Depot Medroxyprogesterone Acetate (DMPA) Injectables
DEPOT MEDROXPROGESTERONE ACETATE

In Jordan, the proportion of married women of reproductive age using depot medroxyprogesterone acetate (DMPA) is less than 1 percent\(^1\). Most women can use DMPA, but health professionals should be aware of the World Health Organization Medical Eligibility Criteria for Contraceptive Use\(^2\).

**Effectiveness**

Depot medroxyprogesterone acetate (Depo Provera\(^\text{®}\)) is highly effective if taken every three months as directed. With correct and consistent use, less than 1 percent will experience a method failure in the first year of use. Typical users though have failure rates about 3 percent in the first year\(^3\). For women who prefer an injectable contraceptive method, duration of use is not associated with any decrease in efficacy or safety. Thus, the use of DMPA does not require a rest period.

**Mode of Action**

There are several modes of action of DMPA in preventing pregnancy. It acts primarily by inhibiting ovulation. Other ways that DMPA may prevent pregnancy are by a thickening of the cervical mucus thus preventing sperm entry into the upper genital tract, or by altering the endometrium thus inhibiting implantation of a fertilized egg\(^4\).

**Advantages of Depot Medroxyprogesterone Acetate**

In addition to being effective, other advantages to using DMPA are:

- the absolute number of ectopic pregnancies are reduced\(^5\)
- it is reversible\(^6,7,8\)
- it is an option throughout reproductive years
- a suggested decrease in menstrual bleeding\(^9\)
- a reduced risk of anemia\(^10\)
- less pain from endometriosis\(^11,12\)
- no apparent increased cardiovascular risks\(^13\)
- is safe for the infant of a breastfeeding woman\(^14\)
Disadvantages of Depot Medroxyprogesterone Acetate

- menstrual cycle disturbances\textsuperscript{9}
- return visits are required every three months
- not possible to discontinue immediately
- return to fertility is likely to be delayed\textsuperscript{6,7,8}

Special Topics

- Cancer

\textit{No apparent elevation of cancer risk though studies of association with breast cancer are not consistent}\textsuperscript{15-20}.

- Bone Mineral Density Loss

\textit{Some loss of bone mineral density which may be associated with a risk of fractures in some women}\textsuperscript{21,22}. 
REFERENCES
Depot Medroxyprogesterone Acetate


15. Lumbiganon P. *Depo-medroxyprogesterone acetate (DMPA) and cancer of the endometrium and ovary.* Contraception March 1994:49;203-209.


20. Mati JG et al. *Depot-medroxyprogesterone acetate (DMPA) and risk...*


List of Critically Appraised Topics

1-Efficacy
2-Ectopic Pregnancy
3-Return to Fertility
4-Menstrual Blood Loss
5-Amenorrhea
6-Anemia
7-Counseling
8-Endometriosis
9-Fibroids
10-Pelvic Inflammatory Disease
11-Weight Gain
12-Acne
13-Depression
14-Hypertension
15-Myocardial Infarction
16-Stroke
17--Venous Thromboembolism
18-Endometrial Cancer
19-Ovarian Cancer
20-Cervical Cancer
21-Breast Cancer
22-Liver Cancer
23-Fractures
24-Breastfeeding

Note that the level of evidence accompanying each publication in each of the CATs refers to the study design.
Depot medroxyprogesterone acetate is an effective contraceptive for both breastfeeding and non-breastfeeding women when used correctly and consistently.

Conclusion
Studies show depot medroxyprogesterone acetate 150 mg IM (DMPA) is a highly effective contraceptive method for both breastfeeding and non-breastfeeding women when used correctly and consistently.

Clinical Question
Is depot medroxyprogesterone an effective contraceptive for women?

Search Terms
Depot medroxyprogesterone, DMPA, Depo Provera, effectiveness

Citation

Object of Research
Depot medroxyprogesterone

Research Outcome
Pregnancy in breastfeeding and non-breastfeeding women

Study Features
This is a review of nine studies assessing the efficacy of depot medroxyprogesterone 150 mg IM as a contraceptive. The sample size for one study was not available, but the other seven included 8,292 women ranging from 209 to 3,857. The median sample size was 650. Trial locations included European countries, the United Kingdom, the United States, as well as those from Africa, Latin America, and Asia. One study in Bangladesh was of 100 women who received their injection immediately postpartum. (Level 1 Evidence)
The Evidence

The one-year results for these studies were:

- No pregnancies in the immediate postpartum study though 100 cases is insufficient to assess a pregnancy rate.
- One-year pregnancy rates ranged from a low of zero to a high of 3.2. The highest rate was based on 209 cases whereas the two studies with over a thousand women reported one-year pregnancy rates of 0.1 and 0.3.

Appraised by: The Jordan Evidence-Based Medicine Reproductive Health Group

Update by: 26 April 2016
Among current users of depot medroxyprogesterone, there is no increased risk of ectopic pregnancy

Conclusion
Based on the results of a review of series reports of ectopic pregnancy, use of depot medroxyprogesterone (DMPA) as a contraceptive method decreases the overall incidence of ectopic pregnancy since there are few pregnancies among women who use an effective contraceptive method. Similarly there is no increased proportion of ectopic pregnancies among women who conceive while using depot medroxyprogesterone acetate though the possibility of ectopic pregnancy should be ruled out.

Clinical Question
Is there an increased risk of ectopic pregnancy among women using depot medroxyprogesterone acetate?

Search Terms
Depo Provera, DMPA, depot medroxyprogesterone, ectopic pregnancy

Citation

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Ectopic pregnancy

Study Features
This is a retrospective study based on a series of reports of pregnancies to the Insurance Division of Planned Parenthood Federation of America during the years 1994 to 1998 inclusive. Cases were included only if a pregnancy was reported after depot medroxyprogesterone acetate had been administered at a
Planned Parenthood site.

*(Level 2 Evidence)*

**The Evidence**
A total of 949,182 users of DMPA users were identified among which there were 402 reported pregnancies with a rate of 0.42 pregnancies/1000 users. Of these, there were 4 identified ectopic pregnancies or 1.5% of all pregnancies.

Comment: Based on data from the US Center for Disease Control as well as the WHO, the current estimated ectopic pregnancy rate without contraceptive use is approximately 2%. The current rate for DMPA based on these data is not significantly different from these estimates.

**Appraised by:** The Jordan Evidence Based Medicine-Reproductive Health Group

**Update by:** 11 March 2016
Among users of depot medroxyprogesterone acetate, there is no apparent association between use and failure to return to fertility though return is often delayed.

