–7.

Fay 1982

Fay RA. Failure with the new triphasic oral contraceptive Logynon. *British Medical Journal* 1982;**284**:17–8.

Gallo 2008

Gallo MF, Nanda K, Grimes DA, Lopez LM, Schulz KF. 20 μg versus >20 μg estrogen combined oral contraceptives for contraception. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: 10.1002/14651858.CD003989]

Graham 1982
Graham H. Failure with the new triphasic oral contraceptive Logynon. *British Medical Journal* 1982;**284**:422.

Guillebaud 1993
Guillebaud J. *Contraception: your questions answered*. 2nd Edition. Edinburgh: Churchill Livingstone, 1993:188–90.

Hale 1987
Hale RW. Phasic approach to oral contraceptives. *American Journal of Obstetrics and Gynecology* 1987;**157**:1052–8.

Higgins 2005
Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]. In: The Cochrane Library 2005, Issue 3. Chichester, UK: John Wiley & Sons, Ltd. Chicester, UK: John Wiley & Sons, Ltd.

ICTRP 2008
World Health Organization (WHO). International Clinical Trials Registry Platform (ICTRP). http://www.who.int/ictrp/search/en/ (accessed 21 Nov 2008).

IPPF 2004
Terki F, Malhotra U. In: Powlson M editor(s). *Medical and Service Delivery Guidelines for Sexual and Reproductive Health Services*. Third Edition. London (UK): International Planned Parenthood Federation, 2004.

Juni 1999
Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *Journal of the American Medical Association* 1999;**282**:1054–60.

Ketting 1988
Ketting, E. The relative reliability of oral contraceptives: findings of an epidemiological study. *Contraception* 1988;**37**:343–8.

Kovacs 1989
Kovacs, GT, Riddoch G, Duncombe P, Welberry L, Chick P, et al.Inadvertent pregnancies in oral contraceptive users. *Medical Journal of Australia* 1989;**150**:549–51.

Lexchin 2003
Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *British Medical Journal* 2003;**326**:1167–70.

Maitra 2004
Maitra N, Kulier R, Bloemenkamp KWM, Helmerhorst FM, Gulmezoglu AM. Progestogens in combined oral contraceptives for contraception. *Cochrane Database of Systematic Reviews* 2004, Issue 3. [DOI: 10.1002/14651858]

Moher 2001
Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel group randomized trials. *Lancet* 2001;**14**:1191–4.

Moreau 2007
Moreau C, Trussell J, Gilbert F, Bajos N, Bouyer J. Oral contraceptive tolerance. Does the type of pill matter?. *Obstetrics and Gynecology* 2007;**109**:1277–85.

NIH 2008
US National Institutes of Health (NIH). ClinicalTrials.gov. http://clinicaltrials.gov/ct2/home (accessed 21 Nov 2008).

Rosenberg 1992
Rosenberg MJ, Long SC. Oral contraceptives and cycle control: a critical review of the literature. *Advances in Contraception* 1992;**8** (Suppl):35–45.

Rosenberg 1995
Rosenberg MJ, Waugh MS, Meehan TE. Use and misuse of oral contraceptives: risk indicators for poor pill taking and discontinuation. *Contraception* 1995;**51**:283–8.

Rosenberg 1998
Rosenberg MJ, Waugh MS. Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons. *American Journal of Obstetrics and Gynecology* 1998;**179**:577–82.

Schulz 1995
Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of the American Medical Association* 1995;**273**:408–12.

Schulz 2002a
Schulz KF, Grimes DA. Sample size slippages in randomised trials: exclusions and the lost and wayward. *Lancet* 2002;**359**:781–5.

Schulz 2002b
Schulz KF, Chalmers I, Altman DG. The landscape and lexicon of blinding in randomized trials. *Annals of Internal Medicine* 2002;**136**: 254–9.

Schulz 2002c
Schulz KF, Grimes DA. Generation of allocation sequences in randomised trials: chance, not choice. *Lancet* 2002;**359**:515–9.

Schulz 2002d
Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. *Lancet* 2002;**359**:614–8.

Schulz 2002e
Schulz KF, Grimes DA. Blinding in randomised trials: hiding who got what. *Lancet* 2002;**359**:696–700.

Strauss 2005
Strauss SE, Richardson WS, Glasziou P, Haynes RB. *Evidence-based Medicine: How to Practice and Teach EBM*. Third Edition. New York: Churchill Livingstone, 2005.

Trussell 1991
Trussell J. Methodological pitfalls in the analysis of contraceptive failure. *Statistics in Medicine* 1991;**10**:201–20.

Upton 1983
Upton GV. The phasic approach to oral contraception:the triphasic concept and its clinical application. *International Journal of Fertility* 1983;**28**:121–40.

van Hylckama 2003
van Hylckama Vlieg A. *Causes of venous thrombosis: procoagulant factors and oral contraceptives [dissertation]*. Leiden (Netherlands): Leiden University, 2003.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Agoestina 1987

Methods	Randomized controlled trial. Randomization by random number tables and allocation concealment by numbered containers. The use of blinding is not described. We were unable to reach the author.
Participants	170 women at 3 sites in Indonesia. Inclusion criteria were healthy women. Exclusion criteria were contraindications to oral contraceptives, use of hormonal contraceptives within the previous 3 cycles before enrollment and current pregnancy. The mean age of the 2 groups of participants differs.
Interventions	Triphasic gestodene/ethinylestradiol (50-70-100 μg GTD and 30-40-30 μg EE in a 6/5/10 days regimen) [SHD 415 G] versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 30 μg EE for 21 days) [Marvelon].
Outcomes	Primary outcomes measures are: efficacy; side effects; cycle control; continuation and reasons for discontinuation; pill intake errors. The method to collect data is not described. The report does not describe the definitions of breakthrough bleeding and spotting.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 3 women in the triphasic group and 5 women in the monophasic group discontinued early. The reasons for discontinuation are described. The report does not mention loss to follow up or withdrawals because of protocol violations. Analysis not according to intention-to-treat principle. The trial was supported by the manufacturer of the studied triphasic gestodene/ethinylestradiol pill (Schering).

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Andrade 1993

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. We were unable to reach the author.
Participants	480 women at 14 study sites in Europe and New Zealand. Inclusion criteria were healthy women under 40 years of age who were at risk of becoming pregnant and had regular 21 to 35 day menstrual cycles. The report does not provide exclusion criteria for the study. Switchers were included in the study.
Interventions	Triphasic gestodene/ethinylestradiol (50-70-100 μg GTD and 30-40-30 μg EE in a 6/5/10 days regimen, N=250 for 6 cycles of whom N=13 continued for an additional 6 cycles) [no brand name described] versus

Andrade 1993 (*Continued*)

	monophasic desogestrel/ethinylestradiol (150 μg DSG and 30 μg EE for 21 days, N=230 for 6 cycles of whom N=8 continued for an additional 6 cycles) [no brand name described].
Outcomes	Principal outcome measures are: pregnancy; cycle control; cycle length and bleeding intensity; side effects; laboratory and cytology changes; blood pressure; bodyweight; compliance; discontinuation and reasons for discontinuation. The method to collect data is not described. The report does not describe the definitions of breakthrough bleeding and spotting.
Notes	The report does not describe an a priori hypothesis or sample size or power calculation. Study duration: 6 and 12 cycles. 49 women in the triphasic group and 50 women in the monophasic group discontinued early. The reasons for discontinuation are described. 7 women in the triphasic group and 5 women in the monophasic group were lost to follow up. 6 women in the triphasic group and 8 women in the monophasic group were withdrawn because of protocol violations. Women who missed pills in cycle 6 were excluded from analysis of cycle control. Analysis not according to intention-to-treat principle. The paper does not report information on support.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Bruni 2000

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. We were unable to reach the authors.
Participants	2419 women in 18 countries worldwide. Inclusion criteria were age 18 to 41 years who had regular menstrual cycles. Exclusion criteria were hypersensitivity to estrogens or progestogens, current pregnancy, breastfeeding, disorders that might interfere with the study protocol. Little information about baseline demographics. The paper does not report if switchers were included in the study.
Interventions	Triphasic gestodene/ethinylestradiol (50-70-100 μg GTD and 30-40-30 μg EE in a 6/5/10 days regimen, N=808) [Tri-Minulet] versus monophasic gestodene/ethinylestradiol (75 μg GTD and 30 μg EE for 21 days, N=806) [Minulet] versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 20 μg EE for 21 days, N=805) [Mercilon].
Outcomes	Primary outcome measures are: cycle control; well-being; side effects and discontinuation. Use of a daily diary card to collect data on cycle control. Use of a modified form of Moos Menstrual Distress Questionnaire (MMDQ) to assess well-being. The method of collecting data on side effects is unclear. The report does not describe the definitions of breakthrough bleeding and spotting.

Bruni 2000 (*Continued*)

Notes	The report does not describe an a priori hypothesis or sample size or power calculation. Study duration: 13 cycles. 234 women in the triphasic group, 245 women in the monophasic gestodene group and 219 women in the monophasic desogestrel group discontinued early. The reasons for discontinuation are described. 92 women in the triphasic group, 101 women in the monophasic gestodene group and 77 women in the monophasic desogestrel group were lost to follow up. 17 women in the triphasic group, 15 women in the monophasic gestodene group and 10 women in the monophasic desogestrel group were withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. The trial was sponsored by the manufacturer of the studied triphasic and monophasic gestodene/ethinylestradiol pills (Wyeth-Ayerst)

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Carlborg 1983

Methods	Randomized controlled trial. The method of randomization, the use of allocation concealment and the use of blinding are not described. Communication with the author indicated a computer-generated random allocation sequence, allocation concealment by numbered pharmacy packages and blinding of participants and investigators. The method of randomizing is unclear.
Participants	862 women at 12 sites in Sweden. Inclusion criteria were that women had to fulfill the current recommendations for oral contraceptive use. Limited information on baseline characteristics. Switchers were included in the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30- 40-30 μg EE in a 6/5/10 days regimen, N=210 for 6 cycles of whom N=89 continued for an additional 6 cycles) [Trionetta 21] versus triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen and 7 days of placebo tablets, N=207 for 6 cycles of whom N=93 continued for an additional 6 cycles) [Trionetta 28] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg ethinylestradiol, N=418 for 6 cycles of whom N=189 continued for an additional 6 cycles) [Neovletta].
Outcomes	Primary outcomes measures are: pregnancy; side effects; cycle control; continuation rate and reasons for discontinuation. Use of diary cards to collect data on pill-intake errors and cycle control. Breakthrough bleeding was defined as intermenstrual bleeding which required the use of sanitary protection and spotting as all other cases. Data on side effects were recorded if reported spontaneously.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 and 12 cycles. 67 women in the triphasic group and 60 women in the monophasic group discontinued early in the 1 to 6 cycles trial period. 26 women in the triphasic group and 24 women in the monophasic group discontinued early in the 7 to 12 cycles trial period. Little information concerning the number and

Carlborg 1983 (*Continued*)

	reasons for discontinuation. 27 women entered in the trial are not included in the analysis because they were lost to follow up. The report does not describe withdrawals because of protocol violations. Analysis not according to intention-to-treat principle. The trial was supported by the manufacturer of the studied monophasic and triphasic levonorgestrel/ethinylestradiol pills (Schering).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Chavez 1999

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Communication with an author indicated allocation concealment by sequentially-numbered opaque envelopes. The author could not elucidate the method of randomization.
Participants	342 women at 11 sites in the USA. 53 women did not start the study after randomization. Inclusion criteria were healthy women aged 18 to 35 years for smokers and no upper age limit for non-smokers with regular menstrual cycles (25 to 31 days) for the 3 months before enrollment who were at risk of becoming pregnant. Exclusion criteria were the standard contraindications for oral contraceptive studies listed in product class labeling, use of oral contraceptives within the previous 3 cycles before enrollment, use of an IUD or injectable or implantable estrogens, progestins or androgens during the 6 months before enrollment, smoking of more than 15 cigarettes per day and drug or alcohol abuse.
Interventions	Triphasic norethindrone/ethinylestradiol (500-750-1000 μg NET and 35 μg ethinylestradiol in a 7/7/7 days regimen and 7 days of placebo tablets, N=173) [Ortho-Novum 7/7/7] versus monophasic levonorgestrel/ethinylestradiol (100 μg LNG and 20 μg EE for 21 days and 7 days of placebo tablets, N=169) [Alesse/Loette].
Outcomes	Principal outcome measures are: pregnancy; side effects; cycle control; discontinuation and reasons for discontinuation. Use of a daily diary card to collect data on pill intake, cycle control, side effects and concomitant medication. Spotting was defined as a light flow that did not require sanitary protection; breakthrough bleeding as a heavier flow, similar to normal menstrual flow, that required sanitary protection; withdrawal bleeding as bleeding or spotting that began during the drug-free interval and stopped by day 4 of the next cycle; intermenstrual bleeding as all other bleeding or spotting; and an amenorrheic cycle as one with no withdrawal bleeding or intermenstrual bleeding. Report describes the results of 4 cycles of exposure. In the article there is a discrepancy in the number of pregnancies. Communication with the authors revealed that one participant in the monophasic group became pregnant before the start of the study.

Chavez 1999 (*Continued*)

Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 4 cycles. 75 women in the triphasic group and 76 women in the monophasic discontinued early. The reasons for discontinuation are described. 23 women in the triphasic group and 30 women in the monophasic group did not start oral contraceptives. 12 women in the triphasic group and 9 women in the monophasic group were lost to follow up. 9 women in the triphasic group and 5 women in the monophasic were withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. Breakthrough bleeding includes both breakthrough bleeding and spotting in this review. The trial was sponsored by the manufacturer of the studied monophasic levonorgestrel/ethinylestradiol pill (Wyeth-Ayerst).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Chen 1987

Methods	Double-blind, randomized controlled trial. Randomization by a WHO random table. The use of allocation concealment and the method of blinding are not described. We were unable to reach the authors.
Participants	279 women aged 23-34 years in China. Inclusion criteria were healthy women aged 23 to 34 who have the ability to record menstrual cycle on a diary and have normal physical examination and PAP smear. Exclusion criteria were diabetes mellitus, heart, liver, kidney or nervous system disease, cancer, hypertension, use of hormones 2 months prior to the study, use of injectable contraceptives 6 months prior to the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen and 7 days of placebo tablets, N=96) [no brand name described] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg EE for 21 days and 7 days of placebo tablets, N=93) [Microgynon] versus monophasic norethindrone/ethinylestradiol (600 μg NET and 35 μg ethinylestradiol for 21 days and 7 days of placebo tablets, N=90) [Pill No 1].
Outcomes	Principal outcomes are: pregnancy; side effects; cycle control; discontinuation and reasons for discontinuation. Use of a diary card to collect data on cycle control. Bleeding pattern was analyzed according to the recommendations of Rodriguez 1976.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 cycles. 17 women in each treatment group discontinued early. The reasons for discontinuation are described. No woman was lost to follow up. One woman in the triphasic group, 2 women in the monophasic levonorgestrel group and one woman in the monophasic norethindrone group were withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. The trial was conducted by the World Health Organization.

Chen 1987 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Dieben 1984

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Communication with the author indicated an allocation sequence in balanced blocks of four and no concealment of the allocation sequence. The method of randomizing the blocks of 4 is unclear.
Participants	948 women at sites in 6 European countries. The report does not provide inclusion/exclusion criteria for the study and scarcely describes the baseline demographics. Communication with the authors provided the inclusion/exclusion criteria. Inclusion criteria were healthy, fertile women with a regular cycle and normally exposed to the risk of pregnancy. Exclusion criteria were history of thromboembolic disease, thrombophlebitis, disturbance of liver function, jaundice or a history of jaundice in pregnancy, mammary carcinoma, estrogen-dependent tumor, undiagnosed genital bleeding, sickle-cell anemia, porphyria cutanea tarda, cardiovascular disease, treatment with rifampicin, tetracyclines, phenylhydantoin and phenobarbitone, no spontaneous menstruation postpartum or postabortal, breastfeeding.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=473 for 6 cycles of whom N=38 continued for an additional 6 cycles) [no brand name described] versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 30 μg EE for 21 days, N=475 for 6 cycles of whom N=54 continued for an additional 6 cycles) [Marvelon].
Outcomes	The primary outcome measures are: pregnancy; side effects; cycle control; discontinuation rates. Use of a record to collect data on cycle control and side effects. Withdrawal bleeding was defined as bleeding which begins in the tablet-free period; spotting as scanty bleeding outside the tablet-free period that does not require any hygienic measures or at most one sanitary pad per day; and breakthrough bleeding as bleeding that is not spotting and which cannot be considered as withdrawal bleeding. Report describes outcome measures unclearly. Communication with the author revealed that there were 3 pregnancies instead of the reported 2.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 and 12 cycles. The report does not describe the number and reasons for discontinuation. Communication with the author gave information that 67 women in both groups discontinued early in the 1 to 6 cycles trial period and 2 women in both groups discontinued early in the 7 to 12 cycles trial period. Three women in the triphasic group and two women in the monophasic were withdrawn because of protocol violations in the first trial period. No women were withdrawn because of protocol violations in the second trial period. The number of women lost to follow up was not clear. Analysis not according to intent-to-treat principle. The trial was supported by the manufacturer of the studied monophasic desogestrel/ethinylestradiol pill (Organon).

Dieben 1984 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	D - Not used

Dunson 1993

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Communication with the authors indicated a computer-generated random allocation sequence and allocation concealment by use of sequentially-numbered, opaque, sealed envelopes.
Participants	1088 women aged 18 to 35 years at 5 sites in Sudan, Sri Lanka, Chile, Ecuador and Dominican Republic. Inclusion criteria were healthy women aged 18 to 35 years who were sexually active and had at least one normal menstrual period since the last pregnancy or the last use of a steroidal contraceptive. Exclusion criteria were contraindications to oral contraceptive use, termination of pregnancy less than 42 days prior to admission if not breastfeeding or termination of pregnancy less than 4 months prior to admission if breastfeeding. Switchers were included in the study. The two groups of participants differed in the complaint dizziness at admission.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen and 7 days of placebo tablets, N=543) [Triquilar] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg EE for 21 days and 7 days of placebo tablets, N=545) [Lo-Femenal].
Outcomes	Primary outcomes measures are: pregnancy; discontinuation rates and reasons for discontinuation; side effects; cycle control. Use of recall method to collect data on cycle control, side effects and reasons for discontinuation. The report does not describe the definitions of breakthrough bleeding and spotting. Outcome measures cycle control and side effects differ between the various sites.
Notes	The report does not provide an a priori hypothesis or a sample size calculation. Study duration: 12 cycles. 418 women in the triphasic group and 420 women in the monophasic group discontinued early. Reasons for discontinuation are described. The paper reported that 39% of the participants were lost to follow up but provides no breakdown of how many were in each group. The report does not mention withdrawals because of protocol violations. Analysis according to intention-to-treat principle. The trial was supported by Family Health International.

