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## Progestin-only contraceptives: effects on weight

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### Abstract

**Background**—Progestin-only contraceptives (POCs) are appropriate for many women who cannot or should not take estrogen. Many POCs are long-acting, cost-effective methods of preventing pregnancy. However, concern about weight gain can deter the initiation of contraceptives and cause early discontinuation among users.

**Objectives**—The primary objective was to evaluate the association between progestin-only contraceptive use and changes in body weight.

**Search strategy**—We searched MEDLINE, CENTRAL, POPLINE, EMBASE, LILACS, [ClinicalTrials.gov](http://ClinicalTrials.gov), and ICTRP, and contacted investigators to identify other trials.

**Selection criteria**—All comparative studies were eligible that examined a POC versus another method or no contraceptive. The primary outcome was mean change in body weight or body composition.

**Data collection and analysis**—Two authors extracted the data. We computed the mean difference with 95% confidence interval (CI) for continuous variables and odds ratio with 95% CI for dichotomous variables.

**Main results**—We did not conduct meta-analysis due to the various contraceptive methods and weight change measures. Fifteen studies examined progestin-only pills (N=1), Norplant (N=4), and depot medroxyprogesterone acetate (DMPA) (N=10). Comparison groups were similar for weight change in 11 studies. Four studies showed differences in weight or body composition

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#### CONTRIBUTIONS OF AUTHORS

L Lopez reviewed the search results, extracted and entered the data, and drafted the review. A Edelman and F Helmerhorst participated in the second extraction. M Chen-Mok provided guidance on study design, data analysis, and interpretation of results. All authors reviewed and commented on the document.

#### DECLARATIONS OF INTEREST

The authors do not have any conflicts of interest to declare regarding this review.

change for POCs compared to no hormonal method. Adolescents using DMPA had a greater increase in body fat (%) versus a group using no hormonal method (mean difference 11.00; 95% CI 2.64 to 19.36). The DMPA group also had a greater decrease in lean body mass (%) (mean difference -4.00; 95% CI -6.93 to -1.07). In another study, weight gain (kg) was greater for the DMPA group than an IUD group (mean difference 2.28, 2.71, 3.17, respectively). The differences were notable within the normal weight and overweight subgroups. One study showed the Norplant (six-capsule) group had greater weight gain (kg) than a non-hormonal IUD group (mean difference 0.47 (95% CI 0.29 to 0.65) and a group using non-hormonal or no method (mean difference 0.74; 95% CI 0.52 to 0.96). Another study also showed a Norplant group also had greater weight gain (kg) than an IUD group (mean difference 1.10; 95% CI 0.36 to 1.84).

**Authors' conclusions**—We found little evidence of weight gain when using POCs. Mean gain was less than 2 kg for most studies up to 12 months, and usually similar for the comparison group using another contraceptive. Appropriate counseling about typical weight gain may help reduce discontinuation of contraceptives due to perceptions of weight gain.

## PLAIN LANGUAGE SUMMARY

### Effects of progestin-only birth control on weight

Progestin-only contraceptives (POCs) can be used by women who cannot or should not take the hormone estrogen. Many POCs are long acting, cost less than some other methods, and work well to prevent pregnancy. Some people worry that weight gain is a side effect of these birth control methods. Concern about weight gain can keep women from using these methods, or cause women to stop using them early, which can lead to unplanned pregnancy. We looked at studies of progestin-only birth control and changes in body weight.

We did computer searches for studies of progestin-only birth control compared to another birth control method or no contraceptive. We also wrote to researchers to find other trials. The main focus was on change in body weight.

Of 15 studies, 4 showed the groups differed in weight gain or body mass. Differences were noted when a POC was compared to no hormonal birth control. In one study, the group using the injectable 'depo' had a greater increase in body fat at six months than a group with no hormonal birth control. The depo group also had a greater decrease in lean body mass than the 'no hormonal' group. In another study, the depo group gained more weight by one, two, and three years compared to an IUD group. The difference was noted in the subgroups of normal weight or overweight (but not obese) women. Two studies showed a Norplant (implant) group had more weight gain at six months and one year than an IUD group. A Norplant group also gained more weight by six months than a group using another non-hormonal method or no birth control.

We found little evidence of weight gain when using progestin-only birth control. Mean weight gain was less than 2 kg for most studies up to 12 months. The groups using other birth control methods had about the same weight gain. Good counseling about typical weight gain may help women avoid stopping birth control early due to worries about weight gain.

## BACKGROUND

### Description of the condition

Weight gain is often considered a side effect of using hormonal contraceptives (Goldberg 2007; Raymond 2007). This perception may be based on self-report of side effects rather than actual weight changes (Paul 1997; Berenson 2008). A Cochrane review revealed no clear evidence of weight gain with the use of combined hormonal contraceptives (Gallo 2008). Many clinicians and women also believe that progestin-only contraceptives cause weight gain (FWHC 2010; WebMD 2010).

Concern about weight gain can deter the initiation of contraceptives and cause early discontinuation among users. In a United States (US) study of bone mineral density, weight gain was reported more often by women using depot medroxyprogesterone acetate (DMPA) than those using a low-dose oral contraceptive (Berenson 2008). A national study in New Zealand found that weight gain was the most common side effect reported with DMPA use after menstrual disturbances (Paul 1997). In the US, weight gain has been reported to be a major reason for discontinuing DMPA use (Bonny 2004). Some evidence suggests that DMPA is a concern for adolescents who are already obese (Curtis 2009). Levonorgestrel implants have also been implicated for weight gain (Sivin 2003). The gain may be greater among women in the US than among those in China, and may be partly attributable to differences in dietary habits. In US studies, half of all implant discontinuations were attributed to the side effects of headache, weight, and mood changes (Sivin 2003).

### Description of the intervention

Progestin-only contraceptives (POCs) do not contain estrogen, unlike combined hormonal contraceptives that have both progestin and estrogen. Therefore, POCs are appropriate for women who cannot or should not take estrogen (ACOG 2006). The World Health Organization classes POCs as category 1 for women who are obese (body mass index  $\geq 30$  kg/m<sup>2</sup>). Category 1 is a condition with no restriction for use of the contraceptive method. For obese adolescents, DMPA is category 2 due to possible effects on bone mineral density (WHO 2010). For category 2, method advantages generally outweigh the theoretical or proven risks. POCs are also category 1 for breastfeeding women who are at least six weeks postpartum (WHO 2010), while combined hormonal contraceptives are category 3 for such women.

Oral contraceptives are the most commonly used reversible method in more developed areas of the world at 16.5% (UN 2007), and include combined oral contraceptives (COCs) as well as progestin-only pills (POPs) (Grimes 2010). The introduction of a new progestin-only oral contraceptive in Europe (Faculty of Family Planning 2003) has renewed interest in this class of oral contraceptives. Intrauterine devices (IUDs) lead in less developed areas at 16.5%, but hormonal IUDs are not widely used. Next in usage are injectables and implants; the combined rate is 3.4% worldwide (UN 2007). Some injectable contraceptives are combined, i.e., contain estrogen and progestin, while others like DMPA are progestin-only.

Injectables and implants are long-acting, thus freeing women from daily action to prevent unintended pregnancy. Long-acting methods are among the most cost-effective

contraceptives in many areas. Studies of long-acting contraceptives are often of longer duration than those for combined oral contraceptives (COCs), making study of weight change over time more feasible.

### How the intervention might work

In general, weight gain is due to an increase in one or more factors: fluid retention, muscle mass, and fat deposition. An early mechanistic study of DMPA and weight gain found no significant changes in fluid compartmental size, creatinine excretion rate, or nitrogen metabolism (Amatayakul 1980). The researchers reported an association between skinfold thickness and weight gain, indicating the gain was related to increased body fat. A study of risk factors for weight gain among adolescent DMPA users showed that appetite decreased while on DMPA (Bonny 2004). However, a brief randomized controlled trial (RCT) of DMPA versus placebo examined energy intake and expenditure as well as weight gain (Pelkman 2001). Meals were provided along with a range of snacks. Menstrual phase (pre-treatment) was associated with differences in energy intake and expenditure, but DMPA did not affect intake, expenditure, or weight gain.

The possible causal association between contraceptives and weight gain is difficult to study. During adolescence, some weight gain is developmentally normal and appropriate. Also, people tend to gain weight over time (Flegal 2000). No consensus exists regarding what is excessive weight gain. Ideally, studies would define a clinically important weight gain a priori, but weight change is rarely a primary outcome in contraceptive studies.

Examining contraceptive use and weight gain can be complicated by the initial weight of the users. We know little about how overweight women metabolize hormonal contraceptives, since many studies exclude overweight women (Edelman 2009; Lopez 2009). Further, concern about contraceptive effectiveness among overweight women (Grimes 2005; Trussell 2009) may lead to different usage by women of greater body weight. Some contraceptive methods that require a medical procedure have been associated with body weight. Among obese women in a US survey of contraceptive use (Schraudenbach 2009), tubal ligation was similar to pill use at nearly 26%. Among lower BMI groups, the figures were 13.5% and 19.5%, respectively. Implant use was relatively low overall, but higher among overweight (0.9%) and obese women (1.2%) than among normal or underweight women (0.4%). IUD use ranged from 4.1% to 4.6% across the BMI groups. In contrast, within an RCT focused on postpartum weight reduction, women with a BMI of 35 or higher were less likely to use 'effective' contraceptive than those with a BMI less than 30 (Chin 2009). Effective contraception referred to hormonal methods, IUDs, or sterilization.

### Why it is important to do this review

Currently no comprehensive systematic review exists on progestin only contraceptives and weight change. Concern about weight gain might deter women from using these effective contraceptives and health care providers from recommending them. We are not examining effectiveness nor focusing on overweight women. Many reviews have examined effectiveness of specific progestin only contraceptives, such as progestin-only pills (Grimes 2010) and IUDs (Grimes 2007). Further, a Cochrane review examined effectiveness of

hormonal contraceptives for overweight women versus women who were not overweight (Lopez 2010).

Progestin-only contraceptives are an attractive option for many women. The cost can be less than that of COCs in some areas, and many postpartum women can use them. Further, POCs are appropriate for many obese women, an important factor given the worldwide epidemic of obesity (Ogden 2007; Prentice 2006).

## OBJECTIVES

The primary objective was to evaluate the potential association between progestin-only contraceptive use and changes in body weight.

## METHODS

### Criteria for considering studies for this review

**Types of studies**—We included studies of progestin-only contraceptives for contraception and the effect on weight change. Reports had to contain information on the specific contraceptive method(s) examined. We did not anticipate finding many randomized controlled trials addressing weight change. Therefore, we searched for studies with comparative data on a progestin-only contraceptive versus another contraceptive (differing in formulation, dose, or regimen) or no contraceptive. This includes comparisons of a progestin-only contraceptive with a combination contraceptive as well as comparisons of two different types of progestin-only contraceptives. We eliminated studies focused on women with specific health problems, such as diabetes or HIV. We also excluded studies of contraceptives as treatment for specific disorders, e.g., acne, hirsutism, or polycystic ovary syndrome.

**Types of participants**—Participants were the women in the studies who used the progestin-only contraceptive for contraception or who had the comparison intervention or placebo.

**Types of interventions**—Any progestin-only contraceptive could have been examined, such as an oral contraceptive, an injectable, an implant, or a hormonal IUD. Treatment duration must have been at least three cycles. Progestin method of interest must have been specified and not combined in a group with another method (e.g., a group that could have used either DMPA or norethisterone enanthate (NET-EN)). The comparison could have been another progestin-only contraceptive or a group of contraceptives, such as COCs. We did not include comparison groups identified only as OC users, since the oral contraceptives could have been POPs or COCs.

**Types of outcome measures**—The primary outcome was the continuous outcome of mean change in body weight, BMI, or body composition (e.g., percent body fat) over time with the use of progestin-only contraceptives. If mean change in body weight or BMI was not available per study arm, we examined the dichotomous outcome of loss or gain of a

specified amount of weight in each study arm. Measured weight was used (not self-reported weight).

### Search methods for identification of studies

**Electronic searches**—We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), POPLINE, EMBASE, and LILACS. We also searched for trials via [ClinicalTrials.gov](http://ClinicalTrials.gov) and the search portal of the International Clinical Trials Registry Platform (ICTRP). The search strategies are shown below.

**MEDLINE via PubMed**—(contraceptive agents, female [Mesh] OR contraceptive devices, female [Mesh] OR contracept\*) AND (progest\* OR “progestin only” OR “progestin only” contracept\* OR “progestin only pill” OR progestin\* OR progesteron\* OR progestational, hormones, synthetic OR progestogen\* OR progesterone OR gestagen OR “progestogen only”) AND (body weight changes OR weight gain OR weight loss OR body mass index OR BMI OR weight) NOT (cancer [ti] OR polycystic [ti] OR exercise [ti] OR physical activity [ti] OR postmenopaus\*[ti])

limited to human, female.

**POPLINE**—(progestin only contracept\*/contraceptive agents, progestin/low-dose progestins) & (weight/weight gain/weight loss/body weight/BMI/body mass index/weight change)

**CENTRAL**—weight OR body mass index OR BMI in Abstract and contraception OR contraceptive in Title, Abstract or Keywords.

NOT premenstrual OR dysmenor\* OR endometr\* OR \*androgen\* OR HIV OR polycystic OR PCOS OR cancer OR exercise OR anorexia OR bulimic in Record Title.

NOT postmenopausal OR post-menopausal OR hormone therapy OR male hormonal OR male contracept\* OR testosterone in Record Title.

**EMBASE**—(contraceptive agent, progestin –side effects

or

((contraceptive device or contraceptives or contracept\*) and (gestagen! or progest? or progestin? or progesterone? or progestational, hormones, synthetic or progestogen?or progestin()only or progestin()only()contracept or progestin()only()pill or progestogen()only)))

and

(body weight! or weight gain or weight reduction or weight()loss or body()mass()index)

not (cancer or polycystic or exercise or physical() activity or postmenopaus? or oral contraceptives, combined)

and body weight/de

limited to human

**LILACS**—contraceptive agents or Agentes Anticoncepcionais Femininos or Anticoncepcionais Femininos or contraceptive devices, female or Dispositivos Anticoncepcionais Femininos or Dispositivos Anticoncepcionais Femininos or contraceptives or Anticoncepcionais [Words]

and weight or body weight or Peso Corporal or weight gain or Aumento de Peso or Ganho de Peso or weight reduction or weight loss or Pérdida de Peso or Perda de Peso or body weight changes or Cambios en el Peso Corporal or Alterações do Peso Corporal or body mass index or BMI [Words]

**ClinicalTrials.gov**—Search terms: overweight OR obese OR obesity OR weight OR body mass index OR BMI

Condition: NOT (HIV OR polycystic OR PCOS OR cancer OR anorexia OR pulmonary OR metabolic OR amenorrhea)

Intervention: contraceptive OR contraception

Study type: interventional studies

Gender: studies with female participants

### **ICTRP**

1. Intervention: contraceptive OR contraception
2. Condition: contraceptive OR contraception

Intervention: progestin OR progestin-only OR IUD OR implant OR medroxyprogesterone OR norethisterone

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

## **Data collection and analysis**

**Selection of studies**—We assessed for inclusion all titles and abstracts identified during the literature searches. One author reviewed the search results and identified reports for inclusion or exclusion. A second author also examined the reports identified for appropriate categorization according to the criteria above.

All comparative study designs were considered. For example, studies could have been randomized controlled trials (RCTs), other prospective studies (provided intervention; assignment not random), observational studies of existing contraceptive users, case control studies, or retrospective chart reviews. Post hoc analysis from any of these types of studies

was also considered. However, the studies had to meet the other Criteria for considering studies for this review.

We excluded studies that only reported mean weight pre- and post-treatment. Even RCTs could not be used with mean weights only, since the comparisons in our review were not necessarily those on which the randomization was based.

**Data extraction and management**—One author abstracted the data and entered the information into RevMan. Another author conducted a second data abstraction and verified correct data entry. Any discrepancies were resolved by discussion or with a third author if necessary.

**Assessment of risk of bias in included studies**—The randomized controlled trials were examined for methodological quality, according to recommended principles (Higgins 2009). Methodology considered included randomization method, allocation concealment, blinding, and losses to follow up and early discontinuation. Adequate methods for allocation concealment include a centralized telephone system and the use of sequentially-numbered, opaque, sealed envelopes (Schulz 2002). In addition, high losses to follow up threaten validity (Strauss 2005).

To assess the non-randomized data, we used the principles outlined in section 13.5 of Higgins 2009 as well as the STROBE statement for reports of observational studies (Von Elm 2007). We assessed whether the analysis included adjustment for potential confounding related to weight change. The study groups could differ in ways related to the outcome, such as initial weight or BMI or previous use of hormonal contraceptives.

For all types of studies, limitations in design were presented in Risk of bias in included studies, and were considered when interpreting the results.

