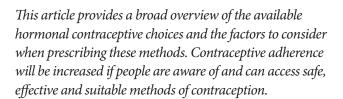
Current choices of hormonal contraception

What are the factors to consider?

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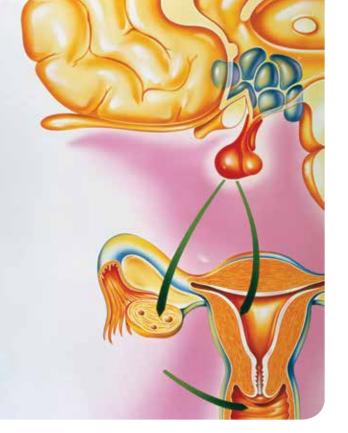


Key points

- There is now a wide array of hormonal contraceptive options for women to choose from. GPs and other primary health providers are well placed to provide evidence-based and balanced guidance to assist in appropriate individualised choice.
- Long-acting reversible contraception, particularly 'fit and forget' implants and intrauterine devices, provide very high efficacy, immediate reversibility and are safe for use by most women. They are, however, underused in the Australian setting.
- The international Medical Eligibility Criteria (MEC) system provides an essential framework for understanding any absolute or relative contraindications when prescribing hormonal contraception.
- Although most women can safely use combined hormonal contraceptives, history taking with reference to the MEC framework is extremely important so that women at higher risk of venous thromboembolism, stroke and ischaemic heart disease can be offered alternative methods.

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he combined hormonal contraceptive pill and condoms remain the most commonly used contraceptive methods in Australia.¹ However, the past decade has seen a welcome expansion in the range of contraceptive options available for women in Australia, with new delivery systems, a wider array of progestogens and, more recently, a new oestrogen in two pill formulations.

Long-acting reversible contraception (LARC) methods, which in Australia include the depot medroxyprogesterone acetate (DMPA) injection, the etonogestrel implant and the copper and levonorgestrel intrauterine devices (IUDs), have few contraindications and are more effective at preventing an unintended pregnancy compared with combined hormonal contraceptives,² yet are used by fewer than 10% of Australian women.¹ The 'top tier' LARC methods (implants and IUDs) share the characteristics of requiring a single act of motivation for long-term use and having rapid reversibility, and have the highest continuation rates of all contraceptive methods.³

This article provides a broad overview of the available hormonal contraceptive choices and the factors to consider when prescribing these methods. For a comprehensive review of all methods of contraception, including practical advice on prescribing and the noncontraceptive benefits of hormonal contraception see parts 1, 2 and 3 of 'A practical guide to contraception', published in *Medicine Today*.⁴⁻⁶

Classification

Classification of hormonal contraception can be organised in several ways (Table 1). Due to contraindications, side effects and benefits specific to oestrogen, it is useful to think of contraceptives that are combined (oestrogen and progestogen) and those that are progestogen only. Contraception can also be classified as short acting (hormonal pills and vaginal rings), long acting (DMPA injection) and very long acting reversible contraception (progestogen implant and IUDs). Another way of classifying hormonal contraception is by the primary mechanism of action: whether the method acts systemically by suppressing ovulation

Table 1. Classifying hormonal methods of contraception					
Hormonal contraceptive method	Classifications				
	Hormonal content	Duration of action	Primary mechanism of action		
Combined oral contraceptive pills	Combined	Short acting	Ovulation suppression		
Vaginal ring	Combined	Short acting	Ovulation suppression		
Progestogen-only pills	Progestogen only	Short acting	Cervical mucus changes		
DMPA injection	Progestogen only	LARC	Ovulation suppression		
Etonorgestrel implant	Progestogen only	LARC (very long)	Ovulation suppression		
Levonorgestrel IUD	Progestogen only	LARC (very long)	Endometrial and cervical mucus changes		
Emergency contraceptive pill	Progestogen only	Single use post coital	Ovulation suppression or delay		

Abbreviations: DMPA = depot medroxyprogesterone acetate; IUD = intrauterine device; LARC = long-acting reversible contraception.

Table 2. Medical eligibility criteria (MEC) categories for contraceptive methods ^{7,8}				
MEC category	Definition			
1	A condition for which there is no restriction for the use of the contraceptive method			
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks			
3	A condition where the theoretical or proven risks generally outweigh the advantages of using the method. The provision of a method requires expert clinical judgement and/or referral to a specialist contraceptive provider, since use of the method is not usually recommended unless other more appropriate methods are not available or acceptable			
4	A condition that represents an unacceptable risk if the contraceptive method is used			

(progestogen implants, DMPA injection, combined pills and vaginal rings) or by mostly local effects on the endometrium (progestogen IUDs) and cervical mucus (progestogen-only pills).