Conclusion
While there is no apparent association between use of depot medroxyprogesterone (DMPA) as a contraceptive and a return to fertility, users tend to experience some delay relative to other contraceptive users such as those using an IUD. That is, DMPA normally causes amenorrhea in the majority of users; however it is very rare for this to lead to infertility. Note that though the studies cited are old (1974, 1984, 1987), the return to fertility rates are consistent in the three studies and thus convincing.

Clinical Question
Is there an association between return to fertility and the use of DMPA as a contraceptive?

Search Terms
Depo Provera, DMPA, return to fertility

Citations


Object of Research
Depo Provera
Research Outcome
Return to fertility after discontinuation of method

Study Features
Schwallie
This is data taken from published and unpublished sources. 188 women who dropped from the Upjohn collaborative DMPA clinical study to become pregnant were included. Of these 74 (39.4%) were lost to follow-up, changed their mind or moved away.
(Level 2 Evidence)

Pardthaisong
This is a study of Thai contraceptive users who discontinued their method for a planned pregnancy. In all there were 796 former DMPA users, 437 former oral contraceptive users, and 125 former IUD users. The patients’ demographic characteristics were not described in this paper.
(Level 2 Evidence)

Study Features (continued)
Affandi
This is a study of Indonesian contraceptive users who discontinued their method for a planned pregnancy. In all there were 47 former DMPA users, 75 former IUD users and 51 former Norplant users. Mean ages (26 years) and parity (1.7 live births) were similar across the 3 groups.
(Level 2 Evidence)

The Evidence
Schwallie
Of the 114 DMPA users followed in this study, all became pregnant. The median time to pregnancy was 10 months. Of the 74 classified as lost to follow-up, 44 (59.5%) were true lost to follow-up, 5 (6.8%) returned to menses and then were lost to follow, 6 (8.1%) moved away, 18 (24.3%), changed their mind about becoming pregnant, and one other was removed because of
treatment for infertility prior to initiation of the study.

Pardthaisong
747 (94%) DMPA users returned to fertility at 36 months as compared to 117 (94%) IUD users. There was no apparent association between the length of use and a return to fertility.

Affandi
42 (89%) of all DMPA discontinuers returned to fertility at 24 months as compared to 65 (87%) IUD discontinuers.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update By: 15 March 2016
The use of depot medroxyprogesterone acetate is associated with a significant decrease in menstrual blood loss

Conclusion
Depot medroxyprogesterone acetate (DMPA) is associated with a significant decrease in menstrual blood loss. If women are counseled about this possibility, continuation rates may be improved.

Clinical Question
Is the use of depot medroxyprogesterone acetate contraceptive associated with an increased risk of menorrhagia?

Search Terms
Depot medroxyprogesterone acetate, DMPA, Depo Provera, menorrhagia.

Citations

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Menorrhagia

Study Features
This is a comprehensive review of 17 relevant studies of long-term data regarding the menstrual patterns among users of DMPA. The studies range from controlled clinical trials to retrospective chart reviews and follow-up surveys.

(Level 1 Evidence)
The Evidence
Based on these data, menstrual changes, such as spotting/irregular bleeding and longer durations of menses, are relatively common in the initial 3 months, but these tend to decrease over time. Bleeding associated with DMPA was more frequently characterized by spotting or light bleeding rather than heavy menstrual flow. Although the irregular bleeding with DMPA declines substantially with time, menstrual cycle changes are a major reason for patient discontinuation.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
The use of depot medroxyprogesterone acetate is associated with a significant increase in amenorrhea

Conclusion
Depot medroxyprogesterone acetate (DMPA) is associated with an increase in amenorrhea. The likelihood of a user experiencing amenorrhea increases with usage.

Clinical Question
Is the use of depot medroxyprogesterone acetate contraceptive associated with an increased risk of amenorrhea?

Search Terms
Depot medroxyprogesterone acetate, DMPA, Depo-Provera, amenorrhea.

Citation

Object of Research
Depot medroxyprogesterone acetate.

Research Outcome
Amenorrhea

Study Features
This a systematic review of 16 published articles including 5 studies of DMPA. The studies involved diaries and standard World Health Organization definitions for menstrual pattern changes for bleeding or spotting days, amenorrhea, or a normal pattern in four consecutive 90 day reference periods. Amenorrhea was defined as no bleeding in the 90 days reference period. The studies documenting amenorrhea included 1600 DMPA users from Vietnam, the United States, and ten WHO centers from Africa, Asia, Europe and North America.

(Level 1 Evidence)
The Evidence
For DMPA use, the prevalence of amenorrhea at successive 90-day periods was 12%, 25%, 37% and 46%. At 12 months, normal menstrual patterns were experienced by only 11% of DMPA users.

Comment: There is some suggestion that counseling women about likely menstrual pattern changes with DMPA use may decrease discontinuation due to amenorrhea with this method.

Appraised by: The Jordan Evidence Based Medicine Reproductive Health Group

Update by: 11 March 2016
The use of depot medroxyprogesterone acetate decreases the incidence of anemia

**Conclusion**
Depot medroxyprogesterone acetate (DMPA) is associated with a decrease in anemia incidence as measured by hemoglobin and ferritin levels.

**Clinical Question**
Is the use of depot medroxyprogesterone acetate contraceptive associated with a decrease in the incidence of anemia?

**Search Terms**
Depot medroxyprogesterone acetate, Depo-Provera, DMPA, hemoglobin, anemia.

**Citation**

**Object of Research**
Depot medroxyprogesterone acetate.

**Research Outcome**
Hemoglobin levels, anemia.

**Study Features**
This is a cross sectional study of current contraceptive users including DMPA. Women were non-pregnant and non-lactating. Countries with DMPA users were Bangladesh (n=51), Pakistan (n=25), and Thailand (two sites n=95 and n=50). The objective was to assess the effects of depot medroxyprogesterone
acetate contraceptive on hemoglobin and ferritin levels. Current users of other contraceptive methods (e.g. combined oral contraceptives, intrauterine devices) were compared with users of DMPA. Women with normal hemoglobin at the time of initiation of their contraceptive were asked to participate in a longitudinal component of the study in which hemoglobin and ferritin levels were assessed at a 3, 6, 9 and 12 months follow-up.