After conducting the review, we assessed the quality of evidence using the GRADE approach (Higgins 2009). Grades could be high, moderate, low, or very low. The initial grade was based on study design: RCTs were high; prospective, not RCTs were moderate; and retrospective studies were low. The initial rating was downgraded a level for each of the following: a) losses to follow up of 25% or more; b) inappropriate exclusions after randomization.

**Measures of treatment effect**—Outcomes listed in Characteristics of included studies are focused on those relevant to this review. For weight gain measure with follow up less than one year, we selected the last date. If multiple time points were reported up to one year, we used the midpoint and one year data. If data were available for more than three years, we used one year as well as the midpoint and last measure.

**Dealing with missing data**—We excluded studies with insufficient data on weight or BMI for analysis in this review. Reports sometimes provided results in figures without specific numbers; others presented means without any variance estimate. Many studies were more than 10 years old, making it difficult to obtain additional data from the researchers.



**Assessment of heterogeneity**—We expected study populations, designs, and interventions to be heterogeneous. We described the clinical and methodological diversity (or heterogeneity) of the studies. We did not pool data from studies that had different contraceptive methods (e.g., DMPA or implants), different doses of the same method, or different criteria for reporting weight change. Therefore, we were not able to conduct meta-analysis due to the range of contraceptive methods examined and different reporting for weight change. Heterogeneity is not an issue when a comparison has a single study.

**Data synthesis**—We examined results by the contraceptive method studied, e.g., injectable or implant, as well as by formulation, dose, or regimen as appropriate. The main comparisons for this review were between users of progestin-only contraceptives and users of another contraceptive (differing in formulation, dose, or regimen) or no hormonal contraceptive. For continuous variables, the mean difference was computed with 95% confidence interval (CI) using a fixed effect model. RevMan uses the inverse variance approach (Higgins 2009). Continuous measures include mean change in weight or BMI or percentage body fat. For dichotomous outcomes, the Mantel-Haenszel odds ratio (OR) with 95% CI was calculated using a fixed-effect model. An example is the proportion of women who gained a specified amount of weight. Fixed and random effects give the same result if no heterogeneity exists, as when a comparison includes only one study. The Peto OR was used when a study arm had no events; the Peto OR does not require correction for zero events (Higgins 2009).

Data were not available to examine weight change in relation to age. A certain amount of weight gain is part of normal development for adolescents. Studies that targeted adolescents are identified. Studies that included both adolescents and adult women did not provide outcome data for age subgroups.

When data were available, we also examined weight change in relation to initial body weight or body mass index (BMI) [weight (kg)/height (m)<sup>2</sup>]. Weight change may differ for women who were initially overweight or obese versus those who were not overweight or obese. We preferred BMI over weight alone, as a higher BMI generally reflects more body fat (CDC 2010). However, the measures and cutoffs depended on those used in the included studies. Frequently used BMI categories are 25 to 29.9 (kg/m<sup>2</sup>) for overweight and 30 or higher for obesity (CDC 2010). We also considered studies that used older US cutoffs derived from the National Health and Nutrition Examination Survey II (NHANES II) conducted from 1976 to 1980 (Najjar 1987). From NHANES II, the BMI cutoffs for women are 27.3 for overweight and 32 for obesity.

### Sensitivity analysis

We conducted sensitivity analysis by removing the retrospective studies, i.e., chart reviews. The remaining prospective studies included RCTs, other prospective designs, and post hoc analysis of data from prospective studies. Further, we examined results after removing studies that had losses or discontinuations totaling 25% or more of the sample.

## RESULTS

### Description of studies

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

Fifteen studies met our inclusion criteria. The nine prospective studies included five RCTs (WHO 1983; Salem 1988; Ball 1991; Sivin 1998; Westhoff 2007) and four with other prospective designs (Tankeyoon 1976; Castle 1978; Salem 1984; Bonny 2009). Six studies used retrospective data (Moore 1995; Taneepanichskul 1998; Espey 2000; Sule 2005; Tuchman 2005; Pantoja 2010).

The progestin-only contraceptives studied were as follows:

- Oral contraceptives (OCs) containing norethisterone 350 µg or levonorgestrel 30 µg
- Injectable: depot medroxyprogesterone acetate (DMPA) 150 mg/mL or 450 mg/mL (intramuscular) or 104 mg/0.65mL (subcutaneous)
- Injectable: norethisterone enanthate (NET-EN) 200 mg
- Implants (levonorgestrel): 6 capsules; 2 rods

Comparison groups included no hormonal contraceptive, a different regimen of the same progestin-only contraceptive, another progestin-only contraceptive, or a contraceptive or supplement containing estrogen. Where IUD users were a comparison group, the IUDs were non-hormonal.

Studies were conducted in the USA, South America, Europe, Africa, Asia, and on multiple continents. Duration of prospective follow up or retrospective data collection was 6 months to 2 years for 10 studies, while 5 studies lasted 3 years or more.

Three studies included adolescents and young women. Bonny 2009 analyzed data from a larger study of hormonal contraceptives and bone mineral density. Moore 1995 and Tuchman 2005 were retrospective chart reviews.

### Risk of bias in included studies

Three of the five RCTs did not have any information on randomization method or allocation concealment (WHO 1983; Ball 1991; Westhoff 2007). The other two RCTs reported the method of randomization and allocation concealment (Salem 1988; Sivin 1998). Two RCTs had information on blinding. Ball 1991 was reportedly “single-blind.” For the trials used in Westhoff 2007, the evaluators were blinded.

**Incomplete outcome data**—Five of 15 studies had losses of 25% or more in at least one group. Three were prospective studies (RCTs or non-randomized) For Tankeyoon 1976, the COC group was reduced by 25%. In Castle 1978, losses to follow up were 39% (DMPA 150) versus 23% (DMPA 450). Westhoff 2007 had study discontinuation rates of 75% (DMPA-SC 104) and 79% (DMPA-IM 150). The retrospective studies generally had complete outcome data due to the inclusion criteria for cases. However, two of the six were missing substantial data from the later years. For Espey 2000 at two years, weight measures

were not available for 70% of interval group and 49% of the postpartum group. In Sule 2005, the sample was reduced to 54% at three years.

**Selective reporting**—Taneepanichskul 1998 excluded those who developed a chronic disease or disorder during method use, which may have biased the results. Weight gain is associated with development of some diseases and disorders.

**Other potential sources of bias**—Two non-randomized studies conducted analysis that adjusted for potential confounders (Moore 1995; Bonny 2009). However, we did not include those analyses because at least one comparison group did not meet our inclusion criteria. Details are in Characteristics of included studies. Consequently, none of the analyses in this review were adjusted for potential confounders of weight gain.

**Effects of interventions**—See: **Summary of findings for the main comparison** All included studies; **Summary of findings 2** Sensitivity analysis; **Summary of findings 3** Quality of evidence by contraceptive method

Results are grouped according to three types of progestin-only contraceptive studied. One trial examined progestin-only pills, 10 studies addressed DMPA, and 4 examined Norplant (one of which also included DMPA). We have subdivided the sections into studies comparing POCs with combination contraceptives, with no hormonal contraceptive, and with other POCs.

**Progestin-only oral contraceptives**—In the RCT of Ball 1991, weight change at six months was similar for the norethisterone 350 µg and the levonorgestrel 30 µg groups. Mean changes were small.

#### **Depot medroxyprogesterone acetate**

**POC versus a combination contraceptive:** Depot medroxyprogesterone acetate 150 mg/mL (DMPA) was compared to a contraceptive or supplement that also contained estrogen in three studies. Bonny 2009 compared mean percentage changes in total body fat and lean body mass at six months for DMPA 150 plus placebo injection versus DMPA plus estradiol cypionate 5 mg (E2C). The study targeted adolescents, ages 12 to 18 years. The DMPA group was similar to the DMPA plus E2C group for mean change in total body fat (%) and in lean body mass (%). However, when compared to a group using no hormonal method, the DMPA group had a greater change in total body fat (%) (mean difference 11.00; 95% CI 2.64 to 19.36) (Analysis 3.1) and a greater change in lean body mass (%) (mean difference -4.00; 95% CI -6.93 to -1.07) (Analysis 3.2). The retrospective study of Tuchman 2005 focused on adolescents and young women, ages 12 to 21 years. At 6 and 12 months, the DMPA group was similar to the group using medroxyprogesterone acetate (MPA) plus E2C and to the COC users for mean weight change and mean percentage weight change (Tuchman 2005). In the small study of Tankeyoon 1976, the DMPA and COC groups were similar in the proportions that gained at least 1 kg by months 6 and 12. For weight loss of 1 kg or more, the groups were slightly different at six months but the confidence interval was very wide.

**POC versus another POC:** DMPA 150 mg/mL was compared with other DMPA formulations or regimens in three studies. In Castle 1978, the mean changes in weight at six months were small and similar for the DMPA 150 and DMPA 450 groups. The retrospective study of Espey 2000 did not show a significant difference in weight gain at one or two years for those who initiated DMPA at 20 weeks or more after pregnancy (interval group) versus initiation at 5 to 8 weeks after pregnancy (postpartum group). In the RCT analyzed in Westhoff 2007, weight change was comparable for the DMPA 150 group and the group with subcutaneous DMPA 104.

Two studies examined DMPA 150 mg/mL versus NET-EN 200 mg. In WHO 1983, mean weight changes at 12 and 24 months did not differ significantly for the DMPA group versus the group administered NET-EN at 60-day intervals. Weight change was also similar for two NET-EN regimens of 60 day-intervals versus 84-day intervals. For the RCT of Salem 1988, the units for weight were not reported (lbs or kg). However, mean changes in weight at one year were similar for the DMPA and the NET-EN groups.

**POC versus no hormonal contraceptive:** DMPA 150 mg/mL was compared to a non-hormonal IUD in two retrospective studies. Taneepanichskul 1998 did not show a difference between the DMPA and IUD groups at 120 months. For Pantoja 2010, mean weight gain (kg) was greater for the DMPA group versus the IUD group at one, two, and three years: mean difference 2.28 (Analysis 11.2), 2.71 (Analysis 11.3), and 3.17 (Analysis 11.4), respectively. For each year, the difference between contraceptive groups was notable within the normal to lower weight group (BMI < 25) and within the overweight group (BMI 25 to 29.9), but not within the obese group (BMI  $\geq$  30).

**Norplant**—Norplant (with 6 capsules) was compared to other hormonal contraceptives and to no hormonal contraceptive use.

For the retrospective study of Sule 2005, the Norplant group had a significantly greater weight increase (kg) than the IUD group at one year (mean difference 1.10; 95% CI 0.36 to 1.84) (Analysis 13.2), but not at three years. The Norplant group was similar in weight change to the COC group.

The retrospective study of Moore 1995 targeted adolescents and young women, ages 15 to 30 years. The Norplant and DMPA groups were similar in mean weight change at one year. Salem 1984 showed a greater weight change (kg) at six months for the Norplant group versus the IUD group (mean difference 0.47; 95% CI 0.29 to 0.65) (Analysis 13.1). The Norplant group also had a greater weight change (kg) than the group that used barrier, 'local', or no contraceptive method (mean difference 0.74; 95% CI 0.52 to 0.96) (Analysis 14.1). In the RCT of Sivin 1998, mean weight change was similar for the Norplant group versus the two-rod LNG group at one, three, and five years.

**Sensitivity analysis**—All study results were summarized in Summary of findings for the main comparison. For the planned sensitivity analysis, we removed retrospective studies as well as studies with high losses to follow up or method discontinuation ( $\geq$  25%) (Summary of findings 2). Two studies showed differences in weight gain or body composition between

the progestin-only group and a comparison group; both lasted only six months. Bonny 2009 was a small study of adolescents from a larger trial. The DMPA group had a greater increase in body fat percentage, and a greater decrease in lean body mass, compared to the group using no hormonal contraceptive. In Salem 1984, Norplant users showed a greater weight gain than the IUD users and the group that used barrier, 'local', or no contraceptive method.

## DISCUSSION

### Summary of main results

We were not able to conduct meta-analysis due to the range of contraceptive methods examined and different reporting for weight change. Four of the 15 studies showed a significant difference between groups in weight change or body composition change (Salem 1984; Sule 2005; Bonny 2009; Pantoja 2010). Two of the four studies examined DMPA and two focused on Norplant (six capsules). The differences were noted in the comparisons with groups using no hormonal contraceptives. Of these four studies, two remained in the sensitivity analysis. Bonny 2009 examined DMPA, focused on adolescents, and appropriately measured change in body fat (%) and lean body mass (%) rather than weight change alone. The DMPA group differed from the group using no hormonal contraceptive at six months. Salem 1984 assessed Norplant and provided mean weight change (kg) at six months. The Norplant group differed from the IUD group and from a group using other non-hormonal or no contraceptive method.

Actual mean weight gain was limited at 6 or 12 months (Summary of findings for the main comparison), i.e., less than 2 kg for most studies. The five studies with multi-year data showed that mean weight change was approximately twice as much at two or three years than at one year, but was generally similar for both study groups (Summary of findings for the main comparison). A total of seven studies had data from two years or more of contraceptive use:

- Three RCTs compared two POCs (WHO 1983; Sivin 1998; Westhoff 2007). The DMPA or implant groups gained similar amounts of weight over one to three years.
- Three retrospective studies compared a POC to a nonhormonal IUD (Taneepanichskul 1998; Sule 2005; Pantoja 2010). Only Pantoja 2010 showed more weight gain for the DMPA group at one, two, and three years, but interestingly not within the obese group (BMI  $\geq 30$ ).
- The retrospective study of Espey 2000 showed two DMPA groups to be similar in weight gain at one and two years.

### Overall completeness and applicability of evidence

Of the 15 studies, 11 had data from a year or more of contraceptive use, of which 7 had data from two years or more. Weight gain (or the perception of weight gain) is frequently cited as a reason for discontinuing a contraceptive method. If a method is associated with weight gain, a year is long enough to detect some change, though the amount may not be significant. Of the seven studies with data from two years or more of contraceptive use, most

showed the study groups to be similar for weight gain, regardless of whether the comparison group used POCs, combination contraceptives, or no hormonal methods.

Studies of progestin-only contraceptives and weight change were limited in type and number. Only one study of progestin-only pills was found that met our inclusion criteria. For implants, we found the most weight change data for Norplant (with six capsules). However, Norplant is no longer marketed, while single-rod and two-rod implants are currently available. However, most studies of currently marketed implants did not meet our inclusion criteria, mainly due to the lack of comparative weight change data. The one exception was a study in which Norplant was compared to a two-rod implant. Consequently, we do not have much evidence regarding weight change with currently marketed implants. Further, we did not find any studies of hormonal IUDs that met our inclusion criteria.

### Quality of the evidence

After conducting the review, we assessed the quality of evidence using the GRADE approach (Higgins 2009). The level was based primarily on study design, which we downgraded one level if losses to follow up were 25% or more or if cases were inappropriately excluded after randomization. The results are shown by contraceptive method of focus and quality level (Summary of findings 3). Seven studies were rated as high or moderate quality. Progestin-only pills had one study of high quality that showed no significant difference in weight change. DMPA had two high quality and two moderate quality studies, one of which showed adolescents using DMPA had increased body fat percentage and decreased lean body mass. The six-capsule Norplant had one high quality and one moderate quality study; the latter showed a greater weight increase for Norplant users.

Sample sizes varied. Three studies had 32 to 51 participants, and were unlikely to have had sufficient power to detect differences in weight gain. Seven studies had 100 to 400 participants, and five ranged from 534 to 3172. A few had comparison groups that were not used in this review, because the group did not meet our inclusion criteria.

Most studies did not adjust for potential confounding factors of weight change. Some had adjusted analyses that we did not use since a comparison group did not meet our inclusion criteria.

### Potential biases in the review process

We selected studies that had data on mean weight change, mean change in body composition, or proportion that gained or lost a specified amount of weight. Several studies were excluded due to not reporting the data we needed. Many studies were older, which limited our ability to obtain additional information from the researchers.

### Agreements and disagreements with other studies or reviews

Many of the concerns about weight gain with POC use are based on perceptions and discontinuation reasons rather than measures of actual weight change (Paul 1997; Bonny 2004; Berenson 2008). We found limited evidence of significant change for POC users

versus those who did not use hormonal contraceptives. Actual weight gain was relatively low up to one year. Similarly, a Cochrane review showed no clear evidence of weight gain with the use of combined hormonal contraceptives (Gallo 2008). People may gain weight over time, regardless of contraceptive use.

However, DMPA may be a concern for adolescents who are already obese (Curtis 2009). One study that focused on adolescents (Bonny 2009) showed an increase in total body fat and a decrease in lean body mass for the DMPA group versus those with no hormonal contraceptive use. Two retrospective studies included adolescents (Moore 1995 (15 to 30 years old); Tuchman 2005(12 to 21 years old). However, they did not show a significant difference between groups nor much weight gain within the DMPA or Nor-plant groups.

