PERSPECTIVE

Contraception for Cancer Survivors

Eleanor Bimla Schwarz, MD, MS[1,2], Rachel Hess, MD, MSc[1], and James Trussell, PhD[3,4]

[1]Center for Research on Health Care, Departments of Medicine and Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA; [2]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh, Pittsburgh, PA, USA; [3]Office of Population Research, Princeton University, Princeton, NJ, USA; [4]The Hull York Medical School, Kingston upon Hill, Hull, England, UK.

Women who have survived cancer may need guidance in choosing a method of contraception. This paper reviews the evidence supporting the safety and efficacy of available methods of contraception for cancer survivors and concludes that the Copper T380A intrauterine device (IUD), a highly effective, reversible, long-acting, hormone-free method should be considered a first-line contraceptive option for women with a history of a hormonally mediated cancer. However, the levonorgestrel-containing IUD may be preferable for women being treated with tamoxifen and women who have survived non-hormonally mediated cancers. Women with IUDs can undergo all forms of imaging, including computed tomography and magnetic resonance imaging.

KEY WORDS: contraception; cancer survivors.
J Gen Intern Med 24(Suppl 2):401–6
DOI: 10.1007/s11606-009-1023-8

Ovarian failure is a common consequence of chemotherapy.[1] However, some women remain fertile despite undergoing chemotherapy.[2,3] Identification of fertility after chemotherapy is challenging and remains an area of active research. New data suggest that anti-Mullerian hormone levels may be the best predictor of future fertility,[4] as pregnancy has been reported in cancer survivors despite amenorrhea and follicle stimulating hormone (FSH) levels suggestive of menopause.[5] Women who are amenorrheic during treatment with gonadotropin-releasing hormone (GnRH) agonists are not at risk of pregnancy. However, when treatment stops, women who ceased menstruation during chemotherapy may find that fertility returns. In a study of young survivors of breast cancer, 67% remained premenopausal.[3] Among childhood cancer survivors, treatment is thought to reduce fertility by 10% to 25% depending on type of treatment.[6] Norwegian data suggest that in the 10 years after a cancer diagnosis women are about half as likely as women without cancer diagnoses to become pregnant.[7]

In general, women are advised to avoid pregnancy during chemotherapy or radiation treatments that may be teratogenic. In addition, women with hormonally sensitive cancers (e.g., breast cancer) are advised to avoid pregnancy until they have passed the period of peak recurrence, 3 years after treatment.[8] After treatment, fertile cancer survivors can be reassured that existing data suggest no subsequent increased risk of birth defects[9,10] or that pregnancy increases the risk of cancer recurrence.[11,12] However, some cancer treatments (e.g., pelvic and ovarian irradiation, central nervous system irradiation, and nonalkylating chemotherapy) do increase the risk of pregnancy loss and low birth weight babies.[9] Contraception may, therefore, be desired to allow women to ensure their pregnancies coincide with a period of optimum health. Alternatively, women may desire to avoid pregnancy indefinitely.

CONTRACEPTIVE OPTIONS

Broadly speaking, there are 6 classes of contraceptive methods: (1) behavioral methods, (2) barrier methods, (3) estrogen-containing methods, (4) progestin-only methods, (5) intrauterine devices (IUDs), and (6) surgical sterilization. There are pros and cons to each of these methods (Table 1) including marked differences in efficacy during typical use. Although contraceptive efficacy is frequently discussed in the context of 1-year failure rates, for women requiring longer term contraception, it is important to consider cumulative rates of failure over more extended periods of time. Over the long term, IUDs, contraceptive implants, and sterilization are dramatically more effective than barrier methods or birth control pills. Unfortunately, birth control pills remain the most widely used form of reversible contraception in the United States.[13,14] Unintended pregnancy remains common in the United States; it is estimated that half of all pregnancies in the United States are unintended.[15] During a lifetime of use of reversible contraceptive methods, the typical woman will experience 1.8 contraceptive failures.[16] Moreover, unintended pregnancy is more common among women with chronic medical conditions,[17,18] perhaps because women with chronic conditions receive less contraceptive counseling.[19,20] In the United States, cancer survivors between the ages of 15 and 30 years were more likely to terminate a pregnancy than age-matched control subjects.[9] Similarly, a recent Danish study found that cancer survivors were slightly more likely to terminate a pregnancy.[21] Other studies have also found that cancer survivors have limited awareness of available contraceptives.[22]

