Managing Adverse Effects of Hormonal Contraceptives

NANCY GROSSMAN BARR, MD, *David Geffen School of Medicine at the University of California, Los Angeles, California*

Adverse effects of hormonal contraceptives usually diminish with continued use of the same method. Often, physicians only need to reassure patients that these symptoms will likely resolve within three to five months. Long-acting injectable depot medroxyprogesterone acetate is the only hormonal contraceptive that is consistently associated with weight gain; other hormonal methods are unlikely to increase weight independent of lifestyle choices. Switching combined oral contraceptives is not effective in treating headaches, nor is the use of multivitamins or diuretics. There are no significant differences among various combined oral contraceptives in terms of breast tenderness, mood changes, and nausea. Breakthrough bleeding is common in the first months of combined oral contraceptive use. If significant abnormal bleeding persists beyond three months, other methods can be considered, and the patient may need to be evaluated for other causes. Studies of adverse sexual effects in women using hormonal contraceptives are inconsistent, and the pharmacologic basis for these symptoms is unclear. If acne develops or worsens with progestin-only contraceptives, the patient should be switched to a combination method if she is medically eligible. There is insufficient evidence of any effect of hormonal contraceptives on breast milk quantity and quality. Patient education should be encouraged to decrease the chance of unanticipated adverse effects. Women can also be assessed for medical eligibility before and during the use of hormonal contraceptives. (*Am Fam Physician*. 2010;82(12):1499-1506. Copyright © 2010 American Academy of Family Physicians.)

▶ **Patient information:** A handout on side effects of hormonal contraceptives, written by the author of this article, is provided on page 1509.

Adverse effects of hormonal contraceptives usually diminish to the point of acceptance with continued use of the same method. Reassurance that symptoms will likely resolve within three to five months is often the only treatment required. Despite the transient course of these effects, a population-based survey found that 64.6 percent of women who discontinued oral contraceptives did so because of adverse effects.[1] Educating patients about common adverse effects of hormonal contraceptives helps to establish realistic expectations *(Table 1)*.[1-22]

Persistent symptoms are often alleviated by changing methods; however, no method has been proven superior in terms of adverse effects.[9] Exogenous estrogen increases production of sex hormone–binding globulin.[23] Progestins bind sex hormone–binding globulin and decrease its synthesis to varying degrees, which should result in different levels of androgenicity. However, despite their biochemical differences, progestins have shown few differences clinically.[5]

Physicians can decrease the likelihood of significant adverse effects by using criteria from the World Health Organization to assess patients for medical eligibility before and during the use of hormonal contraceptives *(Table 2)*.[24,25] *Table 3* outlines potential treatments for adverse effects of hormonal contraceptives.[1,4,7-13,16,19,22,23,25-34]

Weight Gain

Long-acting injectable depot medroxyprogesterone acetate (Depo-Provera) is the only hormonal contraceptive that is consistently associated with weight gain. A prospective study found that women who used Depo-Provera gained an average of 11.2 lb (5.1 kg) over 36 months, whereas women who used combined oral contraceptives did not gain any weight.[8,20]

There are no significant differences among combined oral contraceptives in terms of weight gain.[9] A systematic review of randomized controlled trials did not find a causal connection between combined hormonal contraceptives and weight gain,[21] whereas a Cochrane review found the evidence to be insufficient.[22] Extended-cycle combined oral contraceptives do not cause more weight gain than standard regimens.[11]