## AUTHORS' CONCLUSIONS

### Implications for practice

We found little evidence of weight gain when using progestin-only contraceptives. Some differences were noted when a POC was compared to no hormonal contraceptive. Actual mean weight gain was low for 6 to 12 months, i.e., less than 2 kg for most studies. More weight gain was noted at two and three years, but was generally similar for both comparison groups. People may gain weight over time regardless of contraceptive use. Appropriate and accurate counseling about typical weight gain may help reduce discontinuation of contraceptives due to perceptions of weight gain.

### Implications for research

The five RCTs each compared similar progestin-only contraceptives, which might account for the groups being similar for weight change. Two other prospective studies (not RCTs) and two retrospective studies showed some differences for POCs versus no hormonal contraceptives; one showed a difference at more than a year of contraceptive use. Weight gain is rarely the focus of prospective contraceptive studies. Well-designed RCTs assessing weight change over time would better address this issue. However, careful counseling and follow up are needed to avoid the high rates for losses to follow up and discontinuation found in many contraceptive studies.

## Acknowledgments

Carol Manion of FHI developed the search strategies for several databases. David Grimes of FHI assisted with the second data abstraction.

### SOURCES OF SUPPORT

#### Internal sources

- No sources of support supplied

#### External sources

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

## Appendix

### DATA AND ANALYSES

#### Comparison 1. Norethisterone 350 µg versus levonorgestrel 30 µg

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	39	Mean Difference (IV, Fixed, 95% CI)	-0.6 [-1.76, 0.56]

#### Comparison 2. DMPA 150 mg/mL + placebo versus DMPA 150 mg/mL + E2C

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean change in total body fat (%) at 6 months	1	15	Mean Difference (IV, Fixed, 95% CI)	7.50 [-0.47, 15.47]
2 Mean change in lean body mass (%) at 6 months	1	15	Mean Difference (IV, Fixed, 95% CI)	-2.2 [-3.00, 0.60]

#### Comparison 3. DMPA 150 mg/mL versus control (no hormonal method)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean change in total body fat (%) at 6 months	1	26	Mean Difference (IV, Fixed, 95% CI)	11.0 [2.64, 19.36]
2 Mean change in lean body mass (%) at 6 months	1	26	Mean Difference (IV, Fixed, 95% CI)	-4.0 [-6.93, -1.07]

#### Comparison 4. DMPA 150 mg/mL versus MPA + E2C

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	70	Mean Difference (IV, Fixed, 95% CI)	-0.6 [-3.05, 1.85]
2 Mean weight change (kg) at 12 months	1	46	Mean Difference (IV, Fixed, 95% CI)	-1.3 [-6.37, 3.77]
3 Mean percentage weight change at 6 months	1	70	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-4.04, 2.84]
4 Mean percentage weight change at 12 months	1	46	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-7.58, 6.18]



**Comparison 5. DMPA 150 mg/mL versus COC**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	142	Mean Difference (IV, Fixed, 95% CI)	-0.50 [-2.26, 1.26]
2 Mean weight change (kg) at 12 months	1	81	Mean Difference (IV, Fixed, 95% CI)	0.7 [-1.92, 3.32]
3 Mean percentage weight change at 6 months	1	142	Mean Difference (IV, Fixed, 95% CI)	-0.7 [-3.10, 1.70]
4 Mean percentage weight change at 12 months	1	81	Mean Difference (IV, Fixed, 95% CI)	Not estimable
5 Weight gain $\geq$ 1 kg at month 6	1	31	Odds Ratio (M-H, Fixed, 95% CI)	0.39 [0.09, 1.67]
6 Weight gain $\geq$ 1 kg at month 12	1	26	Odds Ratio (M-H, Fixed, 95% CI)	0.44 [0.08, 2.39]
7 Weight loss $\geq$ 1 kg at month 6	1	31	Peto Odds Ratio (Peto, Fixed, 95% CI)	9.15 [0.88, 95.40]
8 Weight loss $\geq$ 1 kg at month 12	1	26	Odds Ratio (M-H, Fixed, 95% CI)	1.83 [0.15, 23.15]

**Comparison 6. DMPA 150 mg/mL versus DMPA 450 mg/mL**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	651	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.48, 0.50]

**Comparison 7. DMPA 150 mg/mL initiation after pregnancy: interval ( $\geq$ 20 weeks) versus postpartum (5 to 8 weeks)**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight gain (lbs) at 1 year	1	172	Mean Difference (IV, Fixed, 95% CI)	2.30 [-0.94, 5.54]
2 Mean weight gain (lbs) at 2 years	1	64	Mean Difference (IV, Fixed, 95% CI)	1.60 [-4.79, 7.99]

**Comparison 8. DMPA-IM 150 mg versus DMPA-SC 104 mg**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 36 months	1	121	Mean Difference (IV, Fixed, 95% CI)	1.30 [-1.78, 4.38]

**Comparison 9. DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals)**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 12 months	1	1162	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.63, 1.03]
2 Mean weight change (kg) at 24 months	1	604	Mean Difference (IV, Fixed, 95% CI)	Not estimable
3 Mean weight change at 1 year	1	201	Mean Difference (IV, Fixed, 95% CI)	0.80 [-0.10, 1.70]

**Comparison 10. NET-EN 200 mg: 60-day intervals versus 3 intervals of 60 days then 84-day intervals**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 12 months	1	822	Mean Difference (IV, Fixed, 95% CI)	Not estimable
2 Mean weight change (kg) at 24 months	1	453	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-1.35, 1.15]

**Comparison 11. DMPA 150 mg/mL versus IUD**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 120 months	1	100	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-0.83, 0.23]
2 Mean weight change (kg) at 1 year by baseline BMI	1	758	Mean Difference (IV, Fixed, 95% CI)	2.28 [1.79, 2.77]
2.1 BMI < 25 kg/m <sup>2</sup>	1	452	Mean Difference (IV, Fixed, 95% CI)	2.5 [1.90, 3.10]
2.2 BMI 25 to 29.9 kg/m <sup>2</sup>	1	218	Mean Difference (IV, Fixed, 95% CI)	2.10 [1.16, 3.04]
2.3 BMI ≥ 30 kg/m <sup>2</sup>	1	88	Mean Difference (IV, Fixed, 95% CI)	0.7 [-1.26, 2.66]
3 Mean weight change (kg) at 2 years by baseline BMI	1	758	Mean Difference (IV, Fixed, 95% CI)	2.71 [2.12, 3.30]
3.1 BMI < 25 kg/m <sup>2</sup>	1	452	Mean Difference (IV, Fixed, 95% CI)	2.7 [2.02, 3.38]
3.2 BMI 25 to 29.9 kg/m <sup>2</sup>	1	218	Mean Difference (IV, Fixed, 95% CI)	3.0 [1.73, 4.27]
3.3 BMI ≥ 30 kg/m <sup>2</sup>	1	88	Mean Difference (IV, Fixed, 95% CI)	1.5 [-1.33, 4.33]
4 Mean weight change (kg) at 3 years by baseline BMI	1	758	Mean Difference (IV, Fixed, 95% CI)	3.17 [2.51, 3.83]
4.1 BMI < 25 kg/m <sup>2</sup>	1	452	Mean Difference (IV, Fixed, 95% CI)	3.3 [2.52, 4.08]
4.2 BMI 25 to 29.9 kg/m <sup>2</sup>	1	218	Mean Difference (IV, Fixed, 95% CI)	3.20 [1.82, 4.58]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.3 BMI $\geq$ 30 kg/m <sup>2</sup>	1	88	Mean Difference (IV, Fixed, 95% CI)	1.30 [-1.56, 4.16]

### Comparison 12. Norplant versus DMPA 150 mg/mL

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 1 year	1	100	Mean Difference (IV, Fixed, 95% CI)	-0.87 [-1.86, 0.12]

### Comparison 13. Norplant versus IUD

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	99	Mean Difference (IV, Fixed, 95% CI)	0.47 [0.29, 0.65]
2 Mean weight change (kg) at 1 year	1	324	Mean Difference (IV, Fixed, 95% CI)	1.1 [0.36, 1.84]
3 Mean weight change (kg) at 3 years	1	190	Mean Difference (IV, Fixed, 95% CI)	0.90 [-0.39, 2.19]

### Comparison 14. Norplant versus barrier, 'local', or no contraceptive method

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 6 months	1	97	Mean Difference (IV, Fixed, 95% CI)	0.74 [0.52, 0.96]

### Comparison 15. Norplant versus 2-rod LNG

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 1 year	1	1196	Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.33, 0.51]
2 Mean weight change (kg) at 3 years	1	922	Mean Difference (IV, Fixed, 95% CI)	Not estimable
3 Mean weight change (kg) at 5 years	1	614	Mean Difference (IV, Fixed, 95% CI)	0.60 [-0.13, 1.33]

### Comparison 16. Norplant versus COC

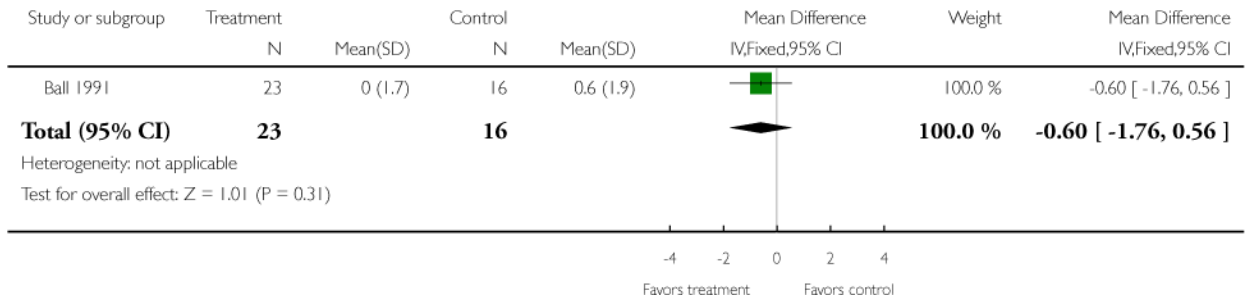
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at 1 year	1	226	Mean Difference (IV, Fixed, 95% CI)	1.1 [-0.13, 2.33]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Mean weight change (kg) at 3 years	1	132	Mean Difference (IV, Fixed, 95% CI)	Not estimable

Review: Progestin-only contraceptives: effects on weight

Comparison: 1 Norethisterone 350 g versus levonorgestrel 30 g

Outcome: 1 Mean weight change (kg) at 6 months



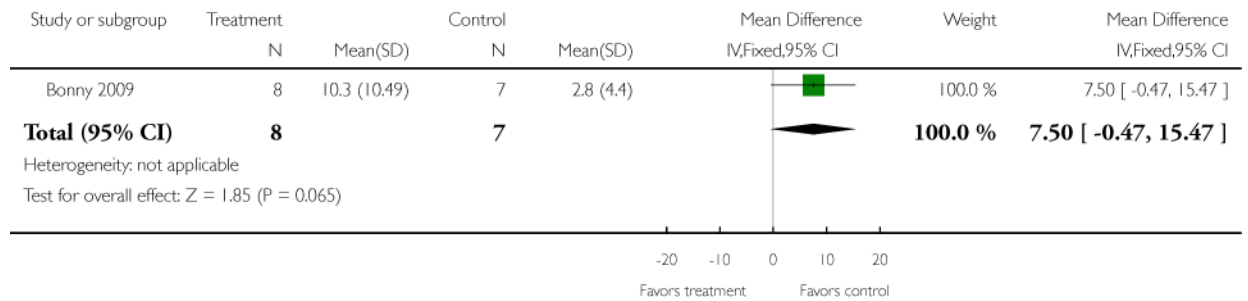
**Analysis 1.1.**

Comparison 1 Norethisterone 350 µg versus levonorgestrel 30 µg, Outcome 1 Mean weight change (kg) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 2 DMPA 150 mg/mL + placebo versus DMPA 150 mg/mL + E2C

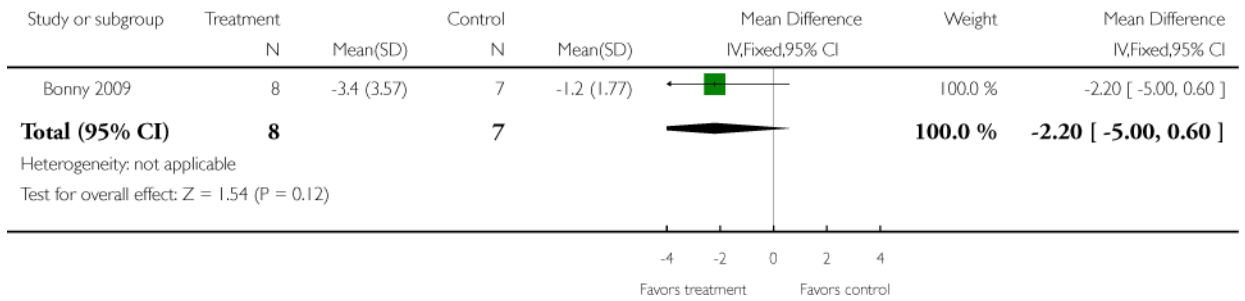
Outcome: 1 Mean change in total body fat (%) at 6 months



**Analysis 2.1.**

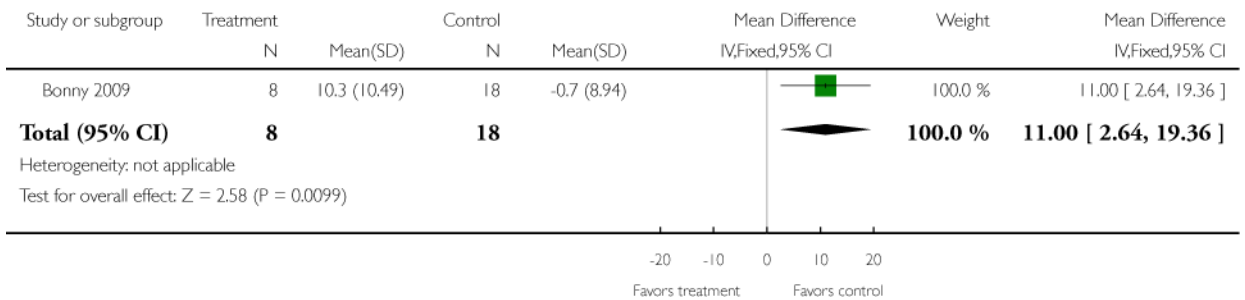
Comparison 2 DMPA 150 mg/mL + placebo versus DMPA 150 mg/mL + E2C, Outcome 1 Mean change in total body fat (%) at 6 months.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 2 DMPA 150 mg/mL + placebo versus DMPA 150 mg/mL + E2C  
 Outcome: 2 Mean change in lean body mass (%) at 6 months



**Analysis 2.2.**  
 Comparison 2 DMPA 150 mg/mL + placebo versus DMPA 150 mg/mL + E2C, Outcome 2  
 Mean change in lean body mass (%) at 6 months.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 3 DMPA 150 mg/mL versus control (no hormonal method)  
 Outcome: 1 Mean change in total body fat (%) at 6 months

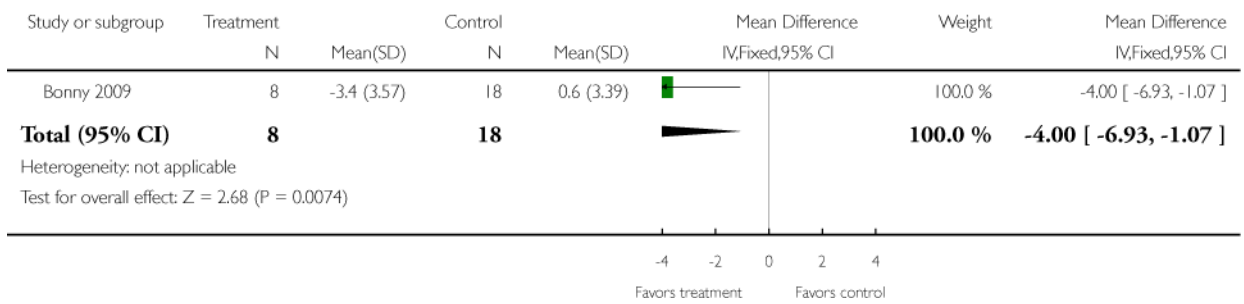


**Analysis 3.1.**  
 Comparison 3 DMPA 150 mg/mL versus control (no hormonal method), Outcome 1 Mean  
 change in total body fat (%) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 3 DMPA 150 mg/mL versus control (no hormonal method)