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Engebretsen 1987

Methods	Randomized controlled trial without blinding. The method of randomization and use of allocation concealment are not described. We were unable to reach the authors.
Participants	300 women aged 15 to 35 years who did not use oral contraceptives in the month prior to the study at 5 sites in Norway. The participants group had a high rate of abortus provocatus. Exclusion criteria were a history of thrombosis or thrombophlebitis, liver-disease, cancer, history of herpes gestationis, pregnancy, hypertension and oral contraceptive use in the month prior to the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=150) [Trinordiol] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg EE for 21 days, N=150) [Follimin].
Outcomes	Primary outcome measures are: pregnancy; cycle control; side effects; continuation rate and reason for discontinuation. Use of a patient diary to collect data on side effects and cycle control. The report does not describe the definitions of spotting and breakthrough bleeding. Limited information on outcome measures.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 45 women in the triphasic group and 44 women in the monophasic group discontinued early. Little information concerning the number and reasons for discontinuation. The report does not describe the number of women lost to follow up or excluded because of protocol violations. Analysis not according to intent-to-threat principle. Cycles with incorrect pill-intake were excluded from the analysis. The paper does not report information on support.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Hampton 2001

Methods	Randomized controlled trial. Randomization in a 3:3:3:2 ratio in blocks of size 11:9. The method of randomization and the use of allocation concealment are not described. NGM/EE regimens were blinded and Loestrin Fe open. Communication with the authors indicated a computer-generated random allocation sequence and allocation concealment by a centralized voice-activated randomization system. The randomization was balanced using permuted blocks and stratified by study center.
Participants	6022 women at 110 sites in the USA and Canada. One-third of the women participated in the study for 13 cycles, two-thirds of the women participated for 6 cycles. Inclusion criteria were women aged 18 to 45 years who had regular menstrual cycles, were sexually active, at risk of pregnancy and agreed to use only the study drug as contraception. Exclusion criteria were positive serum beta-hCG pregnancy test, seated systolic/diastolic blood pressure more than 140/90 mm Hg, lactation or pregnancy within 42 days of study admission, any disorders that were contraindications to steroid hormonal therapy, uncontrolled thyroid disorder, cervical dysplasia, smoking in women older than 35 years, exposure to etretinate, receipt

Hampton 2001 (*Continued*)

	of an experimental drug, device, hepatic enzyme-inducing drug, isotretinoin or tretinoin within 30 days of screening, receipt of Depo-Provera within 6 months of screening and alcohol or substance abuse within 12 months of screening. More than 60 percent of the women used oral contraceptives less than 2 months before admission.
Interventions	Triphasic norgestimate/ethinylestradiol (180-215-250 μg NGM and 25 μg ethinylestradiol in a 7/7/7 days regimen and 7 days of placebo tablets, N=1723 for 6 cycles of whom N=487 continued for an additional 6 cycles) [Ortho Tri-Cyclen Lo] versus monophasic norethindrone acetate/ethinylestradiol and ferrous fumarate (1000 μg NETA and 20 μg EE for 21 days and 7 days of 75 mg ferrous fumarate, N=1171 of whom N=318 continued for an additional 6 cycles) [Loestrin-Fe] versus 'cyclophasic' norgestimate/ethinylestradiol (250-180 μg NGM and 25 μg EE in an alternating 2-day regimen) [Cyclophasic-25] versus 'cyclophasic' norgestimate/ethinylestradiol (180-60 μg NGM and 20 μg EE in an alternating 2-day regimen) [Cyclophasic-20].
Outcomes	Primary outcomes are: pregnancy; cycle control, side effects; laboratory changes; body weight; vital signs; changes in physical examination. Use of daily diary cards to collect data on pill-intake, cycle control and side effects. Data on side effects were recorded if reported in response to a general question or observed during physical examination. Breakthrough bleeding and spotting was defined as bleeding and spotting occurring during the active pill-taking interval, excluding bleeding contiguous with menses. Breakthrough bleeding was defined as bleeding requiring sanitary protection of more than one pad or tampon on any day. The definition of amenorrhea was two consecutive cycles without any bleeding or spotting. Secondary article examined bleeding patterns by age and weight subgroups. Outcomes for 'cyclophasic' norgestimate/ethinylestradiol groups are not described.
Notes	The report does not provide an a priori hypothesis. The paper states that the sample size was determined to meet the US regulatory requirements of at least 10,000 cycles for the evaluation of the safety and efficacy of oral contraceptives with at least 200 participants evaluated for 13 cycles. Study duration: 6 and 13 cycles. In the group of participants enrolled for a trial period of 6 cycles, 258 women taking triphasic pills and 176 women taking monophasic pills discontinued early. In the group of participants enrolled for a trial period of 13 cycles, 204 women using triphasic pills and 126 women using monophasic pills discontinued early. The reasons for discontinuation are partially described. The paper reports that 6.5% of the women in the triphasic group and 5.8% of the women in the monophasic group were lost to follow up but provides no numerator. The number of women withdrawn because of protocol violations is not mentioned. The paper states that the evaluation of contraceptive efficacy was based on an intent-to-treat analysis. The evaluation of cycle control was not according to the intention-to-treat principle. Cycles in which data on dosing and bleeding was lacking and cycles with incorrect pill-intake were excluded from the analysis. The trial was sponsored by the manufacturer of the studied triphasic norgestimate/ethinylestradiol pill (Johnson & Johnson).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Ismail 1991

Methods	Randomized controlled trial without blinding. The method of randomization is not described. Allocation concealment by use of preprinted sealed envelopes opened at the time of admission. Communication with the author indicated a computer-generated random allocation sequence.
Participants	200 women in Malaysia. Inclusion criteria were healthy women aged 18 to 35 years who were sexually active, were willing to rely exclusively upon the pills as the only method of contraception and had at least one menstrual period since the last pregnancy. Exclusion criteria were contraindications to oral contraceptives, termination of pregnancy less than 42 days prior to admission and breastfeeding. Switchers were included in the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=100) versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 30 μg EE for 21 days, N=100) [Marvelon].
Outcomes	Primary outcome measures are: pregnancy; side effects; cycle control; discontinuation and reasons for discontinuation. The method of collecting the data on cycle control and side effects is unclear. The report does not describe the definitions of breakthrough bleeding and spotting.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 41 women in the triphasic group and 33 women in the monophasic group discontinued early. The reasons for discontinuation are described. 2 women in the triphasic group did not start oral contraceptives. 9 women in the triphasic group and 6 women in the monophasic group were lost to follow up. 6 women in the triphasic group and 3 women in the monophasic group were withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. The trial was supported by Family Health International.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Lachnit-Fixson 1984

Methods	Randomized controlled trial. The method of randomization, the use of allocation concealment and the use of blinding are not described. Communication with the author revealed no extra information.
Participants	555 women at sites in Austria, Germany, the Netherlands and the United Kingdom. The report does not provide inclusion/exclusion criteria for the study. Little information about baseline demographics. The paper does not report if switchers were included in the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=278) [Triquilar/Logynon] versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 30 μg EE, N=277) [Marvelon].

Lachnit-Fixson 1984 (*Continued*)

Outcomes	Primary outcome measures are: pregnancy; side effects; cycle control; continuation and reason for discontinuation. Use of a bleeding chart to collect data on cycle control. Data on side effects were recorded if reported spontaneously. The report does not describe the definitions of breakthrough bleeding and spotting.
Notes	The report does not provide an a priori hypothesis. Report states a sample size, yet the sample size calculation is unclear. Study duration: 6 cycles. Limited information on number and reasons for discontinuation. The paper describes that 15.5% of the participants discontinued early but provides no breakdown of how many were in each group. The report does not mention loss to follow up or withdrawals because of protocol violations. Unclear whether the analysis was according to intention-to-treat principle. The trial was supported by the manufacturer of the studied triphasic levonorgestrel/ethinylestradiol pill (Schering).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Percival-Smith 1990

Methods	Randomized controlled trial with blinding of the outcome assessor. The method of randomization, the use of allocation concealment and the method of blinding are not described. Communication with the author revealed no extra information.
Participants	At 4 sites in Canada, 469 women were randomized to one of the pills. However, only 391 women were admitted to the study and used the pills for at least one month. 222 women did not use OC pills at least 90 days before the study, and 247 women did use pills before the study. Inclusion criteria were healthy women aged 15 to 35 years who had a history of regular menses for two months prior to admission. Exclusion criteria were contraindications to oral contraceptives.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=119) [Triphasil] versus triphasic norethindrone/ethinylestradiol (500-750-1000 μg NET and 35 μg EE in a 7/7/7 days regimen, N=117)) [Ortho 7/7/7] versus biphasic norethindrone/ethinylestradiol (500-1000 μg NET and 35 μg ethinylestradiol in a 10/11 days regimen, N=116) [Ortho 10/11] versus monophasic norethindrone acetate/ethinyl estradiol (1500 μg NETA and 30 μg EE, N=117) [Loestrin]. In the pre-study user group, 16 participants already used Triphasil, 5 Loestrin, 8 Ortho 10/11 and 8 Ortho 7/7/7.
Outcomes	Primary outcomes measures are: side effects; cycle control; continuation, discontinuation rates and reason for discontinuation. Use of daily diary method to collect data on cycle control and side effects. Breakthrough bleeding was defined as free flow, much like menses occurring during the 21 days of active medication and requiring sanitary protection; and spotting as bleeding during the active medication, which is limited to minor staining, whether or not sanitary protection was used.

Percival-Smith 1990 (*Continued*)

Notes	The report provides an a priori hypothesis and an adequate sample size calculation. Study duration: 6 cycles. 49 women in the monophasic group, 35 women in the biphasic group, 46 women in the levonorgestrel triphasic group and 39 women in the norethindrone triphasic group discontinued early. The reasons for discontinuation are partially described. The report does not describe the number of women lost to follow up or withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. 78 women who were randomized but did not take the oral contraceptives for at least one cycle were excluded from the analysis. Breakthrough bleeding includes all intermenstrual bleeding except continued menstrual flow in this review. The trial was sponsored by the manufacturer of the monophasic norethindrone acetate/ethinylestradiol pill (Parke-Davis).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Ramos 1989

Methods	Randomized controlled trial with blinding of investigators and participants. Allocation concealment by use of numbered pharmacy packages, blinding by repackaging the pills. The method of randomization is not described. Communication with the authors revealed no extra information.
Participants	1800 women at 18 sites in the Philippines. The report does describe the inclusion and exclusion criteria for the study. Switchers were included in the study. 27% to 32% of the participating women lactated at the time of admission.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen, N=601) [Trinordiol] versus monophasic norethindrone/ethinylestradiol (400 μg NET and 35 μg EE for 21 days, N=599) [Micropil] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg EE for 21 days, N=600) [Nordette].
Outcomes	Primary outcome measures are: pregnancy; side effects; cycle control; continuation rates and reasons for discontinuation. Use of menstrual diary cards to collect data on cycle control. Data on side effects were recorded if reported spontaneously. Information on side effects was specifically asked at discontinuation or method change. Breakthrough bleeding was defined as intermenstrual bleeding that required the use of sanitary protection, and spotting as intermenstrual bleeding which required no use of pads.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 165 women in the triphasic group, 192 women in the NET monophasic group and 151 women in the LNG monophasic group discontinued early. The reasons for discontinuation are described. 13 participants in the triphasic group, 9 participants in the NET monophasic group and 16 participants in the monophasic LNG group were lost to follow up. 11 women in triphasic group, 12 women in the NET monophasic group and 8 women in the LNG monophasic group were withdrawn because of protocol vio-

Ramos 1989 (*Continued*)

	lations. Analysis not according to intention-to-treat principle. The trial was supported by United Nations Population Fund and by the manufacturers of the triphasic levonorgestrel/ethinylestradiol and monophasic levonorgestrel/ethinylestradiol pill (Wyeth-Ayerst) and monophasic norethindrone/ethinylestradiol pill (Pascual Laboratories).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Reisman 1999

Methods	Randomized controlled trial without blinding. The method of randomization is not described. Allocation concealment by sequentially-numbered, sealed envelopes opened at the time of admission. Reports notes stratification using investigational site as the stratification variable. Communication with the investigators revealed no extra information.
Participants	387 women at 11 sites in the USA. 65 women did not start the study after randomization. Inclusion criteria were healthy women aged 18 to 35 years for smokers and no upper age limit for non-smokers with regular menstrual cycles (25 to 31 days) for the 3 months before enrollment who were at risk of becoming pregnant. Exclusion criteria were the standard contraindications for oral contraceptive studies listed in product class labeling, use of oral contraceptives within the previous 3 cycles before enrollment, use of an IUD or injectable or implantable estrogens, progestins or androgens during the 6 months before enrollment and smoking of more than 15 cigarettes per day.
Interventions	Triphasic norethindrone/ethinylestradiol (500-750-1000 μg NET and 35 μg ethinylestradiol in a 7/7/7 days regimen and 7 days of placebo tablets, N=195) [Ortho-Novum 7/7/7; TriNovum] versus monophasic levonorgestrel/ethinylestradiol (100 μg LNG and 20 μg ethinylestradiol for 21 days and 7 days of placebo tablets, N=192) [Alesse;Loette].
Outcomes	Principal outcome measures are: pregnancy; side effects during treatment and after discontinuation; cycle control; discontinuation and reasons for discontinuation; metabolic outcomes. Use of diary cards to collect data on pill intake, cycle control, side effects and concomitant medication. The report describes the results of 4 cycles of exposure. Spotting was defined as a light flow that did not necessitate sanitary protection; breakthrough bleeding as a heavier flow, similar to normal menstrual flow, that did necessitate sanitary protection; withdrawal bleeding as bleeding or spotting that began during the drug-free interval and stopped by day 4 of the next cycle; intermenstrual bleeding as all other bleeding or spotting; and an amenorrheic cycle as one with neither withdrawal bleeding nor intermenstrual bleeding.
Notes	The report provides an adequate sample size calculation. Study duration: 4 cycles. 77 women in the triphasic group and 90 women in the monophasic group discontinued early. Reasons for discontinuation are described. 28 women in the triphasic group and 37 women in the monophasic group did not take the oral contraceptives. 20 women in the triphasic group and 19 women in the monophasic group were

Reisman 1999 (*Continued*)

	lost to follow up. 6 women in both groups were withdrawn because of protocol violations. Analysis not according to intention-to-treat principle. Breakthrough bleeding includes breakthrough bleeding and spotting in this meta-analysis. The trial was sponsored by the manufacturer of the monophasic levonorgestrel/ethinylestradiol pill (Wyeth-Ayerst).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Reiter 1990

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Communication with the authors indicated randomization by use of a random number table and no concealment of treatment allocation.
Participants	477 women at sites in the U.S.A. Inclusion criteria were women aged 18 years or older. Exclusion criteria were contraindications to oral contraceptive use. Little information about baseline demographics. All participants were first-time oral contraceptive users.
Interventions	Triphasic norethindrone/ethinylestradiol (500-750-1000 μg NET and 35 μg EE in a 7/7/7 days regimen and 7 days of placebo tablets) [Ortho-Novum 7/7/7] versus triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 days regimen and 7 days of placebo tablets) [Triphasil] versus monophasic norethindrone/ethinylestradiol (1000 μg norethindrone and 35 μg ethinylestradiol for 21 days and 7 days of placebo tablets) [Ortho-Novum 1/35].
Outcomes	Outcome measures are: side effects; cycle control; continuation rate; satisfaction; side effects after change of OC. Use of recall method to collect data on cycle control, side effects and satisfaction with the method. Breakthrough bleeding was defined as any spotting or bleeding between menstrual periods, and amenorrhea as the absence of spotting or bleeding during the expected time of the menstrual period. Limited information on outcome measures.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 100 women discontinued early, however the paper does not provide a breakdown of the number in each group. No information on reasons for discontinuation. Analysis not according to intent-to-treat principle. The report contains no references to other studies. The trial was conducted by Planned Parenthood Federation of America.

Risk of bias

Item	Authors' judgement	Description

Reiter 1990 (*Continued*)

Allocation concealment?	Unclear	D - Not used

Rosenberg 1999

Methods	Randomized controlled trial without blinding. Randomization in balanced blocks of 6. The method of randomization and the use of allocation concealment are not described. Communication with the author indicated a computer-generated randomization sequence and allocation concealment by sequentially numbered randomization cards with an opaque scratch-off dot.
Participants	463 women at 15 sites in the US. Inclusion criteria were age 18 to 50 years, BMI of 18 to 35, regular menstrual cycles of 21 to 38 days. Exclusion criteria were contraindications to oral contraceptive use, age more than 35 years and smoking more than 15 cigarettes per day, more than 2 alcoholic drinks per day, breastfeeding, fewer than 3 regular cycles after delivery or fewer than 2 regular cycles after an abortion, use of injectable or implant contraceptives within 6 months before enrollment or considered to be poor candidates for follow up or reliability. Analysis of 2 groups: 308 switchers (participants who have used OC in the 2 months before the study); 155 starters. 34 participants were using 20 μg EE preparations and 262 were using 30 or 35 μg EE preparations at study entry. Low percentage of smokers.
Interventions	Triphasic norgestimate/ethinylestradiol (180-215-250 μg NGM and 35 μg EE in a 7/7/7 days regimen, N=155) [Tri-Cyclen] versus monophasic levonorgestrel/ethinylestradiol (100 μg LNG and 20 μg ethinylestradiol for 21 days and 7 hormone-free days, N=154) [Alesse] versus monophasic desogestrel/ethinylestradiol (150 μg DSG and 20 μg EE for the first 21 days, then 2 hormone-free days, and 10 μg EE for the last 5 days, N=154) [Mircette].
Outcomes	Primary outcomes measures are: efficacy; cycle control; side effects; and continuation rates. Use of a daily diary to collect data on pill-intake, side effects and cycle control. Cycle control was assessed by an index that considered duration and severity of intermenstrual bleeding. The report does not describe the definitions of breakthrough bleeding and spotting. Limited information on outcome measures.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 cycles. The paper describes continuation rates; however, the number of women who continue are not described. Communication with the author indicated that 25 women in the triphasic group, 26 women in the levonorgestrel monophasic group and 24 women in the desogestrel monophasic group discontinued early. Reasons for discontinuation are not described. It is unclear whether the analysis was according to intention-to-treat principle. The trial was supported by the manufacturer of the monophasic desogestrel/ethinylestradiol pill (Organon).

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Rowan 1999

Methods	Double-blind, randomized controlled trial. The method of randomization, the use of allocation concealment, and the method of blinding are not described. Communication with the author indicated randomization in a 3:2 ratio in blocks of five, allocation concealment by numbered pharmacy packages and double-blinding by identical pills and packages. The method of randomizing the blocks of five is unclear.
Participants	1277 women at 8 sites. Inclusion criteria were women aged 18 to 35 years with a history of regular menstrual cycles (28 $\pm$ 3 days) for 2 consecutive cycles immediately before study entry. Exclusion criteria were contraindications to oral contraceptives and use of oral contraceptives within 2 months before enrollment. Limited information on baseline demographics.
Interventions	'Estrophasic' norethindrone acetate/ethinylestradiol (1000 μg NETA and 20-30-35 μg EE in a 5/7/9 days regimen, N=769) [Estrostep] versus monophasic norethindrone acetate/ethinylestradiol (1500 μg NETA and 30 μg EE for 21 days, N=508) [Loestrin 1.5/30].
Outcomes	Primary outcome measures are: efficacy; cycle control; side effects; discontinuation due to side effects. Use of special diaries to collect data on cycle control, side effects, pill-intake and concomitant medication. Breakthrough bleeding was defined as vaginal bleeding during the medication-taking period that was not a continuation of menstrual flow and that necessitated pad or tampon protection.
Notes	Report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 cycles. Number of and reasons for discontinuation are not described except discontinuation due to side effects. Unclear whether the analysis was according to intention-to-treat principle. Random assignment in a 2:1 ratio. However, 769 women received the 'estrophasic' preparation and 508 the monophasic preparation. Communication with the author indicated a 3:2 allocation ratio. We only included study 1 in this review. Study number 2 compares the 'estrophasic' combination with a triphasic combination in terms of metabolic outcomes. The trial was sponsored by the manufacturer of the studied monophasic and estrophasic norethindrone acetate/ethinylestradiol pills (Parke-Davis).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Saxena 1992

Methods	Randomized controlled trial. The method of randomization, the use of allocation concealment or the use of blinding are not described. Communication with the authors indicated a computer-generated allocation sequence, allocation concealment by sequentially-numbered sealed envelopes and no blinding.
Participants	721 women in reproductive age at 11 sites in India. Inclusion criteria were healthy women in the reproductive age exposed to the risk of pregnancy. Exclusion criteria were contraindications for oral contraceptive use. The paper does not report if switchers were included.