Table 1. Patient-Reported Adverse Effects of Hormonal Contraceptives

Adverse effect	*More likely*	*Less likely*
Acne	Progestin-only methods[2,3]	Combined oral contraceptives, Nuvaring (ethinyl estradiol/etonogestrel vaginal ring)[4]
Amenorrhea	Mirena (levonorgestrel-releasing intrauterine system),[5,6] Implanon (single-rod etonogestrel implantable device),[2,7] Depo-Provera (long-acting injectable depot medroxyprogesterone acetate),[8] continuous-cycle combined oral contraceptives,[5,9] Nuvaring (continuous use)	Combined oral contraceptives, progestin-only pills[9]
Breakthrough bleeding	Low-dose combined oral contraceptives,[9,10] extended-cycle regimens[9,11] (especially those containing levonorgestrel[12]), progestin-only pills,[9,10] Implanon[2,7]	Higher-dose combined oral contraceptives,[9] Mirena,[6] extended-cycle regimens with norethindrone,[12] Ortho Evra (norelgestromin/ethinyl estradiol contraceptive patch),[4] Nuvaring[4]
Breast tenderness	Ortho Evra[4]	Combined oral contraceptives with 20 mcg of ethinyl estradiol or less,[5] combined oral contraceptives after 18 months of use,[8] Nuvaring[4]
Decreased libido	Very low-dose combined oral contraceptives (15 mcg of estrogen per day)[13]	—
Depressed mood	Depo-Provera (possibly)[14]; hormonal contraceptives generally have no effect[9,12,15]	Nuvaring (possibly)[4]; hormonal contraceptives generally have no effect[9,12,15]
Headache (general)	All hormonal methods, especially in women older than 35 years[9,16]	—
Headache (menses-associated)	—	Extended-cycle combined oral contraceptives[17,18]
Heavy menses	Depo-Provera,[8] Implanon[2,7]	Combined hormonal contraceptives (oral, Ortho Evra, Nuvaring); low-dose combined oral contraceptives[9]; Mirena[5,6]
Hirsutism	Progestin-only methods[3,8]	Combined oral contraceptives
Increased vaginal discharge	Nuvaring[4]	All other methods
Irregular menses	Implanon,[2,5,7] Depo-Provera,[1,8] emergency contraceptive regimens	Ortho Evra
Nausea	Emergency contraceptive regimens with combined oral contraceptives,[19] Ortho Evra[4]	Nuvaring[4]; no differences among combined oral contraceptives[9]
Oily skin	Progestin-only methods[3]	Combined oral contraceptives
Weight gain	Depo-Provera[8,20]	Combined hormonal contraceptives (oral, Ortho Evra, Nuvaring); Mirena; progestin-only pills[9,11,13,21,22]

Information from references 1 through 22.

A randomized prospective trial of two combined oral contraceptive regimens and the ethinyl estradiol/etonogestrel vaginal ring (Nuvaring) did not find significant weight gain in any group.[13]

Headache

Combined oral contraceptives increase the risk of stroke in women who have migraines with aura, and should not be used in these patients.[25] A systematic review found that 10 percent of women have new-onset headache with the use of combined oral contraceptives.[16] The type and dose of progestin do not affect headache,[16] nor does the particular formulation.[9]

Headaches are more common during the first cycle of combined oral contraceptives and in women who are older than 35 years.[16] If headache occurs in a woman who is older than 40 years during the placebo week of a 28-day regimen, the addition of 10 mcg of ethinyl

Table 2. Hormonal Contraceptive Methods to Avoid in Patients with Selected Medical Conditions