(Level 2 Evidence)

The Evidence
Current users of hormonal contraceptive methods generally had higher hemoglobin and ferritin levels than nonusers. The differences between women using a hormonal contraceptive and nonusers in mean values for hemoglobin varied between 3 and 6 g/L and for ferritin between 2 and 18 g/L. Significant mean increases of hemoglobin and ferritin levels at 12 months were observed among the users of oral contraceptives and DMPA, but not among users of copper or stainless steel ring IUDs.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
Users of depot medroxyprogesterone acetate who receive structured pretreatment counseling experience less rates of discontinuation than those with routine counseling

Conclusion
For women using depot medroxyprogesterone (DMPA), discontinuation can be decreased if they are given structured counseling designed to inform them of common use-related adverse effects (e.g. menstrual cycle disruptions).

Clinical Question
Does the provision of structured counseling on expected side effects of DMPA use affect continuation rates for this contraceptive?

Search Terms
Depot medroxyprogesterone acetate, DMPA, Depo-Provera, pretreatment counseling

Citation

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Discontinuation rates after pretreatment counseling on side effects associated with the use of DMPA

Study Features
This was a prospective, comparative study in four clinical sites conducted in China. The objective was to assess the effect of an intensive, detailed, structured pretreatment counseling as compared to routine counseling. Women (n=204) at two of the clinics received the intensive counseling while those
(n=217) at the other two had routine counseling. Women between the ages of 18 and 40 were enrolled at the four different clinics. The structured counseling included information on the mode of action of DMPA as well as common hormonal and possible side effects.

(Level 2 Evidence)

The Evidence
Within 3 months after receiving one DMPA dose, 3% of those who received structured counseling dropped out as compared to 25% who had received routine counseling. At 12 months, the corresponding rates for the two groups were 11% and 42%, respectively. For the structured counseling group, 5% dropped out for irregular bleeding and none left the study because of amenorrhea. For the routine counseling group, the corresponding dropout rates were 19% and 2%, respectively.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
The use of depot medroxyprogesterone acetate is effective in decreasing pain associated with endometriosis

Conclusion
Depot medroxyprogesterone acetate (DMPA) is an effective treatment for pain associated with endometriosis.

Clinical Question
Is the use of depot medroxyprogesterone acetate contraceptive associated with a decrease in pain associated with endometriosis?

Search Terms
Depot medroxyprogesterone acetate, DMPA, Depo Provera, pain associated with endometriosis

Citations


Object of Research
Depot medroxyprogesterone acetate.

Research Outcome
Pain associated with endometriosis
Study Features
Vercellini
Eighty patients with laparoscopic confirmed endometriosis and moderate or severe pelvic pain (dysmenorrhea, deep dyspareunia, and nonmenstrual pelvic pain) were randomly assigned to one of two treatments for 1 year in an open label, prospective clinical study. Treatments were either intramuscular depot medroxyprogesterone acetate 150 mg every 3 months or a cyclic monophasic oral contraceptive (ethinyl estradiol 0.02 mg, desogestrel 0.15 mg) combined with oral danazol 50 mg a day for 21 days of each 28-day cycle. The women were asked to grade the degree of their satisfaction at the end of therapy. Variations in severity of symptoms during treatment were determined by a 10 cm visual analog and a 0- to 3-point verbal rating scale.

(Level 1 Evidence)

Walch
In an open label, one year, prospective clinical study of women with histologically confirmed endometriosis, 21 were randomly assigned to receive Implanon and 20 to receive depot medroxyprogesterone. They were evaluated for pain improvement according to a visual analog scale as well as overall degree of satisfaction.

(Level 1 Evidence)

The Evidence
Vercellini
A significant decrease in symptom scores was observed in both groups. Twenty nine (72.5%) of 40 subjects in the depot medroxyprogesterone acetate group were satisfied after 1 year of therapy compared with 23 (57.5%) of 40 in the oral contraceptive plus danazol group (Odds Ratio=1.95, 95% confidence interval 0.76-4.97). Numerically, the DMPA group had better symptom scores, but the relative risk was not statistically significant.
Walch
During the follow-up period at one year, an improvement in pain intensity was observed in both treatment groups. The average decrease in pain was 68 percent in the implant group and 53 percent in the DMPA group. Numerically, at each quarterly evaluation, the decreases were greater in the Implanon group though the differences with the DMPA group were not statistically significant. However, the overall degree of users satisfied or very satisfied among those using Implanon and those using DMPA was similar (Implanon: 57%; DMPA: 58%).

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
Depot medroxyprogesterone acetate is associated with a decrease in the incidence of uterine fibroids

**Conclusion**
Depot medroxyprogesterone acetate (DMPA) is associated with a decrease in the incidence of uterine fibroids when compared to non-users of contraceptives. When compared with current use of combined oral contraceptives (COCs) this decrease is significantly better.

**Clinical Question**
Is the use of depot medroxyprogesterone acetate contraceptive associated with a decrease incidence of uterine fibroids?

**Search Terms**
Depot medroxyprogesterone acetate, DMPA, Depo-Provera, myomas, uterine fibroids

**Citation**

**Object of Research**
Depot medroxyprogesterone acetate

**Research Outcome**
Uterine fibroids, leiomyomata

**Study Features**
This is a prospective cohort study conducted in the United States as part of the Black Women’s Health Study. Through a questionnaire, women were recruited in 1995 if they subscribed to Essence magazine, were a member of a Black professional organization, or were a friend or relative of a respon-
dent. The baseline questionnaire elicited information on demographic and behavioral characteristics, reproductive and contraceptive histories, health care utilization, and medical conditions. After exclusions, 22,895 premenopausal women with intact uteri and no previous self-reported diagnosis of uterine leiomyomata were subsequently identified and included in the study. Updated information was obtained from the sample every two years. Of these women, 3 percent were depot medroxyprogesterone users. 

*Level 2 Evidence*

**The Evidence**

Among those using DMPA, there appeared to be a significant decrease in the risk of uterine leiomyomata when compared to non-users of a hormonal contraceptive (Rate Ratio=0.5; 95% confidence interval 0.4 - 0.9).

**Appraised by:** The Jordan Evidence Based Medicine-Reproductive Health Group

**Update by:** 15 March 2016
Use of depot medroxyprogesterone acetate does not appear to be associated with an increased risk of pelvic inflammatory disease.

Conclusion
The use of depot medroxyprogesterone acetate (DMPA) does not appear to result in an increased risk of pelvic inflammatory disease, and it may actually protect women from acute pelvic inflammatory disease. The mechanism of this potentially protective effect is not well understood, but is possibly due to the increase of the viscosity of cervical mucus.

Clinical Question
Is the use of DMPA associated with an increased risk of pelvic inflammatory disease?