Saxena 1992 (*Continued*)

Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 regimen and 7 days of placebo tablets, N=383) [Triquilar ED] versus monophasic levonorgestrel/ethinylestradiol (150 μg levonorgestrel and 30 μg ethinylestradiol for 21 days and 7 days of placebo tablets, N=338) [MALA-D]. Report does not describe the composition of the monophasic pill. Communication with the author indicated data described above.
Outcomes	Principal outcome measures are: pregnancy; side effects; cycle control; continuation; discontinuation and reasons for discontinuation; metabolic outcomes. Use of recall method to collect data on pill intake errors, cycle control and side effects. Bleeding pattern was analyzed according to the recommendations by Rodriguez 1976.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 12 cycles. 256 women in the triphasic group and 203 women in the monophasic group discontinued early. The report describes number and reasons for discontinuation. 16 women in the triphasic group and 14 women in the monophasic group were lost to follow up. 9 women in the triphasic group and 14 women in the monophasic group were withdrawn because of protocol violations. Analysis not according to intention-to-treat. The trial was conducted by the Indian Council of Medical Research.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Sulak 1999

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Report notes stratification using postpartum status as the stratification variable. We were unable to reach the authors.
Participants	373 women at 10 sites. Inclusion criteria were healthy women aged 18 to 50 years. Exclusion criteria were disorders considered to be contraindications for steroid hormonal therapy and use of oral contraceptives within 60 days of enrollment. Analysis of 2 groups: safety population (all participants who received at least one dose of study medication); intent-to-treat population (all participants who received at least one dose of study medication and who had at least one cycle control measurement). The safety population consisted of 335 women and the intent-to-treat population of 328 women. Participants used a nonsteroidal contraceptive method for the first 7 days of cycle 1.
Interventions	Triphasic norgestimate/ethinylestradiol (180-215-250 μg NGM and 35 μg EE in a 7/7/7 days regimen and 7 days of placebo tablets, N=187) [Ortho Tri-Cyclen] versus monophasic norethindrone acetate/ethinylestradiol (1000 μg NETA and 20 μg ethinylestradiol for 21 days and 7 days of placebo tablets, N=186) [Loestrin 1/20].

Sulak 1999 (*Continued*)

Outcomes	Primary outcomes measures are: efficacy; side effects; cycle control; continuation and reasons for discontinuation; pill intake errors. The method to collect data is not described. The report does not describe the definitions of breakthrough bleeding and spotting.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 cycles. 72 women in the triphasic group and 70 women in the monophasic group discontinued early. Limited information on reasons for discontinuation. 16 women in the triphasic group and 22 women in the monophasic group did not start oral contraceptives. The report does not describe the number of women lost to follow up or excluded because of protocol violations. The paper indicated an analysis based on the intent-to-treat principle but participants not starting oral contraceptives and invalid cycles were excluded from analysis. Errors in pill intake, a cycle length longer than 31 days, errors in non-active pill intake and errors in recording cycle information all create invalid cycles. The trial was sponsored by the manufacturer of the triphasic norgestimate/ethinylestradiol pill (Ortho-McNeil Pharmaceutical).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Zador 1979

Methods	Randomized controlled trial without blinding. The method of randomization and the use of allocation concealment are not described. Communication with the author revealed no extra information.
Participants	489 women at sites in Sweden, Great Britain and Germany. Inclusion criteria were that women had to meet the requirements for the prescription of oral contraceptives in accordance with established medical practice. Limited information about baseline demographics. The paper does not report if switchers were included in the study.
Interventions	Triphasic levonorgestrel/ethinylestradiol (50-75-125 μg LNG and 30-40-30 μg EE in a 6/5/10 regimen, N=254) [SH B 264 AB] versus monophasic levonorgestrel/ethinylestradiol (150 μg LNG and 30 μg EE for 21 days, N=235) [Neovletta].
Outcomes	Principal outcome measures are: pregnancy; side effects; cycle control; discontinuation and reasons for discontinuation. Use of a chart for collecting data on side effects and cycle control. Breakthrough bleeding was defined as intermenstrual bleeding that required the use of sanitary protection and spotting as all other cases including slight brownish discharge.
Notes	The report does not provide an a priori hypothesis or a sample size or power calculation. Study duration: 6 cycles. 36 women in both groups discontinued early. Limited information on number and reasons for discontinuation. The report does not mention the number of women lost to follow up or excluded because of protocol violations. Whether the analysis was based on the intention-to-treat principle is unclear. The trial was supported by the manufacturer of the studied monophasic and triphasic levonorgestrel/ethinylestradiol pills (Schering).

Zador 1979 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

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

Bancroft 1987	The study examines mood and sexuality.
Christie 1989	The report does not mention how participants were assigned to groups. We attempted without success to reach the author.
Dik 1984	The report does not mention how participants were assigned to groups. We were unable to contact the authors.
Dubnitskaia 1988	Although described as a randomized controlled trial we learned from the author that the study is a matched cohort study.
Grace 1994	Communication with the author indicated no randomization of the allocation sequence.
Kuhl 1985	Insufficient data for analysis of spotting and breakthrough bleeding. Emphasis was on hormonal and metabolic parameters.
Matsumoto 1988	Report does not mention how participants were assigned to groups. We attempted without success to reach the author.
Otolorin 1989	The report describes allocation as systematical. We were unable to contact the author.
Perrone 1987	Report does not mention how participants were assigned to groups. We attempted without success to reach the author.
Rubio-Lotvin 1992	The report does not mention how participants were assigned to groups. We could not reach the authors.

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

Bayer 2008

Trial name or title	Cycle Control and Safety of E2-DRSP
Methods	Randomized, double blind, multicenter
Participants	600 healthy women, 18 to 35 years
Interventions	6 different regimens of drospirenone and ethinyl estradiol (including monophasic and triphasic) over 7 cycles (details not provided)
Outcomes	include bleeding patterns and cycle control
Starting date	March 2008
Contact information	Bayer Study Director (no more information provided)
Notes	estimated completion May 2009

DATA AND ANALYSES

Comparison 1. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	2	678	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.10, 3.91]
2 Pregnancy per woman within 12 cycles	5	4145	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.25, 7.22]
3 Proportion of cycles with spotting within 3 cycles	1	2367	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.41, 0.68]
4 Proportion of cycles with breakthrough bleeding within 3 cycles	1	2367	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.32, 0.72]
5 Proportion of cycles with spotting within 6 cycles	2	7290	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.48, 0.67]
6 Proportion of cycles with breakthrough bleeding within 6 cycles	2	7290	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.50, 0.80]
7 Proportion of cycles with spotting within 12 cycles	1	6472	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.49, 0.72]
8 Proportion of cycles with breakthrough bleeding within 12 cycles	1	6472	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.45, 0.77]
9 Proportion of women with intermenstrual bleeding within 12 cycles	1	979	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.53, 1.31]
10 Proportion of women with spotting at cycle 6	1	1032	Odds Ratio (M-H, Random, 95% CI)	0.24 [0.03, 2.17]
11 Proportion of women with breakthrough bleeding at cycle 6	1	1032	Odds Ratio (M-H, Random, 95% CI)	2.45 [0.47, 12.67]
12 Proportion of women with spotting at cycle 12	1	896	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.06, 16.62]
13 Proportion of women with breakthrough bleeding at cycle 12	1	896	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.05, 5.72]
14 Proportion of women with intermenstrual bleeding within 12 cycles	1	979	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.53, 1.31]
15 Proportion of cycles with amenorrhea within 6 cycles	1	2777	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.28, 1.14]
16 Proportion of cycles with amenorrhea within 12 cycles	1	6472	Odds Ratio (M-H, Random, 95% CI)	0.27 [0.17, 0.45]
17 Total discontinuation within 6 cycles	3	1513	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.79, 1.39]

18 Discontinuation due to medical reasons within 6 cycles	3	1513	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.81, 1.61]
19 Discontinuation due to cycle disturbances within 6 cycles	1	189	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.13, 7.02]
20 Total discontinuation within 12 cycles	4	3310	Odds Ratio (M-H, Random, 95% CI)	1.13 [0.97, 1.31]
21 Discontinuation due to medical reasons within 12 cycles	3	3010	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.71, 1.76]
22 Discontinuation due to cycle disturbances within 12 cycles	3	2109	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.56, 2.21]
23 Discontinuation due to intermenstrual bleeding within 12 cycles	1	1201	Odds Ratio (M-H, Random, 95% CI)	1.40 [0.44, 4.44]
24 Proportion of women with amenorrhea within 12 cycles	1	979	Odds Ratio (M-H, Random, 95% CI)	1.47 [0.24, 8.83]

Comparison 2. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 600 μg/ EE 35 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	186	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.13, 6.79]
2 Total discontinuation within 6 cycles	1	186	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.44, 1.94]
3 Discontinuation due to medical reasons within 6 cycles	1	186	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.35, 2.46]
4 Discontinuation due to cycle disturbances within 6 cycles	1	186	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.10, 3.78]

Comparison 3. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 12 cycles	1	1200	Odds Ratio (M-H, Random, 95% CI)	Not estimable
2 Proportion of women with spotting at cycle 6	1	1018	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.01, 0.94]
3 Proportion of women with breakthrough bleeding at cycle 6	1	1018	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.11, 0.86]
4 Proportion of women with spotting at cycle 12	1	851	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.06, 14.98]

5 Proportion of women with breakthrough bleeding at cycle 12	1	851	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.04, 5.16]
6 Total discontinuation within 12 cycles	1	1200	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.63, 1.03]
7 Discontinuation due to medical reasons within 12 cycles	1	1200	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.55, 1.10]
8 Discontinuation due to intermenstrual bleeding within 12 cycles	1	1200	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.23, 1.47]

Comparison 4. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	555	Odds Ratio (M-H, Random, 95% CI)	3.00 [0.12, 73.96]
2 Pregnancy per woman within 12 cycles	2	1146	Odds Ratio (M-H, Random, 95% CI)	7.22 [0.88, 59.00]
3 Proportion of cycles with spotting within 3 cycles	1	2763	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.88, 1.41]
4 Proportion of cycles with breakthrough bleeding within 3 cycles	1	2763	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.87, 1.56]
5 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles	1	2763	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.31, 1.61]
6 Proportion of cycles with spotting within 6 cycles	2	8295	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.19, 2.11]
7 Proportion of cycles with breakthrough bleeding within 6 cycles	2	8295	Odds Ratio (M-H, Random, 95% CI)	0.70 [0.26, 1.91]
8 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles	2	8295	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.29, 0.86]
9 Proportion of cycles with spotting within 12 cycles	1	5478	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.99, 1.44]
10 Proportion of cycles with breakthrough bleeding within 12 cycles	1	5478	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.88, 1.35]
11 Proportion of cycles with spotting and breakthrough bleeding within 12 cycles	1	5478	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.33, 1.22]
12 Proportion of women with staining/spotting within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	1.55 [0.42, 5.67]

13 Proportion of women with moderate flow intermenstrual bleeding within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	2.61 [0.49, 13.77]
14 Proportion of women with spotting at cycle 3	1	894	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.74, 1.90]
15 Proportion of women with breakthrough bleeding at cycle 3	1	894	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.66, 1.82]
16 Proportion of women with spotting and breakthrough bleeding at cycle 3	1	894	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.04, 5.50]
17 Proportion of women with spotting at cycle 6	1	797	Odds Ratio (M-H, Random, 95% CI)	1.33 [0.68, 2.58]
18 Proportion of women with breakthrough bleeding at cycle 6	1	797	Odds Ratio (M-H, Random, 95% CI)	1.53 [0.80, 2.92]
19 Proportion of women with spotting and breakthrough bleeding at cycle 6	1	797	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.04, 5.51]
20 Proportion of women with spotting at cycle 12	1	10	Odds Ratio (M-H, Random, 95% CI)	Not estimable
21 Proportion of women with breakthrough bleeding at cycle 12	1	10	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.03, 33.32]
22 Proportion of women with spotting and breakthrough bleeding at cycle 12	1	10	Odds Ratio (M-H, Random, 95% CI)	Not estimable
23 Proportion of cycles with amenorrhea within 3 cycles	1	2763	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.82, 1.39]
24 Proportion of cycles with amenorrhea within 6 cycles	2	8295	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.11, 2.59]
25 Proportion of cycles with amenorrhea within 12 cycles	1	5478	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.86, 1.28]
26 Proportion of women with amenorrhea within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	1.53 [0.25, 9.37]
27 Proportion of women with amenorrhea at cycle 3	1	894	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.63, 1.57]
28 Proportion of women with amenorrhea at cycle 6	1	797	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.76, 2.43]
29 Proportion of women with amenorrhea at cycle 12	1	10	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.03, 33.32]
30 Total discontinuation within 3 cycles	1	948	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.50, 1.28]
31 Discontinuation due to medical reasons within 3 cycles	1	948	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.42, 1.19]
32 Discontinuation due to cycle disturbances within 3 cycles	1	948	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.33, 1.61]
33 Total discontinuation within 6 cycles	2	1503	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.75, 1.33]
34 Discontinuation due to medical reasons within 6 cycles	2	1503	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.36, 1.43]

35 Discontinuation due to cycle disturbances within 6 cycles	1	948	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.58, 1.92]
36 Total discontinuation within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	1.44 [0.81, 2.57]
37 Discontinuation due to medical reasons within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	1.45 [0.44, 4.72]
38 Discontinuation due to cycle disturbances within 12 cycles	1	197	Odds Ratio (M-H, Random, 95% CI)	7.29 [0.37, 143.08]

Comparison 5. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NETA 1500 μg/ EE 30 g

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of cycles with intermenstrual bleeding within 6 cycles	1	987	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.56, 1.01]
2 Proportion of cycles with amenorrhea within 6 cycles	1	987	Odds Ratio (M-H, Random, 95% CI)	0.02 [0.00, 0.18]
3 Total discontinuation within 6 cycles	1	236	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.52, 1.47]

Comparison 6. Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NETA 1500 μg/ EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of cycles with intermenstrual bleeding within 6 cycles	1	1005	Odds Ratio (M-H, Random, 95% CI)	1.37 [1.05, 1.80]
2 Proportion of cycles with amenorrhea within 6 cycles	1	1005	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.35, 1.01]
3 Total discontinuation within 6 cycles	1	234	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.41, 1.18]

Comparison 7. Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 1000 μg/ EE 35 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of women with intermenstrual bleeding within 12 cycles	1	260	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.29, 1.18]

2 Proportion of women with amenorrhea within 12 cycles	1	260	Odds Ratio (M-H, Random, 95% CI)	0.03 [0.00, 0.43]

Comparison 8. Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NET 1000 μg/ EE 35 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of women with intermenstrual bleeding within 12 cycles	1	245	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.55, 2.02]
2 Proportion of women with amenorrhea within 12 cycles	1	245	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.08, 0.76]

Comparison 9. Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 4 cycles	2	729	Odds Ratio (M-H, Random, 95% CI)	1.97 [0.36, 10.83]
2 Proportion of cycles with spotting within 3 cycles	1	756	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.70, 1.67]
3 Proportion of cycles with breakthrough bleeding within 3 cycles	1	756	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.50, 1.78]
4 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles	1	756	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.77, 1.57]
5 Proportion of cycles with intermenstrual bleeding within 3 cycles	2	1367	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.96, 1.54]
6 Proportion of women with spotting at cycle 3	1	232	Odds Ratio (M-H, Random, 95% CI)	2.03 [0.74, 5.54]
7 Proportion of women with breakthrough bleeding at cycle 3	1	232	Odds Ratio (M-H, Random, 95% CI)	1.52 [0.53, 4.33]
8 Proportion of women with spotting and breakthrough bleeding at cycle 3	1	232	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.39, 1.38]
9 Proportion of women with intermenstrual bleeding at cycle 3	2	420	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.79, 1.75]
10 Proportion of cycles with amenorrhea within 3 cycles	2	1367	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.51, 1.48]

11 Proportion of women with amenorrhea at cycle 3	2	330	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.07, 1.92]
12 Total discontinuation within 4 cycles	2	729	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.62, 1.11]
13 Discontinuation due to medical reasons within 4 cycles	2	729	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.31, 1.47]

Comparison 10. Estrophasic NETA 1000 μg/ EE 20-30-35 μg versus monophasic NETA 1500 μg/ EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Discontinuation due to adverse events within 6 cycles	1	1277	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.49, 1.60]

Comparison 11. Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	480	Odds Ratio (M-H, Random, 95% CI)	2.77 [0.11, 68.38]
2 Pregnancy per woman within 12 cycles	1	168	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.06, 16.26]
3 Proportion of cycles with spotting within 6 cycles	1	2515	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.72, 1.28]
4 Proportion of cycles with breakthrough bleeding within 6 cycles	1	2515	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.48, 1.43]
5 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles	1	2515	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.33, 0.73]
6 Proportion of women with spotting at cycle 3	2	579	Odds Ratio (M-H, Random, 95% CI)	1.13 [0.54, 2.33]
7 Proportion of women with breakthrough bleeding at cycle 3	1	160	Odds Ratio (M-H, Random, 95% CI)	2.85 [0.73, 11.17]
8 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 3	1	419	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.33, 1.60]
9 Proportion of women with spotting at cycle 6	2	510	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.50, 2.12]
10 Proportion of women with breakthrough bleeding at cycle 6	1	158	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.36, 2.81]

11 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 6	1	352	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.20, 1.65]
12 Proportion of women with spotting at cycle 12	1	144	Odds Ratio (M-H, Random, 95% CI)	1.5 [0.40, 5.56]
13 Proportion of women with breakthrough bleeding at cycle 12	1	144	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.27, 3.51]
14 Proportion of cycles with amenorrhea within 6 cycles	1	2403	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.17, 2.14]
15 Proportion of cycles with amenorrhea within 12 cycles	1	2515	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.20, 2.01]
16 Proportion of women with amenorrhea at cycle 3	2	579	Odds Ratio (M-H, Random, 95% CI)	1.30 [0.15, 11.52]
17 Proportion of women with amenorrhea at cycle 6	2	510	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.04, 5.56]
18 Proportion of women with amenorrhea at cycle 12	2	160	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.03, 3.10]
19 Total discontinuation within 6 cycles	2	648	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.59, 1.35]
20 Discontinuation due to medical reasons within 6 cycles	1	480	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.49, 1.54]
21 Discontinuation due to cycle disturbances within 6 cycles	1	480	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.23, 2.53]
22 Total discontinuation within 12 cycles	1	168	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.35, 1.96]
23 Discontinuation due to medical reasons within 12 cycles	1	168	Odds Ratio (M-H, Random, 95% CI)	2.02 [0.18, 22.76]

Comparison 12. Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 20 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 13 cycles	1	1613	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.14, 7.09]
2 Total discontinuation within 13 cycles	1	1613	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.88, 1.36]
3 Discontinuation due to medical reasons within 13 cycles	1	1613	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.60, 1.21]

Comparison 13. Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic GTD 75 μg/ EE 30 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 13 cycles	1	1614	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.11, 3.99]
2 Total discontinuation within 13 cycles	1	1614	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.75, 1.16]
3 Discontinuation due to medical reasons within 13 cycles	1	1614	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.77, 1.60]

Comparison 14. Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	373	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.14, 7.14]
2 Proportion of women with spotting or breakthrough bleeding at cycle 6	1	231	Odds Ratio (M-H, Random, 95% CI)	0.26 [0.14, 0.51]
3 Proportion of women with amenorrhea at cycle 6	1	231	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.06, 0.45]
4 Total discontinuation within 6 cycles	1	373	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.68, 1.58]
5 Discontinuation due to adverse events within 6 cycles	1	373	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.50, 1.98]

Comparison 15. Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	3.02 [0.31, 29.35]
2 Proportion of cycles with spotting within 6 cycles	1	1650	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.42, 0.81]
3 Proportion of cycles with breakthrough bleeding within 6 cycles	1	1650	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.66, 2.04]
4 Proportion of cycles with amenorrhea within 6 cycles	1	1650	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.34, 0.96]
5 Total discontinuation within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.52, 1.73]

6 Discontinuations due to adverse events within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.21, 3.00]

Comparison 16. Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	7.09 [0.36, 138.46]
2 Proportion of cycles with spotting within 6 cycles	1	1679	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.91]
3 Proportion of cycles with breakthrough bleeding within 6 cycles	1	1679	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.57, 1.68]
4 Proportion of cycles with amenorrhea within 6 cycles	1	1679	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.23, 0.60]
5 Total discontinuation within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.57, 1.92]
6 Discontinuations due to adverse events within 6 cycles	1	309	Odds Ratio (M-H, Random, 95% CI)	1.33 [0.29, 6.06]