What's important when choosing a hormonal method?

The Medical Eligibility Criteria (MEC) is a framework developed by an expert group of the World Health Organization⁷ and adapted by the Faculty of Sexual and Reproductive Healthcare UK to the developed world setting (Table 2).⁸

The 'Efficacy of contraceptive methods available in Australia', a patient counselling card developed by Sexual Health and Family Planning Australia, is a useful tool when discussing contraception

options with patients (see Figure). It presents the available methods on a visual scale of efficacy with typical use.

When considering a method of contraception, efficacy, medical eligibility, side effects of previously used methods, noncontraceptive benefits and patient choice (including consideration of cost, cultural or personal beliefs, convenience and access) are all important. Contraindications to combined hormonal contraceptives are mostly related to identified risk factors for, or a personal history of, arterial and venous disease. Other important MEC 3 and 4 contraindications include migraine with aura, a history of breast cancer, smoking and aged over of 35 years, hypertension, and the concurrent use of liver-enzyme inducing medications.⁸

Although medical contraindications for hormonal methods, especially progestogen-only methods, are uncommon in women of reproductive age, women often raise concerns of adverse effects of hormonal methods on weight, mood and libido. Respectful collaborative exploration with women of their understanding of the risks, side effects and benefits of specific hormonal methods followed by appropriate challenge of misinformation with balanced evidence is a useful strategy. For example, although weight gain is a frequent concern, it has not been demonstrated in studies investigating low-dose pills containing 35 µg or less of ethinyloestradiol.⁹

If nonhormonal methods of contraception are preferred by a woman, the copper IUD, a top-tier LARC method, can be offered as first line to women of all ages; however, condoms (both male and female) are the only methods to offer protection against sexually transmitted infections. Although the copper IUD is associated with heavier, 10 and sometimes more painful periods, it is the most effective reversible nonhormonal method available. It is also the most effective form of emergency contraception if a woman can access it within the five-day time frame after unprotected intercourse. 11

The shorter-acting contraceptives (the pill, vaginal ring and

Efficacy of contraceptive methods available in Australia







Etonogestrel implant Typical & Perfect use 99.95% Lasts 3 years Inserted and removed by clinician



Levonorgestrel IUD Typical & Perfect use 99.8% Lasts 5 years Inserted and removed by clinician

Copper IUD's Typical use 99.2% Perfect use 99.4% Lasts 5 -10 years Inserted and removed by clinician



Typical use 99.85% Perfect use 99.9% Considered permanent Performed by clinician



Sterilisation

Tubal occlusion by metal microinsert (Essure®) Typical & Perfect use 99.8%* Hysteroscopic procedure Considered permanent



Female tubal ligation Typical use 99.5% Perfect use 99.5% Laparoscopic procedure requiring anaesthesia Considered permanent

Other hormonal methods



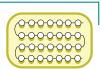
Depot medroxyprogesterone acetate injection Typical use 94% Perfect use 99.8% Injection every 3 months



Combined hormone vaginal ring Typical use 91% Perfect use 99.7% Change every 4 weeks



Combined Oral Contraceptive Pill Typical use 91% Perfect use 99.7% Once daily



Progestogen-Only Pill Typical use 91% Perfect use 99.7% Once daily

Barriers and natural methods



Diaphragm Typical use 88% Perfect use 94% On each occasion of intercourse



Male Condom Typical use 82% Perfect use 98% On each occasion of intercourse



Female Condom Typical use 79% Perfect use 95% On each occasion of intercourse



Withdrawal Typical use 78% Perfect use 96% On each occasion of intercourse



Fertility awareness Typical use 76% Perfect use 95-99.6%

References

Trussell J, 2011. "Contraceptive failure in the UnitedStates". Contraception 83: 397-404

*Lessard CR, Hopkins MR 2011. "Efficacy, safety, and patient acceptability of the Essure procedure". Patient Acceptance and Adherence 5: pp207-212

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Less **Effective**

Figure. Patient counselling card on efficacy of contraceptive methods developed by Sexual Health and Family Planning Australia.