Outcome: 2 Mean change in lean body mass (%) at 6 months



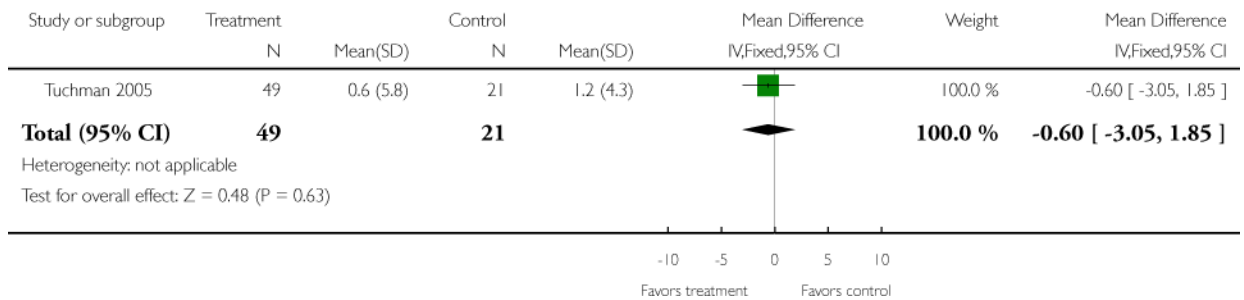
**Analysis 3.2.**

Comparison 3 DMPA 150 mg/mL versus control (no hormonal method), Outcome 2 Mean change in lean body mass (%) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 4 DMPA 150 mg/mL versus MPA + E2C

Outcome: 1 Mean weight change (kg) at 6 months



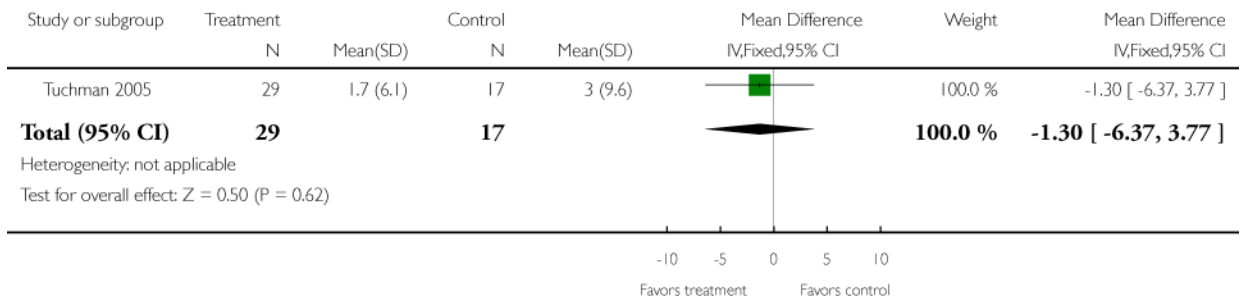
**Analysis 4.1.**

Comparison 4 DMPA 150 mg/mL versus MPA + E2C, Outcome 1 Mean weight change (kg) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 4 DMPA 150 mg/mL versus MPA + E2C

Outcome: 2 Mean weight change (kg) at 12 months



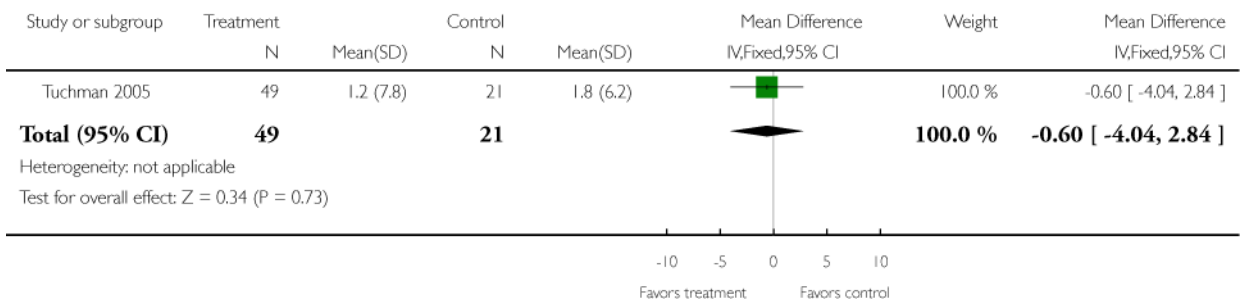
**Analysis 4.2.**

Comparison 4 DMPA 150 mg/mL versus MPA + E2C, Outcome 2 Mean weight change (kg) at 12 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 4 DMPA 150 mg/mL versus MPA + E2C

Outcome: 3 Mean percentage weight change at 6 months



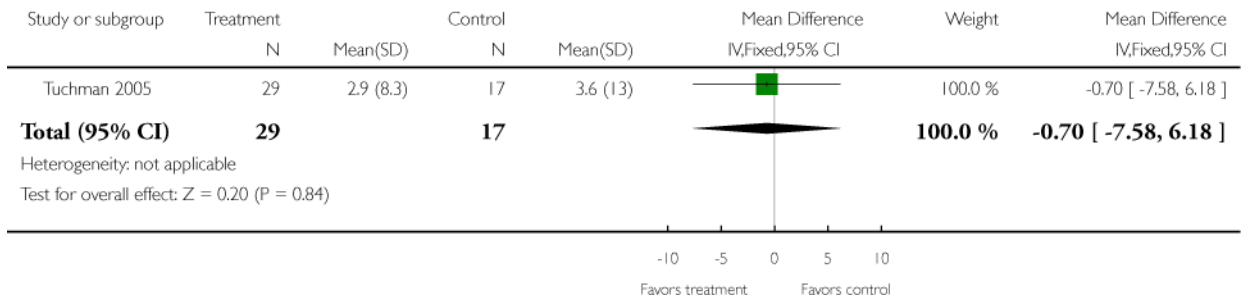
**Analysis 4.3.**

Comparison 4 DMPA 150 mg/mL versus MPA + E2C, Outcome 3 Mean percentage weight change at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 4 DMPA 150 mg/mL versus MPA + E2C

Outcome: 4 Mean percentage weight change at 12 months



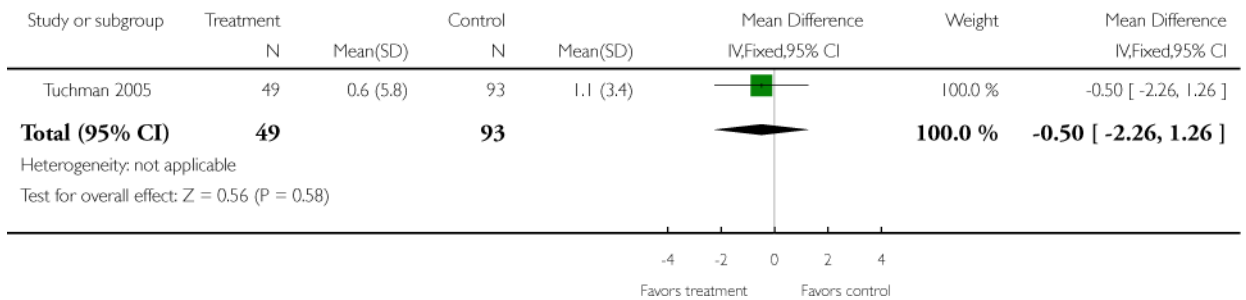
**Analysis 4.4.**

Comparison 4 DMPA 150 mg/mL versus MPA + E2C, Outcome 4 Mean percentage weight change at 12 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

Outcome: 1 Mean weight change (kg) at 6 months



**Analysis 5.1.**

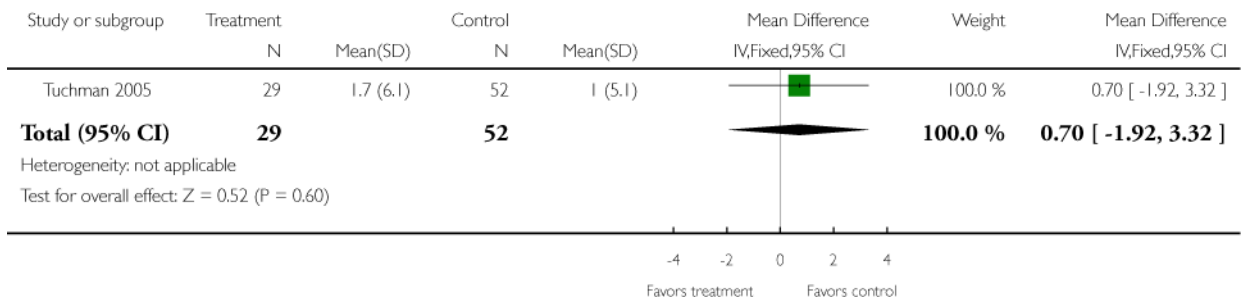
Comparison 5 DMPA 150 mg/mL versus COC, Outcome 1 Mean weight change (kg) at 6 months.



Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

Outcome: 2 Mean weight change (kg) at 12 months



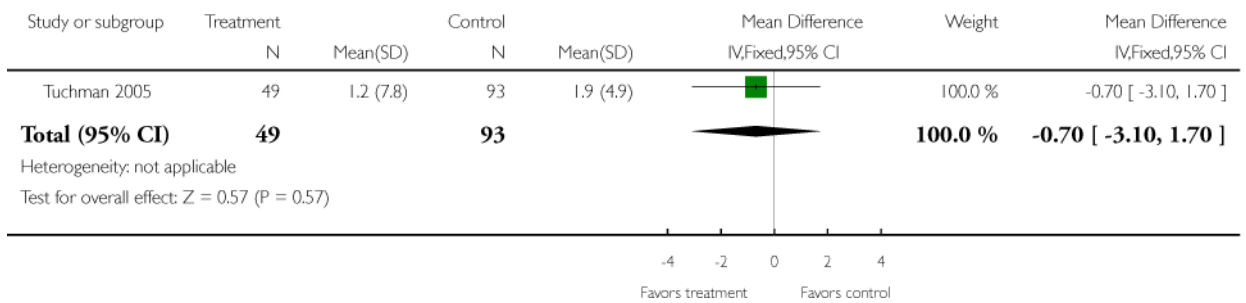
**Analysis 5.2.**

Comparison 5 DMPA 150 mg/mL versus COC, Outcome 2 Mean weight change (kg) at 12 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

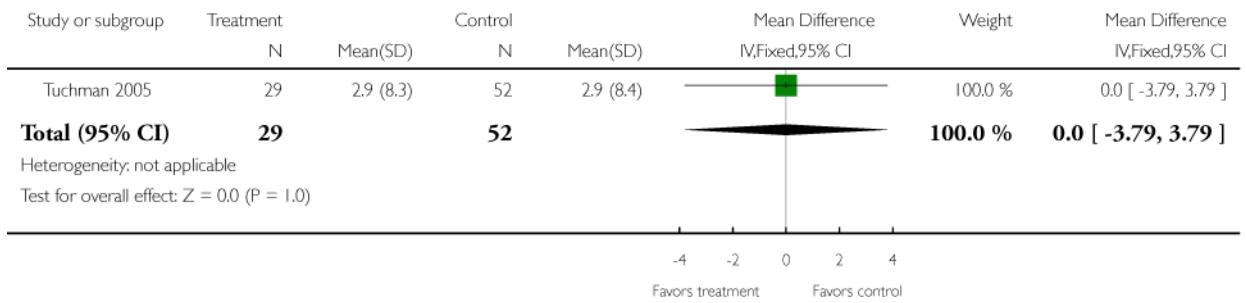
Outcome: 3 Mean percentage weight change at 6 months



**Analysis 5.3.**

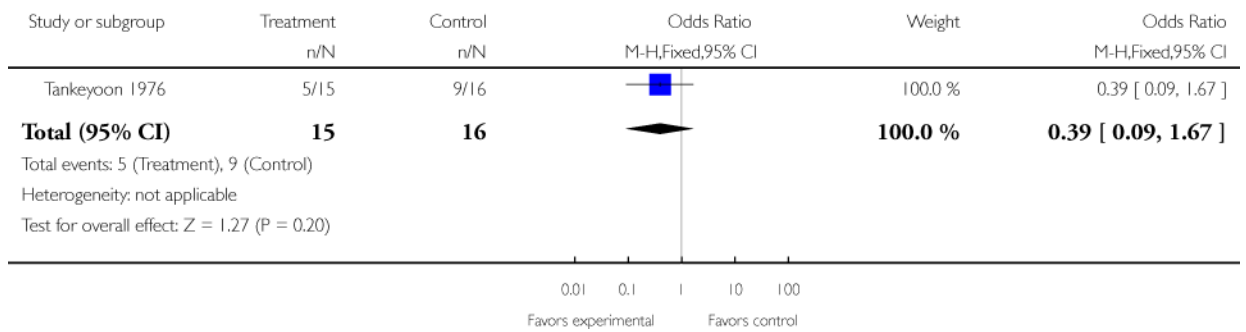
Comparison 5 DMPA 150 mg/mL versus COC, Outcome 3 Mean percentage weight change at 6 months.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 5 DMPA 150 mg/mL versus COC  
 Outcome: 4 Mean percentage weight change at 12 months



**Analysis 5.4.**  
 Comparison 5 DMPA 150 mg/mL versus COC, Outcome 4 Mean percentage weight change at 12 months.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 5 DMPA 150 mg/mL versus COC  
 Outcome: 5 Weight gain >= 1 kg at month 6

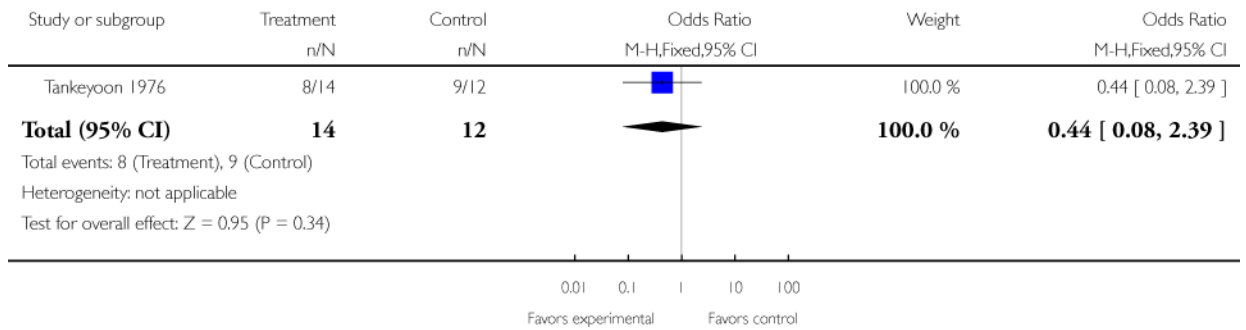


**Analysis 5.5.**  
 Comparison 5 DMPA 150 mg/mL versus COC, Outcome 5 Weight gain >= 1 kg at month 6.

Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

Outcome: 6 Weight gain >= 1 kg at month 12



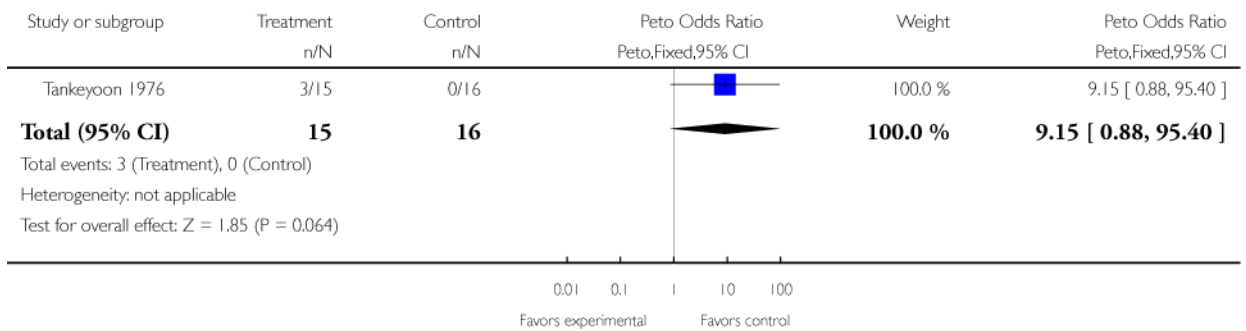
**Analysis 5.6.**

Comparison 5 DMPA 150 mg/mL versus COC, Outcome 6 Weight gain >= 1 kg at month 12.

Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

Outcome: 7 Weight loss >= 1 kg at month 6



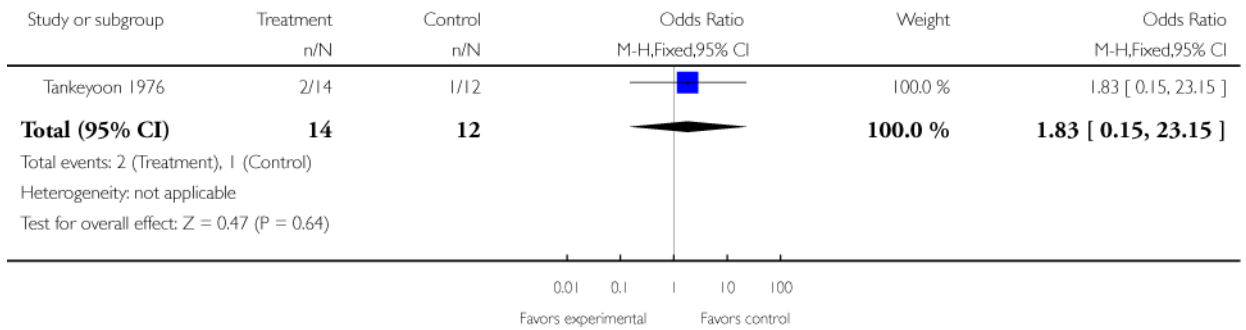
**Analysis 5.7.**

Comparison 5 DMPA 150 mg/mL versus COC, Outcome 7 Weight loss >= 1 kg at month 6.