Without clear guidance from a healthcare provider, women with chronic conditions or complex medical histories who wish to preserve their fertility may limit themselves to barrier and behavioral methods.[23] Unfortunately, with typical use, these methods leave women at high risk of unintended pregnancy (1-year failure rates typically range from 15% to 32%).[24] Alternatively, women may feel that surgical sterilization, either through tubal ligation or partner vasectomy, is their only highly effective option. Worldwide, sterilization is used by more people than any other method of contraception.[25] However, women who undergo sterilization may later regret this decision. There appears to be a consistent inverse relationship

Table 1. Contraceptive Options Currently Available in the United States

Class	Examples	Issues for cancer survivors	Pros	Cons	Number of pregnancies expected in first year of use per 100 women using method[24]	
					Typical use	Perfect use
Sterilization	Tubal ligation	Decreases ovarian cancer	Coitally independent	Irreversible	0.5	0.5
	Essure		Long-term efficacy		0.5	0.5
	Vasectomy				0.15	0.10
Intrauterine	Copper 380A (Paragard)	Decreases endometrial cancer	Coitally independent	Insertion by a trained provider	0.8	0.6
		Hormone free	Reversible	Heavier menses		
			Effective for 10–20 years	May have more cramps		
	Levonorgestrel (Mirena)	Decreases endometrial cancer	Coitally independent	Insertion by a trained provider	0.2	0.2
		Used with caution if concern of breast cancer	Reversible			
			Effective for 5–7 years			
			Decreases vaginal bleeding	Irregular vaginal bleeding		
Progestin-only	Implant (Implanon)	Decreases ovarian cancer	Effective for 3 years	Insertion/removal by a trained provider requires small incision	0.05	0.05
				Irregular vaginal bleeding		
Progestin-only	Injection (Depo-Provera)	Decreases ovarian cancer	Effective for 3 months	Requires prescription and injection	3	0.3
		Transient decrease in bone mineral density		Irregular vaginal bleeding		
				Return to fertility may be delayed		
	Mini-pill (Micronor, Nor-QD, Camilla, Errin)	Decrease ovarian cancer		Taken daily	8	0.3
				Irregular vaginal bleeding		
Estrogen-containing	Pill	Decreases ovarian cancer	Coitally independent	Requires prescription	8	0.3
		May increase breast cancer				
		Increases thromboembolism	Regular withdrawal bleed			
			Generics available			
	Patch (Ortho Evra)	Decreases ovarian cancer	Used weekly	Requires prescription	8	0.3
		May increase breast cancer				
		Increases thromboembolism	Regular withdrawal bleed			
	Ring (Nuvaring)	Decreases ovarian cancer	Used monthly	Requires prescription	8	0.3
		May increase breast cancer				
		Increases thromboembolism	Regular withdrawal bleed			
Barrier Methods	Male/female condoms	Protection from HPV and cervical cancer	No prescription needed	Coitally dependent	15	2
			Protection from infection		21	5
	Diaphragm			Requires prescription	16	6
				Coitally dependent		
	Sponge		No prescription needed	Coitally dependent	16–32	9–20
Emergency contraception	Plan B	No increased risk of thrombosis	No prescription needed if >17 years of age		?	Use <72 hours after intercourse reduces risk by ≥75%
Behavioral	Withdrawal		No prescription needed	Coitally dependent	27	4
	Fertility awareness				25	3–5
No method					85	85

between a woman's age at sterilization and the likelihood of regretting having been sterilized, with women less than 30 years of age expressing regret nearly twice as often. They were also from 3.5 to 18 times as likely to request information about reversing the procedure and about 8 times as likely to undergo an evaluation for in vitro fertilization.[26]

HIGHLY EFFECTIVE REVERSIBLE CONTRACEPTION

Intrauterine contraception is reversible, but offers efficacy similar (or greater) than sterilization.[24] The cumulative pregnancy rate at 5 years for the levonorgestrel-releasing intrauterine system is less than 0.5% and between 0.3% and 0.6% for the Copper T380A IUD.[27] As a result of high levels of user satisfaction,[28] and cost-effectiveness,[29] the IUD is the most widely used reversible method of contraception outside the United States.[30] Women with IUDs can undergo all forms of imaging, including computed tomograph (CT) and magnetic resonance imaging (MRI).[31] Infection after IUD insertion is rare[32] and IUDs can be safely used even by women who are immunocompromised.[33] IUDs can be used by women who have previously had sexually transmitted infections or multiple sexual partners, provided that they have no evidence of infection at the time of insertion.[33] Insertion of an IUD is a simple office procedure and uterine perforation with IUD insertion is rare.[34] IUDs can be successfully used by both nulliparous and parous women,[35] with rapid return of fertility upon removal of the IUD. IUDs do not increase the risk of clotting[33] or osteoporosis,[36] and the levonorgestrel-IUD reduces menstrual blood loss and risk of anemia.[37] While some people worry that IUDs are effective because they destroy embryos that arrive in a woman's uterus, detailed study of the IUD's mechanism of action does not support these concerns.[38] The primary disadvantages of IUDs are the need to have a trained provider insert the device and a one-time out-of-pocket cost of $400 to $800 if a woman's insurance does not cover the cost of IUDs.