Search Terms
Depo-Provera, DMPA, depot medroxyprogesterone acetate, PID, pelvic inflammatory disease

Citations


Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Pelvic inflammatory disease

Study Features
This is a report of a multinational case control study which was conducted in Africa, Asia, South America and Europe by the World Health Organization between March, 1978 and December, 1979. The diagnosis of pelvic inflammatory disease was based on an oral temperature of 38°C, suprapubic tenderness with guarding, and cervical or adnexal tenderness, or a pelvic mass
of PID. Thus, 638 controls were matched with the 319 acute PID cases for parity, age, marital status and inpatients/outpatients status. (Note that the WHO publication is used to define the study design and population. No DMPA results are provided in this publication.)

(Level 3 Evidence)

The Evidence
Of the PID cases, 10 (3.1%) reported current use of injectable contraceptive as compared to 38 (6.0%) controls. The odds ratio of acute pelvic inflammatory disease associated with current injectable contraceptive use was 0.5 (95% CI:0.25-1.0). Though not statistically significant, this suggests that injectable progestin may protect women from acute pelvic inflammatory disease, possibly by increasing the viscosity of cervical mucus.

Comment: The reduced risk of PID in users of injectable contraceptives is of similar magnitude to the risks reported for users of combined oral contraceptives, barrier methods and female sterilization in developed and developing countries.

Developed by: The Jordan Evidence Based Medicine and Reproductive Health Group

Update By: 16 March 2016
The association between the use of depot medroxyprogesterone acetate (DMPA) and with weight gain is not clear

Conclusion
Results from this systematic study of weight gain including depot medroxyprogesterone acetate users are not consistent. For most studies, weight gain among DMPA users was less that 2 kg. Designs without a placebo control make it difficult to assess causality.

Clinical Question
Are women who take DMPA for contraception at an increased risk for weight gain?

Search Terms
DMPA, Depo-Provera depot-medroxyprogesterone acetate, weight gain

Citations

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Weight gain

Study Features
This is a systematic review of different progestin only contraceptives and their effect on weight gain. Ten studies involving DMPA were identified though one is not presented here as it compares interval and postpartum users of DMPA. The primary outcome in these studies was mean change in body
weight. The studies were as follows:

- USA (2009):
- Rhodesia (1976): Two groups, each of 500 women, received DMPA 150 mg every three months or DMPA 450 mg every six months. Weight was measured at each visit.

(Level 1 Evidence)

The Evidence
Mean gain among DMPA users was less than 2 kg for most studies up to one year.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
The use of depot medroxyprogesterone as a contraceptive is not associated with any changes in the incidence of acne.

Conclusion
When compared with women who were not using a hormonal contraceptive method, there does not appear to be any evidence that depot medroxyprogesterone acetate (DMPA) either increases or decreases acne.

Clinical Question
Is the use of depot medroxyprogesterone acetate contraceptive associated with a decrease in acne?

Search Terms
Depot medroxyprogesterone acetate, acne vulgaris.

Citation

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Acne

Study Features
This a prospective, cohort study of 608 women in which 17 symptoms (including acne) were assessed prior to their initiation of contraception and every 6 months thereafter for 24 months. Of the total of 608 women included in the study, 218 selected oral contraceptive pills, 219 DMPA, and 171 non-hormonal contraception. The 3 groups were similar at baseline with regard to race/ethnicity, age, or income but did differ regarding marital status, education, and parity.

(Level 2 Evidence)
The Evidence
Relative to women using a non-hormonal method of contraception, those using depot medroxyprogesterone showed neither a decrease nor an increase in the risk of acne [odds ratio=0.99 (95% confidence interval: 0.65-1.51)]. Consistent with other studies, women who had selected an oral contraceptive showed an improvement in their acne symptoms.

Appraised by: The Jordan Evidence Based Medicine Reproductive Health Group

Update by: 15 March 2016
The relationship between depressive symptoms and the use of depot medroxyprogesterone acetate is not clear

Conclusion
Individual women may experience an increase in depression when they use depot medroxyprogesterone acetate (DMPA). However, data evaluating the impact of DMPA on mood are limited and conflicting. A history of depression is not a contraindication to DMPA user.

Clinical Question
Is the use of depot medroxyprogesterone acetate associated with increased risk of depression?

Search Terms
Depot medroxyprogesterone acetate, DMPA, Depo Provera, depression.

Citations


Object of Research:
Depot medroxyprogesterone acetate

Research Outcome
Depressive Symptoms.
Study Features
Westhoff, Truman et al
Women in a prospective multicenter study were evaluated to identify a possible relationship between depressive symptoms and the use of contraceptives. Baseline depressive symptom scores were assessed for users of DMPA, Norplant implants, sterilization and pills. All women were interviewed at 6 month intervals using a closed ended questionnaire. Of the 2,007 women seen at baseline, 495 (24.8%) selected DMPA. Of these 393 (79.4%) completed follow-up whether or not they continued use of their injectable method. They were interviewed at 12 months after study initiation. Overall, 172 (43.8%) continued to use DMPA and 221 (56.2%) discontinued. (Level 2 Evidence)

Civic et al
This is a prospective, population based study in the United States of 183 women using DMPA and a control group of 274 non-users. The age range was between 18-39 years. Data on depressive symptoms was collected at 6 month intervals for up to three years. The questionnaire included an assessment of the level of depressive symptoms during the last two weeks prior to their evaluation using the Community Epidemiology Survey Depression Scale (CSE-D). (Level 2 Evidence)

Gupta et al
This a prospective study set in urban hospital, adolescent clinic. Thirty-nine young women who chose DMPA as contraceptive method and 24 who chose not to use any hormonal contraception were enrolled as subjects and controls. Two standard questionnaires were used; the Beck Depression Inventory (BDI) and the Multiple Affect Adjective Checklist –Revised (MAACL-R). These questionnaires were administered at baseline to all participants and at 3, 6, 12 months after the initiation of the study. (Level 2 Evidence)
The Evidence
Westhoff, Truman et al:
Among those who discontinued DMPA, there was no change in depressive symptoms at the 12 month follow-up. Among continuing users, there was a decrease in depressive symptoms from 7.4 at baseline to 6.7 at one year. Among those women who entered the study with depressive symptoms and scored in the highest quintile, there was no increase in these symptoms. In fact, the reverse was true in that they experienced a decrease in scores by several points during the study. That is, the use of DMPA did not exacerbate symptoms in women with pre existing symptoms.

Civic et al:
Relative to non-users, women who discontinued DMPA had elevated depressive symptoms prior to discontinuation (Odds Ratio=1.6; 95% CI = 1.03-2.48). Continuing users also experienced an elevated, though not statistically significant, risk compared to non-users (Odds Ratio=1.44; 95% CI= 1.00-2.07). It should be noted that discontinuers had higher depressive symptoms before they started their contraceptive.