Condition	*Methods to avoid*
Anatomic abnormalities with distortion of the uterine cavity	IUD
Breast cancer	All hormonal contraceptives
Breastfeeding in women less than 6 weeks postpartum	Combined oral contraceptives, Ortho Evra (norelgestromin/ethinyl estradiol contraceptive patch), Nuvaring (ethinyl estradiol/etonogestrel vaginal ring)
Cardiovascular disease risk factors (multiple)	Combined oral contraceptives, Ortho Evra, Nuvaring*
Cervical cancer (untreated)	Initiation of IUD (may continue if already placed)
Chlamydia, gonorrhea, or current purulent cervicitis	Initiation of IUD (may continue if already placed)
Cirrhosis (severe)	Combined oral contraceptives, Ortho Evra, Nuvaring
Deep venous thrombosis (current or previous)	Combined oral contraceptives, Ortho Evra, Nuvaring
Diabetes mellitus with nephropathy, retinopathy, neuropathy, or other vascular disease; or diabetes of more than 20 years' duration	Combined oral contraceptives, Ortho Evra, Nuvaring
Endometrial cancer	Initiation of IUD (may continue if already placed)
Gestational trophoblastic disease (malignant or with persistent elevated human chorionic gonadotropin levels)	IUD
Hepatocellular adenoma	Combined oral contraceptives, Ortho Evra, Nuvaring
Hepatocellular carcinoma	Combined oral contraceptives, Ortho Evra, Nuvaring
Hypertension with systolic blood pressure > 160 mm Hg or diastolic blood pressure > 100 mm Hg	Combined oral contraceptives, Ortho Evra, Nuvaring
Ischemic heart disease (current or previous)	Combined oral contraceptives, Ortho Evra, Nuvaring
Leiomyomas with distortion of the uterine cavity	IUD
Major surgery with prolonged immobilization	Combined oral contraceptives, Ortho Evra, Nuvaring
Migraine with aura	Combined oral contraceptives, Ortho Evra, Nuvaring
Migraine without aura (in women older than 35 years)	Ortho Evra, Nuvaring, initiation of combined oral contraceptives (may continue combined oral contraceptives if already in use and if other methods are unavailable)
Pelvic inflammatory disease	Initiation of IUD (may continue if already placed)†
Postpartum sepsis	IUD
Septic abortion (immediately following)	IUD
Smoking more than 15 cigarettes per day (in women older than 35 years)	Combined oral contraceptives, Ortho Evra, Nuvaring
Stroke history	Combined oral contraceptives, Ortho Evra, Nuvaring
Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies	Combined oral contraceptives, Ortho Evra, Nuvaring
Thrombotic mutations (factor V Leiden; prothrombin mutation; protein C, protein S, or antithrombin deficiencies)	Combined oral contraceptives, Ortho Evra, Nuvaring
Tuberculosis with pelvic involvement	Initiation of IUD (may continue if already placed)
Unexplained vaginal bleeding before evaluation	IUD
Valvular heart disease complicated by pulmonary hypertension, risk of atrial fibrillation, or history of bacterial endocarditis	Combined oral contraceptives, Ortho Evra, Nuvaring
Vascular disease	Combined oral contraceptives, Ortho Evra, Nuvaring
Viral hepatitis (acute or flare)	Initiation of combined oral contraceptives, Ortho Evra, or Nuvaring (may continue if method is already in use, and may initiate method if condition is not severe)

IUD = intrauterine device.

**—The use of hormonal contraceptives may increase the risk of cardiovascular disease to an unacceptable level in patients with multiple major risk factors.*

†*—No evidence suggests that IUDs should be removed in women with acute pelvic inflammatory disease. However, close clinical follow-up is mandatory if the IUD remains in place. Rates of treatment failure and recurrent pelvic inflammatory disease in women who continue to use an IUD are not known. There are no data on antibiotic selection and treatment outcomes according to type of IUD (i.e., copper or levonorgestrel-releasing).*[24]

Information from references 24 and 25.

Table 3. Treatment for Adverse Effects of Hormonal Contraceptives

Contraceptive	*Adverse effect*	*Possible treatments*
Combined oral contraceptives	Breakthrough bleeding	Reassure patient that bleeding will likely resolve in three to five cycles[1]; increase estrogen dose if less than 20 mcg per day[9,10]
	Decreased libido	Reassurance[23]; consider increasing estrogen dose if current dose is very low[13]; consider prescribing 10 mcg of estrogen per day during the placebo week if patient is perimenopausal[26]; consider other reasons for decreased libido[8]
	Depressed mood	Reassure patient that mood changes will likely improve with time[1]
	Headache	Discontinue contraceptive if patient has migraine with aura[25]; reassure patient that headache will likely resolve after the first few cycles[16]; if headaches occur during the placebo week and the patient is older than 40 years, add 10 mcg of ethinyl estradiol per day during five days of the placebo week[26]
	Weight gain	Combined oral contraceptives are not associated with weight gain; consider lifestyle factors that may be causing weight gain[22]
Combined oral contraceptives (extended cycle)	Breakthrough bleeding	Reassure patient that bleeding will likely diminish by the fourth month[11]; consider a hormone-free interval of three or four days beginning on the first day of breakthrough bleeding[27]; consider changing progestin from levonorgestrel to norethindrone[12]
Depo-Provera (long-acting injectable depot medroxyprogesterone acetate)	Acne	Consider changing to a combined method if patient is medically eligible[8]
	Amenorrhea	Reassurance
	Hirsutism	Consider changing to a combined method if patient is medically eligible[28]
	Weight gain	Careful adherence to diet and exercise regimen
Emergency contraceptive regimens	Nausea	Metoclopramide (Reglan), 10 mg, or meclizine (Antivert), 50 mg, one hour before taking emergency contraceptive[19,29]; use progestin-only emergency contraceptive[30]
Implanon (single-rod etonogestrel implantable device)	Breakthrough bleeding (single episode)	Mifepristone (Mifeprex), 25 mg twice per day, then ethinyl estradiol, one 10-mg tablet twice per day for four days, beginning on the first day of bleeding[31]
	Breakthrough bleeding (continuous)	No treatment has been proven effective; consider changing contraceptive method[31,32]
	Heavy menses	Reassurance, but it is unclear if bleeding will diminish with time[7]; change contraceptive methods if persistent
Nuvaring (ethinyl estradiol/etonogestrel vaginal ring), standard use	Increased vaginal discharge	Reassure patient that discharge usually does not indicate pathology; consider changing to nonvaginal contraceptive[4]
Nuvaring, continuous use*	Breakthrough bleeding	Remove the contraceptive ring for four days at the start of bleeding, then replace for the remainder of the month[33]
Ortho Evra (norelgestromin/ethinyl estradiol contraceptive patch)	Breast tenderness	Consider changing to a combined oral contraceptive[4]
Progestin-only pills	Acne	Change to a combined oral contraceptive if patient is medically eligible[34]
	Breakthrough bleeding	Change to a combined oral contraceptive if patient is medically eligible[9,10]
	Hirsutism	Change to a combined oral contraceptive if patient is medically eligible[28]