There are currently two types of IUDs available in the United States: the copper T 380A (Paragard) and levonorgestrel-containing IUD (Mirena). The copper-containing IUD contains no hormones, which may make it a preferred option for some women who have survived cancer. The copper T 380A IUD is labeled for use for 10 years, but studies have shown good efficacy of a single IUD used for 12 years[39] to 20 years.[40] While generally well tolerated, some women who have a copper-containing IUD inserted experience increased menstrual cramping and vaginal bleeding.

To reduce this cramping, the levonorgestrel-IUD was developed. This IUD is effective for 5 to 7 years, after which time a new IUD can be safely inserted.[41] With this IUD, women experience less cramping and vaginal bleeding. However, the bleeding that does occur with the levonorgesterel-IUD (as with all progestin-only contraceptive methods) is irregular, and some women may find this bleeding pattern unacceptable. The levels of progestin contained in this IUD are so low that many women continue to ovulate.[42] However, the levonorgestrel-IUD does produce detectable serum levels of levonorgestrel.[43] While women with cancers such as breast cancer are cautioned about the potential for hormonal stimulation of residual disease,[44] several studies (Table 2) have examined the use of the levonorgestrel-IUD by women with histories of breast cancer who are being treated with tamoxifen. One recent study found no higher recurrence risk in breast cancer patients using a levonorgestrel-IUD.[45] However, a subgroup of patients who were using a levonorgestrel-IUD at the time of diagnosis and who continued using it, experienced an increased risk of breast cancer recurrence.[45] More research is, therefore, needed to determine the long-term safety of use of a levonorgestrel-IUD by women at risk of hormonally mediated cancers. For breast cancer survivors treated with tamoxifen, which can cause proliferative changes of the endometrium and even endometrial cancer, the levonorgestrel-IUD, which reduces endometrial proliferation, may be preferred because it decreases the need for investigation of vaginal bleeding.[48]

The third form of highly effective reversible contraception available in the United States is a contraceptive implant, Implanon, which is effective for 3 years after subcutaneous placement.[46] Similar to all progesterone-only methods, women using this method experience irregular vaginal bleeding. Data on whether the use of Implanon contraceptive implants affects the risk of breast cancer in the general population, or the risk of recurrence among breast cancer survivors, are not yet available. Limited data on the Norplant contraceptive implant, which is no longer available in the United States, did not raise concern about increased rates of breast cancer.[47] However, use

Table 2. Studies of Contraceptive Use by Cancer Survivors

Author (year of publication)	Contraceptive Method	Population	Design and Outcomes	Findings
Trinh XB (2008) [45]	Levonorgestrel-IUD	Breast cancer survivors	Case control study of breast cancer recurrence	increased recurrence among women with a levonorgestrel-IUD at time of diagnosis
Kesim MD (2008)[71]	Levonorgestrel-IUD	Breast cancer patients taking tamoxifen	Cohort followed for 36 months for lipid and endometrial changes	Improvement of endometrium, no effect on lipids
Chan SS (2007) [39]	Levonorgestrel-IUD	Breast cancer patients taking tamoxifen	Cohort followed for 12 months for endometrial changes	Improvement of endometrium
Gardner FJ (2000)[40]	Levonorgestrel-IUD	Breast cancer patients taking tamoxifen	Cohort followed for 12 months for endometrial changes	Improvement of endometrium
Kloke O (1999) [57]	Medroxy-progesterone acetate	Advanced breast cancer responding to induction chemotherapy	Randomized phase III trial of time to cancer progression and overall survival	Increased time to cancer progression, no effect on overall survival

of this method is not advised for women who have survived a hormonally mediated cancer, or who have received thoracic radiation which may increase their risk of breast cancer.