Gupta et al:
Adolescents using DMPA did not show depressive symptoms when over a period of 12 months as measured by two standardized questionnaires (Beck Depressive inventory) and the (Multiple Affect Checklist-revised).

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group.

Updated by: 26 April 2016
Use of depot medroxyprogesterone acetate does not appear to be associated with an increased risk of hypertension

**Conclusion**
Depot medroxyprogesterone acetate (DMPA) does not appear to be associated with an increased risk of hypertension. Further, DMPA may be the choice of contraception in hypertensive patients as long term use of this injectable should not have any unfavorable effects on blood pressure.

**Clinical question**
Is the use of depot medroxyprogesterone acetate associated with an increased risk of hypertension?

**Search Terms**
Depo-Provera, DMPA, depot medroxyprogesterone acetate, hypertension, blood pressure

**Citations**


**Object of Research**
Depot medroxyprogesterone acetate

**Research Outcome**
Hypertension

**Study Features**
Cuong and Huong
This is a comparative study of Vietnamese women randomly assigned to either the one month combined injectable, Cyclofem, or the three month inject-
able, DMPA. Four study centers were involved at which 150 women in each received one of the two injectables.

*(Level 1 Evidence)*

**Taneepanichskul**

This is a case control study conducted in Thailand. The two groups were comprised of 50 DMPA users and 50 non-hormonal IUD users. All had been using their contraceptive for at least 10 years. They were matched for selected sociodemographic characteristics (age, parity, income and life style). All of the users were normotensive at the beginning of the study period. WHO/British Hypertension Society guidelines were used for classifications of blood pressure.

*(Level 3 Evidence)*

**The Evidence**

**Coung and Huong**

Both groups experienced a mean drop in blood pressure. In the DMPA group, there was a 1.6 mmHG drop in the systolic blood pressure and 0.5 mmHG drop in the diastolic blood pressure. There were no discontinuations from the study due to changes in blood pressure.

**Taneepanichskul**

Five (10%) users of DMPA developed hypertension compared to 7 (14%) of the IUD users. This difference is not statistically significant. No cases of hypotension were reported. There were no differences in blood pressure changes with long term DMPA or IUD use.

_Developed by:_ The Jordan Evidence Based Medicine-Reproductive Health Group

_Update By:_ 25 April 2016
The use of depot medroxyprogesterone acetate does not increase the risk of myocardial infarction

Conclusion
The use of depot medroxyprogesterone acetate (DMPA) as a contraceptive does not appear to be associated with significant increase in risk of myocardial infarction.

Clinical Question
Is the use of DMPA as a contraceptive associated with an increased risk of myocardial infarction?

Search Terms
Depot medroxyprogesterone acetate, Depo-Provera, DMPA, myocardial infarction

Citation
The WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study.* Contraception 1998;57:315-324.

Object of Research
Depot medroxyprogesterone acetate.

Research Outcome
Myocardial infarction

Study Features
This is a hospital-based, case-control study which was undertaken in 21 centers in 17 countries subdivided into 4 regions (Africa, Asia, Europe, and Latin America). Eligible cases were women aged 15 – 49 years, who had been admitted to collaborating hospitals between 1 February 1989 and 31 January
1995. The medical history and the findings of examinations and investigations were used to classify acute myocardial infarction cases as definite or possible. Up to 3 control subjects were matched for each case.

Of the 3,697 cases included in the analyses, 364 had suffered a myocardial infarction, of which one case was a current user of DMPA. Cases and controls had similar mean ages, body mass indices, and numbers of live births. The prevalence of DMPA use was highest in Asia (2.6%) and lowest in Europe (0.3%). Crude and adjusted odds ratios associated with the current use of DMPA compared with nonusers were estimated. The odds ratios were adjusted for high blood pressure and smoking categories.

*Level 3 Evidence*

**The Evidence**
Crude and adjusted odds ratios for myocardial infarction in relation to current the use of DMPA were 0.52 (95% CI: 0.06 – 4.38) and 0.66 (95% CI: 0.07 – 6.00) respectively. Based on these findings, there is no apparent risk of myocardial infarction among users of DMPA.

**Comment**
Though the number of cases included in this study is small, the results provide reassurance that the use of DMPA was not associated with any significant increase in the risk of myocardial infarction. The small number of cases and control subjects in this study may be attributed to low incidence of myocardial infarction in women of childbearing years and in part because of the limited use of DMPA as contraceptive during the years of the study.

**Appraised by:** The Jordan Evidence Based Medicine-Reproductive Health Group

**Update by:** 15 March 2016
The use of depot medroxyprogesterone acetate does not increase the risk of stroke

Conclusion
The use of depot medroxyprogesterone acetate (DMPA) as a contraceptive does not appear to be associated with a significant increase in risk of stroke. The results of studies to date provide reassurance that the use of DMPA is not associated with any significant increase in the risk of stroke.

Clinical Question
Is the use of DMPA associated with an increased risk of stroke?

Search Terms
DMPA, Depo-Provera, depot medroxyprogesterone acetate, stroke

Citation
The WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study*. Contraception 1998;57:315-324.

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Stroke

Study Features
This is multicenter, hospital-based case-control study which was undertaken in 21 centers in 17 countries subdivided into 4 regions (Africa, Asia, Europe, and Latin America). Eligible cases were women within the age 15 – 49 years who had been admitted to a collaborating hospital between 1 February 1989 and 31 January 1993. Cases included hemorrhagic, ischemic, and unspecified types of stroke. For each case, an average of 3 control subjects were found as matches.
Of the 3,697 cases included in the analyses, 2196 had suffered a stroke. Twenty-five cases were current users of DMPA. These 25 cases were matched to 81 controls. Cases and controls had similar mean ages, body mass indices, and numbers of live births. The prevalence of DMPA use was highest in Asia (2.6%) and lowest in Europe (0.3%).

(Level 3 Evidence)

The Evidence
Crude and adjusted odds ratios for stroke in relation to current use of DMPA were 0.93 (95% CI: 0.58 – 1.48) and 0.89 (95% CI: 0.53 – 1.49), respectively. Based on these results, there is no apparent increased risk of stroke among users of DMPA.

Comment: The small number of cases and control subject in this study may be attributed to low incidence of stroke event in women of childbearing years and in part because of the limited use of DMPA as contraceptive during the years of the study.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 15 March 2016
The use of depot medroxyprogesterone acetate as a contraceptive does not appear to be associated with an increased risk of venous thromboembolism.

Conclusion
The use of depot medroxyprogesterone acetate (DMPA) does not increase the risk of venous thromboembolism. The results of this study provide some reassurance that the use of DMPA is not associated with an increased risk of venous thromboembolism.