**—Patient leaves ring in place for four weeks instead of three, then removes used ring and places new ring on the same day.*

Information from references 1, 4, 7 through 13, 16, 19, 22, 23, and 25 through 34.

estradiol for five of the seven placebo days may help.[26] It is not known if this regimen is effective in younger women. Continuous use of combined oral contraceptives also can be attempted. A Cochrane review comparing extended-cycle with standard 28-day regimens found slightly reduced rates of menses-associated headache in the extended-cycle group.[17] A prospective, open-label, industry-sponsored trial found that switching from a 28-day to a 168-day regimen reduced headache and increased quality-of-life measures in patients with severe headaches, but not in those with mild headaches.[18] Switching to a different combined oral contraceptive or taking diuretics or multivitamin supplements is not effective in treating headaches.[16]

Breast Tenderness

The use of combined oral contraceptives decreases breast tenderness after 18 months, but there are no significant differences among formulations.[8,9] Breast tenderness is more common in women who use the norelgestromin/ethinyl estradiol contraceptive patch (Ortho Evra) than in those who use combined oral contraceptives.[4]

Breakthrough Bleeding

Breakthrough bleeding is common in the first months of combined oral contraceptive use,[1] and patients should be reassured during this time. Variations in the estrogen dose above 20 mcg do not alter bleeding rates,[9] nor does changing the type of progestin.[35] Bleeding patterns are similar among monophasic and biphasic regimens,[33] but the evidence is insufficient to determine whether monophasic and triphasic regimens result in different bleeding patterns.[36] A randomized controlled trial comparing continuous use with a standard 28-day cycle found that spotting increased initially with continuous use, but was less than with the standard regimen by nine months.[11] Increasing the estrogen dosage from 20 to 30 mcg per day does not reduce breakthrough bleeding in extended-cycle regimens.[12] Women on regimens containing norethindrone had significantly more days of amenorrhea than those on levonorgestrel-containing regimens.[12] If breakthrough bleeding occurs with extended-cycle regimens, the pills should be stopped for three or four days, then restarted.[27]

A prospective randomized trial found that women who have breakthrough bleeding for at least five days with continuous Nuvaring use could reduce bleeding by removing the ring at the start of bleeding, storing it for four days, then replacing the same ring.[37]