Review: Progestin-only contraceptives: effects on weight

Comparison: 5 DMPA 150 mg/mL versus COC

Outcome: 8 Weight loss >= 1 kg at month 12



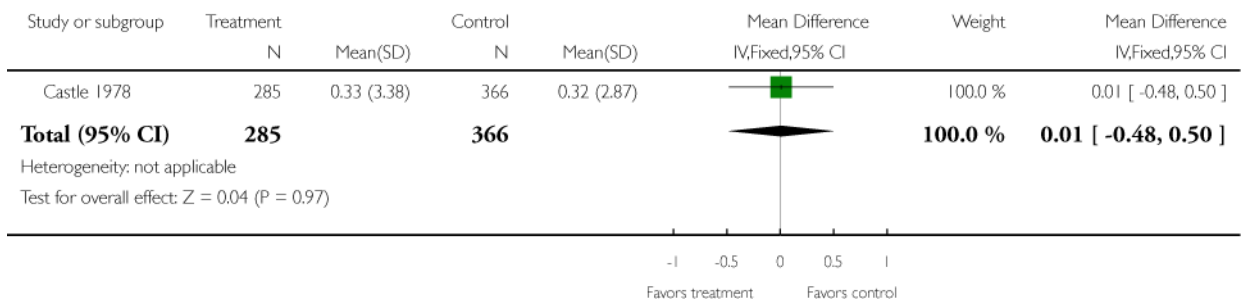
**Analysis 5.8.**

Comparison 5 DMPA 150 mg/mL versus COC, Outcome 8 Weight loss >= 1 kg at month 12.

Review: Progestin-only contraceptives: effects on weight

Comparison: 6 DMPA 150 mg/mL versus DMPA 450 mg/mL

Outcome: 1 Mean weight change (kg) at 6 months



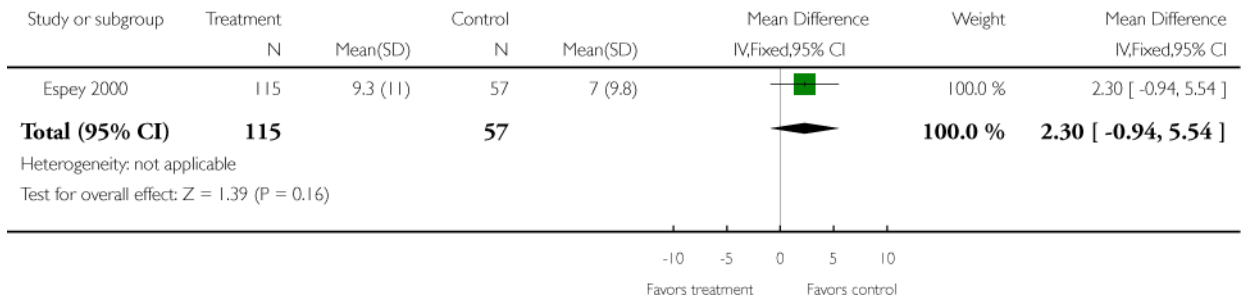
**Analysis 6.1.**

Comparison 6 DMPA 150 mg/mL versus DMPA 450 mg/mL, Outcome 1 Mean weight change (kg) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 7 DMPA 150 mg/mL initiation after pregnancy: interval ( $\geq 20$  weeks) versus postpartum (5 to 8 weeks)

Outcome: 1 Mean weight gain (lbs) at 1 year



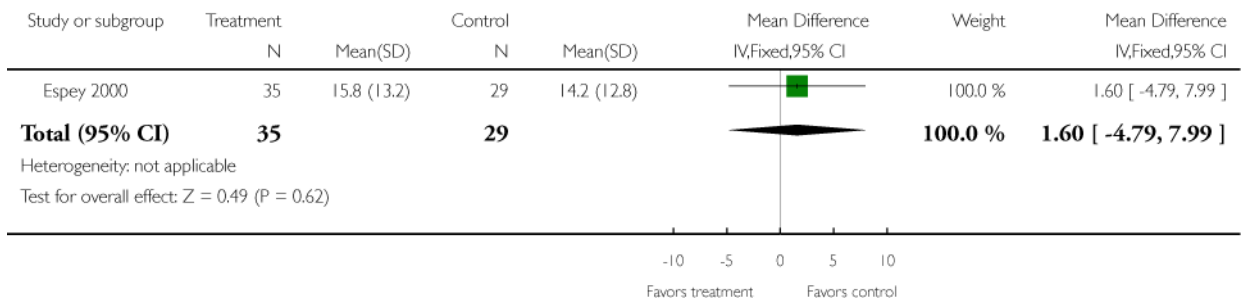
**Analysis 7.1.**

Comparison 7 DMPA 150 mg/mL initiation after pregnancy: interval ( $\geq 20$  weeks) versus postpartum (5 to 8 weeks), Outcome 1 Mean weight gain (lbs) at 1 year.

Review: Progestin-only contraceptives: effects on weight

Comparison: 7 DMPA 150 mg/mL initiation after pregnancy: interval ( $\geq 20$  weeks) versus postpartum (5 to 8 weeks)

Outcome: 2 Mean weight gain (lbs) at 2 years



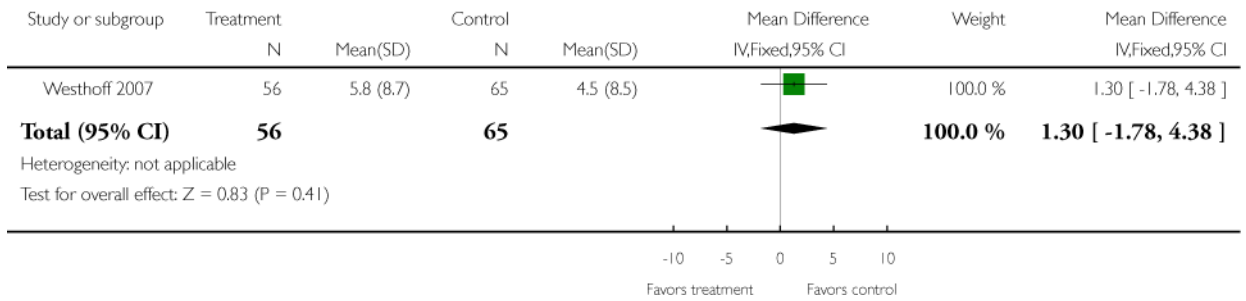
**Analysis 7.2.**

Comparison 7 DMPA 150 mg/mL initiation after pregnancy: interval ( $\geq 20$  weeks) versus postpartum (5 to 8 weeks), Outcome 2 Mean weight gain (lbs) at 2 years.

Review: Progestin-only contraceptives: effects on weight

Comparison: 8 DMPA-IM 150 mg versus DMPA-SC 104 mg

Outcome: 1 Mean weight change (kg) at 36 months



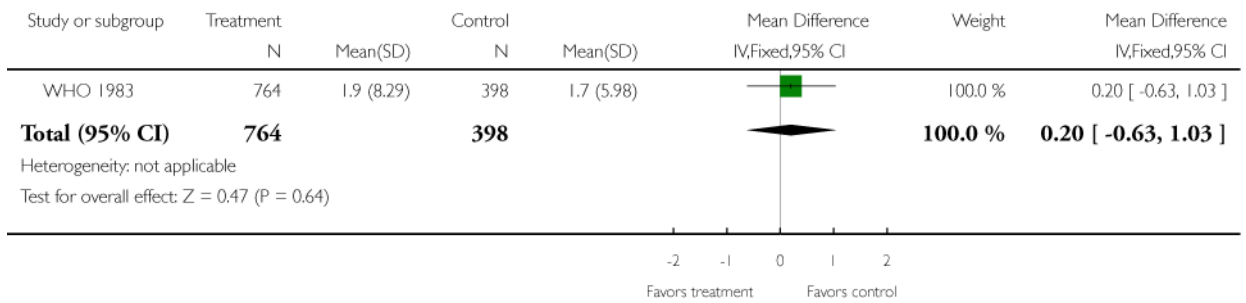
**Analysis 8.1.**

Comparison 8 DMPA-IM 150 mg versus DMPA-SC 104 mg, Outcome 1 Mean weight change (kg) at 36 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals)

Outcome: 1 Mean weight change (kg) at 12 months



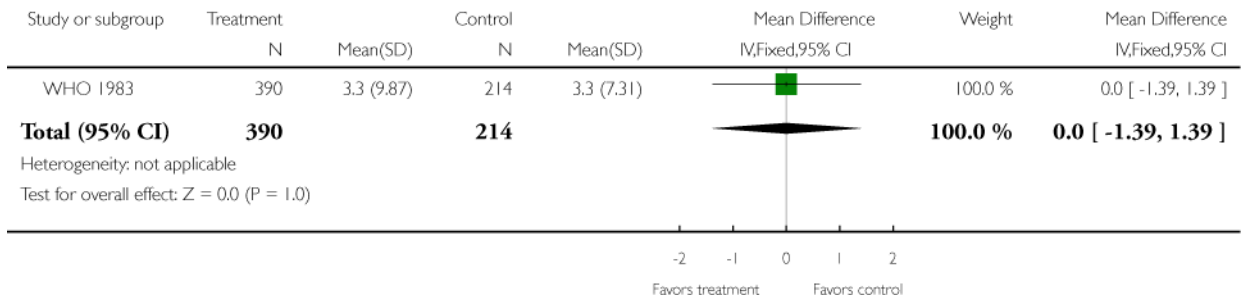
**Analysis 9.1.**

Comparison 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals), Outcome 1 Mean weight change (kg) at 12 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals)

Outcome: 2 Mean weight change (kg) at 24 months



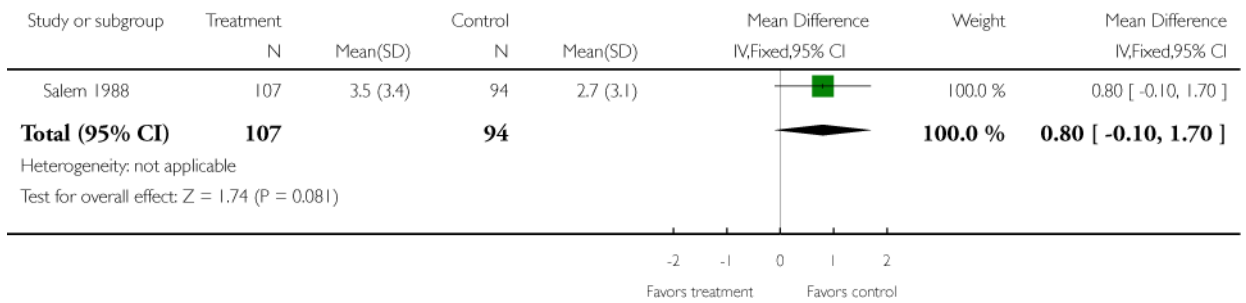
**Analysis 9.2.**

Comparison 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals), Outcome 2  
Mean weight change (kg) at 24 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals)

Outcome: 3 Mean weight change at 1 year



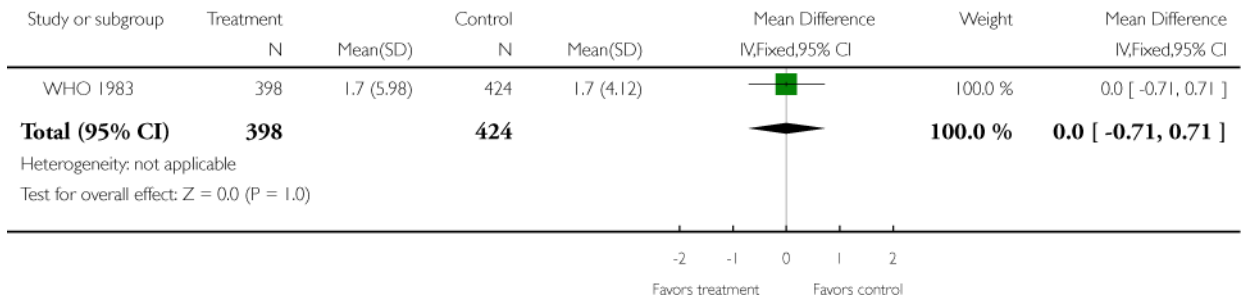
**Analysis 9.3.**

Comparison 9 DMPA 150 mg/mL versus NET-EN 200 mg (60-day intervals), Outcome 3  
Mean weight change at 1 year.

Review: Progestin-only contraceptives: effects on weight

Comparison: 10 NET-EN 200 mg: 60-day intervals versus 3 intervals of 60 days then 84-day intervals

Outcome: 1 Mean weight change (kg) at 12 months



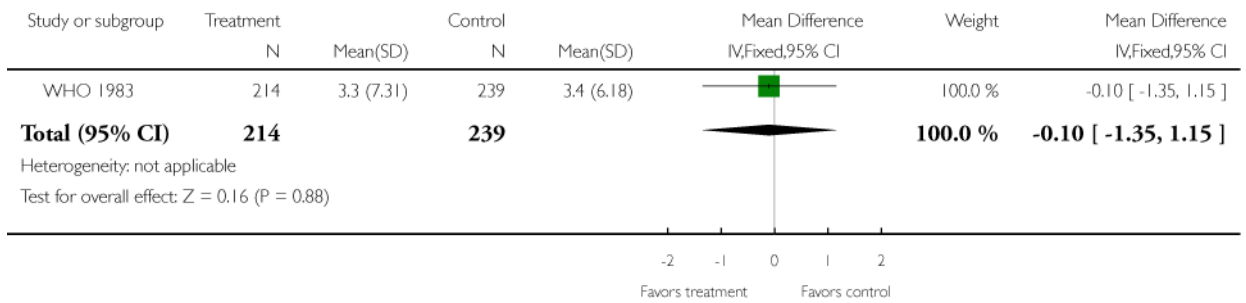
**Analysis 10.1.**

Comparison 10 NET-EN 200 mg: 60-day intervals versus 3 intervals of 60 days then 84-day intervals, Outcome 1 Mean weight change (kg) at 12 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 10 NET-EN 200 mg: 60-day intervals versus 3 intervals of 60 days then 84-day intervals

Outcome: 2 Mean weight change (kg) at 24 months

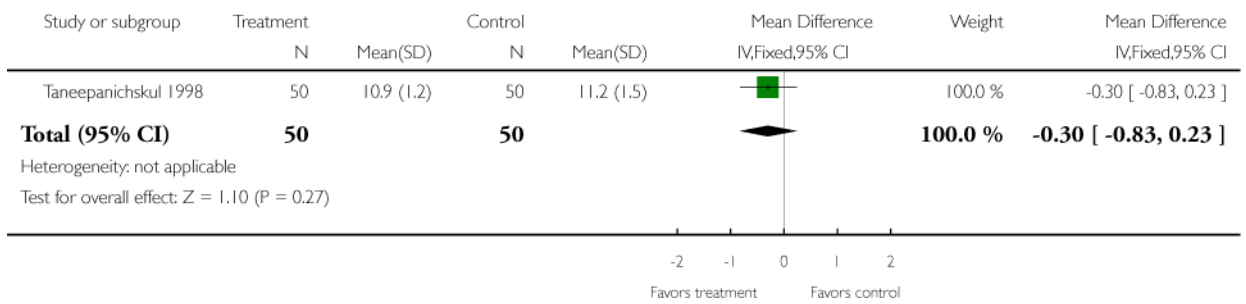


**Analysis 10.2.**

Comparison 10 NET-EN 200 mg: 60-day intervals versus 3 intervals of 60 days then 84-day intervals, Outcome 2 Mean weight change (kg) at 24 months.