Clinical Question
Is the use of DMPA associated with an increased risk of venous thromboembolism?

Search Terms
DMPA, depot medroxyprogesterone, Depo-Provera, venous thromboembolism

Citation
The WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. Contraception 1998;57:315-324.

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Venous thromboembolism

Study Features
This is multicenter, hospital-based case-control study which was undertaken in 21 centers in 17 countries subdivided into 4 regions (Africa, Asia, Europe, and Latin America). Eligible cases were women within the age 15 – 49 years
who had been admitted to a collaborating hospital between 1 February 1989 and 31 January 1993. Cases included those with venous thromboembolism. For each case, an average of 3 control subjects were found as matches.

Of the 3,697 cases included in the analyses, 1137 had suffered venous thromboembolism. Eleven cases were current users of DMPA. These 11 cases were matched to 34 controls. Cases and controls had similar mean ages, body mass indices, and numbers of live births. The prevalence of DMPA use was highest in Asia (2.6%) and lowest in Europe (0.3%).

**(Level 3 Evidence)**

**The Evidence**

Crude and adjusted odds ratios for venous thromboembolism in relation to current use of DMPA were 1.27 (95% CI: 0.63 – 2.57) and 2.19 (95% CI: 0.66 – 7.26), respectively. Based on these results, there does not appear to be any increased risk of venous thromboembolism among users of DMPA.

**Comment**

The small number of cases and control subject in this study may be attributed to low incidence of venous thromboembolism in women of childbearing years and in part because of the limited use of DMPA as contraceptive during the years of the study.

**Appraised by:** The Jordan Evidence Based Medicine- Reproductive Health Group

**Update by:** 15 March 2016
There is no association between the use of depot medroxyprogesterone acetate as a contraceptive and the incidence in endometrial cancer

Conclusion
In this small study, there is not apparent increased risk of endometrial cancer among women using depot medroxyprogesterone acetate (DMPA) for contraception. Suggestions of a possible protective effect require larger studies.

Clinical Question
Is the use of depot medroxyprogesterone acetate associated with an increased risk of endometrial cancer?

Search Terms
DMPA, depot medroxyprogesterone acetate, Depo Provera, endometrial cancer

Citation
Lumbiganon P. Depo-medroxyprogesterone acetate (DMPA) and cancer of the endometrium and ovary. Contraception March 1994;49;203-209.

Object of Research:
Depot medroxyprogesterone acetate

Research Outcome
Endometrial cancer

Study Features
This is a review of two studies of the association between DMPA use and endometrial cancer. The first study was conducted in the United States, the second is WHO collaborative study of neoplasia and steroid hormone contraceptives.
US Study/Atlanta, Georgia: This is a record linkage study of 5000 black women receiving DMPA during a period from 1967 to 1976. These women were followed for four to thirteen years after their initial DMPA injection.

WHO Collaborative Study: This is a hospital-based case-control study carried out in 14 centers in 11 countries. However, there were too few cases to assess the association between DMPA and endometrial cancer outside the three studies in Thailand and results are based only on these three. Controls were selected from among women admitted to the same three hospitals other than the obstetric and gynecologic wards.

(Level 2 Evidence)

The Evidence
US Study/Atlanta, Georgia: The number of cases found in this study linking hospital records (DMPA users and cancer cases) was too small to make any definitive statement about risk. However, the relative risk for all types of uterine cancer in DMPA users was 1.2 (95% CI: 0.1-6.7). Note that this relative risk was calculated comparing the actual incidence in the 5000 DMPA users with the expected number of uterine cancers in this group (0.83) based on National Cancer Institute estimates.

WHO Collaborative Study
In this hospital-based, case control study, 122 women with pathologically confirmed endometrial cancer were identified and matched with 939 controls. The adjusted relative risk was 0.21 (95% CI: 0.06-0.79) suggesting a protective effect of DMPA against endometrial cancer among users.

Appraised by: The Jordan Evidence Based Medicine Reproductive Health Group

Update by: 16 March 2016
There is no association between the use of depot medroxyprogesterone acetate (DMPA) as a contraceptive and the incidence in ovarian cancer.

**Conclusion**
While there is a suggestion of a protective effect of DMPA for ovarian cancer, there is clearly no increased risk among women using this injectable contraceptive.

**Clinical Question**
Is the use of depot medroxyprogesterone acetate associated with an increased risk of ovarian cancer?

**Search Terms**
DMPA, depot medroxyprogesterone acetate, Depo Provera, ovarian cancer

**Citation**
Lumbiganon P. Depo-medroxyprogesterone acetate (DMPA) and cancer of the endometrium and ovary. Contraception March 1994:49;203-209.

**Object of Research:**
Depot medroxyprogesterone acetate

**Research Outcome**
Ovarian cancer

**Study Features**
This is a review of two studies assessing the potential association between DMPA use and ovarian cancer. One study was conducted in the United States while the other was a WHO collaborative study of neoplasia and steroid hormone contraceptives.

**US Study/Atlanta, Georgia:** This study was based on linking hospital records of 5000 women receiving DMPA during the period 1967 o 1976. These women were followed for four to thirteen years.
WHO Collaborative Study: This was also hospital-based and used a case-control approach. Hospitals were in fourteen different centers and eleven countries. However, there were too few cases to assess the association between DMPA and ovarian cancer outside the three studies in Thailand and one in Mexico. Accordingly the study is based only on these four hospitals. Controls were selected from among women admitted to the same four hospitals other than the obstetric and gynecologic wards.

(Level 2 Evidence)

The Evidence
US Study/Atlanta, Georgia: The number of cases found in this study linking hospital records (DMPA users and cancer cases) was too small to make any definitive statement about risk. However, the relative risk for ovarian cancer in DMPA users was 0.8 (95% CI: 0.1-4.6). Note that this relative risk was calculated comparing the actual incidence in the 5000 DMPA users with the expected number of ovarian cancers in this group (1.16) based on National Cancer Institute estimates.

WHO Collaborative Study: In this hospital-based, case control study, 224 women with histologically confirmed epithelial ovarian cancer were found with 1,781 controls. The adjusted relative risk was 1.07 (95% CI: 0.06-1.8) suggesting no increased risk of ovarian cancer among DMPA users.