Table 3. Combined hormonal contraceptive pills available in Australia					
Brand name	Oestrogen	Progestogen	PBS listing		
Femme-tab 20/100 ED Loette Microgynon 20 ED Microlevlen ED	20 μg ethinyloestradiol (EE)	100 μg levonorgestrel	Only Femme-Tab 20/100 ED is PBS listed		
Logynon ED Trifeme 28 Triphasil Triquilar ED	6 x 30 μg EE 5 x 40 μg EE 10 x 30 μg EE	6 x 50 μg levonorgestrel 5 x 75 μg levonorgestrel 10 x 125 μg levonorgestrel			
Femme-Tab ED 30/150 ED Levlen ED Microgynon 30 ED Monofeme Nordette	30 µg EE	150 μg levonorgestrel			
Microgynon 50 ED	50 μg EE	125 µg levonorgestrel	PBS listed		
Brevinor 21 and 28 Norimin 28	35 μg EE	500 μg norethisterone			
Brevinor-1 21 and 28 Norimin-1 28	35 µg EE	1000 µg norethisterone			
Improvil 28 Synphasic 28	7 x 35 µg EE 9 x 35 µg EE 5 x 35 µg EE	7 x 500 µg norethisterone 9 x 1000 µg norethisterone 5 x 500 µg norethisterone			
Norinyl-1 21 and 28	50 µg mestranol	1000 µg norethisterone			
Marvelon28	30 µg EE	150 µg desogestrel			
Femoden ED Minulet ED	30 µg EE	75 µg gestodene			
Brenda-35 ED Carolyn-35 ED Diane-35 ED Estelle-35 ED Juliet-35 ED Laila-35 ED	35 µg EE	2 mg cyproterone acetate			
Isabelle Yasmin	30 µg EE	3 mg drospirenone	Not PBS listed		
YAZ Yaz Flex	20 µg EE	3 mg drospirenone			
Valette	30 µg EE	2 mg dienogest			
Qlaira	2 x 3 mg oestradiol valerate 5 x 2 mg oestradiol valerate 17 x 2 mg oestradiol valerate 2 x 1 mg oestradiol valerate	5 x 2 mg dienogest 17 x 3 mg dienogest			
Zoely	1.5 mg oestradiol	2.5 mg nomegestrol acetate			

progestogen-only pill) are addressed in detail in part 1 of 'A practical guide to contraception' published in *Medicine Today*.⁴

What are the choices?

Combined hormonal contraception (the pill and vaginal ring)

The combined hormonal methods offer excellent cycle control and many other noncontraceptive benefits, such as management of acne, heavy menstrual bleeding and dysmenorrhoea. The combined pill remains a popular choice because it has the ability to manipulate cycles, is easily accessible and can be used under the woman's control. Although most women can safely use combined hormonal contraceptives, history taking with reference to the MEC framework is extremely important, so that women at higher risk of venous thromboembolism, stroke and ischaemic heart disease can be offered alternative methods.

There is a large and sometimes confusing choice of combined contraceptive pills (see Table 3 for a list of combined hormonal contraceptive pills available in Australia). A low-dose pill containing 35 μ g or less of ethinyloestradiol and either levonorgestrel or norethisterone is the recommended first choice. These low-dose pills, including the 20 μ g ethinyloestradiol formulation, are subsidised under the Pharmaceutical Benefits Scheme (PBS) and are associated with the lowest risk of venous thromboembolism.

The vaginal ring (15 μ g ethinyloestradiol and 120 μ g etonogestrel) offers an alternative hormone delivery system to the pill, which may be preferred by some women. Compared with the combined pill, the ring's nondaily action may improve compliance, it offers an advantage when malabsorption might be an issue and its use may be associated with less

Table 4. Risk of venous thromboembolism associated with nonuse and use of combined hormonal contraception over one year²²

Type of contraception	Risk of venous thromboembolism
Women who are not taking any contraception and are not pregnant	2 per 10,000 women
Women taking combined hormonal contraception containing ethinyloestradiol plus levonorgestrel, norgestimate* or norethisterone	5 to 7 per 10,000 women
Women taking combined hormonal contraception containing etonogestrel (vaginal ring) and norelgestromin* (patch)	6 to 12 per 10,000 women
Women taking combined hormonal contraception containing ethinyloestradiol plus gestodene, desogestrel or drospirenone	9 to 12 per 10,000 women
* Not available in Australia.	

unscheduled bleeding.¹³⁻¹⁷ The ethinyloestradiol plus etonogetrel ring is not subsidised by the PBS and so can be too expensive for some women.