Other Bleeding Irregularities

Patients often discontinue hormonal contraceptives because of menstrual cycle disorders.[1] Progestin-only pills and low-dose combined oral contraceptives (less than 20 mcg per day) are associated with a higher incidence of bleeding disturbances.[9,10] Compared with nonhormonal contraceptive methods, Depo-Provera is strongly associated with missed menstrual periods and bleeding for longer than 20 days.[8] A Cochrane review found that no interventions to regulate menstrual bleeding in women using Depo-Provera were useful in the long term.[38] In women using progestin-only injectable contraceptives, short-term treatment with nonsteroidal anti-inflammatory drugs may be helpful for spotting.[39] Nonsteroidal anti-inflammatory drugs or ethinyl estradiol can also be used for heavy or prolonged bleeding until another contraceptive method is chosen.[39,40]

Women who use the single-rod etonogestrel implantable device (Implanon) should expect changes in their menstrual cycle.[7] Before insertion, physicians should inform patients that only about 11 percent of women have a normal bleeding pattern.[2] A combination of mifepristone (Mifeprex) and ethinyl estradiol reduces the duration of a single bleeding episode in women who use Implanon, but does not alter the overall bleeding pattern.[31,32] One study showed that doxycycline shortens a single episode of bleeding in women who use Implanon,[32] but a subsequent larger study did not confirm this finding.[31] If abnormal bleeding persists beyond three months, an alternative contraceptive method may be considered, and the patient may need to be evaluated for other causes.[40]

Mood

No significant differences in effect on mood have been found among various combined oral contraceptives.[9,15] A prospective population-based study found that Depo-Provera was associated with a slightly increased rate of depression, which can persist after discontinuation of therapy.[14] A prospective cohort study, however, found that neither combined oral contraceptives nor Depo-Provera was associated with an increased risk of depressive symptoms.[8,15]

Sexual Effects

Findings from studies of the sexual effects of hormonal contraceptives have been inconsistent, and the pharmacologic basis for these effects is unclear.[23] Bioavailable testosterone is lower in women who use combined oral contraceptives than in nonusers; however, one review found that women who use these contraceptives show more interest in erotic images.[23] Supplementation with androstenedione (illegal in the United States) or testosterone in combined oral contraceptive users with decreased libido is no more effective than placebo.[23]

A prospective analysis of women using Depo-Provera found no change in sexual function after four months, and women using progestin-only pills had no difference in sexual desire compared with those receiving placebo.[23] Another study found that there was no significant change in libido after 24 months among women using Depo-Provera, women taking an oral contraceptive containing 0.15 mg of desogestrel and 20 mcg of ethinyl estradiol, and women using nonhormonal contraception.[8] A prospective randomized study comparing Nuvaring with two combined oral contraceptives (one containing 20 mcg of ethinyl estradiol and 100 mcg of levonorgestrel, and the other containing 15 mcg of ethinyl

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
Physicians should not recommend any combination oral contraceptive over another for decreasing weight gain, headache, breast tenderness, breakthrough bleeding, mood disturbances, acne, or nausea. There are no significant differences among formulations.	C	9	Large population-based cohort
Physicians should not prescribe progestin-only contraceptives for women who are concerned about breakthrough bleeding.	B	9	Large population-based cohort
Breakthrough bleeding associated with continuous contraceptive methods can be alleviated by a three- or four-day hormone-free interval.	B	27, 37	Randomized controlled trial[37]
Nonsteroidal anti-inflammatory drugs and estrogens have only short-term benefits in alleviating heavy menses in women who use progestin-only contraceptives.	C	39, 40	Evidence-based guideline
Patients who have a history of nausea and vomiting with the use of emergency contraceptives should be pretreated with antiemetics.	C	40	Evidence-based guideline

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

estradiol and 60 mcg of gestodene) found that the latter pill had the greatest negative effect on sexual desire.[13] The reason is not known.

If adverse sexual effects persist beyond three months, the method can be changed, but there is little evidence to recommend one method over another. Because sexual function depends on many factors, other causes of sexual dysfunction should be considered before changing methods.[8]

Skin Changes

Acne can develop or worsen with the use of progestin-only contraceptives. A questionnaire-based study of 161 women who used the levonorgestrel-releasing intrauterine system (Mirena) for dysfunctional uterine bleeding found that 22 percent discontinued use secondary to progestin-associated effects (e.g., acne, oily skin, hirsutism, bloating, headaches, weight gain, depression, breast tenderness, decreased libido).[3] A retrospective study of Implanon users found that 11 percent had acne after insertion.[2] If acne worsens with a progestin-only contraceptive, a combination method can be tried if the patient is medically eligible.