HORMONAL CONTRACEPTION

For women who desire pregnancy within 2 to 5 years, a contraceptive pill, patch, or ring may be more cost-effective than an IUD or implant.[48] Estrogen-containing contraceptives are effective because they contain a progestin that suppresses ovulation. However, the combination of estrogen and progestin provides better control of vaginal bleeding, which makes these methods more popular. Women at low risk of breast cancer may choose to use an estrogen-containing contraceptive if they do not have significant risk factors for thrombosis or vascular disease. Concern has been raised that the contraceptive patch may increase the relative risk of thrombosis beyond that of oral contraceptives.[49] However, it is important to remember that the absolute risk of venous thromboembolism while using any form of estrogen-containing contraception remains less than that during pregnancy (when it is estimated to be 57 per 100,000 women-years).

There is mixed data on the effects of combined hormonal contraception on risk of malignancies (Table 3). The large Royal College of General Practitioners' oral contraception study,[50] found an absolute rate reduction of any cancer of 45 per 100,000 years of use among ever-users of oral contraception. Specific tumor types reduced included cancer of the large bowel or rectum, uterus, ovaries, and tumors of unknown site. For ovarian cancer, there is good evidence that the use of combined hormonal contraceptives confers long-term protection.[51] It has been estimated that 10 years use of combined hormonal contraceptives reduces ovarian cancer incidence before the age of 75 years from 1.2 to 0.8 per 100 users and mortality from 0.7 to 0.5 per 100.[51] This reduction in risk was seen for many years after oral contraception was discontinued for both ovarian and uterine cancer.[50] However, combined hormonal contraceptives do appear to increase the risk of being diagnosed with breast cancer. A collaborative reanalysis of 54 studies found that women who were taking combined oral contraceptives (or who had used oral contraceptives in the last 10 years) had a relative risk of 1.24 [95% CI 1.15–1.33].[52] However, use of oral contraceptives before diagnosis of breast cancer has not been shown to have either a harmful or a beneficial effect on breast cancer mortality.[53] Recently, another large study was conducted in China[54] that examined incidence rates for 12 types of cancers in users of oral contraceptives; no associations were observed between oral contraceptives and the risk of breast cancer or all cancers combined.

For women with a history of hormonally mediated cancer, such as breast cancer, and women who received thoracic radiation, which may increase risk of breast cancer, nonhormonal contraceptive methods should be considered as a first-line method.[44,55] Women who do not find any of these methods acceptable may wish to consider a progestin-only method (e.g., pill, injection, or implant). Studies have shown that progestins can have a proliferative, antiproliferative, or neutral effect on breast tissue, depending on the type, timing, and dose of progestin used.[55] Depot medroxyprogesterone (DMPA) injections do not increase the risk of breast cancer.[56] High-dose DMPA has been used as adjunctive treatment for advanced or recurrent breast cancer with significant prolongation of the time to progression.[57] Although not as well-studied as the

Table 3. Studies of Cancer Risk Among Contraceptive Users

Study	Contraceptive	Population	Design and Outcomes	Findings
Beral V (2008)[51]	Oral contraceptives	General population	Case-control study of ovarian cancer	Reduced risk of ovarian cancer
Rosenblatt KA (2008)[54]	Oral contraceptives	Chinese textile workers	Cohort followed for 10 years for all and 12 site-specific cancers	No associations with risk of breast cancer or all cancers combined
Hannaford PC (2007)[50]	Oral contraceptives	General UK population	Large cohort study of all cancers	Less cancer of the large bowel, rectum, uterus, or ovaries
Wingo PA (2007) [53]	Oral contraceptives	General US population	Cohort and cancer registry study of breast cancer mortality	No effect
Collaborative Group on Hormonal Factors in Breast Cancer. (1996)[52]	Oral contraceptives	Women in 25 countries	Case control study of breast cancer	Small increase in relative risk of having breast cancer diagnosed
Vessey M (1989)[72]	Oral contraceptives	General UK population	20-year cohort study of breast, cervical, and ovarian cancer	No effect
Vessey M (1983)[59]	Oral contraceptives	General UK population	Case-control study of breast cancer diagnosis	No significant effect
Shapiro S (2000)[56]	Depomedroxy-progesterone acetate	South African women	Case-control study of breast cancer	No association
Backman T (2005)[60]	Levonorgestrel-IUD	General Finnish population	Incidence rates of breast cancer by IUD use in the Finnish Cancer Registry	No increased risk of breast cancer
International Collaborative Post-Marketing Surveillance of Norplant (2001)[47]	Norplant* contraceptive implant	Women in 8 developing countries	Post marketing surveillance, controlled cohort of all cancer	No increased risk