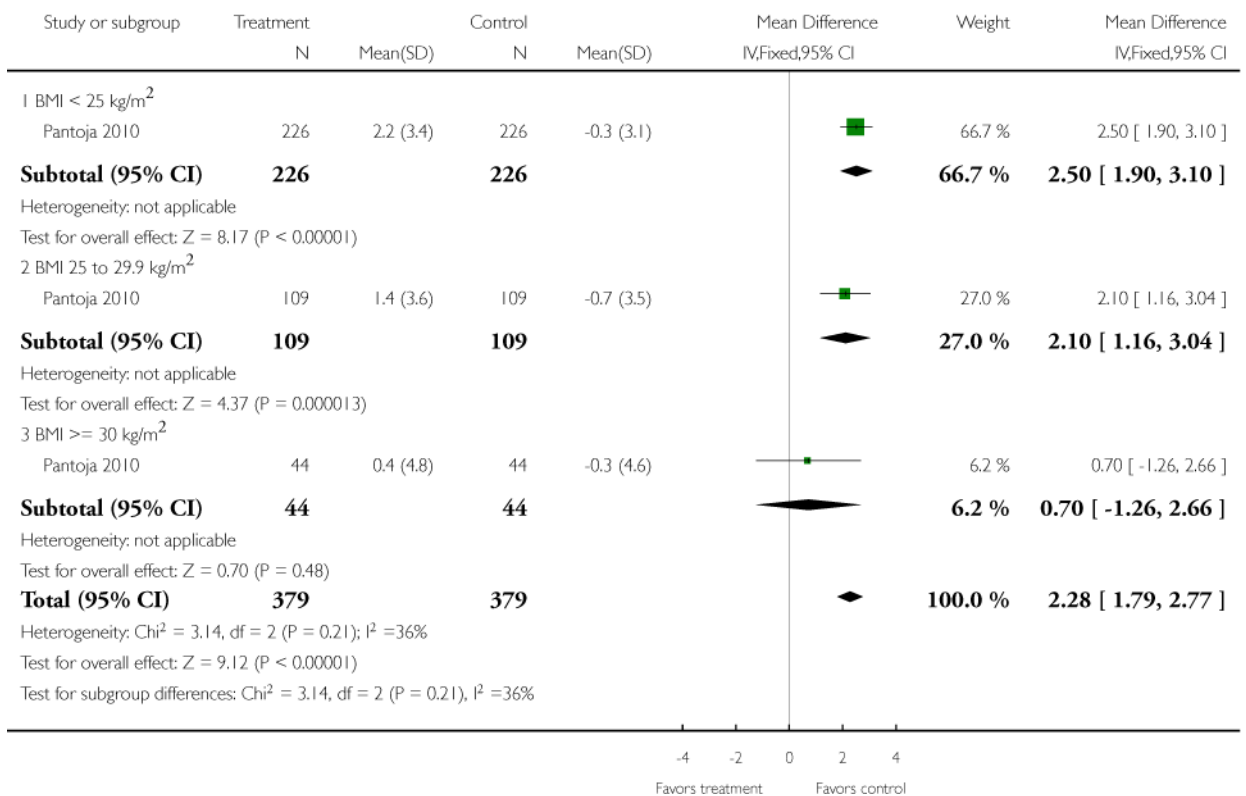


Review: Progestin-only contraceptives: effects on weight  
 Comparison: 11 DMPA 150 mg/mL versus IUD  
 Outcome: 1 Mean weight change (kg) at 120 months



**Analysis 11.1.**  
 Comparison 11 DMPA 150 mg/mL versus IUD, Outcome 1 Mean weight change (kg) at 120 months.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 11 DMPA 150 mg/mL versus IUD  
 Outcome: 2 Mean weight change (kg) at 1 year by baseline BMI

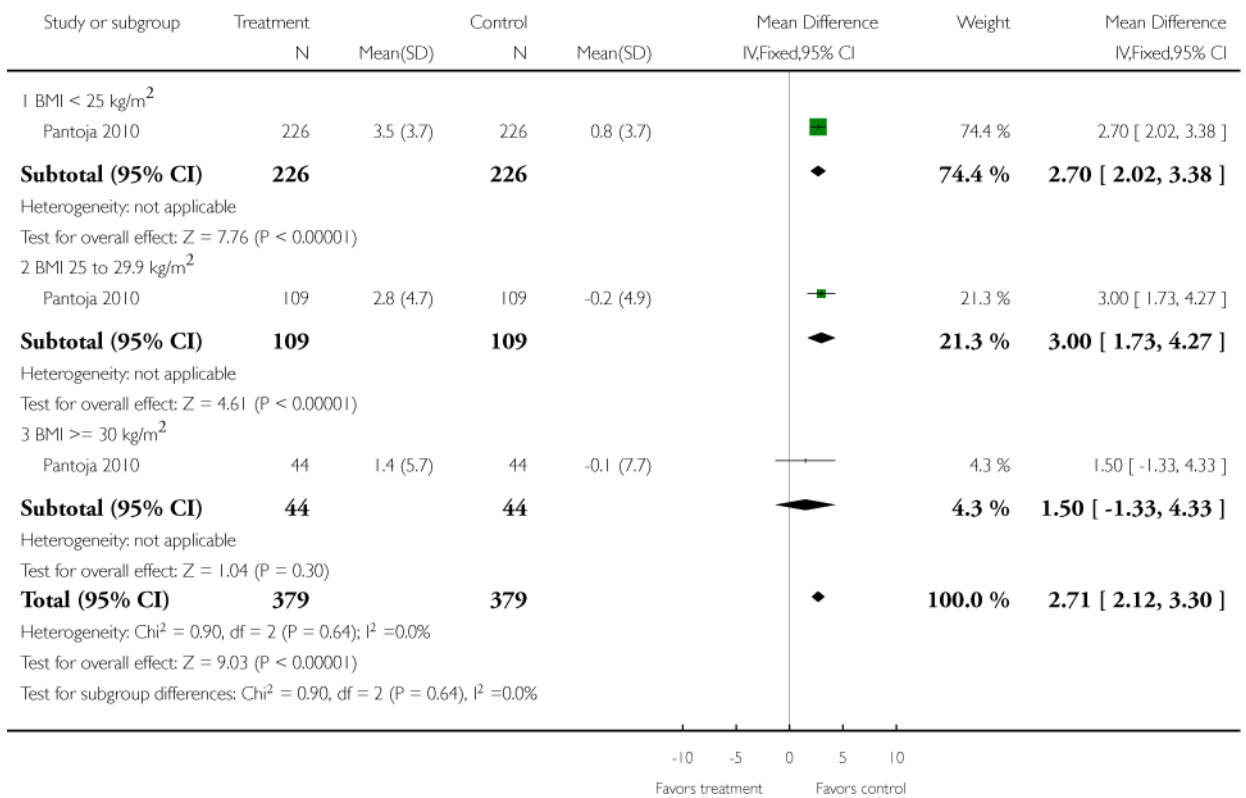


**Analysis 11.2.**  
 Comparison 11 DMPA 150 mg/mL versus IUD, Outcome 2 Mean weight change (kg) at 1 year by baseline BMI.

Review: Progestin-only contraceptives: effects on weight

Comparison: 11 DMPA 150 mg/mL versus IUD

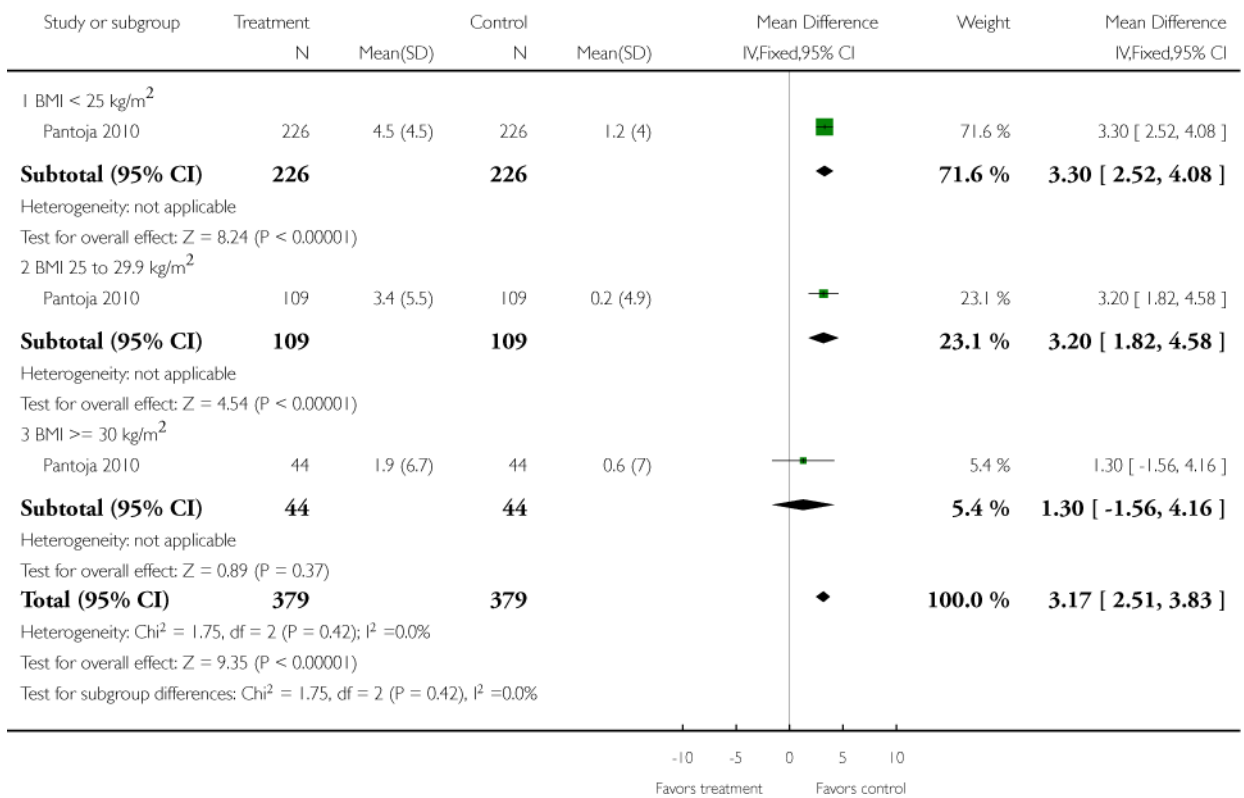
Outcome: 3 Mean weight change (kg) at 2 years by baseline BMI



**Analysis 11.3.**

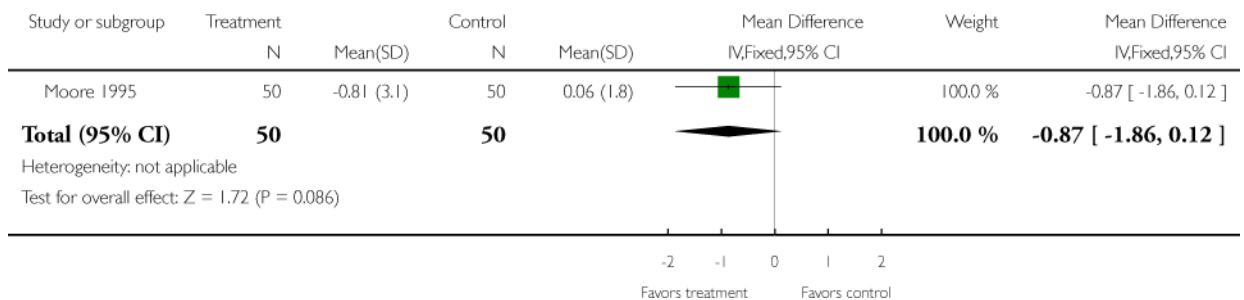
Comparison 11 DMPA 150 mg/mL versus IUD, Outcome 3 Mean weight change (kg) at 2 years by baseline BMI.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 11 DMPA 150 mg/mL versus IUD  
 Outcome: 4 Mean weight change (kg) at 3 years by baseline BMI



**Analysis 11.4.**  
 Comparison 11 DMPA 150 mg/mL versus IUD, Outcome 4 Mean weight change (kg) at 3 years by baseline BMI.

Review: Progestin-only contraceptives: effects on weight  
 Comparison: 12 Norplant versus DMPA 150 mg/mL  
 Outcome: 1 Mean weight change (kg) at 1 year

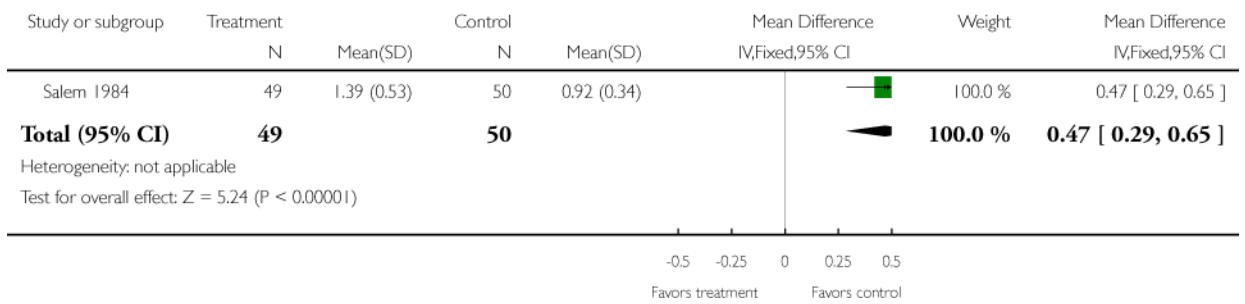


**Analysis 12.1.**  
 Comparison 12 Norplant versus DMPA 150 mg/mL, Outcome 1 Mean weight change (kg) at 1 year.

Review: Progestin-only contraceptives: effects on weight

Comparison: 13 Norplant versus IUD

Outcome: 1 Mean weight change (kg) at 6 months



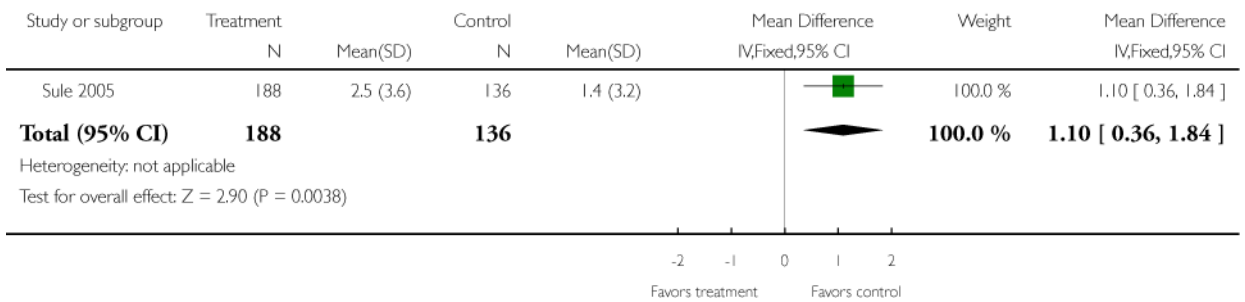
**Analysis 13.1.**

**Comparison 13 Norplant versus IUD, Outcome 1 Mean weight change (kg) at 6 months.**

Review: Progestin-only contraceptives: effects on weight

Comparison: 13 Norplant versus IUD

Outcome: 2 Mean weight change (kg) at 1 year



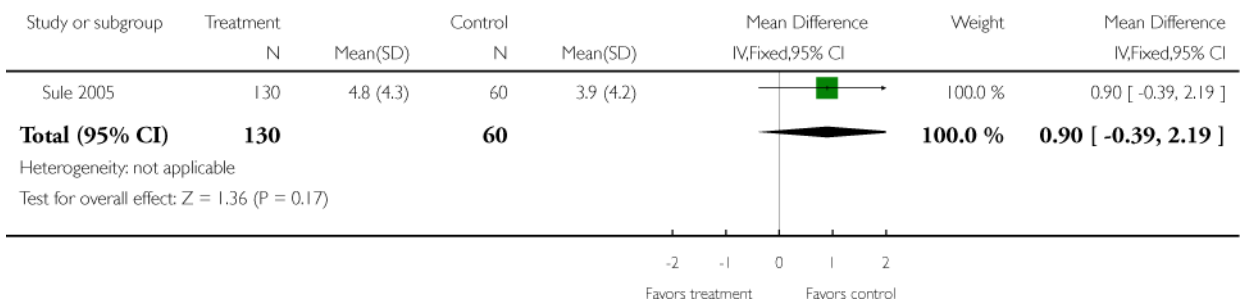
**Analysis 13.2.**

**Comparison 13 Norplant versus IUD, Outcome 2 Mean weight change (kg) at 1 year.**

Review: Progestin-only contraceptives: effects on weight

Comparison: 13 Norplant versus IUD

Outcome: 3 Mean weight change (kg) at 3 years



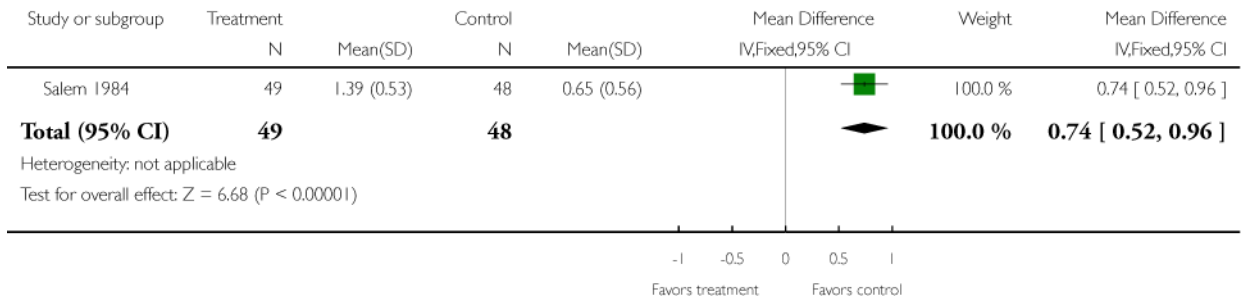
**Analysis 13.3.**

Comparison 13 Norplant versus IUD, Outcome 3 Mean weight change (kg) at 3 years.