Of patients who had acne at baseline and who were using a combined oral contraceptive with 20 mcg of ethinyl estradiol and 0.15 mg of desogestrel, 70 percent had resolution of symptoms at six months.[8] If acne does not improve within six months of combined oral contraceptive use, it typically will not improve with continued use.[8] A Cochrane review analyzing several combined oral contraceptive regimens found that they are effective in treating acne, but that differences in effectiveness among progestins is not clear.[34] A separate Cochrane review found that Nuvaring users reported less acne than women taking combined oral contraceptives.[4]

About 6 percent of Depo-Provera users report new-onset facial hair at six months of use.[8] Combined oral contraceptives are used to treat hirsutism,[28] and a small, prospective, randomized, double-blind study found that those containing levonorgestrel and desogestrel are equally effective.[41]

Nausea

Levonorgestrel-only emergency contraceptives cause less nausea and vomiting than regimens with a combination of ethinyl estradiol and levonorgestrel.[20] Pretreatment with metoclopramide (Reglan) or meclizine (Antivert) can reduce nausea in women using combined oral contraceptives for emergency contraception.[29,30] The World Health Organization advises pretreatment for women who have a history of nausea and vomiting with emergency contraceptive use.[40] For nonemergency use, there are no significant differences in nausea among combined oral contraceptive formulations.[9,12]

Decreased Breast Milk

A Cochrane review found insufficient evidence that hormonal contraceptives affects breast milk quantity or quality.[42] Combined oral contraceptives should not be used for the first six weeks postpartum because of

Table 4. Hormonal Contraceptives: Online Resources

Source	*Title*	*Web site*	*Comment*
Association of Reproductive Health Professionals	Method Match	http://www.arhp.org/methodmatch/	Interactive tool for patients to choose most appropriate methods with comprehensive information on each method
Association of Reproductive Health Professionals	You Decide Tool Kit	http://arhp.org/publications-and-resources/clinical-practice-tools/you-decide	Comprehensive source of tools for physicians to help patients choose appropriate contraception
Bridging the Gap Foundation	Managing Contraception	http://www.managingcontraception.com	Patient education and patient Web-based self-research
Planned Parenthood	Health Topic: Birth Control	http://www.plannedparenthood.org/health-topics/birth-control-4211.htm	Patient education and patient Web-based self-research
Princeton University and the Association of Reproductive Health Professionals	Emergency Contraception Website	http://ec.princeton.edu/	Information on and assistance in obtaining emergency contraception
World Health Organization	Family Planning: A Global Handbook for Providers	http://www.infoforhealth.org/globalhandbook/handbook.pdf	Comprehensive, simplistic reference for contraception counseling and practical management of adverse effects
World Health Organization	Medical eligibility criteria for contraceptive use	http://www.who.int/reproductive health/publications/family_planning/9789241563888/en/index.html	Determination of safe contraceptive options

increased risk of hypercoagulability.[25,43] Depo-Provera and progestin-only pills do not impair lactation.[43,44]

Patient Education

Patient education can decrease the chances of unanticipated adverse effects of hormonal contraceptives. *Table 4* lists resources for physicians and patients.

The Author

NANCY GROSSMAN BARR, MD, is a faculty member in the Department of Family Medicine at the David Geffen School of Medicine at the University of California, Los Angeles.

Address correspondence to Nancy Grossman Barr, MD, UCLA Santa Monica Family Health Center, 1920 Colorado Ave., Santa Monica, CA 90404 (e-mail: ngrossman@mednet.ucla.edu). Reprints are not available from the author.

Author disclosure: Nothing to disclose.