Abbreviations: IUD intrauterine device, UK United Kingdom, US United States

* The Norplant contraceptive implant is no longer available in the United States.

combined contraceptive pill, neither progestin-only pills[52,58,59], progestin-only implants, or the levonorgestrel-releasing intrauterine system appear to increase the risk of breast cancer in the general population.[55,60] However, one study recently suggested an increase in breast cancer recurrence among women who had a levonorgestrel-IUD in place at the time of diagnosis (although an increase in recurrence was not seen among women who had a levonorgestrel-IUD placed after their diagnosis of breast cancer).[45] Further studies of the use of progestin-only methods by cancer survivors are therefore needed.

EMERGENCY CONTRACEPTION

Women who opt for behavioral or barrier methods of contraception should be advised that emergency contraception can decrease the risk of unintended pregnancy if unprotected intercourse occurs. For women who should avoid exposure to exogenous hormones, insertion of a copper-containing IUD is a highly effective way of preventing pregnancy up to 7 days after a contraceptive emergency.[61] Alternatively, emergency contraceptive pills, marketed in the United States under the trade name Plan B, are available to women (and men) ages 17 years or over without a physician's prescription.[62] While these progestin-only pills have been shown to have some efficacy up to 5 days after unprotected intercourse,[63,64], they are more effective the sooner they are used. A number of professional organizations recommend that women be provided emergency contraception in advance of need.[65–67] Studies have shown that women provided a supply of emergency contraception in advance of need are more likely to use it should unprotected intercourse occur, and that easy access to emergency contraception does not increase sexual risk-taking behavior.[68] Detailed study of the mechanism of action of emergency contraception indicates that it does not disrupt implantation or induce abortion.[62]

CONCLUSIONS

In conclusion, contraception is an important issue to discuss with female cancer survivors. Given the prevalence of ovarian failure after chemotherapy, this topic should be broached carefully. As up to one third of women may be ambivalent towards pregnancy,[69] open-ended questions should be used to explore women's intentions to become pregnant. For women who desire contraception and have a history of a hormonally mediated cancer or thoracic radiation, the Copper T 380 A IUD, a highly effective and cost-effective, reversible, long-acting, hormone-free method should be considered a first-line method. However, the levonorgestrel-IUD may be preferred for women being treated with tamoxifen. Prior work has shown that that in many clinical settings, awareness of the benefits of IUDs is limited.[70] This makes comprehensive counseling about contraceptive options an essential part of comprehensive care of cancer survivors.

ACKNOWLEDGMENTS: *Dr. Schwarz was supported by NICHD K23HD051585. Dr. Hess was supported by NIA K23AG024254.*

Conflict of Interest: *None disclosed.*

Corresponding Author: *Eleanor Bimla Schwarz, MD, MS; 230 McKee Place, Suite 600, Pittsburgh, PA 15213, USA (e-mail: schwarzeb@upmc.edu).*