Review: Progestin-only contraceptives: effects on weight

Comparison: 14 Norplant versus barrier, 'local', or no contraceptive method

Outcome: 1 Mean weight change (kg) at 6 months



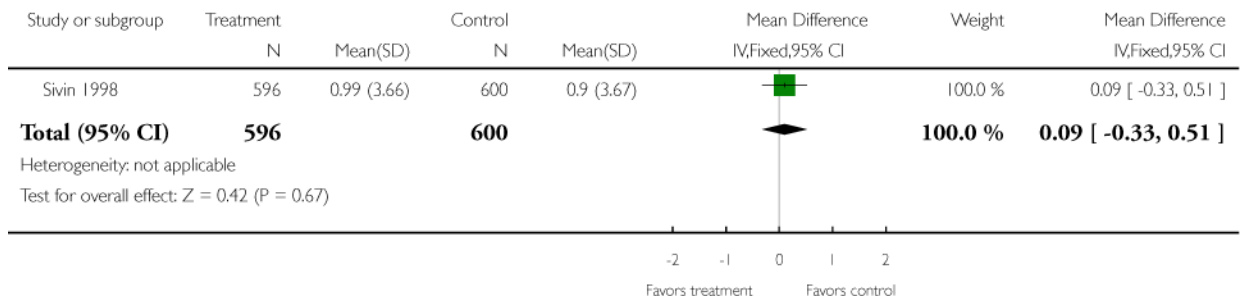
Analysis 14.1.

Comparison 14 Norplant versus barrier, 'local', or no contraceptive method, Outcome 1 Mean weight change (kg) at 6 months.

Review: Progestin-only contraceptives: effects on weight

Comparison: 15 Norplant versus 2-rod LNG

Outcome: 1 Mean weight change (kg) at 1 year



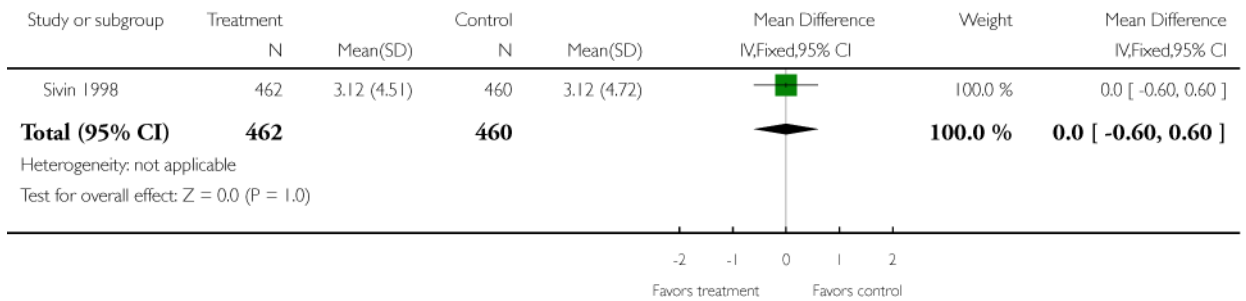
Analysis 15.1.

Comparison 15 Norplant versus 2-rod LNG, Outcome 1 Mean weight change (kg) at 1 year.

Review: Progestin-only contraceptives: effects on weight

Comparison: 15 Norplant versus 2-rod LNG

Outcome: 2 Mean weight change (kg) at 3 years



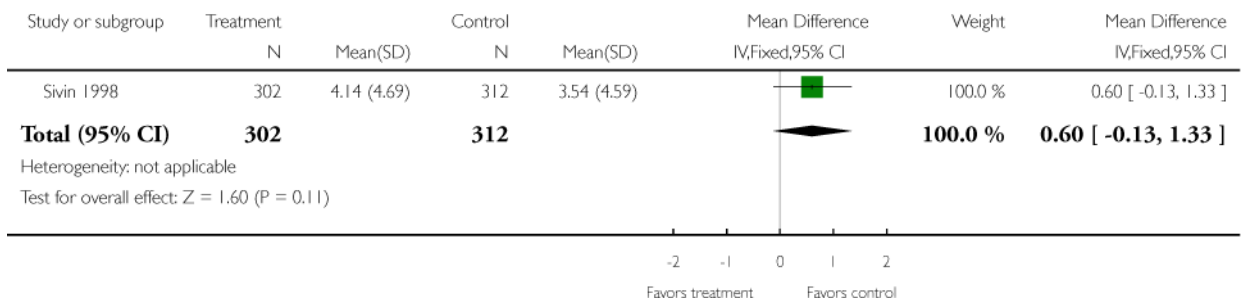
**Analysis 15.2.**

Comparison 15 Norplant versus 2-rod LNG, Outcome 2 Mean weight change (kg) at 3 years.

Review: Progestin-only contraceptives: effects on weight

Comparison: 15 Norplant versus 2-rod LNG

Outcome: 3 Mean weight change (kg) at 5 years



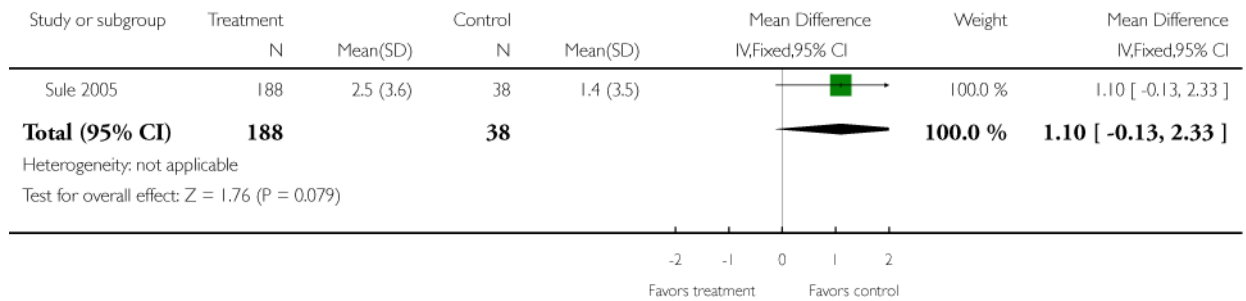
**Analysis 15.3.**

Comparison 15 Norplant versus 2-rod LNG, Outcome 3 Mean weight change (kg) at 5 years.

Review: Progestin-only contraceptives: effects on weight

Comparison: 16 Norplant versus COC

Outcome: 1 Mean weight change (kg) at 1 year



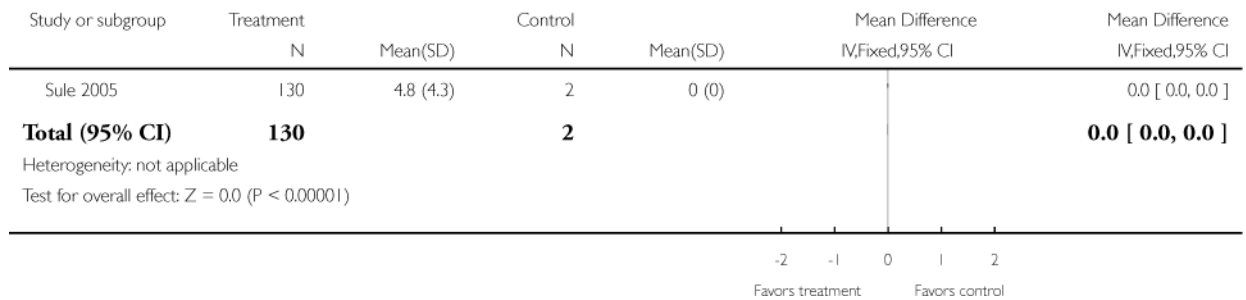
### Analysis 16.1.

Comparison 16 Norplant versus COC, Outcome 1 Mean weight change (kg) at 1 year.

Review: Progestin-only contraceptives: effects on weight

Comparison: 16 Norplant versus COC

Outcome: 2 Mean weight change (kg) at 3 years



### Analysis 16.2.

Comparison 16 Norplant versus COC, Outcome 2 Mean weight change (kg) at 3 years.

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SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [*Explanation*]

Study	Type of study	Sample size	Comparison groups	Groups that differed	Time frame	Mean change <sup>a</sup>
Ball 1991	RCT	51	OC NET 350 µg vs LNG 30 µg	—	6 months	0 vs 0.6
Bonny 2009	Prospective, not randomized	33	DMPA + placebo vs DMPA + E2C	—	6 months	10.3% vs 2.8%; -3.4% vs -1.2% <sup>b</sup>
Castle 1978	Prospective, not randomized	1000	DMPA + placebo vs no hormonal	X	6 months	10.3% vs -0.1%; -3.4% vs 0.6% <sup>b</sup>
Espey 2000	Retrospective	172	DMPA 150 vs DMPA 450	—	6 months	0.33 vs 0.32
Moore 1995	Retrospective	100	DMPA: interval vs postpartum	—	1 year 2 years	4.2 vs 3.2; 7.2 vs 6.5
Pantoja 2010	Retrospective	758	Norplant vs DMPA	—	1 year	-0.81 vs 0.06
Salem 1984	Prospective, not randomized	150	DMPA vs IUD	X (all 3 years)	1 year 2 years 3 years	1.76 vs -0.42; 3.1 vs 0.4; 3.9 vs 0.8
Salem 1988	RCT	400	Norplant vs IUD	X	6 months	1.39 vs 0.92
Sivin 1998	RCT	1200	Norplant vs other non-hormonal	X	6 months	1.39 vs 0.65
Sule 2005	Retrospective	516	DMPA vs NET-EN	—	1 year	3.5 vs 2.7 <sup>a</sup>
Taneepanichskul 1998	Retrospective	100	Norplant vs 2-rod LNG	—	1 year 3 years 5 years	0.99 vs 0.90; 3.12 vs 3.12; 4.14 vs 3.54
Tankeyoon 1976	Prospective, not randomized	32	Norplant vs IUD	X (at 1 year)	1 year 3 years	2.5 vs 1.4 4.8 vs 3.9;
Tuchman 2005	Retrospective	222	Norplant vs COC	—	1 year 3 years	2.5 vs 1.4; 4.8 vs 0.0
Westhoff 2007	RCT	534	DMPA vs IUD	—	10 years	10.9 vs 11.2
WHO 1983	RCT	3172	DMPA vs COC	—	1 year	1.8 vs 3.1 (estimated)
			DMPA vs MPA/E2C	—	6 months; 12 months	0.6 vs 1.2; 1.7 vs 3.0
			DMPA vs COC	—	6 months; 12 months	0.6 vs 1.1; 1.7 vs 1.0
			DMPA-IMI50 vs DMPA-SC 104	—	3 years	5.8 vs 4.5
			DMPA vs NET-EN (60 days)	—	1 year 2 years	1.9 vs 1.7; 3.3 vs 3.3
			NET-EN: 60 days vs 84 days	—	1 year 2 years	1.7 vs 1.7; 3.3 vs 3.4

<sup>a</sup>Weight change in kg unless otherwise specified. Salem 1988 did not report units for weight change (lbs or kg).

<sup>b</sup>Mean change in total body fat or lean body mass, respectively

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ADDITIONAL SUMMARY OF FINDINGS [*Explanation*]

Study <sup>a</sup>	Type of study	Comparison groups	Groups differed significantly	Mean difference (95% CI)
Ball 1991	RCT	OC NET 350 µg vs LNG µg 30	no	—
Bonny 2009	Prospective, not randomized	DMPA + placebo vs DMPA + E2C or no hormonal	DMPA + placebo vs no hormonal	11.00 (2.64 to 19.36); -4.00 (-6.93 to -1.07) <sup>b</sup>
Salem 1984	Prospective, not randomized	Norplant vs IUD or no hormonal	Norplant vs IUD or vs other non-hormonal	0.47 (0.29 to 0.65); 0.74 (0.52 to 0.96) <sup>c</sup>
Sivin 1998	RCT	Norplant vs 2-rod LNG	no	—

<sup>a</sup>Excludes retrospective chart reviews and studies with loss to follow up or discontinuation >= 25%.

<sup>b</sup>Total body fat (%) and lean body mass (%), respectively

<sup>c</sup>Weight change (kg)

Study	Comparison groups	Mean difference (95% CI)*	Quality of evidence**
<b>Progestin-only pills</b>			
Ball 1991	OC NET 350 µg vs LNG 30 µg	—	High
<b>DMPA</b>			
WHO 1983	DMPA vs NET-EN (60 days)	—	High
	NET-EN: 60 days vs 84 days	—	
Salem 1988	DMPA vs NET-EN	—	High
Bonny 2009	DMPA + placebo vs DMPA + E2C	—	Moderate
	DMPA + placebo vs no hormonal	11.00 (2.64 to 19.36); -4.00 (-6.93 to -1.07) <sup>a</sup>	
Westhoff 2007	DMPA-IM 150 vs DMPA-SC 104	—	Moderate
Castle 1978	DMPA 150 vs DMPA 450	—	Low
Pantoja 2010	DMPA vs IUD	3.17(2.51 to 3.83) <sup>b</sup>	Low
Tankeyoon 1976	DMPA vs COC	—	Low
Taneepanichskul 1998	DMPA vs IUD	—	Very low
Tuchman 2005	DMPA vs MPA/E2C	—	Very low
	DMPA vs COC	—	
Espey 2000	DMPA: interval vs postpartum	—	Very low
<b>Norplant</b>			
Sivin 1998	Norplant vs 2-rod LNG	—	High
Salem 1984	Norplant vs IUD	0.47 (0.29 to 0.65) <sup>b</sup>	Moderate
	Norplant vs other non-hormonal	0.74 (0.52 to 0.96) <sup>b</sup>	
Moore 1995	Norplant vs DMPA	—	Low
Sule 2005	Norplant vs IUD	1.10 (0.36 to 1.84) <sup>b</sup>	Very low
	Norplant vs COC	—	

\* Data shown if groups differed significantly

\*\* Grades were initially based on study design (RCT = high; prospective, not RCT = moderate; retrospective = low). Studies were downgraded a level if losses >=25% and if cases inappropriately excluded.

<sup>a</sup>Total body fat (%) and lean body mass (%), respectively

<sup>b</sup>Weight (kg), except Salem 1988, which did not report units (lbs or kg).