REFERENCES

1. Moreau C, Cleland K, Trussell J. Contraceptive discontinuation attributed to method dissatisfaction in the United States. *Contraception.* 2007;76(4):267-272.
2. Bitzer J, Tschudin S, Alder J. Acceptability and side-effects of Implanon in Switzerland: a retrospective study by the Implanon Swiss Study Group. *Eur J Contracept Reprod Health Care.* 2004;9(4):278-284.
3. Daud S, Ewies AA. Levonorgestrel-releasing intrauterine system: why do some women dislike it? *Gynecol Endocrinol.* 2008;24(12):686-690.
4. Lopez LM, Grimes DA, Gallo MF, Schulz KF. Skin patch and vaginal ring versus combined oral contraceptives for contraception. *Cochrane Database Syst Rev.* 2010;(3):CD003552.
5. Practice Committee of American Society for Reproductive Medicine. Hormonal contraception: recent advances and controversies. *Fertil Steril.* 2008;90(5 suppl):S103-S113.
6. Römer T, Linsberger D. User satisfaction with a levonorgestrel-releasing intrauterine system (LNG-IUS): data from an international survey. *Eur J Contracept Reprod Health Care.* 2009;14(6):391-398.
7. Implanon FAQs. http://www.implanon-usa.com/hcp/patientsupport/faqs/index.asp?C=5115440033989108796 3&svarqvp2=0#186833. Accessed March 20, 2010.
8. Berenson AB, Odom SD, Breitkopf CR, Rahman M. Physiologic and psychologic symptoms associated with use of injectable contraception and 20 microg oral contraceptive pills. *Am J Obstet Gynecol.* 2008;199(4):351.e1-351.e12.
9. Moreau C, Trussell J, Gilbert F, Bajos N, Bouyer J. Oral contraceptive tolerance: does the type of pill matter? *Obstet Gynecol.* 2007;109(6):1277-1285.
10. Gallo MF, Nanda K, Grimes DA, Lopez LM, Schulz KF. 20 microg versus >20 microg estrogen combined oral contraceptives for contraception. *Cochrane Database Syst Rev.* 2008;(4):CD003989.
11. Miller L, Hughes JP. Continuous combination oral contraceptive pills to eliminate withdrawal bleeding: a randomized trial. *Obstet Gynecol.* 2003;101(4):653-661.
12. Edelman AB, Koontz SL, Nichols MD, Jensen JT. Continuous oral contraceptives: are bleeding patterns dependent on the hormones given? *Obstet Gynecol.* 2006;107(3):657-665.