REFERENCES

1. **Mitwally MF.** Fertility preservation and minimizing reproductive damage in cancer survivors. Expert Rev Anticancer Ther. 2007;7(7):989–1001.
2. **Hodgson DC, Pintilie M, Gitterman L, Dewitt B, Buckley CA, Ahmed S, et al.** Fertility among female hodgkin lymphoma survivors attempting pregnancy following ABVD chemotherapy. Hematol Oncol. 2007;25(1):11–5.
3. **Partridge AH, Gelber S, Peppercorn J, Gunsburg E, Sampson E, Rosenberg R, et al.** Fertility and menopausal outcomes in young breast cancer survivors. Clin Breast Cancer. 2008;8(1):65–9.
4. **Lie Fong S, Laven JS, Hakvoort-Cammel FG, Schipper I, Visser JA, Themmen AP, et al.** Assessment of ovarian reserve in adult childhood cancer survivors using anti-Mullerian hormone. Hum Reprod. 2009;24(4):982–90.
5. **Sklar C.** Maintenance of ovarian function and risk of premature menopause related to cancer treatment. J Natl Cancer Inst Monogr. 2005;34:25–7.
6. **Byrne J, Mulvihill JJ, Myers MH, Connelly RR, Naughton MD, Krauss MR, et al.** Effects of treatment on fertility in long-term survivors of childhood or adolescent cancer. N Engl J Med. 1987;317(21):1315–21.
7. **Cvancarova M, Samuelsen SO, Magelssen H, Fossa SD.** Reproduction rates after cancer treatment: experience from the Norwegian radium hospital. J Clin Oncol. 2009;27(3):334–43.
8. **Helewa M, Levesque P, Provencher D, Lea RH, Rosolowich V, Shapiro HM.** Breast cancer, pregnancy, and breastfeeding. J Obstet Gynaecol Can. 2002;24(2):64–80, quiz 181–4.
9. **Green DM, Whitton JA, Stovall M, Mertens AC, Donaldson SS, Ruymann FB, et al.** Pregnancy outcome of female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. Am J Obstet Gynecol. 2002;187(4):1070–80.
10. **Edgar AB, Wallace WH.** Pregnancy in women who had cancer in childhood. Eur J Cancer. 2007;43(13):1890–4.
11. **Reinmuth S, Liebeskind AK, Wickmann L, Bockelbrink A, Keil T, Henze G, et al.** Having children after surviving cancer in childhood or adolescence - results of a Berlin survey. Klin Padiatr. 2008;220(3):159–65.
12. **Gelber S, Coates AS, Goldhirsch A, Castiglione-Gertsch M, Marini G, Lindtner J, et al.** Effect of pregnancy on overall survival after the diagnosis of early-stage breast cancer. J Clin Oncol. 2001;19(6):1671–5.
13. **Bensyl DM, Iuliano DA, Carter M, Santelli J, Gilbert BC.** Contraceptive use–United States and territories, Behavioral Risk Factor Surveillance System, 2002. MMWR Surveill Summ. 2005;54(6):1–72.
14. **Mosher WD, Martinez GM, Chandra A, Abma JC, Willson SJ.** Use of contraception and use of family planning services in the United States: 1982–2002. Adv Data. 2004;350:1–36.
15. **Finer LB, Henshaw SK.** Abortion incidence and services in the United States in 2000. Perspect Sex Reprod Health. 2003;35(1):6–15.
16. **Trussell J, Vaughan B.** Contraceptive failure, method-related discontinuation and resumption of use: results from the 1995 National Survey of Family Growth. Fam Plann Perspect. 1999;31(2):64–72, 93.
17. **St James PJ, Younger MD, Hamilton BD, Waisbren SE.** Unplanned pregnancies in young women with diabetes. An analysis of psychosocial factors. Diabetes Care. 1993;16(12):1572–8.
18. **Holing EV, Beyer CS, Brown ZA, Connell FA.** Why don't women with diabetes plan their pregnancies? Diabetes Care. 1998;21(6):889–95.
19. **Schwarz EB, Maselli J, Gonzales R.** Contraceptive counseling of diabetic women of reproductive age. Obstet Gynecol. 2006;107(5):1070–4.
20. **Chuang CH, Chase GA, Bensyl DM, Weisman CS.** Contraceptive use by diabetic and obese women. Womens Health Issues. 2005;15(4):167–73.
21. **Winther JF, Boice JD, Jr., Svendsen AL, Frederiksen K, Olsen JH.** Induced Abortions in Danish Cancer Survivors: A Population-Based Cohort Study. J Natl Cancer Inst 2009.
22. **Mitwally MF.** Management of reproductive needs in cancer patients: clinical perspectives. Expert Rev Anticancer Ther. 2008;8(10):1589–95.
23. **Schwarz EB, Manzi S.** Risk of unintended pregnancy among women with systemic lupus erythematosus. Arthritis Rheum. 2008;59(6):863–6.
24. **Hatcher R, Trussell J, Stewart F, Nelson A, Cates W, Guest F, et al.** Contraceptive Technology. 18 ed. New York: Ardent Media; 2004.
25. **Peterson HB.** Sterilization. Obstet Gynecol. 2008;111(1):189–203.
26. **Curtis KM, Mohllajee AP, Peterson HB.** Regret following female sterilization at a young age: a systematic review. Contraception. 2006;73(2):205–210.