Combined contraceptive pills and vaginal rings can be used continuously without a placebo break, with rings being replaced immediately on removal after four weeks of use. This regimen may be chosen for convenience or to avoid symptoms associated with the withdrawal bleed. There is no upper limit to the number of placebo breaks a woman can miss, provided she remains satisfied with her bleeding pattern/amenorrhoea.¹²

Considerations of using the pill or vaginal ring

Venous thromboembolism risk

All combined hormonal contraceptives increase the risk of venous thromboembolism, with the highest risk being in the first year of use. 18 When prescribing pills containing desogestrel, gestodene, cyproterone acetate or drospirenone, it is important to be aware that although these pills have been associated with a higher risk of venous thromboembolism than pills containing levonorgestrel or norethisterone, the absolute risk remains low and lower than the risk in women during late pregnancy and the postpartum period (Table 4). 19-22 The limited information available on the risk of venous thromboembolism in women using the vaginal ring indicates that the risk of venous thromboembolism is at least that of the risk in women taking levonorgestrel- and norethisterone-containing pills with 35 µg or less ethinyloestradiol. 21

Ischaemic stroke and myocardial infarction

Combined hormonal contraceptive use is associated with approximately double the risk of an ischaemic stroke compared with nonusers. This risk is further increased in users of combined hormonal contraceptives who experience migraine with aura.²³ The risk of myocardial infarction in women using combined hormonal contraception is two to five times that of nonusers.²⁴⁻²⁸ However, the absolute risk of ischaemic stroke or

myocardial infarction in women of reproductive age is very low, with a background risk for nonusers of combined hormonal contraceptives of about 24 and 13 per 100,000 women years for ischaemic stroke and myocardial infarction, respectively.²⁹ Risks are highest in older women and in those with additional risk factors for cardiovascular disease.²⁹

Progestogen-only pill

Two progestogen-only pills are available in Australia: one containing levonorgestrel 30 μg and the other containing norethisterone 350 μg , either of which can be initiated as first choice. The progestogen-only pill is often used in women who are intolerant to or have a contraindication to oestrogen.

The progestogen-only pill is considered to have a more vulnerable efficacy, and strict adherence to taking it, within a daily three-hour timeframe, is important for maximum efficacy.³⁰

Depot medroxyprogesterone acetate

DMPA offers the advantage of high rates of amenorrhoea (50 to 70% of women have amenorrhoea after one year of use)^{31,32} and it is a totally discrete method of contraception. Discontinuation rates are, however, high compared with other LARC methods.³ The disadvantages of DMPA include a need for a three-monthly visit to a healthcare provider (a self-administered subcutaneous injection may be marketed in the future), potential for unpredictable bleeding, weight gain in about 20% of users^{33,34} and a delayed return to fertility.³⁵ Use in women aged under 18 years or over 45 years is MEC 2 category. DMPA is not usually recommended as first line in these women because of an associated decrease in bone density, although this is most likely fully reversible.

Progestogen implants

The contraceptive implant has been gaining popularity, especially among young women. It is a 'set and forget' top tier LARC offering three years of highly effective and immediately reversible contraception with few contraindications. Although up to 20% of women may experience unacceptable bleeding patterns, ³⁶ the continuation rates are higher than with the pill. ³ It is important to realise that, unlike the contraceptive injection, the implant's efficacy is affected by liver enzyme-inducing drugs. It does not appear to affect bone density as it still allows for follicular activity.

Progestogen intrauterine devices

The IUDs currently available in Australia are a five-year hormonal IUD (levonorgestrel IUD) and several five- to 10-year copper IUDs. Again these are 'set and forget' methods that are highly effective and immediately reversible, and have excellent continuation rates. The hormonal IUD has an impressive effect on menstrual bleeding with most women experiencing very light bleeds (if any) after the initial

settling in phase of three to six months.³⁷ The available IUDs are suitable for most women, including young, nulliparous women, and the evidence shows that they are not associated with ongoing risk of pelvic inflammatory disease or infertility. Australian research has demonstrated that IUD insertion in nulliparous women in a primary care setting can be safely achieved without the need for sedation.³⁸

Emergency contraceptive pill

The emergency contraceptive pill currently available in Australia is the progestogen levonorgestrel, which is associated with a far less risk of nausea or vomiting than its predecessor, the Yuzpe method – a combination of oestrogen and progestogen.³⁹ The levonorgestrel emergency contraceptive pill is available over the counter at pharmacies and has no strong contraindications to its use. It is, however, quite expensive (at \$20 to \$30) and offers no ongoing contraception. It is not an abortifacient as its effect has now been shown to be on ovulation alone.⁴⁰ Once ovulation has occurred, the emergency contraceptive pill does not prevent fertilisation or inhibit implantation. Recent concerns have been raised about possible reduced efficacy in women weighing above 70 kg.⁴¹ The evidence for this is under review but there is currently no change to the advice of dosage irrespective of weight.