Comparison 17. Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy per woman within 13 cycles	1	2814	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.38, 1.34]
2 Proportion of cycles with breakthrough bleeding within 3 cycles	1	7272	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.47]
3 Proportion of cycles with breakthrough bleeding/ spotting within 3 cycles	1	7272	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.45]
4 Proportion of cycles with breakthrough bleeding within 6 cycles	1	13692	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.40, 0.50]
5 Proportion of cycles with breakthrough bleeding/ spotting within 6 cycles	1	13692	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.40, 0.48]
6 Proportion of cycles with breakthrough bleeding within 12 cycles	1	16519	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.41, 0.50]

7 Proportion of cycles with breakthrough bleeding/ spotting within 12 cycles	1	16519	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.41, 0.49]
8 Proportion of women with breakthrough bleeding at cycle 3	1	2330	Odds Ratio (M-H, Random, 95% CI)	0.36 [0.27, 0.49]
9 Proportion of women with breakthrough bleeding/ spotting at cycle 3	1	2330	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.35, 0.55]
10 Proportion of women with breakthrough bleeding at cycle 6	1	2118	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.31, 0.57]
11 Proportion of women with breakthrough bleeding/ spotting at cycle 6	1	2118	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.32, 0.52]
12 Proportion of women with breakthrough bleeding at cycle 12	1	444	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.24, 1.16]
13 Proportion of women with breakthrough bleeding/ spotting at cycle 12	1	444	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.27, 0.86]
14 Proportion of cycles with amenorrhea within 13 cycles	1	16957	Odds Ratio (M-H, Random, 95% CI)	0.05 [0.04, 0.07]
15 Total discontinuation within 6 cycles	1	2089	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.82, 1.26]
16 Total discontinuation within 13 cycles	1	805	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.82, 1.46]

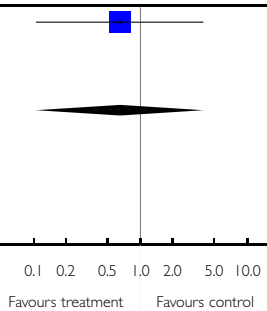
Analysis 1.1. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 1 Pregnancy per woman within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	2/96	3/93		100.0 %	0.64 [0.10, 3.91]
Zador 1979	0/254	0/235		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**350**	**328**		**100.0 %**	**0.64 [0.10, 3.91]**
Total events: 2 (Triphasic), 3 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 0.49 (P = 0.63)					



Analysis 1.2. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 2 Pregnancy per woman within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 2 Pregnancy per woman within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	1/417	0/418		27.3 %	3.01 [0.12, 74.21]
Dunson 1993	1/543	1/545		36.4 %	1.00 [0.06, 16.09]
Engebretsen 1987	1/150	1/150		36.3 %	1.00 [0.06, 16.14]
Ramos 1989	0/601	0/600		0.0 %	0.0 [0.0, 0.0]
Saxena 1992	0/383	0/338		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**2094**	**2051**		**100.0 %**	**1.35 [0.25, 7.22]**

Total events: 3 (Triphasic), 2 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.33$, df = 2 (P = 0.85); $I^2 = 0.0\%$

Test for overall effect: Z = 0.35 (P = 0.72)

Analysis 1.3. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 3 Proportion of cycles with spotting within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 3 Proportion of cycles with spotting within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	106/1180	188/1187		100.0 %	0.52 [0.41, 0.68]
Total (95% CI)	**1180**	**1187**		**100.0 %**	**0.52 [0.41, 0.68]**

Total events: 106 (Triphasic), 188 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 5.00 (P < 0.00001)

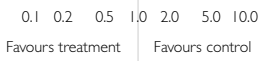
Analysis 1.4. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 4 Proportion of cycles with breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 4 Proportion of cycles with breakthrough bleeding within 3 cycles

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	37/1180	75/1187		100.0 %	0.48 [0.32, 0.72]
Total (95% CI)	**1180**	**1187**		**100.0 %**	**0.48 [0.32, 0.72]**
Total events: 37 (Treatment), 75 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.58 (P = 0.00035)					



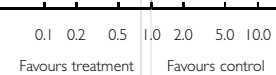
Analysis 1.5. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 5 Proportion of cycles with spotting within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 5 Proportion of cycles with spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	159/2242	268/2271		63.2 %	0.57 [0.46, 0.70]
Zador 1979	95/1440	147/1337		36.8 %	0.57 [0.44, 0.75]
Total (95% CI)	**3682**	**3608**		**100.0 %**	**0.57 [0.48, 0.67]**
Total events: 254 (Triphasic), 415 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.00, df = 1 (P = 0.99); I^2 =0.0%					
Test for overall effect: Z = 6.72 (P < 0.00001)					



Analysis 1.6. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 6 Proportion of cycles with breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 6 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	75/2242	127/2271		62.8 %	0.58 [0.44, 0.78]
Zador 1979	50/1440	63/1337		37.2 %	0.73 [0.50, 1.06]
Total (95% CI)	**3682**	**3608**		**100.0 %**	**0.63 [0.50, 0.80]**
Total events: 125 (Triphasic), 190 (Monophasic)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.81$, df = 1 (P = 0.37); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.87 (P = 0.00011)					

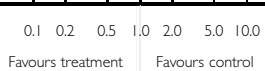
Analysis 1.7. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 7 Proportion of cycles with spotting within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 7 Proportion of cycles with spotting within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	192/3197	318/3275		100.0 %	0.59 [0.49, 0.72]
Total (95% CI)	**3197**	**3275**		**100.0 %**	**0.59 [0.49, 0.72]**
Total events: 192 (Triphasic), 318 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 5.48 (P < 0.00001)					



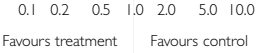
Analysis 1.8. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 8 Proportion of cycles with breakthrough bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 8 Proportion of cycles with breakthrough bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	86/3197	147/3275		100.0 %	0.59 [0.45, 0.77]
Total (95% CI)	**3197**	**3275**		**100.0 %**	**0.59 [0.45, 0.77]**
Total events: 86 (Triphasic), 147 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.84 (P = 0.00012)					



Analysis 1.9. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 9 Proportion of women with intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 9 Proportion of women with intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	38/495	44/484		100.0 %	0.83 [0.53, 1.31]
Total (95% CI)	**495**	**484**		**100.0 %**	**0.83 [0.53, 1.31]**
Total events: 38 (Triphasic), 44 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.80 (P = 0.43)					

Analysis 1.10. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 10 Proportion of women with spotting at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 10 Proportion of women with spotting at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	1/523	4/509		100.0 %	0.24 [0.03, 2.17]
Total (95% CI)	**523**	**509**		**100.0 %**	**0.24 [0.03, 2.17]**
Total events: 1 (Triphasic), 4 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.27 (P = 0.20)					

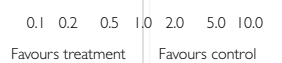
Analysis 1.11. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 11 Proportion of women with breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 11 Proportion of women with breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	5/523	2/509		100.0 %	2.45 [0.47, 12.67]
Total (95% CI)	**523**	**509**		**100.0 %**	**2.45 [0.47, 12.67]**
Total events: 5 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.07 (P = 0.29)					



Analysis 1.12. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 12 Proportion of women with spotting at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 12 Proportion of women with spotting at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	1/440	1/456		100.0 %	1.04 [0.06, 16.62]
Total (95% CI)	**440**	**456**		**100.0 %**	**1.04 [0.06, 16.62]**

Total events: 1 (Triphasic), 1 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.03 (P = 0.98)

Analysis 1.13. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 13 Proportion of women with breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

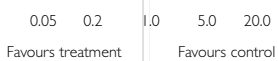
Outcome: 13 Proportion of women with breakthrough bleeding at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	1/440	2/456		100.0 %	0.52 [0.05, 5.72]
Total (95% CI)	**440**	**456**		**100.0 %**	**0.52 [0.05, 5.72]**

Total events: 1 (Triphasic), 2 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.54 (P = 0.59)



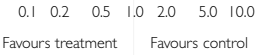
Analysis 1.14. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 14 Proportion of women with intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 14 Proportion of women with intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	38/495	44/484		100.0 %	0.83 [0.53, 1.31]
Total (95% CI)	**495**	**484**		**100.0 %**	**0.83 [0.53, 1.31]**
Total events: 38 (Triphasic), 44 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.80 (P = 0.43)					



Analysis 1.15. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 15 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 15 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Zador 1979	13/1440	21/1337		100.0 %	0.57 [0.28, 1.14]
Total (95% CI)	**1440**	**1337**		**100.0 %**	**0.57 [0.28, 1.14]**
Total events: 13 (Triphasic), 21 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.58 (P = 0.11)					

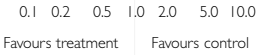
Analysis 1.16. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 16 Proportion of cycles with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 16 Proportion of cycles with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	20/3197	74/3275		100.0 %	0.27 [0.17, 0.45]
Total (95% CI)	**3197**	**3275**		**100.0 %**	**0.27 [0.17, 0.45]**
Total events: 20 (Triphasic), 74 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 5.14 (P < 0.00001)					



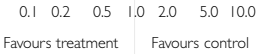
Analysis 1.17. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 17 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 17 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	67/417	59/418		54.4 %	1.16 [0.80, 1.70]
Chen 1987	17/96	17/93		14.2 %	0.96 [0.46, 2.02]
Zador 1979	36/254	36/235		31.3 %	0.91 [0.55, 1.51]
Total (95% CI)	**767**	**746**		**100.0 %**	**1.05 [0.79, 1.39]**
Total events: 120 (Triphasic), 112 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.64, df = 2 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 0.34 (P = 0.73)					



Analysis 1.18. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 18 Discontinuation due to medical reasons within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

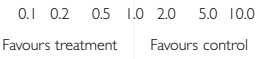
Outcome: 18 Discontinuation due to medical reasons within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Carlborg 1983	47/417	36/418		56.1 %	1.35 [0.85, 2.13]
Chen 1987	9/96	11/93		13.5 %	0.77 [0.30, 1.96]
Zador 1979	23/254	21/235		30.4 %	1.01 [0.55, 1.89]
Total (95% CI)	**767**	**746**		**100.0 %**	**1.15 [0.81, 1.61]**

Total events: 79 (Triphasic), 68 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.33$, df = 2 (P = 0.51); $I^2 = 0.0\%$

Test for overall effect: Z = 0.78 (P = 0.43)



Analysis 1.19. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 19 Discontinuation due to cycle disturbances within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 19 Discontinuation due to cycle disturbances within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	2/96	2/93		100.0 %	0.97 [0.13, 7.02]
Total (95% CI)	**96**	**93**		**100.0 %**	**0.97 [0.13, 7.02]**

Total events: 2 (Triphasic), 2 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.03 (P = 0.97)

Analysis 1.20. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 20 Total discontinuation within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

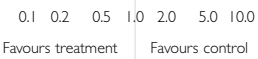
Outcome: 20 Total discontinuation within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	418/543	420/545		29.5 %	1.00 [0.75, 1.32]
Engebretsen 1987	45/150	44/150		9.6 %	1.03 [0.63, 1.69]
Ramos 1989	165/601	151/600		35.6 %	1.13 [0.87, 1.46]
Saxena 1992	256/383	203/338		25.4 %	1.34 [0.99, 1.82]
Total (95% CI)	**1677**	**1633**		**100.0 %**	**1.13 [0.97, 1.31]**

Total events: 884 (Triphasic), 818 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.11$, df = 3 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 1.51 (P = 0.13)



Analysis 1.21. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 21 Discontinuation due to medical reasons within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

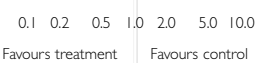
Outcome: 21 Discontinuation due to medical reasons within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	32/543	42/545		33.6 %	0.75 [0.47, 1.21]
Ramos 1989	66/601	61/600		39.4 %	1.09 [0.75, 1.58]
Saxena 1992	33/383	16/338		27.0 %	1.90 [1.02, 3.51]
Total (95% CI)	**1527**	**1483**		**100.0 %**	**1.12 [0.71, 1.76]**

Total events: 131 (Triphasic), 119 (Monophasic)

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 5.47$, df = 2 (P = 0.06); $I^2 = 63\%$

Test for overall effect: Z = 0.47 (P = 0.64)



Analysis 1.22. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 22 Discontinuation due to cycle disturbances within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 22 Discontinuation due to cycle disturbances within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	1/543	1/545		6.2 %	1.00 [0.06, 16.09]
Engebretsen 1987	6/150	8/150		40.5 %	0.74 [0.25, 2.19]
Saxena 1992	12/383	7/338		53.3 %	1.53 [0.60, 3.93]
Total (95% CI)	**1076**	**1033**		**100.0 %**	**1.11 [0.56, 2.21]**

Total events: 19 (Triphasic), 16 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.99$, df = 2 (P = 0.61); $I^2 = 0.0\%$

Test for overall effect: Z = 0.30 (P = 0.77)

Analysis 1.23. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 23 Discontinuation due to intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

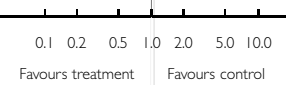
Outcome: 23 Discontinuation due to intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	7/601	5/600		100.0 %	1.40 [0.44, 4.44]
Total (95% CI)	**601**	**600**		**100.0 %**	**1.40 [0.44, 4.44]**

Total events: 7 (Triphasic), 5 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.57 (P = 0.57)



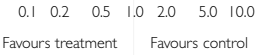
Analysis 1.24. Comparison 1 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic LNG 150 μg/EE 30 μg, Outcome 24 Proportion of women with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 1 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic LNG 150 g/EE 30 g

Outcome: 24 Proportion of women with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunson 1993	3/495	2/484		100.0 %	1.47 [0.24, 8.83]
Total (95% CI)	**495**	**484**		**100.0 %**	**1.47 [0.24, 8.83]**
Total events: 3 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.42 (P = 0.67)					



Analysis 2.1. Comparison 2 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 600 μg/ EE 35 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 2 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 600 g/ EE 35 g

Outcome: 1 Pregnancy per woman within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	2/96	2/90		100.0 %	0.94 [0.13, 6.79]
Total (95% CI)	**96**	**90**		**100.0 %**	**0.94 [0.13, 6.79]**
Total events: 2 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.07 (P = 0.95)					

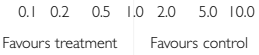
Analysis 2.2. Comparison 2 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 600 μg/ EE 35 μg, Outcome 2 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 2 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 600 g/ EE 35 g

Outcome: 2 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	17/96	17/90		100.0 %	0.92 [0.44, 1.94]
Total (95% CI)	**96**	**90**		**100.0 %**	**0.92 [0.44, 1.94]**
Total events: 17 (Triphasic), 17 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.21 (P = 0.84)					



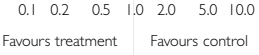
Analysis 2.3. Comparison 2 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 600 μg/ EE 35 μg, Outcome 3 Discontinuation due to medical reasons within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 2 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 600 g/ EE 35 g

Outcome: 3 Discontinuation due to medical reasons within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	9/96	9/90		100.0 %	0.93 [0.35, 2.46]
Total (95% CI)	**96**	**90**		**100.0 %**	**0.93 [0.35, 2.46]**
Total events: 9 (Triphasic), 9 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.14 (P = 0.89)					



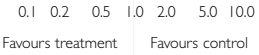
Analysis 2.4. Comparison 2 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 600 μg/ EE 35 μg, Outcome 4 Discontinuation due to cycle disturbances within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 2 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 600 g/ EE 35 g

Outcome: 4 Discontinuation due to cycle disturbances within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chen 1987	2/96	3/90		100.0 %	0.62 [0.10, 3.78]
Total (95% CI)	**96**	**90**		**100.0 %**	**0.62 [0.10, 3.78]**
Total events: 2 (Triphasic), 3 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.52 (P = 0.60)					



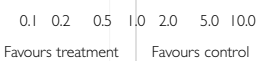
Analysis 3.1. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 1 Pregnancy per woman within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 1 Pregnancy per woman within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	0/601	0/599		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**601**	**599**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (Triphasic), 0 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P < 0.00001)					



Analysis 3.2. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 2 Proportion of women with spotting at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 2 Proportion of women with spotting at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	1/523	8/495		100.0 %	0.12 [0.01, 0.94]
Total (95% CI)	**523**	**495**		**100.0 %**	**0.12 [0.01, 0.94]**
Total events: 1 (Triphasic), 8 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.02 (P = 0.043)					

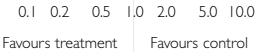
Analysis 3.3. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 3 Proportion of women with breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 3 Proportion of women with breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	5/523	15/495		100.0 %	0.31 [0.11, 0.86]
Total (95% CI)	**523**	**495**		**100.0 %**	**0.31 [0.11, 0.86]**
Total events: 5 (Triphasic), 15 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.26 (P = 0.024)					

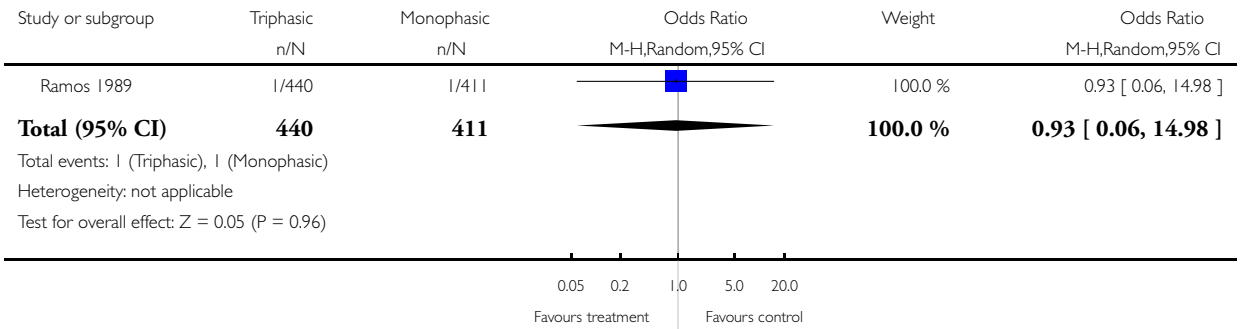


Analysis 3.4. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 4 Proportion of women with spotting at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 4 Proportion of women with spotting at cycle 12

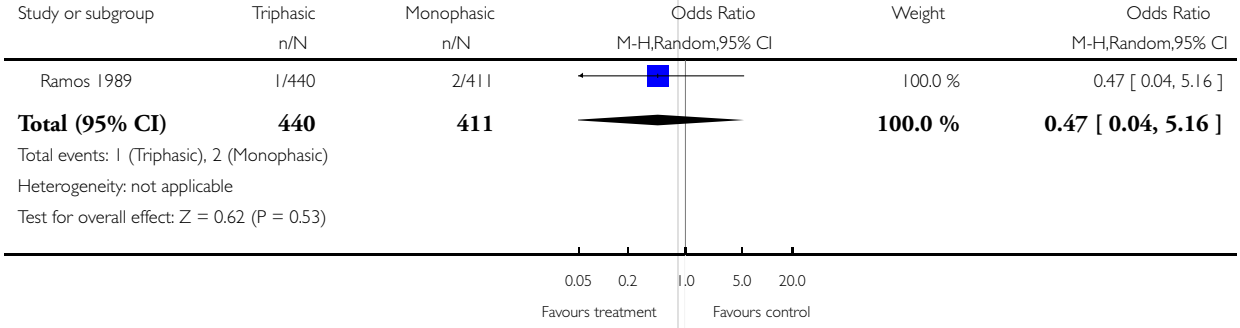


Analysis 3.5. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 5 Proportion of women with breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 5 Proportion of women with breakthrough bleeding at cycle 12



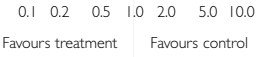
Analysis 3.6. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 6 Total discontinuation within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 6 Total discontinuation within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	165/601	192/599		100.0 %	0.80 [0.63, 1.03]
Total (95% CI)	**601**	**599**		**100.0 %**	**0.80 [0.63, 1.03]**
Total events: 165 (Triphasic), 192 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.74 (P = 0.082)					