27. **Thonneau PF, Almont T.** Contraceptive efficacy of intrauterine devices. Am J Obstet Gynecol. 2008;198(3):248–53.
28. **Tewari R, Kay VJ.** Compliance and user satisfaction with the intrauterine contraceptive device in Family Planning Service: the results of a survey in Fife, Scotland, August 2004. Eur J Contracept Reprod Health Care. 2006;11(1):28–37.
29. **Varney SJ, Guest JF.** Relative cost effectiveness of Depo-Provera, Implanon, and Mirena in reversible long-term hormonal contraception in the UK. Pharmacoeconomics. 2004;22(17):1141–51.
30. **d'Arcangues C.** Worldwide use of intrauterine devices for contraception. Contraception. 2007;75(6 Suppl):S2–7.
31. **Peri N, Graham D, Levine D.** Imaging of intrauterine contraceptive devices. J Ultrasound Med. 2007;26(10):1389–401.
32. **Mohllajee AP, Curtis KM, Peterson HB.** Does insertion and use of an intrauterine device increase the risk of pelvic inflammatory disease among women with sexually transmitted infection? A systematic review. Contraception. 2006;73(2):145–53.
33. World Health Organization. Intrauterine Devices. In: Medical Eligibility Criteria for Contraceptive Use. 3 ed. Geneva: Reproductive Health and Research World Health Organizaiton; 2004.
34. **Van Houdenhoven K, van Kaam KJ, van Grootheest AC, Salemans TH, Dunselman GA.** Uterine perforation in women using a levonorgestrel-releasing intrauterine system. Contraception. 2006;73(3):257–60.
35. **Prager S, Darney PD.** The levonorgestrel intrauterine system in nulliparous women. Contraception. 2007;75(6 Suppl):S12–5.
36. **Bahamondes L, Espejo-Arce X, Hidalgo MM, Hidalgo-Regina C, Teatin-Juliato C, Petta CA.** A cross-sectional study of the forearm bone density of long-term users of levonorgestrel-releasing intrauterine system. Hum Reprod. 2006;21(5):1316–9.
37. **Pisoni CN, Cuadrado MJ, Khamashta MA, Hunt BJ.** Treatment of menorrhagia associated with oral anticoagulation: efficacy and safety of the levonorgestrel releasing intrauterine device (Mirena coil). Lupus. 2006;15(12):877–80.
38. **Ortiz ME, Croxatto HB.** Copper-T intrauterine device and levonorgestrel intrauterine system: biological bases of their mechanism of action. Contraception. 2007;75(6 Suppl):S16–30.
39. Long-term reversible contraception. Twelve years of experience with the TCu380A and TCu220C. Contraception. 1997;56(6):341–52.
40. **Sivin I.** Utility and drawbacks of continuous use of a copper T IUD for 20 years. Contraception. 2007;75(6 Suppl):S70–5.
41. **Inki P.** Long-term use of the levonorgestrel-releasing intrauterine system. Contraception. 2007;75(6 Suppl):S161–6.
42. **Xiao B, Zeng T, Wu S, Sun H, Xiao N.** Effect of levonorgestrel-releasing intrauterine device on hormonal profile and menstrual pattern after long-term use. Contraception. 1995;51(6):359–65.
43. **Lockhat FB, Emembolu JE, Konje JC.** Serum and peritoneal fluid levels of levonorgestrel in women with endometriosis who were treated with an intrauterine contraceptive device containing levonorgestrel. Fertil Steril. 2005;83(2):398–404.
44. Medical Eligibility Criteria for Contraceptive Use. 3 ed. Geneva: Reproductive Health and Research World Health Organization; 2004.
45. **Trinh XB, Tjalma WA, Makar AP, Buytaert G, Weyler J, van Dam PA.** Use of the levonorgestrel-releasing intrauterine system in breast cancer patients. Fertil Steril. 2008;90(1):17–22.
46. **Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM.** Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril 2008.
47. International Collaborative Post-Marketing Surveillance of Norplant. Post-marketing surveillance of Norplant contraceptive implants: I. Contraceptive efficacy and reproductive health. Contraception. 2001;63(4):167–86.
48. **Trussell J, Lalla AM, Doan QV, Reyes E, Pinto L, Gricar J.** Cost effectiveness of contraceptives in the United States. Contraception. 2009;79(1):5–14.
49. **Cole JA, Norman H, Doherty M, Walker AM.** Venous thromboembolism, myocardial infarction, and stroke among transdermal contraceptive system users. Obstet Gynecol. 2007;109(2 Pt 1):339–46.
50. **Hannaford PC, Selvaraj S, Elliott AM, Angus V, Iversen L, Lee AJ.** Cancer risk among users of oral contraceptives: cohort data from the Royal College of General Practitioner's oral contraception study. Bmj. 2007;335(7621):651.
51. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Beral V, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet. 2008;371(9609):303–14.
52. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet. 1996;347(9017):1713–27.
53. **Wingo PA, Austin H, Marchbanks PA, Whiteman MK, Hsia J, Mandel MG, et al.** Oral contraceptives and the risk of death from breast cancer. Obstet Gynecol. 2007;110(4):793–800.
54. **Rosenblatt KA, Gao DL, Ray RM, Nelson ZC, Wernli KJ, Li W, et al.** Oral contraceptives and the risk of all cancers combined and site-specific cancers in Shanghai. Cancer Causes Control 2008.
55. **McNaught J, Reid RL, Provencher DM, Lea RH, Jeffrey JF, Oza A, et al.** Progesterone-only and non-hormonal contraception in the breast cancer survivor: Joint Review and Committee Opinion of the Society of Obstetricians and Gynaecologists of Canada and the Society of Gynecologic Oncologists of Canada. J Obstet Gynaecol Can. 2006;28(7):616–39.
56. **Shapiro S, Rosenberg L, Hoffman M, Truter H, Cooper D, Rao S, et al.** Risk of breast cancer in relation to the use of injectable progestogen contraceptives and combined estrogen/progestogen contraceptives. Am J Epidemiol. 2000; 151(4):396–403.
57. **Kloke O, Klaassen U, Oberhoff C, Hartwich G, Szanto J, Wolf E, et al.** Maintenance treatment with medroxyprogesterone acetate in patients with advanced breast cancer responding to chemotherapy: results of a randomized trial. Essen Breast Cancer Study Group. Breast Cancer Res Treat. 1999;55(1):51–9.
58. Oral-contraceptive use and the risk of breast cancer. The Cancer and Steroid Hormone Study of the Centers for Disease Control and the National Institute of Child Health and Human Development. N Engl J Med. 1986;315(7):405–11.
59. **Vessey M, Baron J, Doll R, McPherson K, Yeates D.** Oral contraceptives and breast cancer: final report of an epidemiological study. Br J Cancer. 1983;47(4):455–62.
60. **Backman T, Rauramo I, Jaakkola K, Inki P, Vaahtera K, Launonen A, et al.** Use of the levonorgestrel-releasing intrauterine system and breast cancer. Obstet Gynecol. 2005;106(4):813–7.
61. **Cheng L, Gulmezoglu AM, Piaggio G, Ezcurra E, Van Look PF.** Interventions for emergency contraception. Cochrane Database Syst Rev. 2008(2):CD001324.
62. **Davidoff F, Trussell J.** Plan B and the politics of doubt. Jama. 2006;296 (14):1775–8.
63. **von Hertzen H, Piaggio G, Ding J, Chen J, Song S, Bartfai G, et al.** Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. Lancet. 2002;360 (9348):1803–10.
64. **Ngai SW, Fan S, Li S, Cheng L, Ding J, Jing X, et al.** A randomized trial to compare 24 h versus 12 h double dose regimen of levonorgestrel for emergency contraception. Hum Reprod. 2005;20(1):307–11.
65. Pediatrics AAo. Policy Statement on Emergency Contraception. Pediatrics. 2005;116(4):1038–1047.
66. **Gold M, Sucato G, Conard L, Adams Hillard P.** Provision of emergency contraception to adolescents Position paper of the society for adolescent medicine. Journal of Adolescent Health. 2004;35(1):66–70.
67. ACOG practice bulletin. Emergency oral contraception. Number 25, March 2001. (Replace Practice Pattern Number 3, December 1996). American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet. 2002;78(2):191–8.
68. **Polis CB, Schaffer K, Blanchard K, Glasier A, Harper CC, Grimes DA.** Advance provision of emergency contraception for pregnancy prevention: a meta-analysis. Obstet Gynecol. 2007;110(6):1379–88.
69. **Schwarz EB, Lohr PA, Gold MA, Gerbert B.** Prevalence and correlates of ambivalence towards pregnancy among nonpregnant women. Contraception. 2007;75(4):305–10.
70. **Stanwood NL, Bradley KA.** Young pregnant women's knowledge of modern intrauterine devices. Obstet Gynecol. 2006;108(6): 1417–22.
71. **Kesim MD, Aydin Y, Atis A, Mandiraci G.** Long-term effects of the levonorgestrel-releasing intrauterine system on serum lipids and the endometrium in breast cancer patients taking tamoxifen. Climacteric. 2008;11(3):252–7.
72. **Vessey MP, Villard-Mackintosh L, McPherson K, Yeates D.** Mortality among oral contraceptive users: 20 year follow up of women in a cohort study. Bmj. 1989;299(6714):1487–91.