Women accessing the emergency contraceptive pill should be given advice on follow up, including the importance of excluding

pregnancy and future contraception. It is important that women using short-acting contraceptive methods are made aware of the superior efficacy and safety of LARC methods. The LARC methods are addressed in detail in part 2 of 'A practical guide to contraception', published in *Medicine Today*.⁵

Conclusion

A wide array of hormonal contraceptive methods is now available for Australian women. Hormonal implants and IUDs are as effective as sterilisation and have excellent continuation rates. GPs and other primary health care providers are well placed to provide evidence-based and balanced guidance to assist in appropriate individualised choice. By ensuring patients are aware of and can access safe, effective and suitable methods, contraceptive adherence can be increased affording women (and men) control over their fertility.

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article

COMPETING INTERESTS: The authors all work for organisations that are paid fees to conduct training for GPs in implant and IUD insertion from MSD and Bayer, respectively. Dr Harvey and Dr McNamee have sat on expert advisory panels for new contraceptive methods for Bayer and MSD. Dr Harvey has received professional development support from MSD to attend conferences.

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References

- Family Planning NSW. Reproductive and sexual health in Australia. Ashfield, Svdnev: FPNSW. 2013.
- 2. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. N Engl J Med 2012; 366: 1998-2007.
- 3. O'Neil-Callahan M, Peipert JF, Zhao Q, Madden T, Secura G. Twenty-four-month continuation of reversible contraception. Obstet Gynecol 2013; 122: 1083-1091.
- 4. McNamee K, Harvey C, Bateson D. A practical guide to contraception. Part 1: Contraceptive pills and vaginal rings. Med Today 2013; 14(7): 18-32.
- 5. Harvey C, McNamee K, Stewart M. A practical guide to contraception. Part 2: Long-acting reversible methods. Med Today 2013; 14(8): 39-51.
- 6. Stewart M, McNamee K, Harvey C. A practical guide to contraception. Part 3: Traditional methods, sterilisation and emergency contraception. Med Today 2013; 14(9): 55-65.
- 7. Medical Eligibility Criteria for Contraceptive Use, 4th edition. World Health Organization. 2010.
- Faculty of Sexual and Reproductive Healthcare. UK medical eligibility criteria for contraceptive use 2009. London: Faculty of Sexual and Reproductive Healthcare, RCOG: 2009.
- Gallo MF, Lopez LM, Grimes DA, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. Cochrane Database Syst Rev 2011; 9: CD003987.
 Nilsson CG. Comparative quantitation of menstrual blood loss with a d-norgestrelreleasing jud and a Nova-T-copper device. Contraception 1977; 15: 379-387.
- 11. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. Hum Reproduction 2012; 8; 27: 1994-2000.
- 12. Bateson D, Harvey C, McNamee K. Contraception: an Australian clinical practice handbook. 3rd ed. Brisbane: Family Planning NSW, Queensland and Victoria; 2012.

 13. Gilliam ML, Neustadt A, Kozloski M, Mistretta S, Tilmon S, Godfrey E. Adherence and acceptability of the contraceptive ring compared with the pill among students: a randomized controlled trial. Obstet Gynecol 2010; 115: 503-510.
- 14. Alexander NJ, Arkin ES, Einhaus KB, Singh M, Thompson MM. Results of a patient acceptance survey administered to women in the NuvaRing Premier Program. Obstet Gynecol 2003; 101: S16-S17.
- 15. Milsom I, Lete I, Bjertnaes A, et al. Effects on cycle control and bodyweight of the combined contraceptive ring, NuvaRing, versus an oral contraceptive containing 30 microg ethinyl estradiol and 3 mg drospirenone. Hum Reprod 2006; 21: 2304-2311. 16. Mohamed AM, El-Sherbiny WS, Mostafa WA. Combined contraceptive ring versus combined oral contraceptive (30-mug ethinylestradiol and 3-mg drospirenone). Int J Gynaecol Obstet 2011: 114: 145-148.
- 17. Oddsson K, Leifels-Fischer B, et al. Superior cycle control with a contraceptive vaginal ring compared with an oral contraceptive containing 30 microg ethinylestradiol and 150 microg levonorgestrel: a randomized trial. Hum Reprod 2005; 20: 557-562.