13. Sabatini R, Cagiano R. Comparison profiles of cycle control, side effects and sexual satisfaction of three hormonal contraceptives. *Contraception*. 2006;74(3):220-223.
14. Civic D, Scholes D, Ichikawa L, et al. Depressive symptoms in users and non-users of depot medroxyprogesterone acetate. *Contraception*. 2000;61(6):385-390.
15. ACOG Committee on Practice Bulletins–Gynecology. ACOG practice bulletin no. 73: use of hormonal contraception in women with coexisting medical conditions. *Obstet Gynecol*. 2006;107(6):1453-1472.
16. Loder EW, Buse DC, Golub JR. Headache as a side effect of combination estrogen-progestin oral contraceptives: a systematic review. *Am J Obstet Gynecol*. 2005;193(3 pt 1):636-649.
17. Edelman AB, Gallo MF, Jensen JT, Nichols MD, Schulz KF, Grimes DA. Continuous or extended cycle vs. cyclic use of combined oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2005;(3):CD004695.
18. Sulak P, Willis S, Kuehl T, Coffee A, Clark J. Headaches and oral contraceptives: impact of eliminating the standard 7-day placebo interval. *Headache*. 2007;47(1):27-37.
19. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet*. 1998;352(9126):428-433.
20. Berenson AB, Rahman M. Changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio associated with injectable and oral contraceptive use. *Am J Obstet Gynecol*. 2009;200(3):329.e1-329.e8.
21. Gallo MF, Grimes DA, Schulz KF, Helmerhorst FM. Combination estrogen-progestin contraceptives and body weight: systematic review of randomized controlled trials. *Obstet Gynecol*. 2004;103(2):359-373.
22. Gallo MF, Lopez LM, Grimes DA, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. *Cochrane Database Syst Rev*. 2008;(4):CD003987.
23. Schaffir J. Hormonal contraception and sexual desire: a critical review. *J Sex Marital Ther*. 2006;32(4):305-314.
24. Workowski KA, Berman SM; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006 [published correction appears in *MMWR Recomm Rep*. 2006;55(36):997]. *MMWR Recomm Rep*. 2006;55(RR-11):1-94.
25. World Health Organization. Medical eligibility criteria for contraceptive use. 4th ed, 2009. http://www.who.int/reproductivehealth/publications/family_planning/9789241563888/en/index.html. Accessed March 20, 2010.
26. Blümel JE, Castelo-Branco C, Binfa L, Aparicio R, Mamani L. A scheme of combined oral contraceptives for women more than 40 years old. *Menopause*. 2001;8(4):286-289.
27. Coffee AL, Sulak PJ, Kuehl TJ. Long-term assessment of symptomatology and satisfaction of an extended oral contraceptive regimen. *Contraception*. 2007;75(6):444-449.
28. Martin KA, Chang RJ, Ehrmann DA, et al. Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2008;93(4):1105-1120.
29. Ragan RE, Rock RW, Buck HW. Metoclopramide pretreatment attenuates emergency contraceptive-associated nausea. *Am J Obstet Gynecol*. 2003;188(2):330-333.
30. Raymond EG, Creinin MD, Barnhart KT, Lovvorn AE, Rountree RW, Trussell J. Meclizine for prevention of nausea associated with use of emergency contraceptive pills: a randomized trial. *Obstet Gynecol*. 2000;95(2):271-277.
31. Weisberg E, Hickey M, Palmer D, et al. A randomized controlled trial of treatment options for troublesome uterine bleeding in Implanon users. *Hum Reprod*. 2009;24(8):1852-1861.
32. Weisberg E, Hickey M, Palmer D, et al. A pilot study to assess the effect of three short-term treatments on frequent and/or prolonged bleeding compared to placebo in women using Implanon. *Hum Reprod*. 2006;21(1):295-302.
33. Van Vliet HA, Grimes DA, Helmerhorst FM, Schulz KF. Biphasic versus triphasic oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2006;(3):CD003283.
34. Arowojolu AO, Gallo MF, Lopez LM, Grimes DA, Garner SE. Combined oral contraceptive pills for treatment of acne. *Cochrane Database Syst Rev*. 2009;(3):CD004425.
35. Maitra N, Kulier R, Bloemenkamp KW, Helmerhorst FM, Gülmezoglu AM. Progestogens in combined oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2004;(3):CD004861.
36. Van Vliet HA, Grimes DA, Lopez LM, Schulz KF, Helmerhorst FM. Triphasic versus monophasic oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2006;(3):CD003553.
37. Sulak PJ, Smith V, Coffee A, Witt I, Kuehl AL, Kuehl TJ. Frequency and management of breakthrough bleeding with continuous use of the transvaginal contraceptive ring: a randomized controlled trial. *Obstet Gynecol*. 2008;112(3):563-571.
38. Abdel-Aleem H, d'Arcangues C, Vogelsong KM, Gülmezoglu AM. Treatment of vaginal bleeding irregularities induced by progestin only contraceptives. *Cochrane Database Syst Rev*. 2007;(4):CD003449.
39. World Health Organization. Selected practice recommendations for contraceptive use: 2008 update. http://whqlibdoc.who.int/hq/2008/WHO_RHR_08.17_eng.pdf. Accessed March 20, 2010.
40. World Health Organization. Selected practice recommendations for contraceptive use. 2nd ed., 2004. http://whqlibdoc.who.int/publications/2004/9241562846.pdf. Accessed March 20, 2010.
41. Breitkopf DM, Rosen MP, Young SL, Nagamani M. Efficacy of second versus third generation oral contraceptives in the treatment of hirsutism. *Contraception*. 2003;67(5):349-353.
42. Truitt ST, Fraser AB, Grimes DA, Gallo MF, Schulz KF. Combined hormonal versus nonhormonal versus progestin-only contraception in lactation. *Cochrane Database Syst Rev*. 2003;(2):CD003988.
43. World Health Organization. Technical consultation on hormonal contraceptive use during lactation and effects on the newborn: summary report. http://whqlibdoc.who.int/hq/2010/WHO_RHR_10.05_eng.pdf. Accessed March 24, 2010.
44. Halderman LD, Nelson AL. Impact of early postpartum administration of progestin-only hormonal contraceptives compared with nonhormonal contraceptives on short-term breast-feeding patterns. *Am J Obstet Gynecol*. 2002;186(6):1250-1256.