Appraised by: The Jordan Evidence Based Medicine Reproductive Health Group

Update by: 16 March 2016
The use of depot medroxyprogesterone acetate does not increase the risk of invasive cervical cancer

Conclusion
Based on the results of these studies, the use of depot medroxyprogesterone acetate (DMPA) as a contraceptive does not appear to be associated with an increase in the risk of invasive carcinoma of the cervix, nor with use of over 12 years. Importantly, the results of these two studies provide reassurance that prolonged use of DMPA does not increase the risk of invasive cervical carcinomas, even after a potential period of non-use over a decade after initiation of DMPA.

Clinical Question
Is the use of depot medroxyprogesterone acetate associated with an increased risk of invasive cervical cancer?

Search Terms
DMPA, depot medroxyprogesterone acetate, Depo-Provera, cervical cancer

Citations


Object of Research
DMPA

Research Outcome
Invasive cervical cancer
Study Features
WHO Collaborative Group
This is hospital-based case-control study. Cases were 2,009 women with invasive squamous cell cervical cancer and 9,583 controls from Thailand, Mexico and Kenya. Risk factors, such as age, center, total number of pregnancies, number of prior Pap smears, and any use of oral contraceptives were controlled for in the analysis. The relative risk estimates of invasive cervical cancer in relation to months of use, months since first initiation, and months since last use of DMPA were estimated.

(\textit{Level 3 Evidence})

Thomas and Ray
This is hospital-based, case control study conducted from October 1979 to September 1988 and included cases and controls from Thailand, Mexico and Kenya. Cases were collected from interviews of 239 women with adenocarcinoma and 85 women with adenosquamous carcinomas, as well as 2,534 controls. The two groups were matched for age, center, parity, year of entry as well as ever use of oral contraception or premenopausal estrogens. The relative risk of adenomatous cervical cancer in women who ever used DMPA was estimated adjusting for known risk factors including sexual behaviors, smoking, genital warts, and months of DMPA use, and months since first and last use of DMPA.

(\textit{Level 3 Evidence})

The Evidence
WHO Collaborative Group
- The relative risk of invasive squamous cell cervical carcinoma in women who ever used DMPA was 1.11 (95\% CI: 0.96 – 1.29). This is not statistically significant.
- No trends in risk with duration of use or times since initial or most recent exposure were observed.
Thomas and Ray
Calculation of relative risks for adeno- and adenosquamous carcinomas yielded similar results, and accordingly, the two groups were combined.

- The combined relative risk of adeno- and adenosquamous cervical carcinomas in women who ever used DMPA was 0.75 (95% CI: 0.51 – 1.1).
- No trends in risk were observed with duration of DMPA use, time since first or last use, or age at first use.

**Appraised by:** The Jordan Evidence Based Medicine-Reproductive Health Group

**Update by:** 16 March 2016
Depot medroxyprogesterone acetate does not appear to increase the risk of breast cancer.

**Conclusion**
There was no increase in breast cancer risk in women who had ever been exposed to depot medroxyprogesterone acetate (DMPA). Risk was not increased among current users, in those who had used in the previous 5 years, in those whose first use was before age 25 or 35, and in those used for 24 months. However, one study found that recent users aged 20 to 44 who used DMPA for more than one year had a two-fold increased risk for breast cancer though this finding was not supported in other similar studies.

**Clinical Question**
Are women who are current or previous users of depot medroxyprogesterone acetate at increased risked for the development of breast cancer?

**Search Terms**
DMPA, depot medroxyprogesterone acetate, Depo Provera, breast cancer; breast neoplasm

**Citations**


**Object of Study**
Depot medroxyprogesterone acetate

**Research Outcome**
Breast cancer

**Study Features**
Strom et al
This is a population-based, multicenter case control study of 4,575 US women who had histologically confirmed breast cancer. Controls were randomly selected from the same geographic area as the cases and were 4,682 in number. Controls had no previous cancer diagnosis and were matched with the cases by age, race and geographic location.

*(Level 3 Evidence)*

**Li et al**

This is a population-based case control study of breast cancer among women 20 to 44 years of age in the United States. Cases were women 20 to 44 years of age diagnosed with a primary invasive breast cancer between June 2004 and June 2010 with no previous history of *in situ* or invasive breast cancer. Controls were identified through the Cancer Surveillance System that serves 13 counties of western Washington State. Controls were ascertained via random digit dialing of landline home telephone numbers. Of the 1,359 eligible controls identified, 1,056 (78%) were interviewed. Controls were matched to cases within 5-year age groups to cases with approximately one control for each case. Three groups of controls were defined; never used hormonal contraception (n=91), ever used DMPA (n=100), and ever used hormonal contraception but never used DMPA (n=728).

*(Level 3 Evidence)*

**The Evidence**

**Strom et al**

A total of 127 subjects were exposed to DMPA (58 cases/69 controls). There was no significant increase in risk for women who had ever been exposed to DMPA. Risk was not increased among current users, defined as women who used DMPA within 1 year of the reference date [Odds Ratio=0.7, 95% CI: 0.4-1.3], those who initiated use in the 5 years immediately preceding the reference date [Odds Ratio=0.9, 95% CI: 0.5-1.4], those whose first use was before age 25 [Odds Ratio=1.3, 95% CI: 0.7-2.3], or those whose use began before age 35 [Odds Ratio=0.9, 95% CI:0.6-1.3]. Risk was significantly reduced among women whose first use was within 1 year of the reference date [Odds Ratio=0.3, 95% CI: 0.07-0.94]. Short-term users (≤6 months duration) were at decreased risk relative to never users [Odds Ratio=0.6, 95% CI: 0.4-1.0]. Among women with at least 24 months of use, risk was not statistically significantly increased relative to never users [Odds Ratio=1.4, 95% CI: 0.8-2.5].
Li et al
A total of 221 subjects were exposed to DMPA (121 cases/100 controls). There was no significant increase in risk for women who had ever been exposed to DMPA [Odds Ratio=1.2, 95% CI: 0.9–1.6], nor in women when the last use was <5 years ago [Odds Ratio=1.5, 95% CI: 0.9-2.7]. However, recent users of DMPA for 12 months or longer had a 2.2-fold increased risk of breast cancer (95% CI: 1.2–4.2).

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update by: 16 March 2016
The use of depot medroxyprogesterone acetate for contraception does not have any effect on the risk of liver cancer in women

Conclusion
Exposure to DMPA does not appear to increase a woman’s risk of contracting liver cancer.

Clinical Question
Are women who take depot medroxyprogesterone acetate for contraception more likely to get liver cancer than those who do not use it?