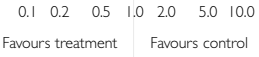
Analysis 3.7. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 7 Discontinuation due to medical reasons within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 7 Discontinuation due to medical reasons within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	66/601	82/599		100.0 %	0.78 [0.55, 1.10]
Total (95% CI)	**601**	**599**		**100.0 %**	**0.78 [0.55, 1.10]**
Total events: 66 (Triphasic), 82 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.42 (P = 0.15)					



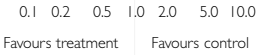
Analysis 3.8. Comparison 3 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 400 μg/ EE 35 μg, Outcome 8 Discontinuation due to intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 3 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 400 g/ EE 35 g

Outcome: 8 Discontinuation due to intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ramos 1989	7/601	12/599		100.0 %	0.58 [0.23, 1.47]
Total (95% CI)	**601**	**599**		**100.0 %**	**0.58 [0.23, 1.47]**
Total events: 7 (Triphasic), 12 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.15 (P = 0.25)					



Analysis 4.1. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 1 Pregnancy per woman within 6 cycles

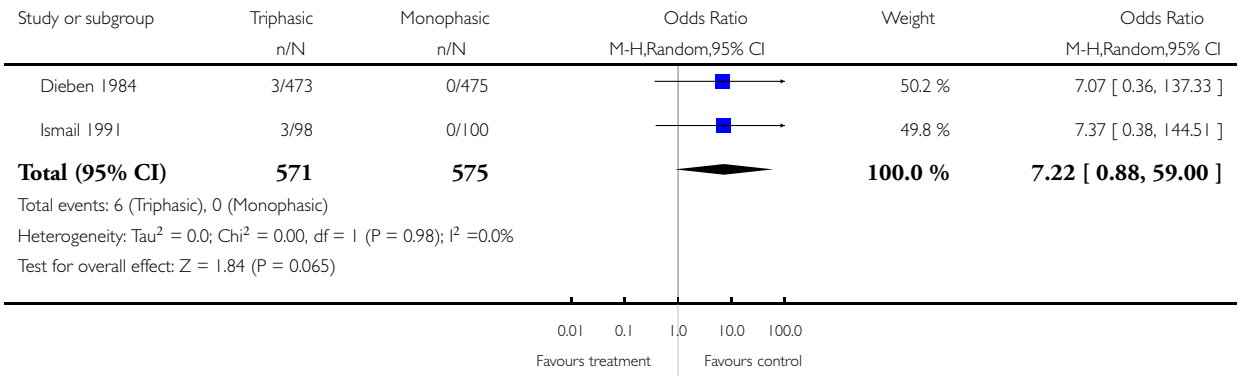
Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Lachnit-Fixson 1984	1/278	0/277		100.0 %	3.00 [0.12, 73.96]
Total (95% CI)	**278**	**277**		**100.0 %**	**3.00 [0.12, 73.96]**
Total events: 1 (Triphasic), 0 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.67 (P = 0.50)					

Analysis 4.2. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 2 Pregnancy per woman within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 2 Pregnancy per woman within 12 cycles

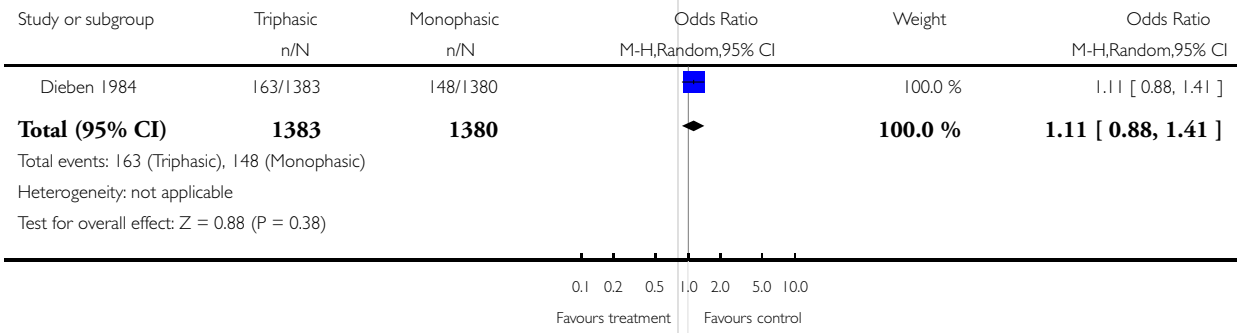


Analysis 4.3. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 3 Proportion of cycles with spotting within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 3 Proportion of cycles with spotting within 3 cycles



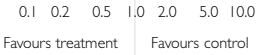
Analysis 4.4. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 4 Proportion of cycles with breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 4 Proportion of cycles with breakthrough bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	105/1383	91/1380		100.0 %	1.16 [0.87, 1.56]
Total (95% CI)	**1383**	**1380**		**100.0 %**	**1.16 [0.87, 1.56]**
Total events: 105 (Triphasic), 91 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.02 (P = 0.31)					



Analysis 4.5. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 5 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 5 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	10/1383	14/1380		100.0 %	0.71 [0.31, 1.61]
Total (95% CI)	**1383**	**1380**		**100.0 %**	**0.71 [0.31, 1.61]**
Total events: 10 (Triphasic), 14 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.82 (P = 0.41)					

Analysis 4.6. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 6 Proportion of cycles with spotting within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 6 Proportion of cycles with spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	251/2617	218/2618		50.2 %	1.17 [0.97, 1.41]
Lachnit-Fixson 1984	98/1536	252/1524		49.8 %	0.34 [0.27, 0.44]
Total (95% CI)	**4153**	**4142**		**100.0 %**	**0.64 [0.19, 2.11]**

Total events: 349 (Triphasic), 470 (Monophasic)

Heterogeneity: $Tau^2 = 0.74$; $Chi^2 = 59.74$, df = 1 ($P<0.00001$); $I^2 = 98\%$

Test for overall effect: Z = 0.74 (P = 0.46)

Analysis 4.7. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 7 Proportion of cycles with breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

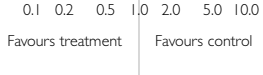
Outcome: 7 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	174/2617	155/2618		53.2 %	1.13 [0.91, 1.42]
Lachnit-Fixson 1984	18/1536	43/1524		46.8 %	0.41 [0.23, 0.71]
Total (95% CI)	**4153**	**4142**		**100.0 %**	**0.70 [0.26, 1.91]**

Total events: 192 (Triphasic), 198 (Monophasic)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 11.17$, df = 1 ($P = 0.00083$); $I^2 = 91\%$

Test for overall effect: Z = 0.69 (P = 0.49)



Analysis 4.8. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 8 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 8 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	14/2617	23/2618		66.2 %	0.61 [0.31, 1.18]
Lachnit-Fixson 1984	6/1536	17/1524		33.8 %	0.35 [0.14, 0.88]
Total (95% CI)	**4153**	**4142**		**100.0 %**	**0.50 [0.29, 0.86]**
Total events: 20 (Triphasic), 40 (Monophasic)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.91$, df = 1 (P = 0.34); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.48 (P = 0.013)					

Analysis 4.9. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 9 Proportion of cycles with spotting within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 9 Proportion of cycles with spotting within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	257/2709	224/2769		100.0 %	1.19 [0.99, 1.44]
Total (95% CI)	**2709**	**2769**		**100.0 %**	**1.19 [0.99, 1.44]**
Total events: 257 (Triphasic), 224 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.83 (P = 0.068)					

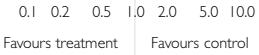
Analysis 4.10. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 10 Proportion of cycles with breakthrough bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 10 Proportion of cycles with breakthrough bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	178/2709	168/2769		100.0 %	1.09 [0.88, 1.35]
Total (95% CI)	**2709**	**2769**		**100.0 %**	**1.09 [0.88, 1.35]**
Total events: 178 (Triphasic), 168 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					



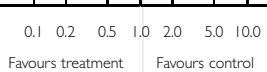
Analysis 4.11. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 11 Proportion of cycles with spotting and breakthrough bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 11 Proportion of cycles with spotting and breakthrough bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	15/2709	24/2769		100.0 %	0.64 [0.33, 1.22]
Total (95% CI)	**2709**	**2769**		**100.0 %**	**0.64 [0.33, 1.22]**
Total events: 15 (Triphasic), 24 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.37 (P = 0.17)					

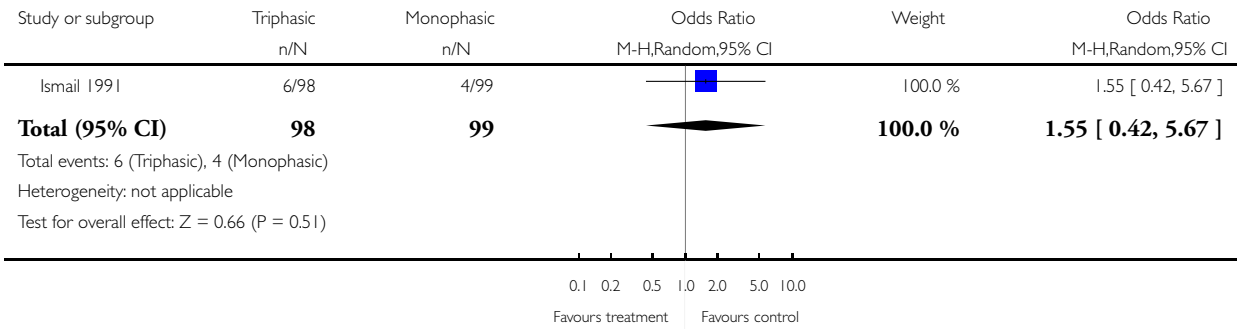


Analysis 4.12. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 12 Proportion of women with staining/spotting within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 12 Proportion of women with staining/spotting within 12 cycles

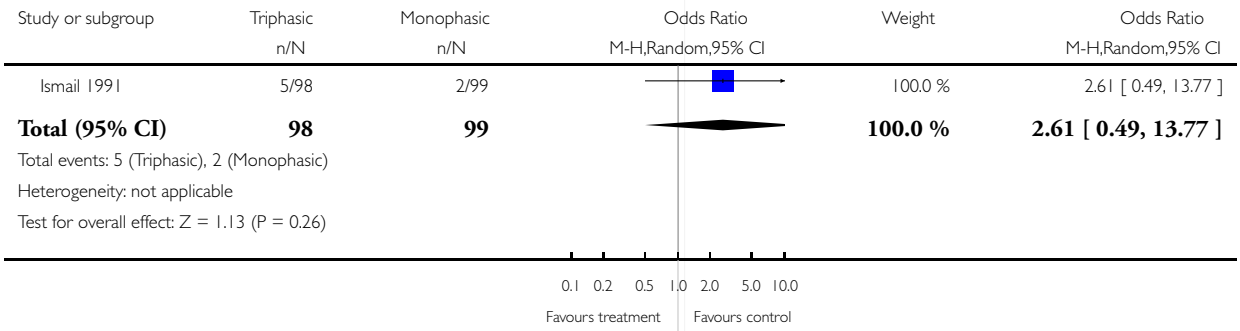


Analysis 4.13. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 13 Proportion of women with moderate flow intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 13 Proportion of women with moderate flow intermenstrual bleeding within 12 cycles

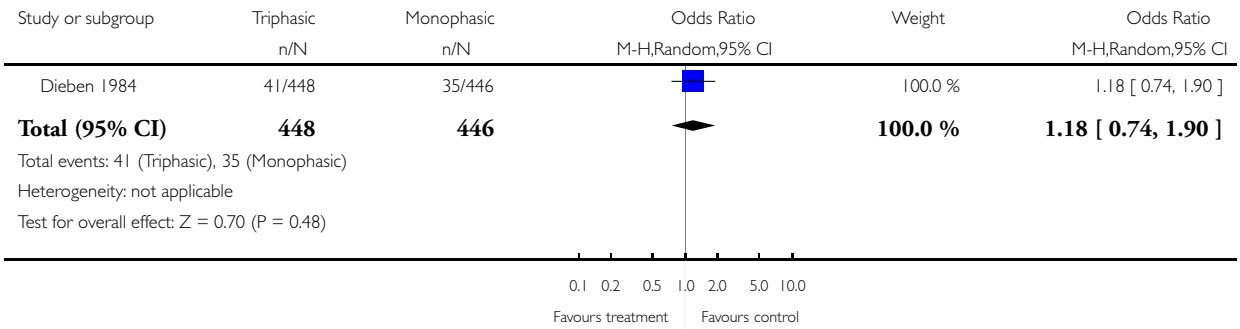


Analysis 4.14. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 14 Proportion of women with spotting at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 14 Proportion of women with spotting at cycle 3

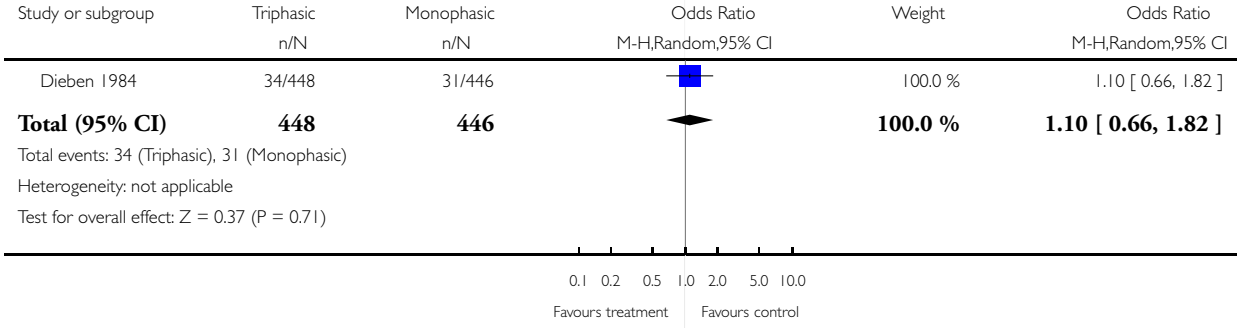


Analysis 4.15. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 15 Proportion of women with breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 15 Proportion of women with breakthrough bleeding at cycle 3



Analysis 4.16. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 16 Proportion of women with spotting and breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 16 Proportion of women with spotting and breakthrough bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	1/448	2/446		100.0 %	0.50 [0.04, 5.50]
Total (95% CI)	**448**	**446**		**100.0 %**	**0.50 [0.04, 5.50]**
Total events: 1 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					

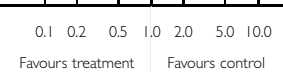
Analysis 4.17. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 17 Proportion of women with spotting at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 17 Proportion of women with spotting at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	21/399	16/398		100.0 %	1.33 [0.68, 2.58]
Total (95% CI)	**399**	**398**		**100.0 %**	**1.33 [0.68, 2.58]**
Total events: 21 (Triphasic), 16 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.83 (P = 0.41)					



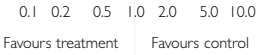
Analysis 4.18. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 18 Proportion of women with breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 18 Proportion of women with breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	24/399	16/398		100.0 %	1.53 [0.80, 2.92]
Total (95% CI)	**399**	**398**		**100.0 %**	**1.53 [0.80, 2.92]**
Total events: 24 (Triphasic), 16 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.28 (P = 0.20)					



Analysis 4.19. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 19 Proportion of women with spotting and breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 19 Proportion of women with spotting and breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	1/399	2/398		100.0 %	0.50 [0.04, 5.51]
Total (95% CI)	**399**	**398**		**100.0 %**	**0.50 [0.04, 5.51]**
Total events: 1 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					

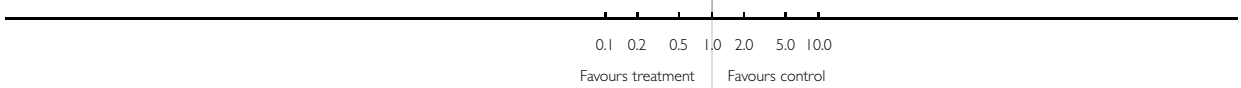
Analysis 4.20. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 20 Proportion of women with spotting at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 20 Proportion of women with spotting at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	0/2	0/8		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**2**	**8**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (Triphasic), 0 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P < 0.00001)					



Analysis 4.21. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 21 Proportion of women with breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 21 Proportion of women with breakthrough bleeding at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	0/2	1/8		100.0 %	1.00 [0.03, 33.32]
Total (95% CI)	**2**	**8**		**100.0 %**	**1.00 [0.03, 33.32]**
Total events: 0 (Triphasic), 1 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					

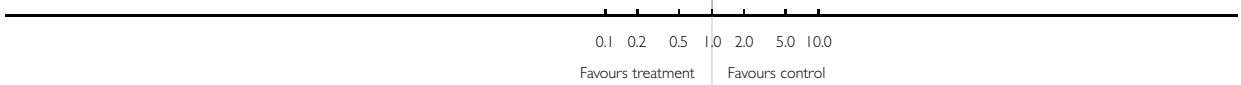
Analysis 4.22. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 22 Proportion of women with spotting and breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 22 Proportion of women with spotting and breakthrough bleeding at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	0/2	0/8		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**2**	**8**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (Triphasic), 0 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P < 0.00001)					



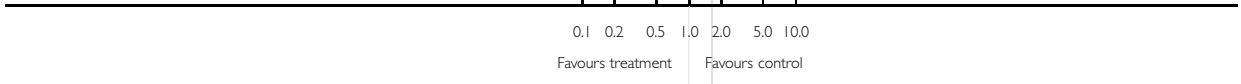
Analysis 4.23. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 23 Proportion of cycles with amenorrhea within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 23 Proportion of cycles with amenorrhea within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	123/1383	116/1380		100.0 %	1.06 [0.82, 1.39]
Total (95% CI)	**1383**	**1380**		**100.0 %**	**1.06 [0.82, 1.39]**
Total events: 123 (Triphasic), 116 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.65)					



Analysis 4.24. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 24 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 24 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	206/2617	194/2618		57.5 %	1.07 [0.87, 1.31]
Lachnit-Fixson 1984	3/1536	14/1524		42.5 %	0.21 [0.06, 0.74]
Total (95% CI)	**4153**	**4142**		**100.0 %**	**0.54 [0.11, 2.59]**

Total events: 209 (Triphasic), 208 (Monophasic)

Heterogeneity: $Tau^2 = 1.11$; $Chi^2 = 6.33$, df = 1 (P = 0.01); $I^2 = 84\%$

Test for overall effect: Z = 0.78 (P = 0.44)

Analysis 4.25. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 25 Proportion of cycles with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

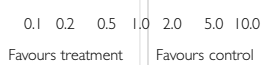
Outcome: 25 Proportion of cycles with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	210/2709	205/2769		100.0 %	1.05 [0.86, 1.28]
Total (95% CI)	**2709**	**2769**		**100.0 %**	**1.05 [0.86, 1.28]**

Total events: 210 (Triphasic), 205 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.49 (P = 0.63)

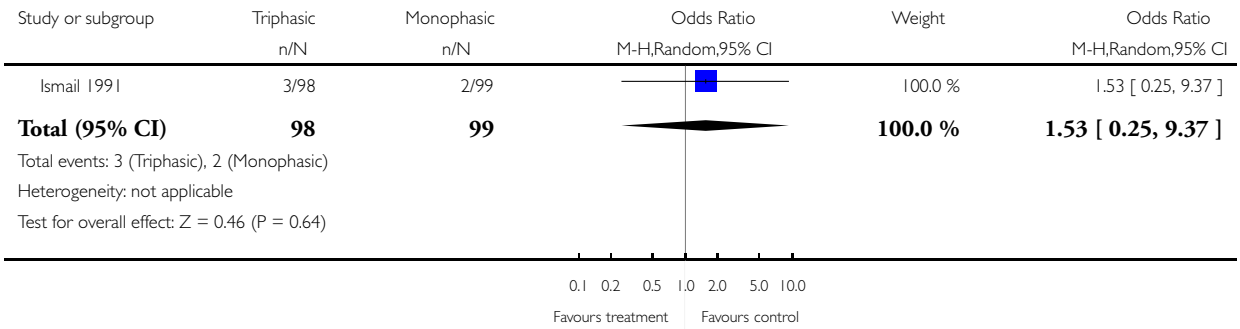


Analysis 4.26. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 26 Proportion of women with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 26 Proportion of women with amenorrhea within 12 cycles