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

Ball 1991		
Methods	Randomized controlled trial, likely conducted in Oxford, England. No information on method for randomization, except stratified according to prior OC use; "single-blind" (unspecified). Main study examined effects of progestin-only OC on lipoprotein levels, glucose tolerance, coagulation factors, and blood pressure.	
Participants	51 women, 17 to 41 years, requesting oral contraceptives (OC). New OC users had not used an OC or hormone therapy for 3 months; switchers were changing from low-dose combined OC. Exclusion criteria: hypertension (diastolic blood pressure (BP) > 100 mm Hg, systolic BP > 140 mm Hg), smoking > 20 cigarettes/day, or diabetes.	
Interventions	Progestin-only pills: norethisterone (NET) 350 µg (N=23) versus levonorgestrel (LNG) 30 µg (N=23); 6 treatment cycles.	
Outcomes	Mean change in weight from baseline to month 6	
Notes		
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	No information
Incomplete outcome data addressed? All outcomes	Yes	Five women did not return for follow up, and were excluded from the analysis (groups not specified). Nine withdrew after 3 months (1 NET; 8 LNG). Analysis for weight included 39 women at 6 months; loss 12/51 = 24%.
Bonny 2009		
Methods	Prospective study in 4 urban adolescent health clinics in large metropolitan area (USA); enrollment 2002 to 2003; part of a larger 2-year study that examined hormonal contraception and bone mineral density	
Participants	Postmenarchal girls 12 to 18 years of age. Inclusion criteria: requesting contraception and selecting DMPA or OC; those who did not want hormonal contraception were eligible for control group. Exclusion criteria: pregnancy or DMPA use in past 6 months; OC use in past 3 months; alcohol or drug dependence; medical condition (e.g., renal disease) or medication use (e.g., corticosteroids) associated with outcomes of interest; contraindication to estrogen use; weight > 250 lbs (upper limit for dual energy x-ray absorptiometry [DEXA] scanner); and need for confidential contraceptive care.	
Interventions	Choice of: 1) Depot medroxyprogesterone acetate (DMPA) (N=15): randomized to additional monthly injections of placebo (N=8) or estradiol cypionate 5 mg (E2C) (N=7) 2) Control (no hormonal contraception) (N=18)	
Outcomes	Change in total body fat (%) and in lean body mass (%) from baseline to 6 months.	
Notes	Researchers also developed multivariate models for change in total body fat and change in lean body mass; models adjusted for potential confounders. However, the analysis also included a third group of those who chose OCs (N=18), which we did not include in our review. Type of OC was not specified and might have included progestin-only OCs as well as combination OCs, so the OC group was excluded here.	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	No information
Incomplete outcome data addressed? All outcomes	Unclear	To remain in study, participants had to adhere to DMPA by appointment. No information on controls.
Castle 1978		
Methods	Prospective study in family planning center in Salisbury, Rhodesia; enrollment Jun to Dec 1976	
Participants	1000 Black women seeking contraception. Ages ranged from 'under 20' to 40 years or older.	
Interventions	1) DMPA 150 mg every 3 months (N=500) 2) DMPA 450 mg every 6 months (N=500)	
Outcomes	Mean increase in weight at 6 months	

Notes	Weight measured at each visit while participant wore only a gown	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	No	Allocation by patient request
Incomplete outcome data addressed? All outcomes	Yes	Withdrawals from study were 21 for DMPA 150 mg and 17 for DMPA 450 mg. Losses to follow-up: 39% DMPA 150 mg and 23% DMPA 450 mg.
Espey 2000		
Methods	Retrospective chart review at 3 Indian Health Service facilities in southwestern USA	
Participants	Female members of Navajo tribe. Inclusion criteria: 18 to 40 years old, completed at least 5 consecutive injections of DMPA at 10- to 14-week intervals, and had weights recorded at 1 - or 2-year intervals. Exclusion criteria: history of diabetes or thyroid disease; women in postpartum group who had pre-eclampsia or multiple gestations within index pregnancy.	
Interventions	DMPA initiation a) Interval (N=15): first injection at least 20 weeks past pregnancy of 20 weeks or more gestation b) Postpartum (N=57): first injection at 5 to 8 weeks after delivery of singleton pregnancy of 20 weeks or more gestation	
Outcomes	Mean weight gain (lbs) for DMPA at 1 and 2 years by initiation group	
Notes	For another group, not included in this review, method of contraception was reportedly extracted from charts but specifics were not provided. Discussion noted that group "more frequently used" IUD or tubal ligation and also included COC users.	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	Not applicable (NA)
Incomplete outcome data addressed? All outcomes	Yes	Women with incomplete records were excluded from this retrospective review. However, at 2 years, weight data were not available for 70% of the interval group and 49% of the postpartum group.
Moore 1995		
Methods	Retrospective chart review at rural obstetrics and gynecology clinic in Arizona (USA)	
Participants	Women who used the contraceptive method and were 15 to 30 years old. Exclusion criteria: prior hormonal contraceptive therapy, height < 62 inches (152.4 cm) or > 70 inches (177.8 cm), weight < 100 lbs (45.5 kg) or > 180 lbs (81.8 kg), presence of diabetes, history of thyroid disease, < 12 months postpartum.	
Interventions	1) Norplant (N=50) 2) DMPA 150 mg (M=50)	
Outcomes	Weight gain (kg) at 1 year by treatment group.	
Notes	Researchers also analyzed weight gain in model adjusted for age, height, weight, and parity. That analysis included a third group of OC users, which we excluded from this review. Type of OC was not specified and may have included progestin-only OCs as well as combination OCs.	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	NA
Pantoja 2010		
Methods	Retrospective chart review at a university department of obstetrics and gynecology in Campina, Brazil. Chart data spanned Jan 1991 to Dec 2000.	
Participants	Women who chose DMPA and used the method continuously for 3 years or more and women who used TCu380A IUD for similar time period. Exclusion criteria: diabetes mellitus, hyper- or hypothyroidism, chronic renal failure, rheumatic diseases requiring chronic use of corticoids, and any type of organ transplant. Mean age was 33.5 years in both groups.	

Interventions	1) DMPA (N=379) 2) TCu380A IUD (N=379)	
Outcomes	Change in weight (kg) at 1, 2, and 3 years by contraceptive group and baseline BMI (kg/m <sup>2</sup> ) group (BMI < 25; 25 to 29.9; >= 30)	
Notes	After pairing for age and baseline BMI, the samples were 379 for each contraceptive group. Weight and height were measured at baseline (time of method initiation) and annually thereafter.	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	NA; charts were selected for those with 3 years of continuous use.
Salem 1984		
Methods	Prospective study in postpartum clinic of university hospital in Assiut, Egypt. Study focused on effect of Norplant use on lactating women and on lactation performance and infant growth.	
Participants	150 lactating women. Inclusion criteria: normal delivery of normal living baby and exclusively breastfeeding, one month after delivery, and infant weight at least 3500 gm. Mean age was 29 years for each group.	
Interventions	Acceptors (50 in each group): 1) Norplant 2) Barrier, "local," or no contraceptive method 3) CuT380A IUD	
Outcomes	Weight gain at 6 months by study group	
Notes		
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	Excluded data: 1 in Norplant group who lost her baby and wanted to get pregnant; 2 who got pregnant in group with barrier, local, or no contraceptive.
Salem 1988		
Methods	Randomized controlled trial of DMPA and NET-EN in family planning center in Assiut, Egypt. Random numbers table was prepared by WHO. Study examined performance of 2 injectables regarding side effects, continuation, and termination.	
Participants	400 women attending family planning clinic. Inclusion criteria: 18 to 40 years old, proven fertility and frequent risk of pregnancy, regular menstrual cycles, willing to rely on one method. Exclusion criteria: breast-feeding; cardiovascular disease; liver disease; known or suspected breast malignancy, genital malignancy, uterine fibroids; undiagnosed vaginal bleeding; suspected pregnancy.	
Interventions	200 in each group: 1) DMPA 150 mg every 3 months 2) Norethisterone enanthate (NET-EN) 200 mg every 2 months Study duration was 1 year	
Outcomes	Mean change in weight at 1 year by contraceptive group. Units were not specified (kg or lbs).	
Notes	Report had mean change for those who had an increase, decrease, or no change in weight. Review authors calculated combined weight change means and standard deviations.	
<b>Risk of bias</b>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Yes	Sealed envelopes contained assignments
Incomplete outcome data addressed? All outcomes	Yes	Losses to follow up were reportedly 19% for DMPA and 13.3% for NET-EN. One-year method continuation rates were 68.8% DMPA and 57.1% NET-EN. Those who finished the study were 54% and 47%, respectively.
Sivin 1998		

Methods	Randomized controlled trial at 7 centers, including USA and Finland. Study focused on effectiveness of reformulated 2-rod LNG implant versus 6-rod implant. Randomization by "linear congruential method"; blocks of 50 per clinic. Enrollment from 1990 to 1994.
Participants	1200 healthy women, 18 to 40 years old, who sought implant contraception. Inclusion criteria: no contraindications to implant use, willing to undergo study procedures. Exclusion criteria: cancer, severe cardiovascular problem, hyperlipidemia, diabetes mellitus, mental illness, epilepsy, severe or frequent headaches, undiagnosed genital bleeding, hyperprolactinaemia or bloody breast discharge, pelvic inflammatory disease since last pregnancy or ectopic pregnancy.
Interventions	Levonorgestrel implants 1) Norplant: 6 capsules, containing levonorgestrel 216 mg (total) 2) LNG rod (Jadelle): 2 rods containing levonorgestrel 150 mg (total); different elastomer in core than earlier implant Follow up: 1, 3, 6 months, and then semi-annually up to 5 years
Outcomes	Mean weight change per year by implant group. Weight change was also presented for the 10th, 50th, and 90th percentiles of body weight (at admission).
Notes	Weighing method not specified

**Risk of bias**

Item	Authors' judgement	Description
Allocation concealment?	Yes	Implants were in sealed opaque envelopes that were numbered sequentially, according to randomization lists.
Incomplete outcome data addressed? All outcomes	Yes	Two sets of Norplant were contaminated and not used (1198 analyzed)

**Sule 2005**

Methods	Retrospective chart review at family planning clinic at a university hospital in Zaria, Nigeria. Study examined hormonal contraceptives and weight changes.
Participants	All new clients registered between 01 Jan 1993 and 31 Dec 1995 and followed for at least 1 year (N=516). Included were those who used hormonal contraceptives (COC, DMPA, NET-EN, or Norplant); IUD users were considered to be controls.
Interventions	Users of 1) Norplant (N=188) 2) Combined oral contraceptives (COC) (N=38) 3) IUD (N=136) (non-hormonal)
Outcomes	Mean weight gain or loss by contraceptive group at 1 year and 3 years
Notes	Report had mean change for those who had an increase, decrease, or no change in weight. Review authors calculated combined weight change means and standard deviations. Injectable users were not used in this review, as DMPA and NET-EN had been grouped for analysis.

**Risk of bias**

Item	Authors' judgement	Description
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	Researchers selected charts with at least one year of data. Only 236 were followed for 3 years, producing an overall loss of 54%: Norplant 31 %, COC 95%, and IUD 56%.

**Taneepanichskul 1998**

Methods	Retrospective study in family planning clinic at a hospital in Bangkok, Thailand. Study examined weight change in long-term users of DMPA versus IUD.
Participants	100 women, aged 37 to 50 years, attending family planning clinic. Inclusion criteria: used DMPA or IUD for 120 months, followed "regularly," no history of smoking or alcohol intake. IUD users had not used any hormonal contraceptive. Exclusion criteria: developed chronic disease or metabolic disorder during DMPA or IUD use.
Interventions	Chosen: 1) DMPA (N=50) 2) Copper T380A IUD (N=50)
Outcomes	Mean change in body weight by 120 months

Notes Weight was measured in standard manner at 120 months; methods used previously were not specified.

**Risk of bias**

Item	Authors' judgement	Description
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	Excluding those who developed a chronic disease or disorder during method use may have biased the results. Weight gain is associated with development of some diseases and disorders.

## Tankeyoon 1976

Methods	Prospective metabolic study in Bangkok, Thailand. Study focused on metabolic effects of the contraceptive methods.	
Participants	Two groups of 16 healthy women attending the family planning clinic. Inclusion criteria: > 6 weeks postpartum and no other steroid use for past 3 months. Age range was 18 to 38 years.	
Interventions	1) DMPA 150 mg (3-month intervals) (N=16) 2) COC: d-norgestrel 50 µg + EE 50 µg (N=16) Follow up at 1, 2, 3, 6, 9, 12 months	
Outcomes	Percent of cases with $\geq 1$ kg increase or decrease in body weight by contraceptive method	

Notes

**Risk of bias**

Item	Authors' judgement	Description
Allocation concealment?	Unclear	No information
Incomplete outcome data addressed? All outcomes	Unclear	Losses by 12 months: DMPA 2/16 (13%); COC 4/16 (25%) Reasons for missing data not specified.

## Tuchman 2005

Methods	Retrospective chart review at urban, hospital-based, teen health center (USA)	
Participants	222 females, aged 12 to 21 years, attending health center for contraception between 01 Jan 2001 and 31 Dec 2001. Inclusion criteria: first-time use of oral or injectable contraceptive. 'New start' was defined as no OC in past 3 months or DMPA in past 6 months prior to new method initiation.	
Interventions	Choice of: 1) DMPA every 3 months 2) Medroxyprogesterone acetate + estradiol cypionate 5 mg (MPA/E2C) monthly 2) COC	
Outcomes	Mean weight change (kg) and mean percent weight change at 3, 6, 9, 12 months by contraceptive method	
Notes	Standardized weight and height measures described. Measures closest to baseline and each follow up were used.	

**Risk of bias**

Item	Authors' judgement	Description
Allocation concealment?	Unclear	NA
Incomplete outcome data addressed? All outcomes	Yes	Numbers were provided for those who continued method use at each follow-up time. At 12 months, discontinuation rates were 54% to 58%.

## Westhoff 2007

Methods	Randomized controlled trial at sites in North and South America. Trial was evaluator-blinded.	
Participants	Women, 18 to 49 years old, sexually active and wanting long-term contraception. Inclusion criteria: no OC use for past 2 months, regular menstruation in past 3 months, willing to rely on DMPA for a year. Exclusion criteria: used OCs, implants, or hormonal IUD in past 2 months or DMPA-IM in past 10 months, pregnant or infertile, abnormal Pap, undiagnosed genital bleeding, other contraindications to hormonal contraceptives.	
Interventions	DMPA-SC 104 mg (N=266) or DMPA-IM 150 mg (N=268) every 3 months for 3 years	
Outcomes	Weight change at 36 months	

Notes Weight assessed as safety endpoint. Researchers also analyzed weight change by BMI group:  $\leq 25$ , 25 to 30,  $> 30$  kg/m<sup>2</sup>. Report notes that no consistent differences were found by BMI groups.

<i>Risk of bias</i>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	No information
Incomplete outcome data addressed? All outcomes	Unclear	By 3 years, continuation in the study was 25% for DMPA-SC 104 and 21% for DMPA-IM 150. Reasons for discontinuation were unclear.
WHO 1983		
Methods	Phase III randomized controlled trial in 13 centers in Africa, Asia, Central and South America, and Europe. No information on method for randomization and whether any blinding was done (e.g., assessors).	
Participants	Non-breastfeeding women who chose injectable contraception. Exclusion criteria: contraindication for long-acting contraceptive methods. Mean age was 27.4 years.	
Interventions	1) DMPA 150 mg at 90-day intervals (N=1587) 2) NET-EN 200 mg at 60-day intervals (N=789) 3) NET-EN 200 mg at 60-day intervals for 6 months then 84-day intervals (N=796)	
Outcomes	Mean weight change at 12 and 24 months by contraceptive group	
Notes	Method for measuring weight not mentioned	
<i>Risk of bias</i>		
<b>Item</b>	<b>Authors' judgement</b>	<b>Description</b>
Allocation concealment?	Unclear	No information
Incomplete outcome data addressed? All outcomes	Yes	Losses to follow up were reportedly 10.7% DMPA, 8.9% NET-EN 60 days, and 9.8% NET-EN 84 days. Life-table rates for total discontinuation were 71 to 74.

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

Study	Reason for exclusion
Agoestina 1978	Insufficient weight change data: presented in figure without any specific numbers, other than mean gain for DMPA group in text.
Barsivala 1974	Insufficient data: study duration not reported (our criteria was $\geq 3$ months); also, authors did not specify whether the variance reported is standard deviation or standard error.
Beksinska 2010	Analysis combined users of DMPA, NET-EN, or both. Authors noted the subgroups were too small to analyze separately and that differences in weight gain were not significant.
Berenson 1997	Insufficient weight change data: means reported without any variance measure
Berenson 2009	Insufficient weight change data: mean change reported without any variance. Of 240 who chose DMPA, 182 (76%) discontinued the method. Of the 182, 68 remained in study $\leq 2$ more years (44 began the COC used in the study and 24 chose non-hormonal methods). Reportedly, DMPA users who had $> 5\%$ increase in weight at 6-month visit were more likely to be lost to follow up at the next visit than those who had not gained weight.
Bonny 2006	Analysis combined groups that received DMPA or DMPA with estradiol supplement; researchers reported the two DMPA groups did not differ in weight gain. Method discontinuation for DMPA was 37% at 18 months.
Clark 2005	Insufficient weight change data: means (not mean change) presented in a figure. Text mentions mean change for DMPA at 30 months (no variance measure) and that the control group was basically unchanged. Due to discontinuations of DMPA and initiation of hormonal contraception among controls, the samples sizes were 17% (DMPA) and 19% (controls) of baseline by the last visit.
Dahlberg 1982	Insufficient weight change data: means reported without any variance measure
El Mahgoub 1980	Insufficient weight change data: mean change reported without any variance measure. Also, percent that lost or gained weight was reported, but no specific amount of weight was provided.
Hall 1980	Insufficient weight change data: mean change in 'ideal body weight' shown in figure, except for mean change for progestin-only group reported in text.
Havranek 1972	Insufficient weight data: mean change for one group reported without any variance measure
Mangan 2002	Comparison groups were DMPA users and OC users. Types of OC were not specified and might have included progestin-only as well as combination OC.
Olsson 1988	Insufficient data for analysis: no N per group for analysis. First-year continuation rate was 59% for Norplant and 77% for Norplant-2; methods suggest these were life-table rates.
Ortayli 2001	Insufficient data: report does not provide sample sizes used for analysis. Outcome data are from a pilot conducted in 1995 and the main study conducted from 1996 to 1998.
Risser 1999	Comparison groups were DMPA users and OC users. Types of OC were not specified and might have included progestin-only as well as combination OC.
WHO 1978	Insufficient weight data: mean gains reported without any variance measure
Yela 2006	Insufficient weight change data: tables show weight and BMI means (not change) by year; text mentions mean change per group over 5 years without any variance measure. Study began in 1998.
Zheng 1999	Insufficient weight change data: means reported without any variance measure