Search Terms
Depo medroxyprogesterone acetate, liver cancer

Citation

Object of Research
Depot medroxyprogesterone acetate

Research Outcome
Liver cancer

Study Features
This is a hospital-based, case-control study conducted at three centers in Thailand and one in Kenya. Women more than 15 years of age and who had used a steroid contraceptive during their fertile years were identified through hospital admission records. All women in Thailand with diagnosed liver cancer were histologically confirmed though this was not always the case in Kenya. In all, 71 liver cancer cases were identified and interviewed. Controls from the same hospital were identified though they were not matched individually. In total, there were 530 controls. The data from Thailand and Kenya were analyzed separately because the estimates of the relative risk in ever-users in these countries were so dissimilar. Thus data from these two sites were not combined. *(Level 3 Evidence)*
The Evidence
In Kenya, 18.2% of the cases and 8.5% of the controls had ever used DMPA. In contrast, 8.2% of the cases and 16.8% of the controls in Thailand had used DMPA. Because of this dissimilarity, the relative risk (RR) was calculated separately for each country (Kenya: RR=1.64 95% CI 0.4-6.6, Thailand: RR=0.33 95% CI 0.1-1.0). Neither risk was statistically significant suggesting that there is no likely association between the use of DMPA and liver cancer.

Appraised by: The Jordan Evidence Based Medicine-Reproductive Health Group

Update By: 16 March 2016
For long term use of depot medroxyprogesterone acetate, there may be an increased risk of fracture though the studies are not confirming

**Conclusion**
In a study comparing depot medroxyprogesterone acetate (DMPA) users and users of other contraceptives, non-users had lower fracture rates though there is a suggestion that there may be inherent differences in the groups. Further, fracture rates among DMPA users remained similar over time suggesting that no causal effect between loss of bone mass density and the incidence of fractures can be assumed. In a second review of studies assessing the relationship of fractures and DMPA use, there was a consistent pattern showing an increased risk for fractures.

**Clinical Question**
In a healthy woman of childbearing age, does long term depot medroxyprogesterone acetate (DMPA) use result in significantly increased risk of fractures?

**Search Terms**
Depot medroxyprogesterone, Depo Provera, DMPA, fractures, bone health

**Citation**


**Object of Research**
Depot medroxyprogesterone acetate (DMPA)

**Research Outcome**
Bone mineral density and fracture
Study Features
Lanza et al
Two cohorts of women, DMPA users and women using non-prescription contraceptives, were selected from the General Practice Research Database. The objective was to compare the incidence of fractures in these two cohorts. Cumulative DMPA exposure for each woman was categorized as low (1 to 7 injections) or high (more than 7 injections). The full cohort included 312,395 women and the subcohort with at least six months of baseline history included 166,637 (53%). The incidence of fracture after initiation of contraception in the sub-cohort was similar to that in the full cohort.
(Level 3 Evidence)

Lopez et al
This is a review of cohort and case control studies involving steroidal contraceptives and the risk of fracture. Four studies involving depot medroxyprogesterone acetate were identified; two cohort studies and two case control studies though one of the cohort studies did not have a comparable cohort and is not referenced here. The studies were as follows:
• **Kaunitz 2010**: This is a cohort study which included women using DMPA before age 50 and using the UK based General Practice Research Database. Interventions were users of DMPA versus other hormonal contraceptives. The primary outcome was incident fractures.
• **Meir 2010**: This is a case control study using the UK based General Practice Research Database. Interventions were users of DMPA versus other hormonal contraceptives. The primary outcome was incident first time fractures.
• **Vestergaard 2006**: This is a case control study in Demark using the National Hospital Discharge Register. The study includes DMPA users and nonusers of DMPA. The primary outcome was fractures sustained in the year 2000.
(Level 2 Evidence)

The Evidence
Lanza et al
Before starting their contraceptive, the crude fracture rate for DMPA users was 8.4 per 1000 person-years as compared to non-DMPA users of 6.6 per 1000 person years. The difference was statistically significant. After starting their contraceptive, the crude fracture rate was 7.3 per 1000 person-years for non-use of DMPA and 9.1 per 1000 person-years during DMPA use. The crude
incidence rate ratio was 1.37 (95% CI: 1.29-1.45) and the crude incidence rate difference was 2.42 per 1000 person-years (95% CI: 1.94-2.91). Although DMPA users had a higher fracture risk than nonusers, the risk did not increase after DMPA was initiated nor did the fractures in the DMPA group correlate with bone mass density losse.

**Lopez et al**
- Kaunitz 2010: Overall, DMPA users had a greater risk of fractures with an incident rate ratio of 1.44 (95% CI: 1.38 – 1.50).
- Meier 2010: Current and past users of DMPA were more likely to have a fracture than non users. The odds increased slightly with the number of prescriptions.
- Vestergaard 2006: DMPA ever users were slightly more likely to have a fracture than non users.

**Appraised by:** The Jordan Evidence Based Medicine-Reproductive Health Group

**Update by:** 16 March 2016
Among breast feeding women using depot-medroxyprogesterone acetate as a contraceptive, there is no decrease in milk volume nor is the growth of the infant affected.

**Conclusion**
DMPA is safe as a method of contraception for the infants of breast feeding women as it does not adversely affect milk secretion or infant growth.

**Clinical Question**
For breastfeeding women, does DMPA affect the volume of breast milk and infant growth?

**Search Terms**
Depo Provera, depot medroxyprogesterone acetate, DMPA, breast milk composition, infant growth

**Citation**

**Object of Research**
Depot medroxyprogesterone acetate

**Research Outcome**
Infant safety measured by breast milk changes and growth

**Study Features**
This is a WHO study of breastfeeding women assessing the effect of four contraceptive groups on breast milk volume and composition as well as infant growth. Measurements were taken at three and four week intervals up to six months after delivery. The four groups included two in which the women were randomly assigned to receive either a combined oral contraceptive (COC) or a progestin only pill (POP). A non-random group using non-hor-
monal methods was also studied in three centers (one in Hungary and two in Thailand) and a fourth group at two Thai centers that elected to use depot medroxyprogesterone acetate (DMPA) were also included. Altogether 341 women entered the study and in the two Thai centers, 59 were DMPA users and 83 were non-hormonal controls. Only the DMPA and non-hormonal contraceptive group outcomes are presented here.

*Level 2 Evidence*

**The Evidence**
Comparing DMPA users and the non-hormonal control group, no significant differences in changes from baseline were noted in milk volume at any of the follow-up visits. At one center, numerical changes from baseline were smaller for the DMPA group while at the other, corresponding changes were smaller for the control group. Only minor shifts occurred in milk composition when compared to controls. Finally, relative to the controls no significant differences in infant weight were noted for DMPA users.

**Appraised by:** The Jordan Evidence Based Medicine and Reproductive Health Group

**Update By:** 16 March 2016