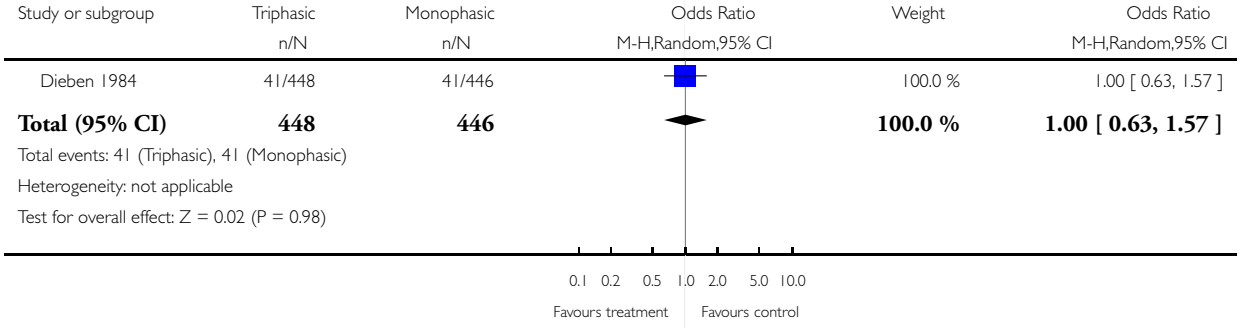


Analysis 4.27. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 27 Proportion of women with amenorrhea at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 27 Proportion of women with amenorrhea at cycle 3



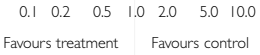
Analysis 4.28. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 28 Proportion of women with amenorrhea at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 28 Proportion of women with amenorrhea at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	28/399	21/398		100.0 %	1.35 [0.76, 2.43]
Total (95% CI)	**399**	**398**		**100.0 %**	**1.35 [0.76, 2.43]**
Total events: 28 (Triphasic), 21 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.02 (P = 0.31)					



Analysis 4.29. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 29 Proportion of women with amenorrhea at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 29 Proportion of women with amenorrhea at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	0/2	1/8		100.0 %	1.00 [0.03, 33.32]
Total (95% CI)	**2**	**8**		**100.0 %**	**1.00 [0.03, 33.32]**
Total events: 0 (Triphasic), 1 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					

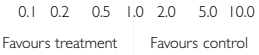
Analysis 4.30. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 30 Total discontinuation within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 30 Total discontinuation within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	35/473	43/475		100.0 %	0.80 [0.50, 1.28]
Total (95% CI)	**473**	**475**		**100.0 %**	**0.80 [0.50, 1.28]**
Total events: 35 (Triphasic), 43 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.92 (P = 0.36)					



Analysis 4.31. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 31 Discontinuation due to medical reasons within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 31 Discontinuation due to medical reasons within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	26/473	36/475		100.0 %	0.71 [0.42, 1.19]
Total (95% CI)	**473**	**475**		**100.0 %**	**0.71 [0.42, 1.19]**
Total events: 26 (Triphasic), 36 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					

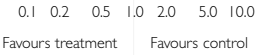
Analysis 4.32. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 32 Discontinuation due to cycle disturbances within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 32 Discontinuation due to cycle disturbances within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	11/473	15/475		100.0 %	0.73 [0.33, 1.61]
Total (95% CI)	**473**	**475**		**100.0 %**	**0.73 [0.33, 1.61]**
Total events: 11 (Triphasic), 15 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					



Analysis 4.33. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 33 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 33 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	67/473	67/475		61.3 %	1.00 [0.70, 1.45]
Lachnit-Fixson 1984	43/278	43/277		38.7 %	1.00 [0.63, 1.58]
Total (95% CI)	**751**	**752**		**100.0 %**	**1.00 [0.75, 1.33]**
Total events: 110 (Triphasic), 110 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.00, df = 1 (P = 0.98); I^2 =0.0%					
Test for overall effect: Z = 0.01 (P = 0.99)					

Analysis 4.34. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 34 Discontinuation due to medical reasons within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 34 Discontinuation due to medical reasons within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	52/473	53/475		55.3 %	0.98 [0.66, 1.48]
Lachnit-Fixson 1984	17/278	33/277		44.7 %	0.48 [0.26, 0.89]
Total (95% CI)	**751**	**752**		**100.0 %**	**0.71 [0.36, 1.43]**

Total events: 69 (Triphasic), 86 (Monophasic)

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 3.65$, df = 1 (P = 0.06); $I^2 = 73\%$

Test for overall effect: Z = 0.95 (P = 0.34)

Analysis 4.35. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 35 Discontinuation due to cycle disturbances within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

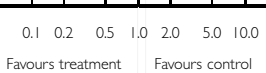
Outcome: 35 Discontinuation due to cycle disturbances within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dieben 1984	23/473	22/475		100.0 %	1.05 [0.58, 1.92]
Total (95% CI)	**473**	**475**		**100.0 %**	**1.05 [0.58, 1.92]**

Total events: 23 (Triphasic), 22 (Monophasic)

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.87)

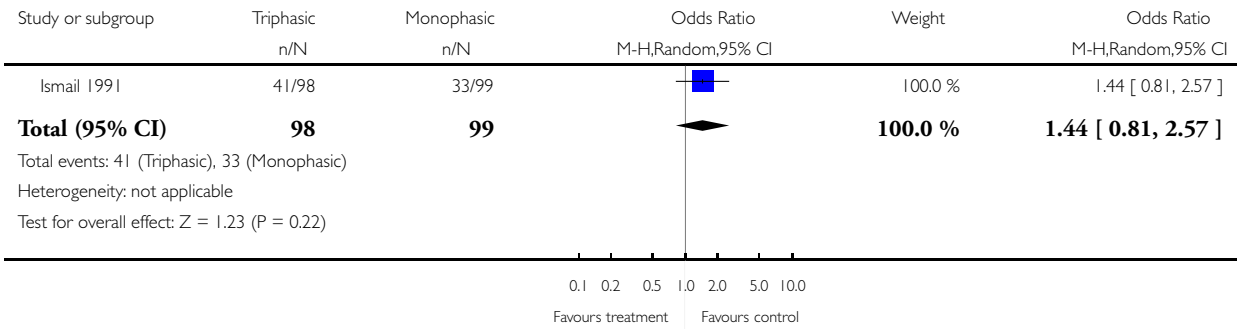


Analysis 4.36. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 36 Total discontinuation within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 36 Total discontinuation within 12 cycles

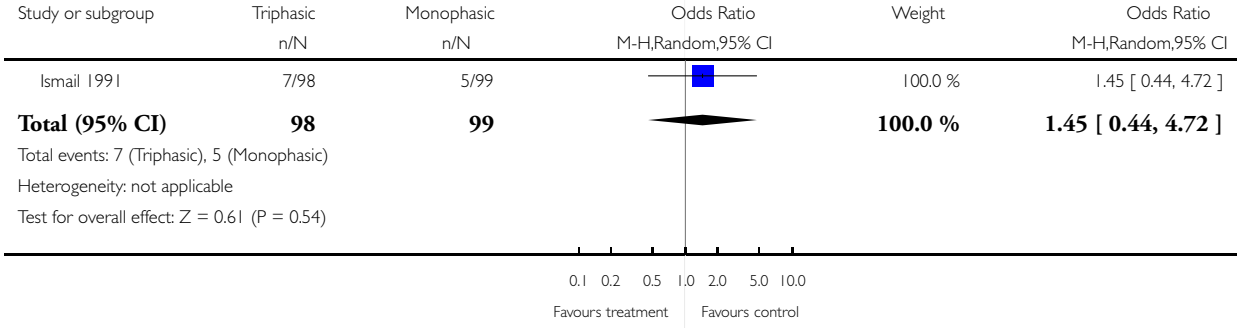


Analysis 4.37. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 37 Discontinuation due to medical reasons within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 37 Discontinuation due to medical reasons within 12 cycles

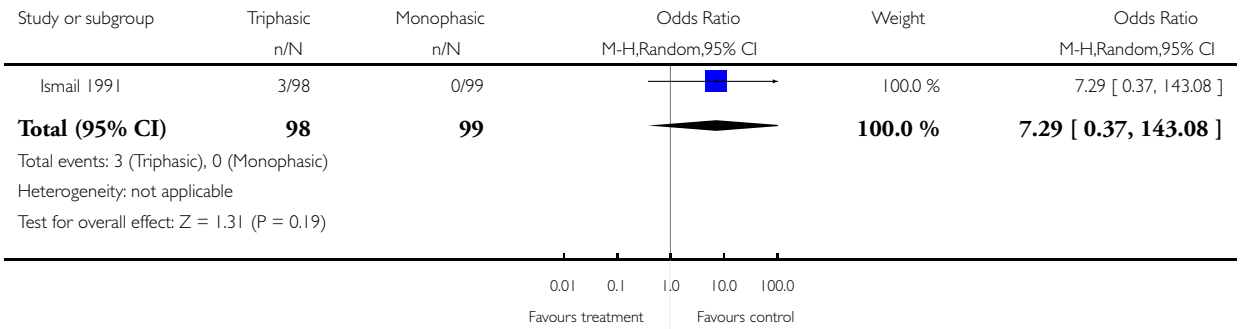


Analysis 4.38. Comparison 4 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 38 Discontinuation due to cycle disturbances within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 4 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 38 Discontinuation due to cycle disturbances within 12 cycles

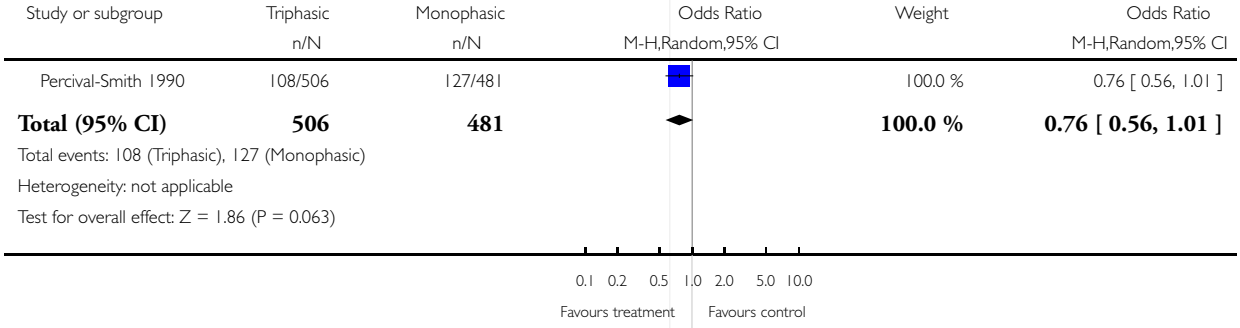


Analysis 5.1. Comparison 5 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NETA 1500 μg/ EE 30 g, Outcome 1 Proportion of cycles with intermenstrual bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 5 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 1 Proportion of cycles with intermenstrual bleeding within 6 cycles

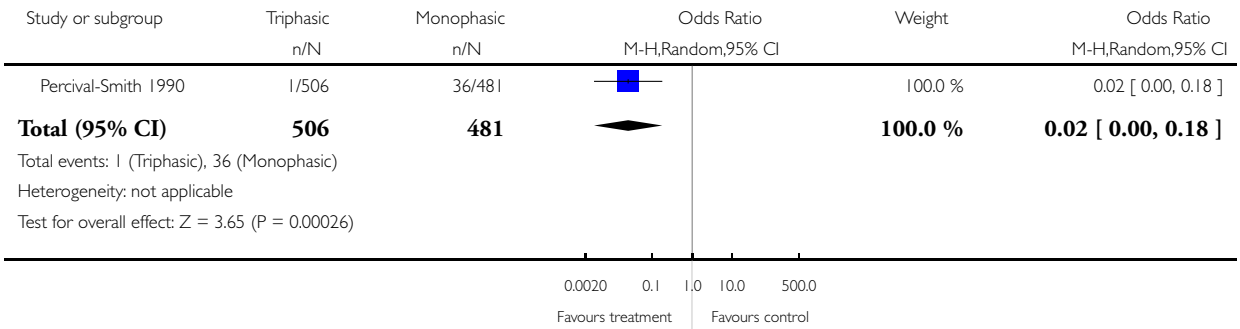


Analysis 5.2. Comparison 5 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NETA 1500 μg/ EE 30 g, Outcome 2 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 5 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 2 Proportion of cycles with amenorrhea within 6 cycles

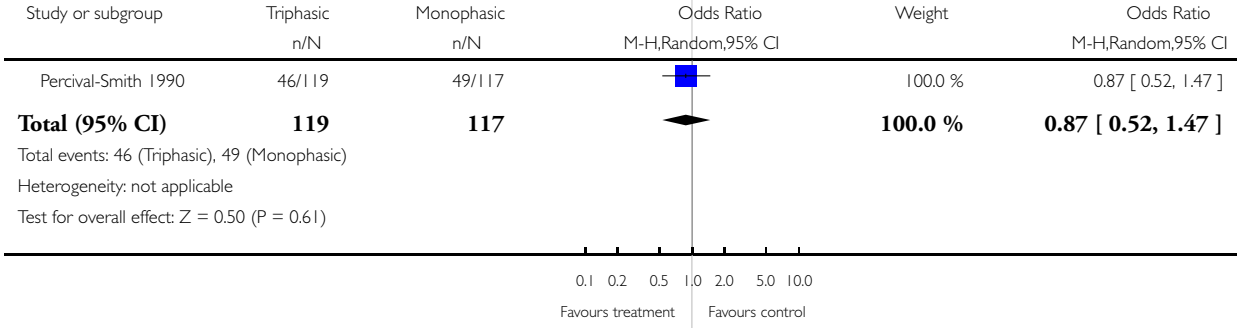


Analysis 5.3. Comparison 5 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NETA 1500 μg/ EE 30 g, Outcome 3 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 5 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 3 Total discontinuation within 6 cycles



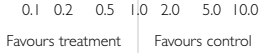
Analysis 6.1. Comparison 6 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NETA 1500 μg/ EE 30 μg, Outcome 1 Proportion of cycles with intermenstrual bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 6 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 1 Proportion of cycles with intermenstrual bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Percival-Smith 1990	173/524	127/481		100.0 %	1.37 [1.05, 1.80]
Total (95% CI)	**524**	**481**		**100.0 %**	**1.37 [1.05, 1.80]**
Total events: 173 (Triphasic), 127 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.28 (P = 0.022)					



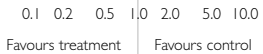
Analysis 6.2. Comparison 6 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NETA 1500 μg/ EE 30 μg, Outcome 2 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 6 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 2 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Percival-Smith 1990	24/524	36/481		100.0 %	0.59 [0.35, 1.01]
Total (95% CI)	**524**	**481**		**100.0 %**	**0.59 [0.35, 1.01]**
Total events: 24 (Triphasic), 36 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.92 (P = 0.054)					



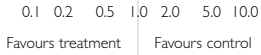
Analysis 6.3. Comparison 6 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NETA 1500 μg/ EE 30 μg, Outcome 3 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 6 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 3 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Percival-Smith 1990	39/117	49/117		100.0 %	0.69 [0.41, 1.18]
Total (95% CI)	**117**	**117**		**100.0 %**	**0.69 [0.41, 1.18]**
Total events: 39 (Triphasic), 49 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.35 (P = 0.18)					



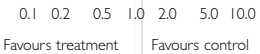
Analysis 7.1. Comparison 7 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 1000 μg/ EE 35 μg, Outcome 1 Proportion of women with intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 7 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 1000 g/ EE 35 g

Outcome: 1 Proportion of women with intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reiter 1990	15/132	23/128		100.0 %	0.59 [0.29, 1.18]
Total (95% CI)	**132**	**128**		**100.0 %**	**0.59 [0.29, 1.18]**
Total events: 15 (Triphasic), 23 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.50 (P = 0.13)					



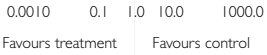
Analysis 7.2. Comparison 7 Triphasic LNG 50-75-125 μg/ EE 30-40-30 μg versus monophasic NET 1000 μg/ EE 35 μg, Outcome 2 Proportion of women with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 7 Triphasic LNG 50-75-125 g/ EE 30-40-30 g versus monophasic NET 1000 g/ EE 35 g

Outcome: 2 Proportion of women with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reiter 1990	0/132	16/128		100.0 %	0.03 [0.00, 0.43]
Total (95% CI)	**132**	**128**		**100.0 %**	**0.03 [0.00, 0.43]**
Total events: 0 (Triphasic), 16 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.54 (P = 0.011)					



Analysis 8.1. Comparison 8 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NET 1000 μg/ EE 35 μg, Outcome 1 Proportion of women with intermenstrual bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 8 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic NET 1000 g/ EE 35 g

Outcome: 1 Proportion of women with intermenstrual bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reiter 1990	22/117	23/128		100.0 %	1.06 [0.55, 2.02]
Total (95% CI)	**117**	**128**		**100.0 %**	**1.06 [0.55, 2.02]**
Total events: 22 (Triphasic), 23 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.17 (P = 0.87)					

Analysis 8.2. Comparison 8 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic NET 1000 μg/ EE 35 μg, Outcome 2 Proportion of women with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 8 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic NET 1000 g/ EE 35 g

Outcome: 2 Proportion of women with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reiter 1990	4/117	16/128		100.0 %	0.25 [0.08, 0.76]
Total (95% CI)	**117**	**128**		**100.0 %**	**0.25 [0.08, 0.76]**
Total events: 4 (Triphasic), 16 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.43 (P = 0.015)					

Analysis 9.1. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 1 Pregnancy per woman within 4 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 1 Pregnancy per woman within 4 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	2/173	1/169		50.0 %	1.96 [0.18, 21.87]
Reisman 1999	2/195	1/192		50.0 %	1.98 [0.18, 22.01]
Total (95% CI)	**368**	**361**		**100.0 %**	**1.97 [0.36, 10.83]**
Total events: 4 (Triphasic), 2 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.00, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 0.78 (P = 0.43)					

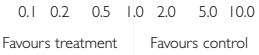
Analysis 9.2. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 2 Proportion of cycles with spotting within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 2 Proportion of cycles with spotting within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	51/397	43/359		100.0 %	1.08 [0.70, 1.67]
Total (95% CI)	**397**	**359**		**100.0 %**	**1.08 [0.70, 1.67]**
Total events: 51 (Triphasic), 43 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.36 (P = 0.72)					



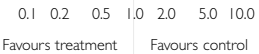
Analysis 9.3. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 3 Proportion of cycles with breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 3 Proportion of cycles with breakthrough bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	21/397	20/359		100.0 %	0.95 [0.50, 1.78]
Total (95% CI)	**397**	**359**		**100.0 %**	**0.95 [0.50, 1.78]**
Total events: 21 (Triphasic), 20 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.17 (P = 0.86)					



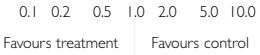
Analysis 9.4. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 4 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 4 Proportion of cycles with spotting and breakthrough bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	81/397	68/359		100.0 %	1.10 [0.77, 1.57]
Total (95% CI)	**397**	**359**		**100.0 %**	**1.10 [0.77, 1.57]**
Total events: 81 (Triphasic), 68 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.50 (P = 0.61)					



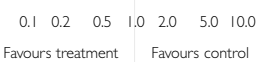
Analysis 9.5. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 5 Proportion of cycles with intermenstrual bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 5 Proportion of cycles with intermenstrual bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	142/310	114/301		46.1 %	1.39 [1.00, 1.91]
Reisman 1999	153/397	131/359		53.9 %	1.09 [0.81, 1.47]
Total (95% CI)	**707**	**660**		**100.0 %**	**1.22 [0.96, 1.54]**
Total events: 295 (Triphasic), 245 (Monophasic)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.15, df = 1 (P = 0.28); I^2 =13%					
Test for overall effect: Z = 1.66 (P = 0.097)					