 18. Clinical Effectiveness Unit. Combined hormonal contraception. London: Faculty of Sexual and Reproductive Healthcare; 2012.
- 19. van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009; 339: b2921. 20. Lidegaard O, Lokkegaard E, Svendsen AL, Agger C. Hormonal contraception and of venous thromboembolism: national follow-up study. BMJ 2009; 339: b2890. 21. Lidegaard O, Nielsen LH, Skovlund CW, Skjeldestad FE, Lokkegaard E. Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001-9. BMJ 2011; 343: d6423.
- 22. Faculty of Sexual and Reproductive Healthcare. Combined hormonal contraception communication, 2014. Available online at: www.fsrh.org/pdfs/FacultyStatementCombinedPill.pdf (accessed June 2014).
- 23. Schurks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and

- cardiovascular disease: systematic review and meta-analysis. BMJ 2009; 339: b3914. 24. Baillargeon JP, McClish DK, Essah PA, Nestler JE. Association between the current use of low-dose oral contraceptives and cardiovascular arterial disease: a meta-analysis. J Clin Endocrinol Metab 2005; 90: 3863-3870.
- 25. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Contraception 1998; 57: 315-324.
- 26. Gillum LA, Mamidipudi SK, Johnston SC. Ischemic stroke risk with oral contraceptives: A meta-analysis. JAMA 2000; 284: 72-78.
- 27. Acute myocardial infarction and combined oral contraceptives: results of an international multicentre case-control study. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet 1997; 349: 1202-1209.
 28. Khader YS. Rice J. John L. Abueita O. Oral contraceptives use and the risk of
- Khader YS, Rice J, John L, Abueita O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. Contraception 2003; 68: 11-17.
 Lidegaard O, Lokkegaard E, Jensen A, Skovlund CW, Keiding N. Thrombotic stroke
- and myocardial infarction with hormonal contraception. N Engl J Med 2012; 366: 2257-2266.
- 30. Trussell J. Contraceptive failure in the United States. Contraception 2004; 70: 89-96.
- 31. Said S, Omar K, Koetsawang S, et al. A multicentred phase III comparative clinical trial of depot-medroxyprogesterone acetate given three-monthly at doses of 100 mg or 150 mg: 1. Contraceptive efficacy and side effects. World Health Organization Task Force on Long-Acting Systemic Agents for Fertility Regulation. Special Programme of Research, Development and Research Training in Human Reproduction. Contraception 1986; 34: 223-235.
- 32. Sangi-Haghpeykar H, Poindexter AN, 3rd, Bateman L, Ditmore JR. Experiences of injectable contraceptive users in an urban setting. Obstet Gynecol 1996; 88: 227-233. 33. Bonny AE, Secic M, Cromer B. Early weight gain related to later weight gain in adolescents on depot medroxyprogesterone acetate. Obstet Gynecol 2011; 117: 793-797.
- 34. Le YC, Rahman M, Berenson AB. Early weight gain predicting later weight gain among depot medroxyprogesterone acetate users. Obstet Gynecol 2009; 114: 279-284.
- 35. Schwallie PC, Assenzo JR. The effect of depo-medroxyprogesterone acetate on pituitary and ovarian function, and the return of fertility following its discontinuation: a review. Contraception 1974; 10: 181-202.
- 36. Mansour D, Korver T, Marintcheva-Petrova M, Fraser IS. The effects of Implanon on menstrual bleeding patterns. Eur J Contracept Reprod Health Care 2008; 13 Suppl 1: 13-28.
- 37. Lethaby AE, Cooke I, Rees M. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev 2005; 4:
- 38. Harvey C, Bateson D, Wattimena J, Black KI. Ease of intrauterine contraceptive device insertion in family planning settings. Aust N Z J Obstet Gynaecol 2012; 52: 534-539.
- 39. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. Task Force on Postovulatory Methods of Fertility Regulation. Lancet 1998; 352: 428-433. 40. Noe G, Croxatto HB, Salvatierra AM, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. Contraception 2011; 84: 486-492
- 41. Glasier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. Contraception 2011; 84: 363-367.