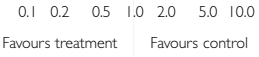
Analysis 9.6. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 6 Proportion of women with spotting at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 6 Proportion of women with spotting at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	13/123	6/109		100.0 %	2.03 [0.74, 5.54]
Total (95% CI)	**123**	**109**		**100.0 %**	**2.03 [0.74, 5.54]**
Total events: 13 (Triphasic), 6 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.38 (P = 0.17)					



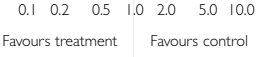
Analysis 9.7. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 7 Proportion of women with breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 7 Proportion of women with breakthrough bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	10/123	6/109		100.0 %	1.52 [0.53, 4.33]
Total (95% CI)	**123**	**109**		**100.0 %**	**1.52 [0.53, 4.33]**
Total events: 10 (Triphasic), 6 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					



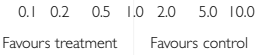
Analysis 9.8. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 8 Proportion of women with spotting and breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 8 Proportion of women with spotting and breakthrough bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Reisman 1999	23/123	26/109		100.0 %	0.73 [0.39, 1.38]
Total (95% CI)	**123**	**109**		**100.0 %**	**0.73 [0.39, 1.38]**
Total events: 23 (Triphasic), 26 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					



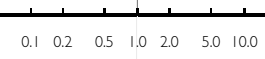
Analysis 9.9. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 9 Proportion of women with intermenstrual bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 9 Proportion of women with intermenstrual bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	40/95	34/93		45.6 %	1.26 [0.70, 2.27]
Reisman 1999	46/123	38/109		54.4 %	1.12 [0.65, 1.91]
Total (95% CI)	**218**	**202**		**100.0 %**	**1.18 [0.79, 1.75]**
Total events: 86 (Triphasic), 72 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.09, df = 1 (P = 0.76); I^2 =0.0%					
Test for overall effect: Z = 0.82 (P = 0.41)					



Analysis 9.10. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 10 Proportion of cycles with amenorrhea within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

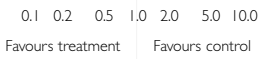
Outcome: 10 Proportion of cycles with amenorrhea within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	12/310	14/301		46.2 %	0.83 [0.38, 1.82]
Reisman 1999	15/397	15/359		53.8 %	0.90 [0.43, 1.87]
Total (95% CI)	**707**	**660**		**100.0 %**	**0.87 [0.51, 1.48]**

Total events: 27 (Triphasic), 29 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.03$, df = 1 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 0.53 (P = 0.60)



Analysis 9.11. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 11 Proportion of women with amenorrhea at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 11 Proportion of women with amenorrhea at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	1/95	3/93		50.8 %	0.32 [0.03, 3.13]
Reisman 1999	3/123	1/19		49.2 %	0.45 [0.04, 4.56]
Total (95% CI)	**218**	**112**		**100.0 %**	**0.38 [0.07, 1.92]**

Total events: 4 (Triphasic), 4 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.04$, df = 1 (P = 0.83); $I^2 = 0.0\%$

Test for overall effect: Z = 1.17 (P = 0.24)

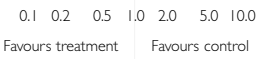
Analysis 9.12. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 12 Total discontinuation within 4 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 12 Total discontinuation within 4 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	75/173	76/169		47.2 %	0.94 [0.61, 1.44]
Reisman 1999	77/195	90/192		52.8 %	0.74 [0.49, 1.11]
Total (95% CI)	**368**	**361**		**100.0 %**	**0.83 [0.62, 1.11]**
Total events: 152 (Triphasic), 166 (Monophasic)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.62$, df = 1 (P = 0.43); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.27 (P = 0.20)					



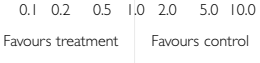
Analysis 9.13. Comparison 9 Triphasic NET 500-750-1000 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 13 Discontinuation due to medical reasons within 4 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 9 Triphasic NET 500-750-1000 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 13 Discontinuation due to medical reasons within 4 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Chavez 1999	18/173	18/169		54.0 %	0.97 [0.49, 1.94]
Reisman 1999	9/195	19/192		46.0 %	0.44 [0.19, 1.00]
Total (95% CI)	**368**	**361**		**100.0 %**	**0.68 [0.31, 1.47]**
Total events: 27 (Triphasic), 37 (Monophasic)					
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 2.11$, df = 1 (P = 0.15); $I^2 = 53\%$					
Test for overall effect: Z = 0.99 (P = 0.32)					

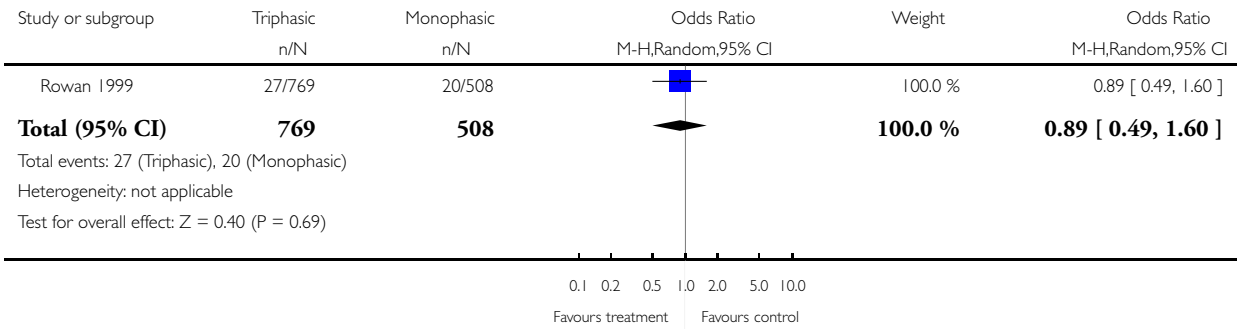


Analysis 10.1. Comparison 10 Estrophasic NETA 1000 μg/ EE 20-30-35 μg versus monophasic NETA 1500 μg/ EE 30 μg, Outcome 1 Discontinuation due to adverse events within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 10 Estrophasic NETA 1000 g/ EE 20-30-35 g versus monophasic NETA 1500 g/ EE 30 g

Outcome: 1 Discontinuation due to adverse events within 6 cycles

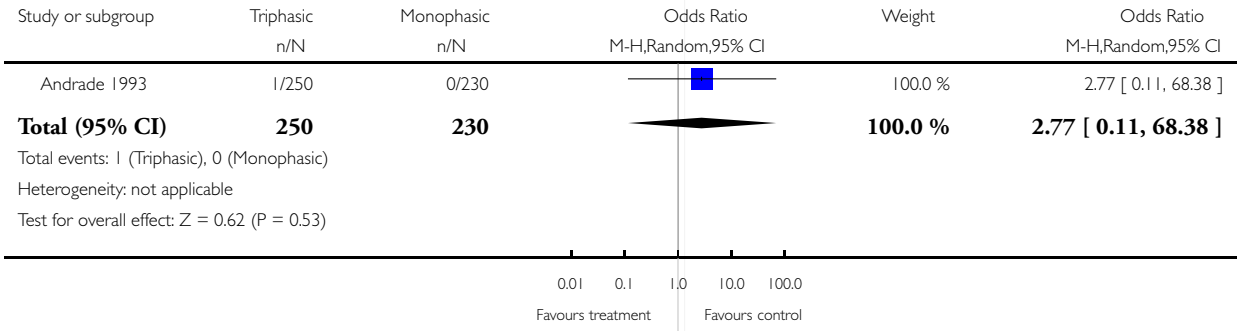


Analysis 11.1. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 1 Pregnancy per woman within 6 cycles



Analysis 11.2. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 2 Pregnancy per woman within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 2 Pregnancy per woman within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	1/84	1/84		100.0 %	1.00 [0.06, 16.26]
Total (95% CI)	**84**	**84**		**100.0 %**	**1.00 [0.06, 16.26]**
Total events: 1 (Triphasic), 1 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					

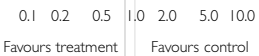
Analysis 11.3. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 3 Proportion of cycles with spotting within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 3 Proportion of cycles with spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	108/1328	100/1187		100.0 %	0.96 [0.72, 1.28]
Total (95% CI)	**1328**	**1187**		**100.0 %**	**0.96 [0.72, 1.28]**
Total events: 108 (Triphasic), 100 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.27 (P = 0.79)					



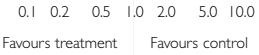
Analysis 11.4. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 4 Proportion of cycles with breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 4 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	25/1328	27/1187		100.0 %	0.82 [0.48, 1.43]
Total (95% CI)	**1328**	**1187**		**100.0 %**	**0.82 [0.48, 1.43]**
Total events: 25 (Triphasic), 27 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					



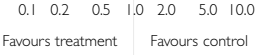
Analysis 11.5. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 5 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 5 Proportion of cycles with spotting and breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	40/1328	71/1187		100.0 %	0.49 [0.33, 0.73]
Total (95% CI)	**1328**	**1187**		**100.0 %**	**0.49 [0.33, 0.73]**
Total events: 40 (Triphasic), 71 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.55 (P = 0.00038)					



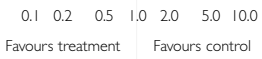
Analysis 11.6. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 6 Proportion of women with spotting at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 6 Proportion of women with spotting at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	9/80	5/80		33.3 %	1.90 [0.61, 5.95]
Andrade 1993	16/217	17/202		66.7 %	0.87 [0.43, 1.76]
Total (95% CI)	**297**	**282**		**100.0 %**	**1.13 [0.54, 2.33]**
Total events: 25 (Triphasic), 22 (Monophasic)					
Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 1.31$, df = 1 (P = 0.25); $I^2 = 24\%$					
Test for overall effect: Z = 0.32 (P = 0.75)					



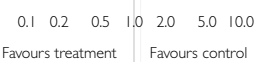
Analysis 11.7. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 7 Proportion of women with breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 7 Proportion of women with breakthrough bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	8/80	3/80		100.0 %	2.85 [0.73, 11.17]
Total (95% CI)	**80**	**80**		**100.0 %**	**2.85 [0.73, 11.17]**
Total events: 8 (Triphasic), 3 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.50 (P = 0.13)					



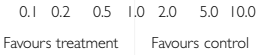
Analysis 11.8. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 8 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 8 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	12/217	15/202		100.0 %	0.73 [0.33, 1.60]
Total (95% CI)	**217**	**202**		**100.0 %**	**0.73 [0.33, 1.60]**
Total events: 12 (Triphasic), 15 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.79 (P = 0.43)					



Analysis 11.9. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 9 Proportion of women with spotting at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 9 Proportion of women with spotting at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	5/79	3/79		24.2 %	1.71 [0.39, 7.42]
Andrade 1993	12/187	12/165		75.8 %	0.87 [0.38, 2.00]
Total (95% CI)	**266**	**244**		**100.0 %**	**1.03 [0.50, 2.12]**
Total events: 17 (Triphasic), 15 (Monophasic)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.61, df = 1 (P = 0.43); I^2 =0.0%					
Test for overall effect: Z = 0.08 (P = 0.94)					

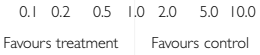
Analysis 11.10. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 10 Proportion of women with breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 10 Proportion of women with breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	8/79	8/79		100.0 %	1.00 [0.36, 2.81]
Total (95% CI)	**79**	**79**		**100.0 %**	**1.00 [0.36, 2.81]**
Total events: 8 (Triphasic), 8 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					



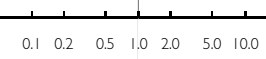
Analysis 11.11. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 11 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 11 Proportion of women with breakthrough bleeding (with or without spotting) at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Andrade 1993	6/187	9/165		100.0 %	0.57 [0.20, 1.65]
Total (95% CI)	**187**	**165**		**100.0 %**	**0.57 [0.20, 1.65]**
Total events: 6 (Triphasic), 9 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					



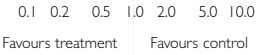
Analysis 11.12. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 12 Proportion of women with spotting at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 12 Proportion of women with spotting at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	6/73	4/71		100.0 %	1.50 [0.40, 5.56]
Total (95% CI)	**73**	**71**		**100.0 %**	**1.50 [0.40, 5.56]**
Total events: 6 (Triphasic), 4 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.61 (P = 0.54)					



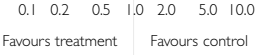
Analysis 11.13. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 13 Proportion of women with breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 13 Proportion of women with breakthrough bleeding at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	5/73	5/71		100.0 %	0.97 [0.27, 3.51]
Total (95% CI)	**73**	**71**		**100.0 %**	**0.97 [0.27, 3.51]**
Total events: 5 (Triphasic), 5 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.05 (P = 0.96)					



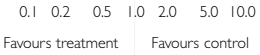
Analysis 11.14. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 14 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 14 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	4/1261	6/1142		100.0 %	0.60 [0.17, 2.14]
Total (95% CI)	**1261**	**1142**		**100.0 %**	**0.60 [0.17, 2.14]**
Total events: 4 (Triphasic), 6 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					



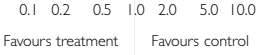
Analysis 11.15. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 15 Proportion of cycles with amenorrhea within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 15 Proportion of cycles with amenorrhea within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	5/1328	7/1187		100.0 %	0.64 [0.20, 2.01]
Total (95% CI)	**1328**	**1187**		**100.0 %**	**0.64 [0.20, 2.01]**
Total events: 5 (Triphasic), 7 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					



Analysis 11.16. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 16 Proportion of women with amenorrhea at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 16 Proportion of women with amenorrhea at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	3/80	1/80		62.4 %	3.08 [0.31, 30.24]
Andrade 1993	0/217	1/202		37.6 %	0.31 [0.01, 7.62]
Total (95% CI)	**297**	**282**		**100.0 %**	**1.30 [0.15, 11.52]**

Total events: 3 (Triphasic), 2 (Monophasic)

Heterogeneity: $Tau^2 = 0.63$; $Chi^2 = 1.31$, df = 1 (P = 0.25); $I^2 = 24\%$

Test for overall effect: Z = 0.23 (P = 0.81)

Analysis 11.17. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 17 Proportion of women with amenorrhea at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

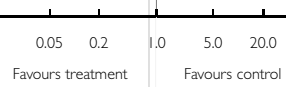
Outcome: 17 Proportion of women with amenorrhea at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	1/79	2/79		100.0 %	0.49 [0.04, 5.56]
Andrade 1993	0/187	0/165		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**266**	**244**		**100.0 %**	**0.49 [0.04, 5.56]**

Total events: 1 (Triphasic), 2 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.57 (P = 0.57)



Analysis 11.18. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 18 Proportion of women with amenorrhea at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 18 Proportion of women with amenorrhea at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	1/73	3/71		100.0 %	0.31 [0.03, 3.10]
Andrade 1993	0/9	0/7		0.0 %	0.0 [0.0, 0.0]
Total (95% CI)	**82**	**78**		**100.0 %**	**0.31 [0.03, 3.10]**

Total events: 1 (Triphasic), 3 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.99 (P = 0.32)

Analysis 11.19. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 19 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 19 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	5/84	5/84		10.7 %	1.00 [0.28, 3.59]
Andrade 1993	49/250	50/230		89.3 %	0.88 [0.56, 1.37]
Total (95% CI)	**334**	**314**		**100.0 %**	**0.89 [0.59, 1.35]**

Total events: 54 (Triphasic), 55 (Monophasic)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.04$, df = 1 (P = 0.85); $I^2 = 0.0\%$

Test for overall effect: Z = 0.55 (P = 0.58)

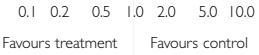
Analysis 11.20. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 20 Discontinuation due to medical reasons within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 20 Discontinuation due to medical reasons within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	26/250	27/230		100.0 %	0.87 [0.49, 1.54]
Total (95% CI)	**250**	**230**		**100.0 %**	**0.87 [0.49, 1.54]**
Total events: 26 (Triphasic), 27 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.47 (P = 0.64)					



Analysis 11.21. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 21 Discontinuation due to cycle disturbances within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 21 Discontinuation due to cycle disturbances within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Andrade 1993	5/250	6/230		100.0 %	0.76 [0.23, 2.53]
Total (95% CI)	**250**	**230**		**100.0 %**	**0.76 [0.23, 2.53]**
Total events: 5 (Triphasic), 6 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.44 (P = 0.66)					

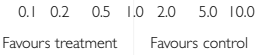
Analysis 11.22. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 22 Total discontinuation within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 22 Total discontinuation within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	11/84	13/84		100.0 %	0.82 [0.35, 1.96]
Total (95% CI)	**84**	**84**		**100.0 %**	**0.82 [0.35, 1.96]**
Total events: 11 (Triphasic), 13 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.44 (P = 0.66)					



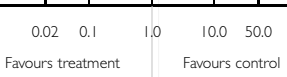
Analysis 11.23. Comparison 11 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 30 μg, Outcome 23 Discontinuation due to medical reasons within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 11 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 30 g

Outcome: 23 Discontinuation due to medical reasons within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Agoestina 1987	2/84	1/84		100.0 %	2.02 [0.18, 22.76]
Total (95% CI)	**84**	**84**		**100.0 %**	**2.02 [0.18, 22.76]**
Total events: 2 (Triphasic), 1 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					



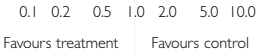
Analysis 12.1. Comparison 12 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 20 μg, Outcome 1 Pregnancy per woman within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 12 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 20 g

Outcome: 1 Pregnancy per woman within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	2/808	2/805		100.0 %	1.00 [0.14, 7.09]
Total (95% CI)	**808**	**805**		**100.0 %**	**1.00 [0.14, 7.09]**
Total events: 2 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.00 (P = 1.0)					



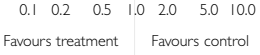
Analysis 12.2. Comparison 12 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 20 μg, Outcome 2 Total discontinuation within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 12 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 20 g

Outcome: 2 Total discontinuation within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	234/808	219/805		100.0 %	1.09 [0.88, 1.36]
Total (95% CI)	**808**	**805**		**100.0 %**	**1.09 [0.88, 1.36]**
Total events: 234 (Triphasic), 219 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					



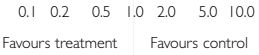
Analysis 12.3. Comparison 12 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic DSG 150 μg/ EE 20 μg, Outcome 3 Discontinuation due to medical reasons within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 12 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic DSG 150 g/ EE 20 g

Outcome: 3 Discontinuation due to medical reasons within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	65/808	75/805		100.0 %	0.85 [0.60, 1.21]
Total (95% CI)	**808**	**805**		**100.0 %**	**0.85 [0.60, 1.21]**
Total events: 65 (Triphasic), 75 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.91 (P = 0.36)					



Analysis 13.1. Comparison 13 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic GTD 75 μg/ EE 30 μg, Outcome 1 Pregnancy per woman within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 13 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic GTD 75 g/ EE 30 g

Outcome: 1 Pregnancy per woman within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	2/808	3/806		100.0 %	0.66 [0.11, 3.99]
Total (95% CI)	**808**	**806**		**100.0 %**	**0.66 [0.11, 3.99]**
Total events: 2 (Triphasic), 3 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.45 (P = 0.65)					

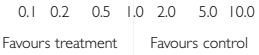
Analysis 13.2. Comparison 13 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic GTD 75 μg/ EE 30 μg, Outcome 2 Total discontinuation within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 13 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic GTD 75 g/ EE 30 g

Outcome: 2 Total discontinuation within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	234/808	245/806		100.0 %	0.93 [0.75, 1.16]
Total (95% CI)	**808**	**806**		**100.0 %**	**0.93 [0.75, 1.16]**
Total events: 234 (Triphasic), 245 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.63 (P = 0.53)					



Analysis 13.3. Comparison 13 Triphasic GTD 50-70-100 μg/ EE 30-40-30 μg versus monophasic GTD 75 μg/ EE 30 μg, Outcome 3 Discontinuation due to medical reasons within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 13 Triphasic GTD 50-70-100 g/ EE 30-40-30 g versus monophasic GTD 75 g/ EE 30 g

Outcome: 3 Discontinuation due to medical reasons within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bruni 2000	65/808	59/806		100.0 %	1.11 [0.77, 1.60]
Total (95% CI)	**808**	**806**		**100.0 %**	**1.11 [0.77, 1.60]**
Total events: 65 (Triphasic), 59 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.55 (P = 0.58)					

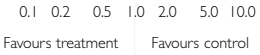
Analysis 14.1. Comparison 14 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 14 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 1 Pregnancy per woman within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Sulak 1999	2/187	2/186		100.0 %	0.99 [0.14, 7.14]
Total (95% CI)	**187**	**186**		**100.0 %**	**0.99 [0.14, 7.14]**
Total events: 2 (Triphasic), 2 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.01 (P = 1.0)					



Analysis 14.2. Comparison 14 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 2 Proportion of women with spotting or breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 14 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 2 Proportion of women with spotting or breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Sulak 1999	16/115	44/116		100.0 %	0.26 [0.14, 0.51]
Total (95% CI)	**115**	**116**		**100.0 %**	**0.26 [0.14, 0.51]**
Total events: 16 (Triphasic), 44 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.02 (P = 0.000057)					

Analysis 14.3. Comparison 14 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 3 Proportion of women with amenorrhea at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 14 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 3 Proportion of women with amenorrhea at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Sulak 1999	5/115	25/116		100.0 %	0.17 [0.06, 0.45]
Total (95% CI)	**115**	**116**		**100.0 %**	**0.17 [0.06, 0.45]**
Total events: 5 (Triphasic), 25 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.53 (P = 0.00042)					

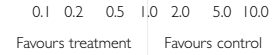
Analysis 14.4. Comparison 14 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 4 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 14 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 4 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Sulak 1999	72/187	70/186		100.0 %	1.04 [0.68, 1.58]
Total (95% CI)	**187**	**186**		**100.0 %**	**1.04 [0.68, 1.58]**
Total events: 72 (Triphasic), 70 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.17 (P = 0.86)					

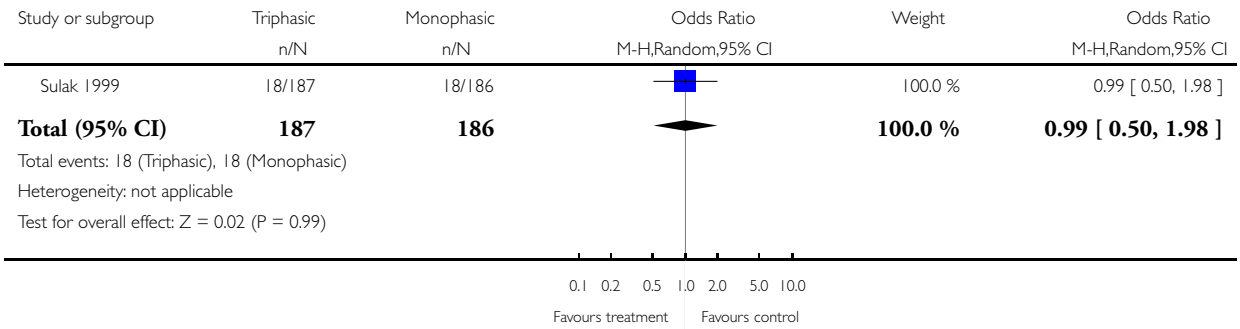


Analysis 14.5. Comparison 14 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 5 Discontinuation due to adverse events within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 14 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 5 Discontinuation due to adverse events within 6 cycles

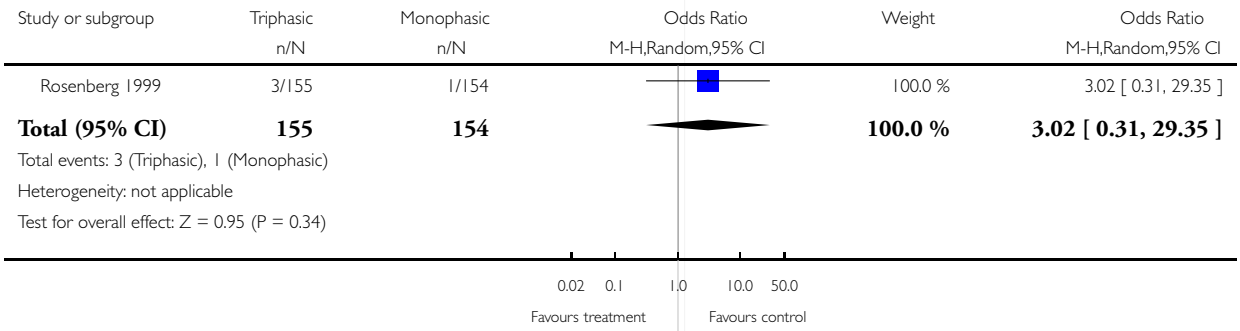


Analysis 15.1. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 1 Pregnancy per woman within 6 cycles



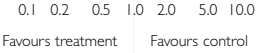
Analysis 15.2. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 2 Proportion of cycles with spotting within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 2 Proportion of cycles with spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	66/831	105/819		100.0 %	0.59 [0.42, 0.81]
Total (95% CI)	**831**	**819**		**100.0 %**	**0.59 [0.42, 0.81]**
Total events: 66 (Triphasic), 105 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.22 (P = 0.0013)					



Analysis 15.3. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 3 Proportion of cycles with breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 3 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	27/831	23/819		100.0 %	1.16 [0.66, 2.04]
Total (95% CI)	**831**	**819**		**100.0 %**	**1.16 [0.66, 2.04]**
Total events: 27 (Triphasic), 23 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.52 (P = 0.60)					

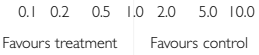
Analysis 15.4. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 4 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 4 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	23/831	39/819		100.0 %	0.57 [0.34, 0.96]
Total (95% CI)	**831**	**819**		**100.0 %**	**0.57 [0.34, 0.96]**
Total events: 23 (Triphasic), 39 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.10 (P = 0.035)					



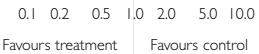
Analysis 15.5. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 5 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 5 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	25/155	26/154		100.0 %	0.95 [0.52, 1.73]
Total (95% CI)	**155**	**154**		**100.0 %**	**0.95 [0.52, 1.73]**
Total events: 25 (Triphasic), 26 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.18 (P = 0.86)					



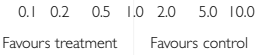
Analysis 15.6. Comparison 15 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic LNG 100 μg/ EE 20 μg, Outcome 6 Discontinuations due to adverse events within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 15 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic LNG 100 g/ EE 20 g

Outcome: 6 Discontinuations due to adverse events within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	4/155	5/154		100.0 %	0.79 [0.21, 3.00]
Total (95% CI)	**155**	**154**		**100.0 %**	**0.79 [0.21, 3.00]**
Total events: 4 (Triphasic), 5 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.35 (P = 0.73)					



Analysis 16.1. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 1 Pregnancy per woman within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 1 Pregnancy per woman within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	3/155	0/154		100.0 %	7.09 [0.36, 138.46]
Total (95% CI)	**155**	**154**		**100.0 %**	**7.09 [0.36, 138.46]**
Total events: 3 (Triphasic), 0 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					

Analysis 16.2. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 2 Proportion of cycles with spotting within 6 cycles.

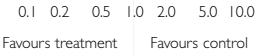
Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 2 Proportion of cycles with spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	66/831	99/848		100.0 %	0.65 [0.47, 0.91]
Total (95% CI)	**831**	**848**		**100.0 %**	**0.65 [0.47, 0.91]**

Total events: 66 (Triphasic), 99 (Monophasic)
Heterogeneity: not applicable
Test for overall effect: Z = 2.55 (P = 0.011)



Analysis 16.3. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 3 Proportion of cycles with breakthrough bleeding within 6 cycles.

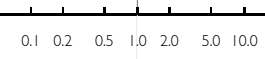
Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 3 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	27/831	28/848		100.0 %	0.98 [0.57, 1.68]
Total (95% CI)	**831**	**848**		**100.0 %**	**0.98 [0.57, 1.68]**

Total events: 27 (Triphasic), 28 (Monophasic)
Heterogeneity: not applicable
Test for overall effect: Z = 0.06 (P = 0.95)



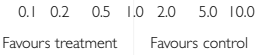
Analysis 16.4. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 4 Proportion of cycles with amenorrhea within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 4 Proportion of cycles with amenorrhea within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	23/831	61/848		100.0 %	0.37 [0.23, 0.60]
Total (95% CI)	**831**	**848**		**100.0 %**	**0.37 [0.23, 0.60]**
Total events: 23 (Triphasic), 61 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.01 (P = 0.000061)					



Analysis 16.5. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 5 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 5 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	25/155	24/154		100.0 %	1.04 [0.57, 1.92]
Total (95% CI)	**155**	**154**		**100.0 %**	**1.04 [0.57, 1.92]**
Total events: 25 (Triphasic), 24 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.13 (P = 0.90)					

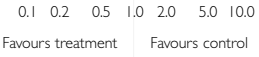
Analysis 16.6. Comparison 16 Triphasic NGM 180-215-250 μg/ EE 35 μg versus monophasic DSG 150 μg/ EE 20 μg + 5 days EE 10 μg, Outcome 6 Discontinuations due to adverse events within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 16 Triphasic NGM 180-215-250 g/ EE 35 g versus monophasic DSG 150 g/ EE 20 g + 5 days EE 10 g

Outcome: 6 Discontinuations due to adverse events within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Rosenberg 1999	4/155	3/154		100.0 %	1.33 [0.29, 6.06]
Total (95% CI)	**155**	**154**		**100.0 %**	**1.33 [0.29, 6.06]**
Total events: 4 (Triphasic), 3 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.37 (P = 0.71)					



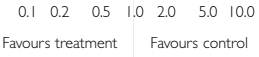
Analysis 17.1. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 1 Pregnancy per woman within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 1 Pregnancy per woman within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	20/1673	19/1141		100.0 %	0.71 [0.38, 1.34]
Total (95% CI)	**1673**	**1141**		**100.0 %**	**0.71 [0.38, 1.34]**
Total events: 20 (Triphasic), 19 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.04 (P = 0.30)					



Analysis 17.2. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 2 Proportion of cycles with breakthrough bleeding within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 2 Proportion of cycles with breakthrough bleeding within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	299/4278	469/2994		100.0 %	0.40 [0.35, 0.47]
Total (95% CI)	**4278**	**2994**		**100.0 %**	**0.40 [0.35, 0.47]**
Total events: 299 (Triphasic), 469 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 11.56 (P < 0.00001)					

Analysis 17.3. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 3 Proportion of cycles with breakthrough bleeding/spotting within 3 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 3 Proportion of cycles with breakthrough bleeding/spotting within 3 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	591/4278	860/2994		100.0 %	0.40 [0.35, 0.45]
Total (95% CI)	**4278**	**2994**		**100.0 %**	**0.40 [0.35, 0.45]**
Total events: 591 (Triphasic), 860 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 15.38 (P < 0.00001)					

Analysis 17.4. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 4 Proportion of cycles with breakthrough bleeding within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 4 Proportion of cycles with breakthrough bleeding within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	564/8089	799/5603		100.0 %	0.45 [0.40, 0.50]
Total (95% CI)	**8089**	**5603**		**100.0 %**	**0.45 [0.40, 0.50]**
Total events: 564 (Triphasic), 799 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 13.74 (P < 0.00001)					

Analysis 17.5. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 5 Proportion of cycles with breakthrough bleeding/spotting within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 5 Proportion of cycles with breakthrough bleeding/spotting within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	1053/8089	1419/5603		100.0 %	0.44 [0.40, 0.48]
Total (95% CI)	**8089**	**5603**		**100.0 %**	**0.44 [0.40, 0.48]**
Total events: 1053 (Triphasic), 1419 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 18.13 (P < 0.00001)					

Analysis 17.6. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 6 Proportion of cycles with breakthrough bleeding within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 6 Proportion of cycles with breakthrough bleeding within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	646/9770	911/6749		100.0 %	0.45 [0.41, 0.50]
Total (95% CI)	**9770**	**6749**		**100.0 %**	**0.45 [0.41, 0.50]**
Total events: 646 (Triphasic), 911 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 14.61 (P < 0.00001)					

Analysis 17.7. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 7 Proportion of cycles with breakthrough bleeding/spotting within 12 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 7 Proportion of cycles with breakthrough bleeding/spotting within 12 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	1190/9770	1595/6749		100.0 %	0.45 [0.41, 0.49]
Total (95% CI)	**9770**	**6749**		**100.0 %**	**0.45 [0.41, 0.49]**
Total events: 1190 (Triphasic), 1595 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 19.03 (P < 0.00001)					

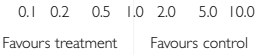
Analysis 17.8. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 8 Proportion of women with breakthrough bleeding at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 8 Proportion of women with breakthrough bleeding at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	74/1374	130/956		100.0 %	0.36 [0.27, 0.49]
Total (95% CI)	**1374**	**956**		**100.0 %**	**0.36 [0.27, 0.49]**
Total events: 74 (Triphasic), 130 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 6.68 (P < 0.00001)					



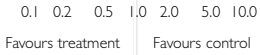
Analysis 17.9. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 9 Proportion of women with breakthrough bleeding/spotting at cycle 3.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 9 Proportion of women with breakthrough bleeding/spotting at cycle 3

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	158/1374	219/956		100.0 %	0.44 [0.35, 0.55]
Total (95% CI)	**1374**	**956**		**100.0 %**	**0.44 [0.35, 0.55]**
Total events: 158 (Triphasic), 219 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 7.23 (P < 0.00001)					



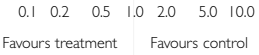
Analysis 17.10. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 10 Proportion of women with breakthrough bleeding at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 10 Proportion of women with breakthrough bleeding at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	79/1260	117/858		100.0 %	0.42 [0.31, 0.57]
Total (95% CI)	**1260**	**858**		**100.0 %**	**0.42 [0.31, 0.57]**
Total events: 79 (Triphasic), 117 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 5.61 (P < 0.00001)					



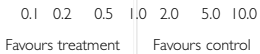
Analysis 17.11. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 11 Proportion of women with breakthrough bleeding/spotting at cycle 6.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 11 Proportion of women with breakthrough bleeding/spotting at cycle 6

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	130/1260	190/858		100.0 %	0.40 [0.32, 0.52]
Total (95% CI)	**1260**	**858**		**100.0 %**	**0.40 [0.32, 0.52]**
Total events: 130 (Triphasic), 190 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 7.31 (P < 0.00001)					



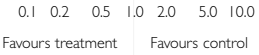
Analysis 17.12. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 12 Proportion of women with breakthrough bleeding at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 12 Proportion of women with breakthrough bleeding at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	12/263	15/181		100.0 %	0.53 [0.24, 1.16]
Total (95% CI)	**263**	**181**		**100.0 %**	**0.53 [0.24, 1.16]**
Total events: 12 (Triphasic), 15 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.59 (P = 0.11)					



Analysis 17.13. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 13 Proportion of women with breakthrough bleeding/spotting at cycle 12.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 13 Proportion of women with breakthrough bleeding/spotting at cycle 12

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	22/263	29/181		100.0 %	0.48 [0.27, 0.86]
Total (95% CI)	**263**	**181**		**100.0 %**	**0.48 [0.27, 0.86]**
Total events: 22 (Triphasic), 29 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.45 (P = 0.014)					

Analysis 17.14. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 14 Proportion of cycles with amenorrhea within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 14 Proportion of cycles with amenorrhea within 13 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	50/10032	609/6925		100.0 %	0.05 [0.04, 0.07]
Total (95% CI)	**10032**	**6925**		**100.0 %**	**0.05 [0.04, 0.07]**
Total events: 50 (Triphasic), 609 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 19.98 (P < 0.00001)					

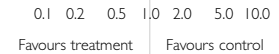
Analysis 17.15. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 15 Total discontinuation within 6 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 15 Total discontinuation within 6 cycles

Study or subgroup	Triphasic n/N	Monophasic n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hampton 2001	258/1236	176/853		100.0 %	1.01 [0.82, 1.26]
Total (95% CI)	**1236**	**853**		**100.0 %**	**1.01 [0.82, 1.26]**
Total events: 258 (Triphasic), 176 (Monophasic)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.13 (P = 0.89)					

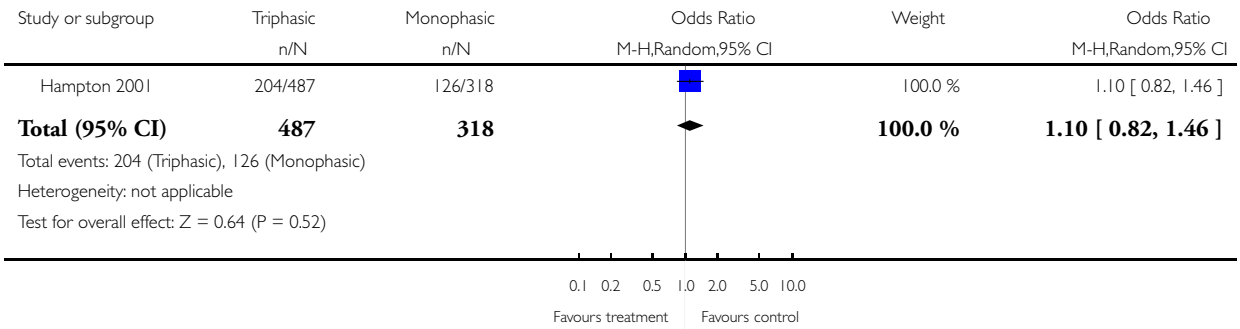


Analysis 17.16. Comparison 17 Triphasic NGM 180-215-250 μg/ EE 25 μg versus monophasic NETA 1000 μg/ EE 20 μg, Outcome 16 Total discontinuation within 13 cycles.

Review: Triphasic versus monophasic oral contraceptives for contraception

Comparison: 17 Triphasic NGM 180-215-250 g/ EE 25 g versus monophasic NETA 1000 g/ EE 20 g

Outcome: 16 Total discontinuation within 13 cycles



WHAT'S NEW

Last assessed as up-to-date: 24 November 2008.

25 November 2008	New search has been performed	Searches were updated; included a secondary article from earlier trial (Hampton 2001). Also added searches of clinical trials databases.

HISTORY

Protocol first published: Issue 2, 2002

Review first published: Issue 3, 2006

15 April 2008	Amended	Converted to new review format.
8 May 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

F Helmerhorst developed the idea. H van Vliet and D Grimes wrote the protocol and performed the literature search. H van Vliet, D Grimes and F Helmerhorst abstracted the data. H van Vliet drafted the review. L Lopez drafted the synopsis and parts of the abstract, and edited the review for Cochrane style. For the 2009 update, L Lopez reviewed the search results and updated the text. All authors edited and advised on the review drafts.

DECLARATIONS OF INTEREST

Dr. Grimes has consulted with or served on a speakers bureau for Bayer Healthcare Pharmaceuticals, Ortho-McNeil, Schering-Plough, Barr Laboratories, and Wyeth.

FM Helmerhorst had contacts with Asta Medica, Ferring, Hoechst Marion Roussel, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Organon, Pharmacia-Upjohn, Schering, SmithKline & Beecham, Serono, Wyeth Ayerst and Zeneca. He supervised studies sponsored or assigned by Hoechst Marion Roussel, Johnson & Johnson, Merck, Novartis, Organon, Schering, Serono and Wyeth Ayerst. These pharmaceutical companies have marketed oral contraceptive pills.

Three of the authors (DA Grimes, KF Schulz, LM Lopez) are employed by Family Health International, which sponsored two of the trials included in this review.

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- No sources of support supplied

External sources

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- U.S. Agency for International Development, USA.

INDEX TERMS

Medical Subject Headings (MeSH)

Contraception [*methods]; Contraceptives, Oral, Hormonal [adverse effects; *therapeutic use]; Drug Combinations; Ethinyl Estradiol [adverse effects; therapeutic use]; Levonorgestrel [adverse effects; therapeutic use]; Menstruation Disturbances [chemically induced]; Norethindrone [adverse effects; therapeutic use]; Patient Compliance; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans