Part II

Using the recommendations

2.1 Background

The *Medical eligibility criteria for contraceptive use* (MEC) provides guidance regarding which clients can use contraceptive methods safely. The goal of the document is to improve access to, and quality of, family planning services by providing policy-makers, decision-makers and the scientific community with recommendations that can be used for developing or revising national guidelines on the medical eligibility criteria for the use of specific contraceptive methods. Methods covered by this guidance include all hormonal contraceptives, intrauterine devices, barrier methods, fertility awareness-based methods, coitus interruptus, lactational amenorrhoea method, male and female sterilization, and emergency contraception. These evidence-based recommendations do not indicate a "best" method that should be used in a particular medical context; rather, review of the recommendations allows for consideration of multiple methods that could be used safely by people with certain health conditions (e.g. hypertension) or relevant characteristics (e.g. age).

2.1.1 Reproductive and sexual health care as a human right

The Programme of Action of the International Conference on Population and Development (ICPD) defines reproductive health as: "a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity, in all matters relating to the reproductive system and to its functions and processes"[1]. The Programme of Action also states that the purpose of sexual health "is the enhancement of life and personal relations, and not merely counselling and care related to reproduction and sexually transmitted diseases". Recognizing the importance of agreements made at the ICPD and other international conferences and summits, the Beijing Declaration and Platform for Action defines reproductive rights in the following way:

> Reproductive rights embrace certain human rights that are already recognized in national laws, international human rights documents and other relevant consensus documents. These rights rest on the recognition of the basic right of all couples and individuals to decide freely and responsibly the number and spacing and timing of their children and to have the information and means to do so, and the right to attain the highest standard of sexual and reproductive health.[2]

Among the Millennium Development Goals (MDGs) agreed by states in 2001, target 5b calls for universal access to reproductive health by 2015. Reproductive and sexual health care, including family planning services and information, is recognized not only as a key intervention for improving the health of men, women and children but also as a human right. International and regional human rights treaties, national constitutions and laws provide guarantees specifically relating to access to contraceptive information and services. These include the guarantee that states should ensure timely and affordable access to good quality sexual and reproductive health information and services, including contraception, which should be delivered in a way that ensures fully informed decision-making, respects dignity, autonomy, privacy and confidentiality, and is sensitive to individuals' needs and perspectives in a client–provider partnership.[3] A rights-based approach to the provision of contraceptives assumes a holistic view of clients, which includes taking into account clients' sexual and reproductive health care needs and considering all appropriate eligibility criteria when helping clients choose and use a family planning method safely.

Evidence shows that the respect, protection and fulfilment of human rights contribute to positive health outcomes. The provision of contraceptive information and services that respect individual privacy, confidentiality and informed choice, along with a wide range of safe contraceptive

1 Programme of Action of the International Conference on Population and Development. In: Report of the International Conference on Population and Development (Cairo, 5–13 September 1994). United Nations; 1994: para. 7.2 (A/CONF.171/13, http://www.un.org/popin/icpd/conference/offeng/poa.html, accessed 24 April 2015).

2 Beijing Declaration and Platform for Action. In: Report of the Fourth World Conference on Women (Beijing, 4–15 September, 1995). United Nations; 1995: para. 95 (A/CONF.177/20; http://www.un.org/documents/ga/conf177/aconf177–20en.htm, accessed 17 April 2015).

3 Ensuring human rights in the provision of contraceptive information and services: guidance and recommendations. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/102539/1/9789241506748_eng.pdf, accessed 24 April 2015).

methods, increase people's satisfaction and continued use of contraception.[4 5 6 7]

Delivery of care in accordance with the client's human and reproductive rights is fundamental to quality of care. The development of international norms for medical eligibility criteria and practice recommendations for contraceptive use is only one aspect of improving the quality of reproductive health care. Many family planning programmes have included screening, treatment and follow-up procedures that reflect high standards of public health and clinical practice, but these should not be seen as eligibility requirements for specific contraceptive methods. These procedures include the screening and treatment of cervical cancer, anaemia and sexually transmitted infections (STIs), and the promotion of breastfeeding and cessation of smoking. Such procedures should be strongly encouraged if the human and material resources are available to carry them out, but they should not be seen as prerequisites for the acceptance and use of family planning methods since they are not necessary to establish eligibility for the use or continuation of a particular method.

2.1.2 Contraceptive choice

While this document primarily addresses medical eligibility criteria for contraceptive use, considerations of social, behavioural and other non-medical criteria – particularly client preference – must also be taken into account. To provide contraceptive choices to clients in a way that respects and fulfils their human rights necessitates enabling clients to make informed choices for themselves. Women's choices, however, are often taken away from them or limited by direct or indirect social, economic and cultural factors. From a woman's point of view, her choices are made at a particular time, in a particular societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making regarding contraceptive methods usually requires the need to make trade-offs among the advantages and disadvantages of different methods, and these vary according to individual circumstances, perceptions and interpretations. Factors to consider when choosing a particular contraceptive method include the characteristics of the potential user, the baseline risk of disease, the adverse effects profile of different products, cost, availability and patient preferences.

This document does not provide recommendations about which specific product or brand to use after selecting a particular type of contraceptive method. Instead, it provides guidance for whether women with specific medical conditions or medically relevant physiological or personal characteristics are eligible to use various contraceptive methods. Decisions about what methods to use should also take into account clinical judgment and user preferences.

Issues of service quality and access that affect method use and choice

The following service-delivery criteria are universally relevant to the initiation and follow-up of all contraceptive method use:

- Clients should be given adequate information to help them make an informed, voluntary choice of a contraceptive method. This information should at least include:
  - the relative effectiveness of the method;
  - correct usage of the method;
  - how it works;
  - common side-effects;
  - health risks and benefits of the method;
  - signs and symptoms that would necessitate a return to the clinic;
  - information on return to fertility after discontinuing method use; and
  - information on STI protection.

  Information should be presented using language and formats that can be easily understood and accessed by the client.
- In order to offer methods that require surgical approaches, insertion, fitting and/or removal by a trained health-care provider (i.e. sterilization, implants, IUDs, diaphragms, cervical caps), appropriately trained personnel in adequately equipped and accessible facilities must be available, and appropriate infection-prevention procedures must be followed.
- Adequate and appropriate equipment and supplies need to be maintained and held in stock (e.g. contraceptive commodities, and supplies for infection-prevention procedures).
- Service providers should be provided with guidelines, client cards or other screening tools.

4 Koenig MA. The impact of quality of care on contraceptive use: evidence from longitudinal data from rural Bangladesh. Baltimore (MD): Johns Hopkins University; 2003.

5 Arends-Kuenning M, Kessy FL. The impact of demand factors, quality of care and access to facilities on contraceptive use in Tanzania. J Biosoc Sci. 2007;39:1–26.

6 RamaRao S, Lacuest M, Costello M, Pangolibay B, Jones H. The link between quality of care and contraceptive use. Int Fam Plann Perspect. 2003;29(2):76–83.

7 Sanogo D, RamaRao S, Johnes H, N'diaye P, M'bow B, Diop CB. Improving quality of care and use of contraceptives in Senegal. Afr J Reprod Health. 2003;7:57–73.

2.1.3 Effectiveness of method

Contraceptive choice is in part dependent on the effectiveness of the contraceptive method in preventing unplanned pregnancy, which, in turn, is dependent for some methods not only on the protection afforded by the method itself, but also on how consistently and correctly it is used. Table 2.1 compares the percentage of women experiencing an unintended pregnancy during the first year of contraceptive method use when the method is used perfectly (consistently and correctly) and when it is used typically (assuming occasional non-use and/or incorrect use). Consistent and correct usage can both vary greatly with client characteristics such as age, income, desire to prevent or delay pregnancy, and culture. Methods that depend on consistent and correct usage by clients (e.g condoms and pills) have a wide range of effectiveness. Most men and women tend to be more effective users as they become more experienced with a method. However, programmatic aspects also have a profound effect on how effectively (consistently and correctly) the method will be used.

2.1.4 Conditions that expose a woman to increased risk as a result of unintended pregnancy

Women with conditions that may make unintended pregnancy an unacceptable health risk should be advised that, because of their relatively higher typical-use failure rates, sole use of barrier methods for contraception and behaviour-based methods of contraception may not be the most appropriate choice for them. These conditions are noted in Box 2.1.

Box 2.1 Conditions that expose a woman to increased health risk as a result of unintended pregnancy

- Breast cancer
- Complicated valvular heart disease
- Diabetes: insulin-dependent; or with nephropathy/ retinopathy/neuropathy or other vascular disease; or of > 20 years' duration
- Endometrial or ovarian cancer
- Epilepsy
- High blood pressure (systolic > 160 mm Hg or diastolic > 100 mm Hg)[a]
- HIV (WHO stages 1–4)[b]
- Ischaemic heart disease
- Malignant gestational trophoblastic disease
- Malignant liver tumours (hepatoma) and hepatocellular carcinoma of the liver (HCA)
- Schistosomiasis with fibrosis of the liver
- Severe (decompensated) cirrhosis
- Sickle cell disease
- STI[b]
- Stroke
- Systemic lupus erythematosus (SLE)
- Thrombogenic mutations
- Tuberculosis

a Throughout this document, blood pressure measurements are given in mm Hg. To convert to kPa, multiply by 0.1333 (e.g. 120/80 mm Hg = 16.0/10.7 kPa).

b Dual protection is strongly recommended for protection against HIV/AIDS and other STIs when a risk of STI/HIV transmission exists. This can be achieved through the simultaneous use of condoms with other methods, or the consistent and correct use of condoms alone.

Table 2.1 Percentage of women experiencing an unintended pregnancy during the first year of typical use and the first year of perfect use of contraception and the percentage continuing use at the end of the first year, United States

	% of women experiencing an unintended pregnancy within the first year of use		% of women continuing use at one year[3]
Method	Typical use[1]	Perfect use[2]	
No method[4]	85	85	–
Spermicides[5]	28	18	42
Fertility awareness-based methods	24	–	47
Standard Days Method®[6]	–	5	–
TwoDay Method®[6]	–	4	–
Ovulation Method[6]	–	3	–
Sympto-thermal method	–	0.4	–
Withdrawal	22	4	46
Sponge	–	–	36
Parous women	24	20	–
Nulliparous women	12	9	–
Condom[7]			
Female	21	5	41
Male	18	2	43
Diaphragm[8]	12	6	57
Combined pill and progestin-only pill	9	0.3	67
Evra patch	9	0.3	67
NuvaRing®	9	0.3	67
Depo-Provera	6	0.2	56
Intrauterine devices			
Paragard® (copper T)	0.8	0.6	78
Mirena® (LNG)	0.2	0.2	80
Implanon®	0.05	0.05	84
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100
Emergency contraceptives: Emergency contraceptive pills or insertion of a copper-bearing intrauterine device after unprotected intercourse substantially reduces the risk of pregnancy.[9] **Lactational amenorrhea method**: LAM is a highly effective, temporary method of contraception.[10]			

Source: Trussell J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Nelson AL, Cates W, Kowal D, Policar M, editors. *Contraceptive technology: twentieth revised edition*. New York (NY): Ardent Media; 2011.

Notes:

1 Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. Estimates of the probability of pregnancy during the first year of typical use for spermicides and the diaphragm are taken from the 1995 National Survey of Family Growth corrected for underreporting of abortion; estimates for fertility-awareness-based methods, withdrawal, the male condom, the pill and Depo-Provera are taken from the 1995 and 2002 National Survey of Family Growth corrected for underreporting of abortion. See the text for the derivation of estimates for the other methods (Trussell, 2011).

2 Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. See the text for the derivation of the estimate for each method (Trussell, 2011).

3 Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

4 The percentages becoming pregnant in columns 2 and 3 are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percentage who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

5 Foams, creams, gels, vaginal suppositories and vaginal film.

6 The Ovulation Method and TwoDay Method® are based on evaluation of cervical mucus. The Standard Days Method® avoids intercourse on cycle days 8–19. The sympto-thermal method is a double-check method based on evaluation of cervical mucus to determine the first fertile day and evaluation of cervical mucus and temperature to determine the last fertile day.

7 Without spermicides.

8 With spermicidal cream or jelly.

9 Plan B One-Step®, ella® and Next Choice One Dose® are the only dedicated products specifically marketed for emergency contraception in the United States at the time of writing. The label for Plan B One-Step (one dose is one white pill) says to take the pill within 72 hours after unprotected intercourse. Research has shown that all of the brands listed here are effective when used within 120 hours after unprotected sex. The label for Next Choice One Dose (one dose is one peach pill) says to take one pill within 72 hours after unprotected intercourse. The United States Food and Drug Administration has in addition declared the following 19 brands of oral contraceptives to be safe and effective for emergency contraception: Ogestrel® (one dose is two white pills), Nordette® (one dose is four light-orange pills), Cryselle®, Levora®, Low-Ogestrel®, Lo/Ovral®, or Quasence® (one dose is four white pills), Jolessa®, Portia®, Seasonale® or Trivora® (one dose is four pink pills), Seasonique® (one dose is four light-blue-green pills), Enpresse® (one dose is four orange pills), Lessina® (one dose is five pink pills), Aviane® or LoSeasonique® (one dose is five orange pills), Lutera® or Sronyx® (one dose is five white pills), and Lybrel® (one dose is six yellow pills).

10 However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches 6 months of age.

2.1.5 Return to fertility

Among contraceptive methods, only male and female sterilization are regarded as irreversible (or permanent). All other methods are reversible, usually with prompt return to fertility upon method discontinuation, with the exception of depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN). The median delay in return to fertility with these methods is 10 and 6 months, respectively, from the date of the last injection, regardless of the duration of their use. Male and female sterilization should be regarded as permanent methods (no possibility of future childbearing), and all individuals and couples considering these methods should be counselled accordingly. No other methods result in permanent infertility.

2.1.6 STIs and contraception: dual protection

In addition to the imperative of international norms for contraceptive provision to assure quality of care in services, the social, cultural and behavioural context of each client must also be considered. In this regard, the problems of exposure to STIs, including HIV, deserve special consideration because of the equal importance of preventing pregnancy and preventing transmission of infections among sexually active clients of reproductive age. When a risk of HIV and other STI transmission exists,[8] it is important that health-care providers offer information on safer sexual practices to prevent transmission and strongly recommend dual protection to all persons at significant risk, either through the simultaneous use of condoms with other methods or through the consistent and correct use of condoms alone for prevention of both pregnancy and STIs, including HIV. Women and men seeking contraceptive advice must always be reminded of the importance of condom use for preventing the transmission of STI/HIV and such use should be encouraged and facilitated where appropriate. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

2.2 How to use this document

The present document is intended for use by policy-makers, family planning programme managers and the scientific community. It aims to provide guidance to national family planning and reproductive health programmes in the preparation of guidelines for delivery of contraceptive services. It is not meant to serve as the actual guidelines but rather as a reference.

The guidance in this document is intended for interpretation at country and programme levels in a manner that reflects the diversity of situations and settings in which contraceptives are provided. While it is unlikely that the classification of categories in this document would change during this process, it is very likely that the application of these categories at country level will vary. In particular, the level of clinical knowledge and experience of various types of providers and the resources available at the service-delivery point will have to be taken into consideration.

Recommendations are presented in tables according to the contraceptive methods included in the guidance with each condition. Each condition was defined as representing either a known pre-existing medical/pathological condition (e.g. diabetes, hypertension) or a medically relevant individual characteristic (e.g. age, history of pregnancy).

It is expected that national and institutional health-care and service-delivery environments will decide the most suitable means for screening for conditions according to their public health importance. Client history will often be the most appropriate approach. A family planning provider may want to consult an expert in the underlying condition.

Initiation and continuation

The medical eligibility criteria for the initiation and continuation of all contraceptive methods are used in the evaluation of eligibility. The assessment of continuation criteria is clinically relevant whenever a woman develops the condition while she is using the method. Where medical eligibility for initiation and continuation of a contraceptive method differ, these differences are noted in the columns of the tables for each contraceptive method (I = initiation; C = continuation). Where I and C are not denoted, the category is the same for initiation and continuation of use.

As shown in Table 2.2 in a simplified template of the tables for each contraceptive (provided in section 2.7), the first column indicates the conditions (each in a separate row). Several conditions are subdivided to differentiate between varying degrees of the condition. The second column classifies the condition for initiation and/or continuation into one of the four MEC categories, as described in section 2.3. The third column provides space for any necessary clarifications or presentation of evidence regarding the classification

8 This can be context specific. These may include high prevalence rates of STIs and HIV in the geographic area, and/or individual risk behaviour such as multiple partners without using condoms.

2.3 Using the categories in practice

Categories 1 and 4 are self-explanatory. Classification of a method/condition as Category 2 indicates the method can generally be used, but careful follow-up may be required. However, provision of a method to a woman with a condition classified as Category 3 requires careful clinical judgement and access to clinical services; for such a woman, the severity of the condition and the availability, practicality and acceptability of alternative methods should be taken into account. For a method/condition classified as Category 3, use of that method is not usually recommended unless other more appropriate methods are not available or acceptable. Careful follow-up will be required.

Where resources for clinical judgment are limited, such as in community-based services, the four-category classification framework can be simplified into two categories. With this simplification, a classification of Category 1 or 2 indicate that a woman can use a method, and a classification of Category 3 or 4 indicate that a woman is not medically eligible to use the method (see Table 2.3).

Medical eligibility criteria (MEC) categories for contraceptive use

Category 1	A condition for which there is no restriction for the use of the contraceptive method
Category 2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
Category 3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
Category 4	A condition which represents an unacceptable health risk if the contraceptive method is used

Table 2.2 Template of contraceptive method tables

Type of contraceptive			
Condition	**Category**		**Clarifications/evidence**
	I = initiation	**C = continuation**	
Condition	Condition classified as Category 1, 2, 3 or 4 Different categories are used for fertility awareness-based (FAB) methods and surgical sterilization; these are described at the beginning of the relevant sections.		Clarifications and evidence regarding the classification

Table 2.3 Interpretation and application of the categories in practice

Category	With good resources for clinical judgement	With limited resources for clinical judgement
1	Use method in any circumstances	**Yes** (Use the method)
2	Generally use the method	
3	Use of method not usually recommended unless other more appropriate methods are not available or not acceptable	**No** (Do not use the method)
4	Method not to be used	

2.4 Programmatic implications

The following issues need to be addressed when applying the medical eligibility criteria in this document to programmes:

- informed choice
- elements of quality of care
- essential screening procedures for administering the methods
- provider training and skills
- referral and follow-up for contraceptive use as appropriate.

Service-delivery practices that are essential for the safe use of the particular contraceptive method should be distinguished from practices that may be appropriate for good health care but are not related to use of the method. The promotion of good health-care practices unrelated to safe contraception should be considered neither as a prerequisite nor as an obstacle to the provision of a contraceptive method, but as complementary to it.

As a next step, the recommendations on medical eligibility criteria need to be considered in light of the country context, so as to be applicable to providers at all levels of the service-delivery system. It is expected that national and institutional health-care and service-delivery environments will decide the most suitable means for screening for conditions according to their public health importance. Client history will often be the most appropriate approach. A family planning provider may want to consult an expert in the underlying condition. Countries will need to determine how far and by what means it may be possible to extend their services to the more peripheral levels of the health system. This may involve upgrading both staff and facilities where feasible and affordable, or it may require or a modest addition of equipment and supplies, and redeployment of space. It will also be necessary to address misperceptions sometimes held by providers and users about the risks and side-effects of particular methods, and to look closely at the needs and perspectives of women and men in the context of informed choice.

Adaptation is not always an easy task and is best done by those well acquainted with prevailing health conditions, behaviours and cultures. These improvements must be made within the context of users' informed choices and medical safety.

2.5 Clients with special needs

2.5.1 People with disabilities

According to United Nations Convention on the Rights of Persons with Disabilities (CRPD), people with disabilities must have access, on an equal basis with others, to all forms of sexual and reproductive health care (Article 25) as part of the general right to marry, found a family and retain their fertility (Article 23)[9]. Health-care professionals often fail to offer sexual and reproductive health services to people with disabilities, based on the common misconception that they are not sexually active.[10] Provision of contraceptive services to people with disabilities may, however, require decisions regarding appropriate contraception considering the preferences of the individual, the nature of the disability and the specifics of different contraceptive methods.

For example, some barrier methods may be difficult to use for those with limited manual dexterity; COCs may not be an appropriate method for women with impaired circulation or immobile extremities, even in the absence of known thrombogenic mutations, because of concerns about an increased risk of DVT; and other methods will be preferable for individuals with intellectual or mental health disabilities who have difficulty remembering to take daily medications. For women who have difficulty with menstrual hygiene, the impact of the contraceptive method on menstrual cycles should also be considered.

In all instances, medical decisions must be based upon informed choice, based on adequate sexual and reproductive health education. When the nature of the disability makes it more challenging to discern the will and preferences of the individual, contraceptives should only be provided in a manner consistent with Article 12 of the CRPD. Specifically, in such cases a process of supported decision-making should be instituted in which individuals who are trusted by the individual with disabilities, personal ombudsman and other support persons jointly participate with the individual in reaching a decision that is, to the greatest extent possible, consistent with the will and preference of that individual. Given the history of involuntary sterilization of persons with disabilities, often as

9 United Nations Convention on the Rights of Persons with Disabilities. Resolution adopted by the United Nations General Assembly. United Nations; 2006 (A/RES/61/106; http://www.un-documents.net/a61r106.htm, accessed 24 April 2015).

10 World report on disability 2011. Geneva: World Health Organization; 2011 (http://www.who.int/disabilities/world_report/2011/report/en/, accessed 9 April 2015).

a technique for menstrual management in institutions,[11] it is especially important to ensure that decisions about sterilization are only made with the full, uncoerced and informed consent of the individual, either alone or with support.

2.5.2 Adolescents

Adolescents in many countries lack adequate access to contraceptive information and services that are necessary to protect their sexual and reproductive health. There is an urgent need to implement programmes that both meet the contraceptive needs of adolescents and remove barriers to services. In general, adolescents are eligible to use all the same methods of contraception as adults, and must have access to a variety of contraceptive choices. Age alone does not constitute a medical reason for denying any method to adolescents. While some concerns have been expressed about the use of certain contraceptive methods by adolescents (e.g. the use of progestogen-only injectables by those below 18 years), these concerns must be balanced against the advantages of preventing unintended pregnancy. It is clear that many of the same eligibility criteria that apply to older clients also apply to young people. However, some conditions (e.g. cardiovascular disorders) that may limit the use of some methods in older women do not generally affect young people, since these conditions are rare in this age group.

Political and cultural factors may affect adolescents' ability to access contraceptive information and services. For example, where contraceptive services are available, adolescents (in particular unmarried ones) may not be able to obtain them because of restrictive laws and policies. Even if adolescents are able to obtain contraceptive services, they may not do so because of fear that their confidentiality will not be respected, or that health workers may be judgmental. All adolescents, regardless of marital status, have a right to privacy and confidentiality in health matters, including reproductive health care. Appropriate sexual and reproductive health services, including contraception, should be available and accessible to all adolescents without necessarily requiring parental or guardian authorization by law, policy or practice.

Social and behavioural issues should be key considerations in the choice of contraceptive methods by adolescents. For example, in some settings, adolescents are also at increased risk for STIs, including HIV. While adolescents may choose to use any one of the contraceptive methods available in their communities, in some cases, using methods that do not require a daily regimen may be more convenient. Adolescents, married or unmarried, have also been shown to be less tolerant of side-effects and therefore have high discontinuation rates. Method choice may also be influenced by factors such as sporadic patterns of intercourse and the need to conceal sexual activity and contraceptive use. For instance, sexually active adolescents who are unmarried have very different needs from those who are married and want to postpone, space or limit pregnancy. Expanding the number of method choices offered can lead to improved satisfaction, increased acceptance and increased prevalence of contraceptive use. Proper education and counselling – both before and at the time of method selection – can help adolescents address their particular needs and make informed and voluntary decisions. Every effort should be made to prevent the costs of services and/or methods from limiting the options available.

2.6 Summary of changes within the MEC fifth edition

The following tables highlight changes within the fifth edition of the MEC, compared with the fourth edition (see Tables 2.4–2.6). These changes include: changes to MEC categories between the earlier editions and the fifth edition; recommendations for new conditions issued in the fifth edition; changes to the labelling of certain conditions (in order to be consistent with current clinical practice); and details for the new contraceptive methods included in this fifth edition.

11 *Ibid.*

Table 2.4 Summary of changes from the fourth edition to the fifth edition of the MEC (changes are highlighted in bold)

Condition	COC/P/ CVR	CIC	POP	DMPA NET-EN	LNG/ ETG implants	Cu-IUD		LNG-IUD	
Breastfeeding									
a) < 6 weeks postpartum	4	4	**2**[a]	3[a]	**2**[a]				
b) ≥ 6 weeks to < 6 months (primarily breastfeeding)	3	3	1	1	1				
c) ≥ 6 months postpartum	2	2	1	1	1				
Postpartum (non-breastfeeding women)									
a) < 21 days			1	1	1				
(i) without other risk factors for VTE	3[a]	3[a]							
(ii) with other risk factors for VTE	**4[a]**	**4[a]**							
b) ≥ 21 days to 42 days			1	1	1				
(i) without other risk factors for VTE	2[a]	2[a]							
(ii) with other risk factors for VTE	**3[a]**	**3[a]**							
c) ≥ 42 days	1	1	1	1	1				
Postpartum (breastfeeding or non-breastfeeding women, including after caesarean section)									
a) < 48 hours including insertion immediately after delivery of the placenta						1		**not BF=1; BF=2**	
b) ≥ 48 hours to < 4 weeks						3		3	
c) ≥ 4 weeks						1		1	
d) Puerperal sepsis						4		4	
Superficial venous disorders									
a) Varicose veins	1	1	1	1	1	1		1	
b) Superficial venous thrombosis	2[a]	2[a]	1	1	1	1		1	
Known dyslipidaemias without other known cardiovascular risk factors	**2[a]**	**2[a]**	2[a]	2[a]	2[a]	1[a]		2[a]	
STIs						**I**	**C**	**I**	**C**
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	1	1	4	2[a]	4	2[a]
b) Other STIs (excluding HIV and hepatitis)	1	1	1	1	1	2	2	2	2
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	1	1	2	2	2	2
d) Increased risk of STIs	1	1	1	1	1	**2/3[a]**	2	**2/3[a]**	2

Condition	COC/P/ CVR	CIC	POP	DMPA NET-EN	LNG/ ETG implants	Cu-IUD		LNG-IUD	
HIV/AIDS						I	C	I	C
High risk of HIV	1	1	1	**1[a]**	1	2	2	2	2
Asymptomatic or mild HIV clinical disease (WHO stage 1 or 2)	1[a]	1[a]	1[a]	1[a]	1[a]	2	2	2	2
Severe or advanced HIV clinical disease (WHO stage 3 or 4)	1[a]	1[a]	1[a]	1[a]	1[a]	3	2[a]	3	2[a]
Antiretroviral therapy									
a) Nucleoside reverse transcriptase inhibitors (NRTIs)						I	C	I	C
Abacavir (ABC)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Tenofovir (TDF)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Zidovudine (AZT)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Lamivudine (3TC)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Didanosine (DDI)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Emtricitabine (FTC)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Stavudine (D4T)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)									
Efavirenz (EFV)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Etravirine (ETR)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Nevirapine (NVP)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Rilpivirine (RPV)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
c) Protease inhibitors (PIs)									
Ritonavir-boosted atazanavir (ATV/r)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Ritonavir-boosted lopinavir (LPV/r)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Ritonavir-boosted darunavir (DRV/r)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
Ritonavir (RTV)	**2[a]**	**2[a]**	**2[a]**	**1 = DMPA; 2 = NET-EN[a]**	**2[a]**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**
d) Integrase inhibitors									
Raltegravir (RAL)	**1**	**1**	**1**	**1**	**1**	**2/3[a]**	**2[a]**	**2/3[a]**	**2[a]**

BMI: body mass index; **COC**: combined oral contraceptives; **CIC**: combined injectable contraceptives; **CVR**: combined contraceptive vaginal ring; **Cu-IUD**: copper-bearing IUD; **DMPA**: depomedroxyprogesterone acetate (intramuscular and sub-cutaneous) injectable; **ETG**: etonogestrel; **LNG**: levonorgestrel; **LNG-IUD**: levonorgestrel-releasing intrauterine device; **NET-EN**: norethisterone enanthate injectable contraceptive; **P**: combined patch; **POP**: progestogen-only pills; **STI**: sexually transmitted infection; **VTE**: venous thromboembolism.

[a] Please consult the relevant table for each contraceptive method in section 2.7 for a clarification to this classification.

Table 2.5 Emergency contraceptive pills (ECPs) (changes are highlighted in bold)

Condition	COC	LNG	UPA
Pregnancy	NA[a]	NA[a]	**NA[a]**
Breastfeeding	1	1	**2[a]**
Past ectopic pregnancy	1	1	**1**
Obesity	**1[a]**	**1[a]**	**1[a]**
History of severe cardiovascular disease (ischaemic heart disease, cerebrovascular attack, or other thromboembolic conditions)	2	2	**2**
Migraine	2	2	**2**
Severe liver disease (including jaundice)	2	2	**2**
CYP3A4 inducers (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, efavirenz, fosphenytoin, nevirapine, oxcarbazepine, primidone, rifabutin, St John's wort/Hypericum perforatum)	**1[a]**	**1[a]**	**1[a]**
Repeated ECP use	1[a]	1[a]	**1[a]**
Rape	1	1	**1**

COC: combined oral contraceptives; CYP3A4: cytochrome P450 3A4 enzyme; LNG: levonorgestrel; UPA: ulipristal acetate.

a Please consult the relevant table for each contraceptive method in section 2.7 for a clarification to this classification.

Table 2.6 Progesterone-releasing vaginal ring (PVR) (changes are highlighted in bold)

Condition	Category
Pregnancy	**NA**
Breastfeeding and ≥ 4 weeks postpartum	**1**

2.7 Tables

2.7.1 Combined hormonal contraceptives (CHCs)

COMBINED ORAL CONTRACEPTIVES (COCs)

The recommendations in this guidance refer to low-dose COCs containing ≤ 35 mcg ethinyl estradiol combined with a progestogen.

Venous thrombosis is rare among women of reproductive age. All COCs are associated with an increased risk for venous thromboembolism (VTE) compared to non-use. A number of studies have found differences in risk for VTE associated with COCs containing different types of progestogens *(1–19)*. Current evidence suggests that COCs containing levonorgestrel, norethisterone and norgestimate are associated with the lowest risk *(20)*. The absolute differences, however, are very small.

Limited data do not suggest that the small absolute risk for arterial events associated with COC use varies according to the type of progestogen *(5, 6, 20–34)*.

Recommendations in this guidance are the same for all COC formulations, irrespective of their progestogen content.

COMBINED INJECTABLE CONTRACEPTIVES (CICs)

Two CIC formulations, are considered here:

1. Cyclofem = medroxyprogesterone acetate 25 mg plus estradiol cypionate 5 mg
2. Mesigyna = norethisterone enanthate 50 mg plus estradiol valerate 5 mg

CICs contain the naturally occurring estrogen, estradiol plus a progestogen *(35–39)*. Estradiol is less potent, has a shorter duration of effect and is more rapidly metabolized than the synthetic estrogens used in other contraceptive formulations such as COCs, the combined contraceptive patch (P) and the combined contraceptive vaginal ring (CVR). These differences imply that the type and magnitude of estrogen-related side-effects associated with CICs may be different from those experienced by COC/P/CVR users. In fact, short-term studies of CICs have shown little effect on blood pressure, haemostasis and coagulation, lipid metabolism and liver function in comparison with COCs *(40–42)*. As CICs are administered by injection, the first-pass metabolism by the liver is avoided, thereby minimizing estradiol's effect on the liver.

However, CICs are a relatively new contraceptive method, and there are few epidemiological data on their long-term effects. There is also the concern that, while the effect of the hormonal exposure associated with use of COCs and progestogen-only pills (POPs) can be reduced immediately by discontinuing their use, this is not the case with injectables, for which the effect continues for some time after the last injection.

Pending further evidence, the Guideline Development Group (GDG) concluded that the evidence available for COCs applies to CICs in many but not all instances. Therefore, the GDG assigned categories for CICs somewhere between the categories for COCs and POPs. However, for severe pathologies (e.g. ischaemic heart disease), the classification of conditions was the same as for COCs. The assigned categories should, therefore, be considered a preliminary, best judgement, which will be re-evaluated as new data become available.

COMBINED CONTRACEPTIVE PATCH (P) AND COMBINED CONTRACEPTIVE VAGINAL RING (CVR)

The combined contraceptive patch (P) and combined vaginal ring (CVR) are relatively new contraceptive methods. Limited information is available on the safety of these methods among women with specific medical conditions. Moreover, epidemiological data on the long-term effects of P and CVR use were not available for the GDG to review. Most of the available studies received support from the manufacturers of these methods.

According to available evidence, the P provides a comparable safety and pharmacokinetic profile to COCs with similar hormone formulations *(43–60)*. Reports of transient, short-term breast discomfort and skin-site reactions were greater among P users; however, less than 25% of users experienced these events *(45, 49, 50, 56–58, 61)*. Limited evidence suggests the effectiveness of the P may decline for women weighing 90 kg or more *(58, 60)*.

According to available evidence, the CVR provides a comparable safety and pharmacokinetic profile and has similar effects on ovarian function to COCs with similar hormone formulations in healthy women *(61–75)*. Evidence from use in obese women (BMI ≥ 30 kg/m^2) found that weight gain for women in this category was not different between CVR users and COC users *(76)*. Limited evidence from use in women post medical and surgical abortion found no serious adverse events and no infection related to use during three cycles of follow-up post-abortion *(77)*, and limited evidence on women with low-grade squamous intraepithelial lesions found that use of the vaginal ring did not worsen the condition *(64)*.

Pending further evidence, the GDG concluded that the evidence available for COCs applies to the combined contraceptive P and CVR, and therefore the P and CVR should have the same categories as COCs. The assigned categories should, therefore, be considered a preliminary, best judgement, which will be re-evaluated as new data become available.

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY					
PREGNANCY	NA	NA	NA	NA	NA = not applicable **Clarification**: Use of COCs, P, CVR or CICs is not required. There is no known harm to the woman, the course of her pregnancy, or the fetus if COCs, P, CVR or CICs are accidentally used during pregnancy.
AGE†* a) Menarche to < 40 years b) ≥ 40 years	 1 2	 1 2	 1 2	 1 2	**Evidence**: Evidence about whether CHC use affects fracture risk is inconsistent *(78–89)*, although 3 recent studies show no effect *(90–92)*. CHC use may decrease bone mineral density (BMD) in adolescents, especially in those choosing very low dose formulations (< 30 µg ethinyl estradiol-containing COCs) *(91, 93–105)*. CHC use has little to no effect on BMD in premenopausal women *(90, 93–102, 106–109)*, and may preserve bone mass in those who are perimenopausal *(103, 104, 110–117)*. BMD is a surrogate marker for fracture risk that may not be valid for premenopausal women, and which, therefore, may not accurately predict current or future (postmenopausal) fracture risk *(118–120)*.
PARITY a) Nulliparous b) Parous	 1 1	 1 1	 1 1	 1 1	

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CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
BREASTFEEDING †					**Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported *(121–126)*. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to combined contraceptives through breast-milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk of either serious or subtle long-term effects exists.
a) < 6 weeks postpartum	4	4	4	4	
b) ≥ 6 weeks to < 6 months postpartum (primarily breastfeeding)	3	3	3	3	
c) ≥ 6 months postpartum	2	2	2	2	
POSTPARTUM (IN NON-BREASTFEEDING WOMEN) †					
Although the risk of venous thromboembolism (VTE) is the same in breastfeeding and non-breastfeeding women, use of CHCs is generally not recommended prior to 6 months postpartum in women who are breastfeeding.					
a) < 21 days					**Clarification:** For women up to 6 weeks postpartum with other risk factors for VTE, such as immobility, transfusion at delivery, BMI > 30 kg/m^2, postpartum haemorrhage, immediately post-caesarean delivery, pre-eclampsia or smoking, use of CHCs may pose an additional increased risk for VTE. **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with non-users at all time points postpartum. Rates were significantly different only after 13 weeks postpartum, but the numbers needed to harm were lowest in the first 6 weeks postpartum (132). VTE risk is elevated during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, declining to near baseline levels by 42 days postpartum (127-131).
i) without other risk factors for VTE	3	3	3	3	
ii) with other risk factors for VTE	4	4	4	4	
b) ≥ 21 days to 42 days					
i) without other risk factors for VTE	2	2	2	2	
ii) with other risk factors for VTE	3	3	3	3	
c) > 42 days	1	1	1	1	

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
POST-ABORTION					**Clarification**: COCs, P, CVR or CICs may be started immediately post-abortion. **Evidence**: Women who started taking COCs immediately after first-trimester medical or surgical abortion did not experience more side-effects or adverse vaginal bleeding outcomes or clinically significant changes in coagulation parameters compared with women who used a placebo, an IUD, a non-hormonal contraceptive method, or delayed COC initiation *(134–141)*. Limited evidence on women using the CVR immediately after first-trimester medical or surgical abortion indicated no serious adverse events and no infection related to CVR use during 3 cycles of follow-up post-abortion *(77)*.
a) First trimester	1	1	1	1	
b) Second trimester	1	1	1	1	
c) Immediate post-septic abortion	1	1	1	1	
PAST ECTOPIC PREGNANCY*	1	1	1	1	
HISTORY OF PELVIC SURGERY	1	1	1	1	
SMOKING					**Evidence**: COC users who smoked were at increased risk of cardiovascular diseases, especially myocardial infarction (MI), compared with those who did not smoke. Studies also showed an increased risk of MI with increasing number of cigarettes smoked per day *(30, 31, 142–151)*.
a) Age < 35 years	2	2	2	2	
b) Age ≥ 35 years					
i) < 15 cigarettes/day	3	3	3	2	
ii) ≥ 15 cigarettes/day	4	4	4	3	

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
OBESITY					**Evidence:** Obese women who use COCs are more likely to experience VTE than obese women who do not use COCs. The absolute risk of VTE in healthy women of reproductive age is small. Limited evidence suggests that obese women who use COCs do not have a higher risk of acute MI or stroke than obese non-users *(146, 147, 151–156)*. Limited evidence suggests obese women are no more likely to gain weight after 3 cycles of using CVR or COCs than overweight or normal-weight women. A similar weight gain during 3 months was noted in both the COC group and the CVR group across all BMI categories *(76)*. Overall, evidence suggests that contraceptive effectiveness is maintained among obese CHC users *(157–172)*; however, among women with very high BMI using COC, evidence is inconsistent *(161, 167, 171)*. No association was found between pregnancy risk and BMI among P users *(161, 167, 171)*. The effectiveness of the patch decreased among women who weighed > 90 kg in 1 study *(172)*.
a) ≥ 30 kg/m^2 BMI	2	2	2	2	
b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	2	2	2	2	
BLOOD PRESSURE MEASUREMENT UNAVAILABLE	NA	NA	NA	NA	NA = not applicable **Clarification**: It is desirable to have blood pressure measurements taken before initiation of COC, P, CVR or CIC use. However, in some settings, blood pressure measurements are unavailable. In many of these settings, pregnancy-related morbidity and mortality risks are high, and COCs, P, CVR or CICs may be among the few methods widely available. In such settings, women should not be denied use of COCs, P, CVR or CICs simply because their blood pressure cannot be measured.

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

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CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
CARDIOVASCULAR DISEASE					
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (e.g. older age, smoking, diabetes, hypertension and known dyslipidaemias)	3/4	3/4	3/4	3/4	**Clarification**: When a woman has multiple major risk factors, any of which alone would substantially increase the risk of cardiovascular disease, use of COCs, P, CVR or CICs may increase her risk to an unacceptable level. However, a simple addition of categories for multiple risk factors is not intended; for example, a combination of 2 risk factors assigned a Category 2 may not necessarily warrant a higher category.
HYPERTENSION For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, the risk of cardiovascular disease may increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive.					
a) History of hypertension, where blood pressure CANNOT be evaluated (including hypertension in pregnancy)	3	3	3	3	**Clarification**: Evaluation of cause and level of hypertension is recommended, as soon as feasible. **Evidence**: Women who did not have a blood pressure check before initiation of COC use had an increased risk of acute MI and stroke *(26, 32, 33, 173, 174)*.
b) Adequately controlled hypertension, where blood pressure CAN be evaluated	3	3	3	3	**Clarification**: Women adequately treated for hypertension are at reduced risk of acute MI and stroke as compared with untreated women. Although there are no data, COC, P, CVR or CIC users with adequately controlled and monitored hypertension should be at reduced risk of acute MI and stroke compared with untreated hypertensive COC, P, CVR or CIC users.
c) Elevated blood pressure levels (properly taken measurements)					**Evidence**: Among women with hypertension, COC users were at increased risk of stroke, acute MI, and peripheral arterial disease compared with non-users *(14, 26, 31, 33, 142, 144, 150, 151, 173–185)*. Discontinuation of COCs in women with hypertension may improve blood pressure control *(186)*.
i) systolic 140–159 or diastolic 90–99 mm Hg	3	3	3	3	
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	4	4	4	4	
d) Vascular disease	4	4	4	4	

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

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CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	2	2	2	2	**Evidence**: Women using COCs who had a history of high blood pressure in pregnancy had an increased risk of MI and VTE, compared with COC users who did not have a history of high blood pressure during pregnancy. The absolute risks of acute MI and VTE in this population remained small *(32, 33, 151, 174, 176, 187–192)*.
DEEP VEIN THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)*					
a) History of DVT/PE	4	4	4	4	
b) Acute DVT/PE	4	4	4	4	
c) DVT/PE and established on anticoagulant therapy	4	4	4	4	
d) Family history (first-degree relatives)	2	2	2	2	
e) Major surgery					
i) with prolonged immobilization	4	4	4	4	
ii) without prolonged immobilization	2	2	2	2	
f) Minor surgery without immobilization	1	1	1	1	
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	4	4	4	4	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening. **Evidence**: Among women with thrombogenic mutations, COC users had a 2- to 20-fold higher risk of thrombosis than non-users *(3, 155, 193–214)*.

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

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CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
SUPERFICIAL VENOUS DISORDERS†					
a) Varicose veins	1	1	1	1	**Evidence**: One study suggested that among women with varicose veins, the rate of VTE and superficial venous thrombosis (SVT) was higher in oral contraceptive users compared with non-users; however, statistical significance was not reported and the number of events was small *(215)*.
b) Superficial venous thrombosis (SVT)	2	2	2	2	**Clarification**: SVT may be associated with an increased risk of VTE. **Evidence**: One study demonstrated that among women with SVT, the risk of VTE was higher in oral contraceptive users compared with non-users *(216)*.
CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE	4	4	4	4	
STROKE (history of cerebrovascular accident)	4	4	4	4	

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS †	2	2	2	2	**Clarification**: Routine screening is not appropriate because of the rarity of the condition and the high cost of screening. Increased levels of total cholesterol, low-density lipoprotein (LDL) and triglycerides, as well as a decreased level of high-density lipoprotein (HDL), are known risk factors for cardiovascular disease. Women with known severe genetic lipid disorders are at much higher lifetime risk for cardiovascular disease and may warrant further clinical consideration. **Evidence**: Limited evidence on use of CHCs among women with dyslipidaemia and risk of cardiovascular outcomes provided inconsistent results. One study suggested an increased risk for MI among COC users with hypercholesterolaemia compared to non-users without hypercholesterolaemia *(217)*; 1 study suggested an increased risk for VTE and for stroke among COC users with dyslipidaemia compared to COC users without dyslipidaemia *(22)*; and 1 study suggested no worsening of lipid abnormalities among CHC users with dyslipidaemia compared to non-users with dyslipidaemia *(218)*. No evidence of risk for pancreatitis was identified.
VALVULAR HEART DISEASE*					
a) Uncomplicated	2	2	2	2	
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	4	4	4	4	

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

CHCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation				CLARIFICATIONS/EVIDENCE
	COC	P	CVR	CIC	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**COC** = combined oral contraceptive **P** = combined contraceptive patch **CVR** = combined contraceptive vaginal ring **CIC** = combined injectable contraceptive				
RHEUMATIC DISEASES					
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) People with SLE are at increased risk of ischaemic heart disease, stroke and venous thromboembolism (VTE). Categories assigned to such conditions in the *Medical eligibility criteria for contraceptive use* should be the same for women with SLE who present with these conditions. For all categories of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Available evidence indicates that many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives *(219–236)*.					
a) Positive (or unknown) antiphospholipid antibodies	4	4	4	4	**Evidence**: Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis *(237–239)*.
b) Severe thrombocytopenia	2	2	2	2	
c) Immunosuppressive treatment	2	2	2	2	
d) None of the above	2	2	2	2	
NEUROLOGIC CONDITIONS					

HEADACHES*	COC I	COC C	P I	P C	CVR I	CVR C	CIC I	CIC C	
a) Non-migrainous (mild or severe)	1	2	1	2	1	2	1	2	**Clarification**: Classification depends on accurate diagnosis of those severe headaches that are migrainous and those that are not. Any new headaches or marked changes in headaches should be evaluated. Classification is for women without any other risk factors for stroke. Risk of stroke increases with age, hypertension and smoking. **Evidence**: Among women with migraine, women who also had aura had a higher risk of stroke than those without aura *(240–242)*. Women with a history of migraine who use COCs are about 2–4 times as likely to have an ischaemic stroke as non-users with a history of migraine *(142, 154, 181, 182, 240–246)*.
b) Migraine									
i) without aura									
age < 35 years	2	3	2	3	2	3	2	3	
age ≥ 35 years	3	4	3	4	3	4	3	4	
ii) with aura, at any age	4	4	4	4	4	4	4	4	
EPILEPSY	1		1		1		1		**Clarification**: If a woman is taking anticonvulsants, refer to the last section of this table, on drug interactions. Certain anticonvulsants lower COC effectiveness. The extent to which P, CVR or CIC use is similar to COC use in this regard remains unclear.

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

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	COC	P	CVR	CIC	
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DEPRESSIVE DISORDERS					
DEPRESSIVE DISORDERS	1	1	1	1	**Clarification**: The classification is based on data for women with selected depressive disorders. No data on bipolar disorder or postpartum depression were available. There is a potential for drug interactions between certain antidepressant medications and hormonal contraceptives. **Evidence**: COC use did not increase depressive symptoms in women with depression compared to baseline or to non-users with depression *(247–256)*.
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS					
VAGINAL BLEEDING PATTERNS*					
a) Irregular pattern without heavy bleeding	1	1	1	1	
b) Heavy or prolonged bleeding (includes regular and irregular patterns)	1	1	1	1	**Clarification**: Unusually heavy bleeding should raise the suspicion of a serious underlying condition. **Evidence**: A Cochrane Collaboration review identified 1 randomized controlled trial evaluating the effectiveness of COC use compared with naproxen and danazol in treating menorrhagic women. Women with menorrhagia did not report worsening of the condition or any adverse events related to COC use *(257)*.
UNEXPLAINED VAGINAL BLEEDING* (suspicious for serious condition)					
a) Before evaluation	2	2	2	2	**Clarification**: If pregnancy or an underlying pathological condition (such as pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation.

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ENDOMETRIOSIS	1	1	1	1	**Evidence**: A Cochrane review identified 1 randomized controlled trial evaluating the effectiveness of COC use compared with a gonadotropin-releasing hormone (GnRH) analogue in treating the symptoms of endometriosis. Women with endometriosis did not report worsening of the condition or any adverse events related to COC use *(258)*.
BENIGN OVARIAN TUMOURS (INCLUDING CYSTS)	1	1	1	1	
SEVERE DYSMENORRHOEA	1	1	1	1	**Evidence**: There was no increased risk of side-effects with COC use among women with dysmenorrhoea compared with women not using COCs. Some COC users had a reduction in pain and bleeding *(259, 260)*.
GESTATIONAL TROPHOBLASTIC DISEASE					**Evidence**: Following molar pregnancy evacuation, the balance of evidence found COC use did not increase the risk of post-molar trophoblastic disease, and some COC users experienced a more rapid regression in human chorionic gonadotropin (hCG) levels, compared with non-users *(261–268)*. Limited evidence suggests that use of COCs during chemotherapeutic treatment does not significantly affect the regression or treatment of post-molar trophoblastic disease compared with women who used a non-hormonal contraceptive method or depot medroxyprogesterone acetate (DMPA) during chemotherapeutic treatment *(269)*.
a) Decreasing or undetectable β-hCG levels	1	1	1	1	
b) Persistently elevated β-hCG levels or malignant disease	1	1	1	1	
CERVICAL ECTROPION*	1	1	1	1	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)	2	2	2	2	**Evidence**: Among women with persistent human papillomavirus (HPV) infection, long-term COC use (≥ 5 years) may increase the risk of carcinoma in situ and invasive carcinoma *(64, 270)*. Limited evidence on women with low-grade squamous intraepithelial lesions found use of the vaginal ring did not worsen the condition *(64)*.

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CERVICAL CANCER* (AWAITING TREATMENT)	2	2	2	2	
BREAST DISEASE*					
a) Undiagnosed mass	2	2	2	2	**Clarification**: Evaluation should be pursued as early as possible.
b) Benign breast disease	1	1	1	1	
c) Family history of cancer	1	1	1	1	**Evidence**: Women with breast cancer susceptibility genes (such as *BRCA1* and *BRCA2*) have a higher baseline risk of breast cancer than women without these genes. The baseline risk of breast cancer is also higher among women with a family history of breast cancer than among those who do not have such a history. Current evidence, however, does not suggest that the increased risk of breast cancer among women with either a family history of breast cancer or breast cancer susceptibility genes is modified by the use of combined oral contraceptives *(175, 271–293)*.
d) Breast cancer					
i) current	4	4	4	4	
ii) past and no evidence of current disease for 5 years	3	3	3	3	
ENDOMETRIAL CANCER*	1	1	1	1	
OVARIAN CANCER*	1	1	1	1	
UTERINE FIBROIDS*					
a) Without distortion of the uterine cavity	1	1	1	1	
b) With distortion of the uterine cavity	1	1	1	1	

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PELVIC INFLAMMATORY DISEASE (PID)*					
a) Past PID (assuming no current risk factors for STIs)					
i) with subsequent pregnancy	1	1	1	1	
ii) without subsequent pregnancy	1	1	1	1	
b) PID – current	1	1	1	1	
STIs					
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	1	
b) Other STIs (excluding HIV and hepatitis)	1	1	1	1	
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	1	
d) Increased risk of STIs	1	1	1	1	**Evidence**: Evidence suggests that there may be an increased risk of chlamydial cervicitis among COC users at high risk of STIs. For other STIs, there is either evidence of no association between COC use and STI acquisition or too limited evidence to draw any conclusions *(289–369)*.
HIV/AIDS†					
High risk of HIV	1	1	1	1	**Evidence**: Eight studies assessed the use of COCs and were considered to be "informative but with important limitations" *(370)*. Seven of these studies found no statistically significant association between use of COCs and HIV acquisition *(371–378)*, although 1 study among sex workers in Kenya did *(379)*.

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Asymptomatic or mild HIV clinical disease (WHO stage 1 or 2)	1	1	1	1	**Clarification** for asymptomatic or mild HIV disease (WHO stage 1 or 2) and severe or advanced HIV disease (WHO stage 3 or 4): Because there may be drug interactions between hormonal contraceptives and ARV therapy, refer to the last section of this table, on drug interactions. **Evidence** for asymptomatic or mild HIV disease (WHO stage 1 or 2) and severe or advanced HIV disease (WHO stage 3 or 4): Out of 8 available studies, 7 suggested no association between use of COCs and progression of HIV, as measured by CD4 count < 200 cells/mm3, initiation of antiretroviral therapy (ART), or mortality *(380–386)*. One randomized controlled trial found an increased risk of a composite outcome of declining CD4 count or death among COC users when compared with users of copper-bearing IUDs *(387, 388)*. Two prospective observational studies directly assessed the effects of different hormonal contraceptive methods on female-to-male HIV transmission by measuring seroconversions in male partners of women known to be using hormonal contraceptives. One of these studies reported an elevated, but not statistically significant, point estimate for COCs *(378)*. The other study also did not find a statistically significant association for COCs *(389)*. Studies indirectly assessing the effect of various hormonal contraceptive methods on female-to-male HIV transmission by measuring genital viral shedding as a proxy for infectivity have had mixed results. The majority of indirect studies measuring whether various hormonal contraceptive methods affect plasma HIV viral load have found no effect *(381, 390–404)*.
Severe or advanced HIV clinical disease (WHO stage 3 or 4)	1	1	1	1	

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OTHER INFECTIONS					
SCHISTOSOMIASIS					
a) Uncomplicated	1	1	1	1	**Evidence**: Among women with uncomplicated schistosomiasis, COC use had no adverse effects on liver function *(405–411)*.
b) Fibrosis of the liver (if severe, see cirrhosis)	1	1	1	1	
TUBERCULOSIS					
a) Non-pelvic	1	1	1	1	**Clarification**: If a woman is taking rifampicin, refer to the last section of this table, on drug interactions. Rifampicin is likely to decrease COC effectiveness. The extent to which P or CVR use is similar to COC use in this regard remains unclear.
b) Pelvic	1	1	1	1	
MALARIA	1	1	1	1	
ENDOCRINE CONDITIONS					
DIABETES					
a) History of gestational disease	1	1	1	1	**Evidence**: The development of non-insulin-dependent diabetes in women with a history of gestational diabetes is not increased by the use of COCs *(412–419)*. Likewise, lipid levels appear to be unaffected by COC use *(420–422)*.
b) Non-vascular disease					**Evidence**: Among women with insulin- or non-insulin-dependent diabetes, COC use had limited effect on daily insulin requirements and no effect on long-term diabetes control (e.g. haemoglobin A1c levels) or progression to retinopathy. Changes in lipid profile and haemostatic markers were limited, and most changes remained within normal values *(419, 422–430)*.
i) non-insulin dependent	2	2	2	2	
ii) insulin dependent	2	2	2	2	
c) Nephropathy/retinopathy/ neuropathy	3/4	3/4	3/4	3/4	**Clarification**: The category should be assessed according to the severity of the condition.
d) Other vascular disease or diabetes of > 20 years' duration	3/4	3/4	3/4	3/4	**Clarification**: The category should be assessed according to the severity of the condition.

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THYROID DISORDERS					
a) Simple goitre	1	1	1	1	
b) Hyperthyroid	1	1	1	1	
c) Hypothyroid	1	1	1	1	
GASTROINTESTINAL CONDITIONS					
GALL BLADDER DISEASE*					
a) Symptomatic					
i) treated by cholecystectomy	2	2	2	2	
ii) medically treated	3	3	3	2	
iii) current	3	3	3	2	
b) Asymptomatic	2	2	2	2	
HISTORY OF CHOLESTASIS*					
a) Pregnancy related	2	2	2	2	
b) Past-COC related	3	3	3	2	

VIRAL HEPATITIS	I	C	I	C	I	C	I	C	
a) Acute or flare	3/4	2	3/4	2	3/4	2	3	2	**Clarification**: The category should be assessed according to the severity of the condition.
b) Carrier	1	1	1	1	1	1	1	1	**Evidence**: Data suggest that in women with chronic hepatitis, COC use does not increase the rate or severity of cirrhotic fibrosis, nor does it increase the risk of hepatocellular carcinoma *(431, 432)*. For women who are carriers, COC use does not appear to trigger liver failure or severe dysfunction *(408, 433, 434)*. Evidence is limited for COC use during active hepatitis *(435, 436)*.
c) Chronic	1	1	1	1	1	1	1	1	

CIRRHOSIS					
a) Mild (compensated)	1	1	1	1	
b) Severe (decompensated)	4	4	4	3	

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LIVER TUMOURS*					
a) Benign					
i) focal nodular hyperplasia	2	2	2	2	**Evidence**: There is limited, direct evidence that hormonal contraceptive use does not influence either progression or regression of liver lesions among women with focal nodular hyperplasia *(437–439)*.
ii) hepatocellular adenoma	4	4	4	3	
b) Malignant (hepatoma)	4	4	4	3/4	
ANAEMIAS					
THALASSAEMIA*	1	1	1	1	
SICKLE CELL DISEASE	2	2	2	2	
IRON-DEFICIENCY ANAEMIA*	1	1	1	1	
DRUG INTERACTIONS					
ANTIRETROVIRAL THERAPY (ART) †					
a) Nucleoside reverse transcriptase inhibitors (NRTIs)					**Evidence**: NRTIs do not appear to have significant risk of interactions with hormonal contraceptive methods *(440, 441)*.
Abacavir (ABC)	1	1	1	1	
Tenofovir (TDF)	1	1	1	1	
Zidovudine (AZT)	1	1	1	1	
Lamivudine (3TC)	1	1	1	1	
Didanosine (DDI)	1	1	1	1	
Emtricitabine (FTC)	1	1	1	1	
Stavudine (D4T)	1	1	1	1	

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b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)					**Clarification**: Antiretroviral drugs have the potential to either decrease or increase the levels of steroid hormones in women using hormonal contraceptives. Pharmacokinetic data suggest potential drug interactions between some antiretroviral drugs (particularly some NNRTIs and ritonavir-boosted PIs) and some hormonal contraceptives. These interactions may reduce the effectiveness of the hormonal contraceptive. **Evidence**: Three clinical studies, including 1 large study, found use of nevirapine-containing ART did not increase ovulation or pregnancy rates in women taking COCs *(442–445)*. For efavirenz-containing ART, a pharmacokinetic study showed consistent significant decreases in contraceptive hormone levels in women taking COCs, and a small clinical study showed higher ovulation rates in women taking efavirenz-containing ART and COCs *(445–447)*. Etravirine and rilpivirine do not interact with COCs *(448, 449)*.
Efavirenz (EFV)	2	2	2	2	
Etravirine (ETR)	1	1	1	1	
Nevirapine (NVP)	2	2	2	2	
Rilpivirine (RPV)	1	1	1	1	
c) Protease inhibitors (PIs)					**Evidence**: Pharmacokinetic data suggest decreases in COC progestin levels with ritonavir and ritonavir-boosted PIs. In women using the patch, co-administration resulted in higher progestin levels *(452)*.
Ritonavir-boosted atazanavir (ATV/r)	2	2	2	2	
Ritonavir-boosted lopinavir (LPV/r)	2	2	2	2	
Ritonavir-boosted darunavir (DRV/r)	2	2	2	2	
Ritonavir (RTV)	2	2	2	2	
d) Integrase inhibitors					**Evidence**: The integrase inhibitor raltegravir does not appear to interact with COCs *(440, 441, 454, 455)*.
Raltegravir (RAL)	1	1	1	1	

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ANTICONVULSANT THERAPY					
a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	3	3	3	2	**Clarification**: Although the interaction of certain anticonvulsants with COCs, P or CVR is not harmful to women, it is likely to reduce the effectiveness of COCs, P or CVR. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. When a COC is chosen, a preparation containing a minimum of 30 µg of ethinyl estradiol (EE) should be used. **Evidence**: Use of certain anticonvulsants may decrease the effectiveness of COCs *(456–459)*.
b) Lamotrigine	3	3	3	3	**Clarification**: The recommendation for lamotrigine does not apply when lamotrigine is already being taken with other drugs that strongly inhibit (such as sodium valproate) or induce (such as carbamazepine) its metabolism, since, in these cases, the moderate effect of the combined contraceptive is unlikely to be apparent. **Evidence**: Pharmacokinetic studies show levels of lamotrigine decrease significantly during COC use and increase significantly during the pill-free interval *(460–464)*. Some women who used both COCs and lamotrigine experienced increased seizure activity in 1 trial *(464)*.
ANTIMICROBIAL THERAPY					
a) Broad-spectrum antibiotics	1	1	1	1	**Evidence**: Most broad-spectrum antibiotics do not affect the contraceptive effectiveness of COCs *(465–501)*, P *(502)*, or CVR *(503)*.
b) Antifungals	1	1	1	1	**Evidence**: Studies of antifungal agents have shown no clinically significant pharmacokinetic interactions with COCs *(504–513)* or CVR *(514)*.
c) Antiparasitics	1	1	1	1	**Evidence**: Studies of antiparasitic agents have shown no clinically significant pharmacokinetic interactions with COCs *(411, 515–519)*.

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d) Rifampicin or rifabutin therapy	3	3	3	2	**Clarification**: Although the interaction of rifampicin or rifabutin therapy with COCs, P, CVR or CICs is not harmful to women, it is likely to reduce the effectiveness of COCs, P, CVR or CICs. Use of other contraceptives should be encouraged for women who are long-term users of either of these drugs. When a COC is chosen, a preparation containing a minimum of 30 µg EE should be used. **Evidence**: The balance of the evidence suggests that rifampicin reduces the effectiveness of COCs *(520–535)*. Data on rifabutin are limited, but effects on metabolism of COCs are less than with rifampicin, and small studies have not shown evidence of ovulation *(363, 522, 535)*.

RECOMMENDATIONS REVIEWED FOR FIFTH EDITION

These recommendations were reviewed according to WHO requirements for guideline development, as part of the preparation of the *Medical eligibility criteria for contraceptive use, fifth edition*. The Population, Intervention, Comparator, Outcome (PICO) questions developed by the Guideline Development Group (GDG) and the databases searched to retrieve the evidence, which guided the preparation of systematic reviews, are described in greater detail in Part I of this document. Additionally, GRADE evidence profiles, the overall GRADE assessment of the quality of the evidence, summaries of the evidence supporting the recommendation(s), and other supplementary remarks from the GDG regarding the recommendations, are available in Part I.

ADDITONAL COMMENTS

AGE

Age ≥ 40 years: The risk of cardiovascular disease increases with age and may also increase with combined hormonal contraceptive (CHC) use. In the absence of other adverse clinical conditions, CHCs can be used until menopause.

PAST ECTOPIC PREGNANCY

The risk of future ectopic pregnancy is increased in these women. CHCs provide protection against pregnancy in general, including ectopic gestation.

DEEP VEIN THROMBOSIS/PULMONARY EMBOLISM

Family history of DVT/PE (first-degree relatives): Some conditions which increase the risk of DVT/PE are heritable.

VALVULAR HEART DISEASE

Among women with valvular heart disease, CHC use may further increase the risk of arterial thrombosis; women with complicated valvular heart disease are at greatest risk.

HEADACHES

Aura is a specific focal neurologic symptom. For more information on this and other diagnostic criteria, see: Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. Cephalalgia. 2004;24(Suppl 1):1–150.[12]

VAGINAL BLEEDING PATTERNS

Irregular menstrual bleeding patterns are common among healthy women.

UNEXPLAINED VAGINAL BLEEDING

There are no conditions that cause vaginal bleeding that will be worsened in the short term by use of CHCs.

CERVICAL ECTROPION

Cervical ectropion is not a risk factor for cervical cancer, and there is no need for restriction of CHC use.

CERVICAL CANCER (AWAITING TREATMENT)

There is some theoretical concern that CHC use may affect prognosis of the existing disease. While awaiting treatment, women may use CHCs. In general, treatment of this condition renders a woman sterile.

BREAST DISEASE

Breast cancer: Breast cancer is a hormonally sensitive tumour, and the prognosis of women with current or recent breast cancer may worsen with CHC use.

ENDOMETRIAL CANCER

COC use reduces the risk of developing endometrial cancer.

Awaiting treatment: Women may use COCs, CICs, P or CVR. In general, treatment of this condition renders a woman sterile.

OVARIAN CANCER

COC use reduces the risk of developing ovarian cancer.

Awaiting treatment: Women may use COCs, CICs, P or CVR. In general, treatment of this condition renders a woman sterile.

UTERINE FIBROIDS

COCs do not appear to cause growth of uterine fibroids, and CICs, P and CVR are not expected to either.

12 Available at: http://ihs-classification.org/en/02_klassifikation

PELVIC INFLAMMATORY DISEASE (PID)

COCs may reduce the risk of PID among women with STIs, but do not protect against HIV or lower genital tract STIs. Whether CICs, P or CVR reduce the risk of PID among women with STIs is unknown but they do not protect against HIV or lower genital tract STIs.

GALL BLADDER DISEASE

COCs, CICs, P or CVR may cause a small increased risk of gall bladder disease.

There is also concern that COCs, CICs, P or CVR may worsen existing gall bladder disease.

Unlike COCs, CICs have been shown to have minimal effect on liver function in healthy women, and have no first-pass effect on the liver.

HISTORY OF CHOLESTASIS

Pregnancy-related: History of pregnancy-related cholestasis may predict an increased risk of developing COC-related cholestasis.

Past-COC-related: History of COC-related cholestasis predicts an increased risk with subsequent COC use.

LIVER TUMOURS

There is no evidence regarding hormonal contraceptive use among women with hepatocellular adenoma.

COC use in healthy women is associated with development and growth of hepatocellular adenoma.

THALASSAEMIA

There is anecdotal evidence from countries where thalassaemia is prevalent that COC use does not worsen the condition.

IRON-DEFICIENCY ANAEMIA

CHC use may decrease menstrual blood loss.

References

1. Effect of different progestagens in low oestrogen oral contraceptives on venous thromboembolic disease. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1995;346(8990):1582–8.
2. Bergendal A, Persson I, Odeberg J, Sundstrom A, Holmstrom M, Schulman S, et al. Association of venous thromboembolism with hormonal contraception and thrombophilic genotypes. Obstet Gynecol. 2014;124(3):600–9.
3. Bloemenkamp KW, Rosendaal FR, Helmerhorst FM, Buller HR, Vandenbroucke JP. Enhancement by factor V Leiden mutation of risk of deep-vein thrombosis associated with oral contraceptives containing a third-generation progestagen. Lancet. 1995;346(8990):1593–6.
4. Dinger J, Assmann A, Mohner S, Minh TD. Risk of venous thromboembolism and the use of dienogest- and drospirenone-containing oral contraceptives: results from a German case-control study. J Fam Plann Reprod Health Care. 2010;36(3):123–9.
5. Dinger J, Bardenheuer K, Heinemann K. Cardiovascular and general safety of a 24-day regimen of drospirenone-containing combined oral contraceptives: final results from the international active surveillance study of women taking oral contraceptives. Contraception. 2014. 89: 253–63
6. Dinger JC, Heinemann LA, Kuhl-Habich D. The safety of a drospirenone-containing oral contraceptive: final results from the European Active Surveillance Study on oral contraceptives based on 142,475 women-years of observation. Contraception. 2007;75(5):344–54.
7. Farmer RD, Lawrenson RA, Thompson CR, Kennedy JG, Hambleton IR. Population-based study of risk of venous thromboembolism associated with various oral contraceptives. Lancet. 1997;349(9045):83–8.
8. Farmer RD, Lawrenson RA, Todd JC, Williams TJ, MacRae KD, Tyrer F, et al. A comparison of the risks of venous thromboembolic disease in association with different combined oral contraceptives. Br J Clin Pharmacol. 2000;49(6):580–90.
9. Herings RM, Urquhart J, Leufkens HG. Venous thromboembolism among new users of different oral contraceptives. Lancet. 1999;354(9173):127–8.
10. Jick H, Jick SS, Gurewich V, Myers MW, Vasilakis C. Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestagen components. Lancet. 1995;346(8990):1589–93.
11. Jick H, Kaye JA, Vasilakis-Scaramozza C, Jick SS. Risk of venous thromboembolism among users of third generation oral contraceptives compared with users of oral contraceptives with levonorgestrel before and after 1995: cohort and case-control analysis. BMJ. 2000;321(7270):1190–5.
12. Jick SS, Hernandez RK. Risk of non-fatal venous thromboembolism in women using oral contraceptives containing drospirenone compared with women using oral contraceptives containing levonorgestrel: case-control study using United States claims data. BMJ. 2011;342:d2151.
13. Jick SS, Kaye JA, Russmann S, Jick H. Risk of nonfatal venous thromboembolism in women using a contraceptive transdermal patch and oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. Contraception. 2006;73(3):223–8.
14. Lidegaard O, Edstrom B, Kreiner S. Oral contraceptives and venous thromboembolism: a five-year national case-control study. Contraception. 2002;65(3):187–96.
15. Parkin L, Sharples K, Hernandez RK, Jick SS. Risk of venous thromboembolism in users of oral contraceptives containing drospirenone or levonorgestrel: nested case-control study based on UK General Practice Research Database. BMJ. 2011;342:d2139.
16. Todd J, Lawrenson R, Farmer RD, Williams TJ, Leydon GM. Venous thromboembolic disease and combined oral contraceptives: a re-analysis of the MediPlus database. Hum Reprod. 1999;14(6):1500–5.
17. van Hylckama V, 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.
18. Vasilakis-Scaramozza C, Jick H. Risk of venous thromboembolism with cyproterone or levonorgestrel contraceptives. Lancet. 2001;358(9291):1427–9.
19. Ziller M, Ziller V, Haas G, Rex J, Kostev K. Risk of venous thrombosis in users of hormonal contraceptives in German gynaecological practices: a patient database analysis. Arch Gynecol Obstet. 2014;289(2):413–9.
20. 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.
21. Dunn N, Thorogood M, Faragher B, de Caestecker L, MacDonald TM, McCollum C, et al. Oral contraceptives and myocardial infarction: results of the MICA case-control study. BMJ. 1999;318(7198):1579–83.

22. Gronich N, Lavi I, Rennert G. Higher risk of venous thrombosis associated with drospirenone-containing oral contraceptives: a population-based cohort study. CMAJ. 2011;183(18):E1319–25.

23. Heinemann LA, Lewis MA, Thorogood M, Spitzer WO, Guggenmoos-Holzmann I, Bruppacher R. Case-control study of oral contraceptives and risk of thromboembolic stroke: results from International Study on Oral Contraceptives and Health of Young Women. BMJ. 1997;315(7121):1502–4.

24. Kemmeren JM, Algra A, Grobbee DE. Third generation oral contraceptives and risk of venous thrombosis: meta-analysis. BMJ. 2001;323(7305):131.

25. Lewis MA. The Transnational Study on Oral Contraceptives and the Health of Young Women. Methods, results, new analyses and the healthy user effect. Hum Reprod Update. 1999;5(6):707–20.

26. Lewis MA, Heinemann LA, Spitzer WO, MacRae KD, Bruppacher R. The use of oral contraceptives and the occurrence of acute myocardial infarction in young women. Results from the Transnational Study on Oral Contraceptives and the Health of Young Women. Contraception. 1997;56:129–40.

27. Lidegaard O. The influence of thrombotic risk factors when oral contraceptives are prescribed. A control-only study. Acta Obstet Gynecol Scand. 1997;76(3):252–60.

28. Lidegaard O, Kreiner S. Cerebral thrombosis and oral contraceptives. A case-control study. Contraception. 1998;57(5):303–14.

29. Lidegaard O, Lokkegaard E, Jensen A, Skovlund CW, Keiding N. Thrombotic stroke and myocardial infarction with hormonal contraception. N Engl J Med. 2012;366(24):2257–66.

30. Rosenberg L, Palmer JR, Rao RS, Shapiro S. Low-dose oral contraceptive use and the risk of myocardial infarction. Arch Intern Med. 2001;161:1065–70.

31. Tanis BC, van den Bosch MA, Kemmeren JM, Cats VM, Helmerhorst FM, Algra A, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med. 2001;345:1787–93.

32. World Health Organization. Ischaemic stroke and combined oral contraceptives: results of an international, multicentre, case-control study. WHO Collaborative Study on Cardiovascular Disease and Steroid Hromone Contraception. Lancet. 1996;348:498–505.

33. World Health Organization. Acute myocardial infarction and combined oral contraceptives: results of an international multicentre case-control study. WHO Collaborative Study on Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1997;349:1202–9.

34. Yang L, Kuper H, Sandin S, Margolis KL, Chen Z, Adami HO, et al. Reproductive history, oral contraceptive use, and the risk of ischemic and hemorrhagic stoke in a cohort study of middle-aged Swedish women. Stroke. 2009;40(4):1050–8.

35. Aedo AR, Landgren BM, Johannisson E, Diczfalusy E. Pharmacokinetics and pharmacodynamic investigations with monthly injectable contraceptive preparations. Contraception. 1985;31:453–69.

36. Fotherby K, Benagiano G, Toppozada HK, Abdel-Rahman A, Navaroli F AB, Ramos-Cordero R, et al. A preliminary pharmacological trial of the montly injectable contraceptive Cycloprovera. Contraception. 1982;25:261–72.

37. Garza-Flores J. Pharmacokinetics of once-a-month injecatable contraceptives. Contraception. 1994;49:347–59.

38. Garza-Flores J, Rodriguez V, Perez-Palacios G, Virutamasen P, Tang-Keow P, Konsayreepong R, et al. A multicentered pharmacokinetic, pharmacodynamic study of once-a-month injectable contraceptives. I. Different doses of HRP112 and of Depoprovera. Contraception. 1987;36:441–57.

39. World Health Organization Task Force on Long-Acting Systemic Agents for Fertility Regulation. A multicentered phase III comparative study of two hormonal contraceptive preparations given once-a-month by intramuscular injection: I. Contraceptive efficacy and side effects. Contraception. 1988;37:455–66.

40. Haiba NA, el-Habashy MA, Said SA, Darwish EA, Abdel-Sayed WS, Nayel SE. Clinical evaluation of two monthly injectable contraceptives and their effects on some metabolic parameters. Contraception. 1989;39:619–32.

41. Kesseru EV, Aydinlik S, Etchepareborda JJ, Kaufmann J. A multicentered, two-year, phase III clinical trial of norethisterone enanthate 50 mg plus estradiol valerate 5 mg as a monthly injectable contraceptive. Contraception. 1991;44:589–98.

42. Meng Y-X, Jiang HY, Chen AJ, Lu FY, Yang H, Zhang MY, et al. Hemostatic changes in women using a montly injectable contraceptive for one year. Contraception. 1990;37:1–20.

43. Abrams LS, Skee D, Natarajan J, Wong FA, Lasseter KC. Multiple-dose pharmacokinetics of a contraceptive patch in healthy women participants. Contraception. 2001;64:287–94.

44. Audet M-C, Moreau M, Koltun WD, Waldbaum AS, Shangold GA, Fisher AC, et al. Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs. an oral contraceptive: a randomized trial. JAMA. 2001;285:2347–54.

45. Boonyarangkul A, Taneepanichskul S. Comparison of cycle control and side effects between transdermal contraceptive patch and an oral contraceptive in women older than 35 years. J Med Assoc Thai. 2007;90(9):1715–9.

46. Burkman RT. The transdermal contraceptive patch: a new approach to hormonal contraception. Int J Fertil. 2002;47(2):69–76.

47. Cole JA, Norman H, Doherty M, Walker AM. Venous thromboembolism, myocardial infarction, and stroke among transdermal contraceptive system users. Obstet Gynecol. 2007;109(2):339–46.

48. Devineni D, Skee D, Vaccaro N, Masserella J, Janssens L, LaGuardia KD, et al. Pharmacokinetics and pharmacodynamics of a transdermal contraceptive patch and an oral contraceptive. J Clin Pharmacol. 2007;47:497–509.

49. Dittrich R, Parker L, Rosen JB, Shangold GA, Creasy GW, Fisher AC. Transdermal contraception: evaluation of three transdermal norelgestromin/ethinyl estradiol doses in a randomized, multicenter, dose-response study. Am J Obstet Gynecol. 2002;186:15–20.

50. Helmerhorst FM, Cronje HS, Hedon B, Shangold GA, Fisher AC, Creasy GW. Comparison of efficacy, cycle control, compliance and safety in users of a contraceptive patch vs. an oral contraceptive. Int J Gynaecol Obstet. 2000;70(suppl 1):78.

51. Jick S, Kaye J, Li L, Jick H. Further results on the risk of nonfatal venous thromboembolism in users of the contraceptive transdermal patch compared to users of oral contraceptives containing norgestimate and 35 ug of ethinyl estradiol. Contraception. 2007;76:4–7.

52. Jick SS, Jick H. Cerebral venous sinus thrombosis in users of four hormonal contraceptives: levonorgestrel-containing oral contraceptives, norgestimate-containing oral contraceptives, desogestrel-containing oral contraceptives and the contraceptive patch. Contraception. 2006;74:290–2.

53. Jick SS, Jick H. The contraceptive patch in relation to ischemic stroke and acute myocardial infarction. Pharmacotherapy. 2007;27(2):218–20.

54. Jick SS, Kaye J, Russmaann S, Jick H. Risk of nonfatal venous thromboembolism in women using a contraceptive transdermal patch and oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. Contraception. 2006;73:223–8.

55. Pierson RA, Archer DF, Moreau M, Shangold GA, Fisher AC, Creasy GW. Ortho Evra versus oral contraceptives: follicular development and ovulation in normal cycles and after an intentional dosing error. Fertil Steril. 2003;80(1):34–42.

56. Radowicki S, Skorzeqska K, Szlendak K. Safety evaluation of a transdermal contraceptive system with an oral contraceptive. Ginekol Pol. 2005;76:884–9 (in Polish).

57. Smallwood GH, Meador ML, Lenihan JP, Shangold GA, Fisher AC, Creasy GW. Efficacy and safety of a transdermal contraceptive system. Obstet Gynecol. 2001;98:799–805.

58. Urdl W, Apter D, Alperstein A, Koll P, Schonian S, Bringer J, et al. Contraceptive efficacy, compliance and beyond: factors related to satisfaction with once-weekly transdermal compared with oral contraception. Eur J Obstet Gynecol Reprod Biol. 2005;121:202–10.

59. White T, Ozel B, Jain JK, Stanczyk FZ. Effects of transdermal and oral contraceptives on estrogen-sensitive hepatic proteins. Contraception. 2006;74:293–6.

60. Zieman M, Guillebaud JG, E W, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril. 2002; 77:s13–s8.

61. van den Heuvel MW, van Bragt AJM, Alnabawy AKM, Kaptein MCJ. Comparison of ethylestradiol pharmacokinetics in three hormonal contraceptive formulations: the vaginal ring, the transdermal patch and an oral contraceptive. Contraception. 2005;72:168–74.

62. Ahrendt HJ, Nisand I, Bastianelli C, Gómez MA, Gemzell-Danielsson K, Urdl W, et al. Efficacy, acceptability and tolerability of the combined contraceptive ring, NuvaRing, compared with an oral contraceptive containing 30 microg of ethinyl estradiol and 3 mg of drospirene. Contraception. 2006;74:451–7.

63. Bjarnadottir RI, Tuppurainen M, Killick SR. Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ethinyl estradiol. Am J Obstet Gynecol. 2002;186:389–95.

64. Dieben TO, Roumen FJ, Apter D. Efficacy, cycle control, and user acceptibility of a novel combined contraceptive vaginal ring. Obstet Gynecol. 2002;100:585–93.

65. Duijkers I, Killick SR, Bigrigg A, Dieben TO. A comparative study on the effects of a contraceptive vaginal ring NuvaRing and an oral contraceptive on carbohydrate metabolism and adrenal and thyroid function. Eur J Contracept Reprod Health Care. 2004;9:131–40.

66. Duijkers I, Klipping C, Verhoeven CH, Dieben TO. Ovarian function with the contraceptive vaginal ring or an oral contraceptive: a randomized study. Hum Reprod. 2004;19:2668–73.

67. Elkind-Hirsch KE, Darensbourg C, Ogden B, Ogden LF, Hindelang P. Contraceptive vaginal ring use for women has less adverse metabolic effets than an oral contraceptive. Contraception. 2007;76:348–56.

68. Magnusdottir EM, Bjarnadottir RI, Onundarson PT, Gudmundsdóttir BR, Geirsson RT, Magnusdóttir SD, et al. The contraceptive vaginal ring (NuvaRing) and hemostasis: a comparative study. Contraception. 2004;69:461–7.

69. Massai R, Makarainen L, Kuukankorpi A, Klipping C, Duijkers I, Dieben T. The combined contraceptive vaginal ring (NuvaRing) and bone mineral density in healthy premenopausal women. Hum Reprod. 2005;20:2764–8.

70. Milsom I, Lete I, Bjertnaes A, Rokstad K, Lindh I, Gruber CJ, 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;21:2304–11.

71. Oddsson K, Leifels-Fischer B, de Melo NR, Wiel-Masson D, Benedetto C, Verhoeven CH, et al. Efficacy and safety of a contraceptive vaginal ring (NuvaRing) compared with a combined oral contraceptive: a 1-year randomized trial. Contraception. 2005;71:176–82.

72. Sabatini R, Cagiano R. Comparison profiles of cycle control, side effects and sexual satisfaction of three hormonal contraceptives. Contraception. 2006;74:220–3.

73. Timmer CJ, Mulders TM. Pharmacokinetics of etonogestrel and ethinylestradiol released from a combined contraceptive vaginal ring. Clin Pharmacokinet. 2000;39:233–42.

74. Tuppurainen M, Klimscheffskij R, Venhola M, Dieben TO. The combined contraceptive vaginal ring (NuvaRing) and lipid metabolism: a comparative study. Contraception. 2004;69:389–94.

75. Veres S, Miller L, Burington B. A comparison between the vaginal ring and oral contraceptives. Obstet Gynecol. 2004;104:555–63.

76. O'Connell KJ, Osborne LM, Westoff C. Measured and reported weight change for women using a vaginal contraceptive ring vs. a low-dose oral contraceptive. Contraception. 2005;72:323–7.

77. Fine PM, Tryggestad J, Meyers NJ, Sangi-Haghpeykar H. Safety and acceptability with the use of a contraceptive vaginal ring after surgical or medical abortion. Contraception. 2007;75:367–71.

78. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk in very young women using combined oral contraceptives. Contraception. 2008;78(5):358–64.

79. Vestergaard P, Rejnmark L, Mosekilde L. Oral contraceptive use and risk of fractures. Contraception. 2006;73(6):571–6.

80. Vessey M, Mant J, Painter R. Oral contraception and other factors in relation to hospital referral for fracture. Findings in a large cohort study. Contraception. 1998;57(4):231–5.

81. Michaelsson K, Baron JA, Farahmand BY, Persson I, Ljunghall S. Oral-contraceptive use and risk of hip fracture: a case-control study. Lancet. 1999;353(9163):1481–4.

82. Memon S, Iversen L, Hannaford PC. Is the oral contraceptive pill associated with fracture in later life? New evidence from the Royal College of General Practitioners Oral Contraception Study. Contraception. 2011;84(1):40–7.

83. Meier C, Brauchli YB, Jick SS, Kraenzlin ME, Meier CR. Use of depot medroxyprogesterone acetate and fracture risk. J Clin Endocrinol Metab. 2010;95(11):4909–16.

84. La Vecchia C, Tavani A, Gallus S. Oral contraceptives and risk of hip fractures. Lancet. 1999;354(9175):335–6.

85. Cooper C, Hannaford P, Croft P, Kay CR. Oral contraceptive pill use and fractures in women: a prospective study. Bone. 1993;14(1):41–5.

86. Barad D, Kooperberg C, Wactawski-Wende J, Liu J, Hendrix SL, Watts NB. Prior oral contraception and postmenopausal fracture: a Women's Health Initiative observational cohort study. Fertil Steril. 2005;84(2):374–83.

87. Michaelsson K, Baron JA, Farahmand BY, Ljunghall S. Influence of parity and lactation on hip fracture risk. Am J Epidemiol. 2001;153(12):1166–72.

88. O'Neill TW, Marsden D, Adams JE, Silman AJ. Risk factors, falls, and fracture of the distal forearm in Manchester, UK. J Epidemiol Community Health. 1996;50(3). 288–92.

89. Mallmin H, Ljunghall S, Persson I, Bergstrom R. Risk factors for fractures of the distal forearm: a population-based case-control study. Osteoporosis Int. 1994;4(6):298–304.

90. Berenson AB, Radecki CM, Grady JJ, Rickert VI, Thomas A. A prospective, controlled study of the effects of hormonal contraception on bone mineral density. Obstet Gynecol. 2001;98(4):576–82.

91. Berenson AB, Rahman M, Breitkopf CR, Bi LX. Effects of depot medroxyprogesterone acetate and 20-microgram oral contraceptives on bone mineral density. Obstet Gynecol. 2008;112(4):788–99.

92. Cromer BA, Bonny AE, Stager M, Lazebnik R, Rome E, Ziegler J, et al. Bone mineral density in adolescent females using injectable or oral contraceptives: a 24-month prospective study. Fertil Steril. 2008;90(6):2060–7.

93. Burr DB, Yoshikawa T, Teegarden D, Lyle R, McCabe G, Mccabe LD, et al. Exercise and oral contraceptive use suppress the normal age-related increase in bone mass and strength of the femoral neck in women 18–31 years of age. Bone. 2000;27(6):855–63.

94. Cobb KL, Kelsey JL, Sidney S, Ettinger B, Lewis CE. Oral contraceptives and bone mineral density in white and black women in CARDIA. Coronary Risk Development in Young Adults. Osteoporos Int. 2002;13(11):893–900.

95. Elgan C, Dykes AK, Samsioe G. Bone mineral density changes in young women: a two year study. Gynecol Endocrinol. 2004;19(4):169–77.

96. Elgan C, Samsioe G, Dykes AK. Influence of smoking and oral contraceptives on bone mineral density and bone remodeling in young women: a 2-year study. Contraception. 2003;67(6):439–47.

97. Endrikat J, Mih E, Dusterberg B, Land K, Gerlinger C, Schmidt W, et al. A 3–year double-blind, randomized, controlled study on the influence of two oral contraceptives containing either 20 microg or 30 microg ethinylestradiol in combination with levonorgestrel on bone mineral density. Contraception. 2004;69(3):179–87.

98. Mazess RB, Barden HS. Bone density in premenopausal women: effects of age, dietary intake, physical activity, smoking, and birth-control pills. Am J Clin Nutr. 1991;53(1):132–42.

99. Nappi C, Di Spiezio SA, Acunzo G, Bifulco G, Tommaselli GA, Guida M, et al. Effects of a low-dose and ultra-low-dose combined oral contraceptive use on bone turnover and bone mineral density in young fertile women: a prospective controlled randomized study. Contraception. 2003;67(5):355–9.

100. Paoletti AM, Orru M, Lello S, Floris S, Ranuzzi F, Etzi R, et al. Short-term variations in bone remodeling markers of an oral contraception formulation containing 3 mg of drospirenone plus 30 microg of ethinyl estradiol: observational study in young postadolescent women. Contraception. 2004;70(4):293–8.

101. Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. Bone gain in young adult women. JAMA. 1992;268(17):2403–8.

102. Reed SD, Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Longitudinal changes in bone density in relation to oral contraceptive use. Contraception. 2003;68(3):177–82.

103. Gambacciani M, Cappagli B, Ciaponi M, Benussi C, Genazzani AR. Hormone replacement therapy in perimenopause: effect of a low dose oral contraceptive preparation on bone quantitative ultrasound characteristics. Menopause. 1999;6(1):43–8.

104. Gambacciani M, Cappagli B, Lazzarini V, Ciaponi M, Fruzzetti F, Genazzani AR. Longitudinal evaluation of perimenopausal bone loss: Effects of different low dose oral contraceptive preparations on bone mineral density. Maturitas. 2006;54(2):176–80.

105. Gambacciani M, Ciaponi M, Cappagli B, Benussi C, Genazzani AR. Longitudinal evaluation of perimenopausal femoral bone loss: effects of a low-dose oral contraceptive preparation on bone mineral density and metabolism. Osteoporos Int. 2000;11(6):544–8.

106. Sordal T, Grob P, Verhoeven C. Effects on bone mineral density of a monophasic combined oral contraceptive containing nomegestrol acetate/17beta-estradiol in comparison to levonorgestrel/ethinylestradiol. Acta Obstet Gynecol Scand. 2012;91(11):1279–85.

107. Nappi C, Di Spiezio SA, Greco E, Tommaselli GA, Giordano E, Guida M. Effects of an oral contraceptive containing drospirenone on bone turnover and bone mineral density. Obstet Gynecol. 2005;105(1):53–60.

108. Gargano V, Massaro M, Morra I, Formisano C, Di CC, Nappi C. Effects of two low-dose combined oral contraceptives containing drospirenone on bone turnover and bone mineral density in young fertile women: a prospective controlled randomized study. Contraception. 2008;78(1):10–5.

109. Berenson AB, Breitkopf CR, Grady JJ. Effects of hormonal contraception on bone mineral density after 24 months of use. Obstet Gynecol. 2004;103:899–906.

110. Gambacciani M, Ciaponi M, Cappagli B, Benussi C, Genazzani AR. Longitudinal evaluation of perimenopausal femoral bone loss: effects of a low-dose oral contraceptive preparation on bone mineral density and metabolism. Osteoporos Int. 2000;11(6):544–8.

111. Gambacciani M, Spinetti A, Cappagli B, Taponeco F, Maffei S, Piaggesi L, et al. Hormone replacement therapy in perimenopausal women with a low dose oral contraceptive preparation: effects on bone mineral density and metabolism. Maturitas. 1994;19(2):125–31.

112. Gambacciani M, Spinetti A, Taponeco F, Cappagli B, Piaggesi L, Fioretti P. Longitudinal evaluation of perimenopausal vertebral bone loss: effects of a low-dose oral contraceptive preparation on bone mineral density and metabolism. Obstet Gynecol. 1994;83(3):392–6.

113. Hansen M, Overgaard K, Riis B, Christiansen C. Potential risk factors for development of postmenopausal osteoporosis – examined over a 12-year period. Osteoporos Int. 1991;1(2):95–102.

114. Shargil AA. Hormone replacement therapy in perimenopausal women with a triphasic contraceptive compound: a three-year prospective study. Int J Fertil. 1985;30(1): 18–20.

115. Taechakraichana N, Jaisamrarn U, Panyakhamlerd K, Chaikittisilpa S, Limpaphayom K. Difference in bone acquisition among hormonally treated postmenopausal women with normal and low bone mass. J Med Assoc Thai. 2001;84 Suppl 2:S586–S92.

116. Taechakraichana N, Limpaphayom K, Ninlagarn T, Panyakhamlerd K, Chaikittisilpa S, Dusitsin N. A randomized trial of oral contraceptive and hormone replacement therapy on bone mineral density and coronary heart disease risk factors in postmenopausal women. Obstet Gynecol. 2000;95(1):87–94.

117. Volpe A, Amram A, Cagnacci A, Battaglia C. Biochemical aspects of hormonal contraception: effects on bone metabolism. Eur J Contracept Reprod Health Care. 1997;2(2):123–6.

118. Cohen A, Shane E. Treatment of premenopausal women with low bone mineral density. Curr Osteoporos Rep. 2008;6(1):39–46.

119. Grimes D, Schulz K. Surrogate end points in clinical research: hazardous to your health. Obstet Gynecol. 2005;105:1114–8.

120. Schonau E. The peak bone mass concept: is it still relevant? Pediatric Nephrol. 2004;19:825–31.

121. Bahamondes L, Bahamondes MV, Modesto W, Tilley IB, Magalhaes A, Pinto e Silva JL, et al. Effect of hormonal contraceptives during breastfeeding on infant's milk ingestion and growth. Fertil Steril. 2013;100(2):445–50.

122. Espey E, Ogburn T, Leeman L, Singh R, Ostrom K, Schrader R. Effect of progestin compared with combined oral contraceptive pills on lactation: a randomized controlled trial. Obstet Gynecol. 2012;119(1):5–13.

123. Kamal I, Hefnawi F, Ghoneim M, Abdallah M, Abdel Razek S. Clinical, biochemical, and experimental studies on lactation. V. Clinical effects of steroids on the initiation of lactation. Am J Obstet Gynecol. 1970;108(4):655–8.

124. Kamal I, Hefnawi F, Ghoneim M, Talaat M, Younis N, Tagui A, et al. Clinical, biochemical, and experimental studies on lactation. II. Clinical effects of gestagens on lactation. Am J Obstet Gynecol. 1969;105(3):324–34.

125. Kapp N, Curtis KM. Combined oral contraceptive use among breastfeeding women: a systematic review. Contraception. 2010;82(1):10–6.

126. Koetsawang S, Bhiraleus P, Chiemprajert T. Effects of oral contraceptives on lactation. Fertil Steril. 1972;23(1):24–8.

127. Jackson E, Curtis KM, Gaffield ME. Risk of venous thromboembolism during the postpartum period: a systematic review. Obstet Gynecol. 2011;117(3):691–703.

128. Kamel H, Navi BB, Sriram N, Hovsepian DA, Devereux RB, Elkind MS. Risk of a thrombotic event after the 6-week postpartum period. N Engl J Med. 2014;370(14):1307–15.

129. Sultan AA, Tata LJ, West J, Fiaschi L, Fleming KM, Nelson-Piercy C, et al. Risk factors for first venous thromboembolism around pregnancy: a population-based cohort study from the United Kingdom. Blood. 2013;121(19):3953–61.

130. Sultan AA, West J, Tata LJ, Fleming KM, Nelson-Piercy C, Grainge MJ. Risk of first venous thromboembolism in and around pregnancy: a population-based cohort study. Br J Haematol. 2012;156(3):366–73.

131. Tepper NK, Boulet SL, Whiteman MK, Monsour M, Marchbanks PA, Hooper WC, et al. Postpartum venous thromboembolism: incidence and risk factors. Obstet Gynecol. 2014;123(5):987–96.

132. Petersen JF, Bergholt T, Nielsen AK, Paidas MJ, Lokkegaard EC. Combined hormonal contraception and risk of venous thromboembolism within the first year following pregnancy. Danish nationwide historical cohort 1995–2009. Thromb Haemost. 2014;112(1):73–8.

133. Jackson E, Glasier A. Return of ovulation and menses in postpartum nonlactating women: a systematic review. Obstet Gynecol. 2011;117(3):657–62.

134. Lahteenmaki P. Influence of oral contraceptives on immediate postabortal pituitary-ovarian function. Acta Obstet Gynecol Scand. 1978;76:1–38.

135. Lahteenmaki P, Rasi V, Luukkainen T, Myllyä G. Coagulation factors in women using oral contraceptives or intrauterine contraceptive devices immediately after abortion. Am J Obstet Gynecol. 1981;141:175–9.

136. Martin CW, Brown AH, Baird DT. A pilot study of the effect of methotrexate or combined oral contraceptive on bleeding patterns after induction of abortion with mifepristone and a prostaglandin pessary. Contraception. 1998;58:99–103.

137. Niswonger JW, London GD, Anderson GV, Wolfe L. Oral contraceptives during immediate postabortal period. Obstet Gynecol. 1968;32(3):325–7.

138. Peterson WF. Contraceptive therapy following therapeutic abortion. Obstet Gynecol. 1974;44(6):853–7.

139. Tang OS, Xu J, Cheng L, Lee SW, Ho PC. The effect of contraceptive pills on the measured blood loss in medical termination of pregnancy by mifepristone and misoprostol: a randomized placebo controlled trial. Hum Reprod. 2002;17(1):99–102.

140. Tang OS, Gao PP, Cheng L, Lee SW, Ho PC. A randomized double-blind placebo-controlled study to assess the effect of oral contraceptive pills on the outcome of medical abortion with mifepristone and misoprostol. Hum Reprod. 1999;14(3):722–5.

141. Gaffield ME, Kapp N, Ravi A. Use of combined oral contraceptives post abortion. Contraception. 2009;80(4):355–62.

142. Gillum LA, Mamidipudi SK, Johnston SC. Ischaemic stroke risk with oral contraceptives: a meta-analysis. JAMA. 2000;284:72–8.

143. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. Br J Cancer. 1989;59:618–21.

144. Khader YS, Rice J, John L, Abueita O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. Contraception. 2003;68(1):11–7.

145. Lawson DH, Davidson JF, Jick H. Oral contraceptive use and venous thromboembolism: absence of an effect of smoking. Br Med J. 1977;2:729–30.

146. Lidegaard O, Edstrom B, Kreiner S. Oral contraceptives and venous thromboembolism. A case-control study. Contraception. 1998;57:291–301.

147. Nightingale AL, Lawrenson RA, Simpson EL, Williams TJ, MacRae KD, Farmer RD. The effects of age, body mass index, smoking and general health on the risk of venous thromboembolism in users of combined oral contraceptives. Eur J Contracept Reprod Health Care. 2000;5:265–74.

148. Petitti D, Wingerd J, Pellegrin F, Ramcharan S. Risk of vascular disease in women. Smoking, oral contraceptives, noncontraceptive estrogens, and other factors. JAMA. 1979;242:1150–4.

149. Straneva P, Hinderliter A, Wells E, Lenahan H, Girdler S. Smoking, oral contraceptives, and cardiovascular reactivity to stress. Obstet Gynecol. 2000;95:78–83.

150. Van den bosch MA, Kemmeren JM, Tanis BC, Mali WP, Helmerhorst FM, Rosendaal FR, et al. The RATIO study: oral contraceptives and the risk of peripheral arterial disease in young women. J Thromb Haemost. 2003;1:439–44.

151. World Health Organization. Venous thromboembolic disease and combined oral contraceptives: results of international multicentre case-control study. Lancet. 1995;346:1575–82.

152. Abdollahi M, Cushman M, Rosendaal FR. Obesity: risk of venous thrombosis and the interaction with coagulation factor levels and oral contraceptive use. Thromb Haemost. 2003;89(3):493–8.

153. Pomp ER, le CS, Rosendaal FR, Doggen CJ. Risk of venous thrombosis: obesity and its joint effect with oral contraceptive use and prothrombotic mutations. Br J Haematol. 2007;139(2):289–96.

154. Schwartz SM, Petitti DB, Siscovick DS, Longstreth WT, Jr., Sidney S, Raghunathan TE, et al. Stroke and use of low-dose oral contraceptives in young women: a pooled analysis of two US studies. Stroke. 1998;29(11):2277–84.

155. Sidney S, Petitti DB, Soff GA, Cundiff DL, Tolan KK, Quesenberry CP, Jr. Venous thromboembolic disease in users of low-estrogen combined estrogen-progestin oral contraceptives. Contraception. 2004;70(1):3–10.

156. Sidney S, Siscovick DS, Petitti DB, Schwartz SM, Quesenberry CP, Psaty BM, et al. Myocardial infarction and use of low-dose oral contraceptives: a pooled analysis of 2 US studies. Circulation. 1998;98(11):1058–63.

157. Brunner Huber LR, Hogue CJ, Stein AD, Drews C, Zieman M. Body mass index and risk for oral contraceptive failure: a case-cohort study in South Carolina. Ann Epidemiol. 2006;16(8):637–43.

158. Brunner Huber LR, Toth JL. Obesity and oral contraceptive failure: findings from the 2002 National Survey of Family Growth. Am J Epidemiol. 2007;166(11):1306–11.

159. Brunner LR, Hogue CJ. The role of body weight in oral contraceptive failure: results from the 1995 national survey of family growth. Ann Epidemiol. 2005;15(7):492–9.

160. Burkman RT, Fisher AC, Wan GJ, Barnowski CE, LaGuardia KD. Association between efficacy and body weight or body mass index for two low-dose oral contraceptives. Contraception. 2009;79(6):424–7.

161. Dinger J, Minh TD, Buttmann N, Bardenheuer K. Effectiveness of oral contraceptive pills in a large U.S. cohort comparing progestogen and regimen. Obstet Gynecol. 2011;117(1):33–40.

162. Dinger JC, Cronin M, Mohner S, Schellschmidt I, Minh TD, Westhoff C. Oral contraceptive effectiveness according to body mass index, weight, age, and other factors. Am J Obstet Gynecol. 2009;201(3):263 e1–9.

163. Holt VL, Cushing-Haugen KL, Daling JR. Body weight and risk of oral contraceptive failure. Obstet Gynecol. 2002;99(5 Pt 1):820–7.

164. Holt VL, Scholes D, Wicklund KG, Cushing-Haugen KL, Daling JR. Body mass index, weight, and oral contraceptive failure risk. Obstet Gynecol. 2005;105(1):46–52.

165. Jick SS, Hagberg KW, Kaye JA, Jick H. The risk of unintended pregnancies in users of the contraceptive patch compared to users of oral contraceptives in the UK General Practice Research Database. Contraception. 2009;80(2):142–51.

166. Kaunitz AM, Portman D, Westhoff CL, Archer DF, Mishell DR, Jr., Rubin A, et al. Low-dose levonorgestrel and ethinyl estradiol patch and pill: a randomized controlled trial. Obstet Gynecol. 2014;23(2 Pt 1):295–303.

167. McNicholas C, Zhao Q, Secura G, Allsworth JE, Madden T, Peipert JF. Contraceptive failures in overweight and obese combined hormonal contraceptive users. Obstet Gynecol. 2013;121(3):585–92.

168. Schramm GA, Schrah G. The efficacy and safety of an oral contraceptive containing chlormadinone acetate: results of a pooled analysis of noninterventional trials in adult and adolescent women. Contraception. 2011;84(4):390–401.

169. Urdl W, Apter D, Alperstein A, Koll P, Schonian S, Bringer J, et al. Contraceptive efficacy, compliance and beyond: factors related to satisfaction with once-weekly transdermal compared with oral contraception. Eur J Obstet Gynecol Reprod Biol. 2005;121(2):202–10.

170. Vessey M. Oral contraceptive failures and body weight: findings in a large cohort study. J Fam Plann Reprod Health Care. 2001;27(2):90–1.

171. Westhoff CL, Hait HI, Reape KZ. Body weight does not impact pregnancy rates during use of a low-dose extended-regimen 91-day oral contraceptive. Contraception. 2012;85(3):235–9.

172. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril. 2002;77(2 Suppl 2):S13–8.

173. Heinemann LA, Lewis MA, Spitzer WO, Thorogood M, Guggenmoos-Holzmann I, Bruppacher R. Thromboembolic stroke in young women. A European case-control study on oral contraceptives. Contraception. 1998;57:29–37.

174. World Health Organization. Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: results of an international, multicentre, case-control study. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Lancet. 1996;348:505–10.

175. Collaborative Group for the Study of Stroke in Young Women. Oral contraceptives and stroke in young women: associated risk factors. JAMA. 1975;231:718–22.

176. Croft P, Hannaford P. Risk factors for acute myocardial infarction in women: evidence from the Royal College of General Practitioners' Oral Contraception Study. BMJ. 1989;298:165–8.

177. D'Avanzo B, La Vecchia C, Negri E, Parazzini F, Franceschi S. Oral contraceptive use and risk of myocardial infarction: an Italian case-control study. J Epidemiol Community Health. 1994;48:324–8.

178. Dunn NR, Faragher B, Thorogood M, de Caestecker L, MacDonald TM, McCollum C, et al. Risk of myocardial infarction in young female smokers. Heart (British Cardiac Society). 1999;82:581–3.

179. Hannaford P, Croft P, Kay CR. Oral contraception and stroke: evidence from the Royal College of General Practitioners' Oral Contraception Study. Stroke. 1994;25:935–42.

180. Kemmeren JM, Tanis BC, van den Bosch MA, Bollen EL, Helmerhorst FM, van der Graaf Y, et al. Risk of Arterial Thrombosis in Relation to Oral Contraceptives (RATIO) study: oral contraceptives and the risk of ischemic stroke. Stroke. 2002;33:1202–8.

181. Lidegaard O. Oral contraception and risk of a cerebral thromboembolic attack: results of a case-control study. BMJ. 1993;306(6883):956–63.

182. Lidegaard O. Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: the influence of diabetes, hypertension, migraine and previous thrombotic disease. Br J Obstet Gynaecol. 1995;102(2):153–9.

183. Lubianca JN, Faccin CS, Fuchs FD. Oral contraceptives: a risk factor for uncontrolled blood pressure among hypertensive women. Contraception. 2003;67:19–24.

184. Narkiewicz K, Graniero GR, D'Este D, Mattarei M, Zonzin P, Palatini P. Ambulatory blood pressure in mild hypertensive women taking oral contraceptives: a case-control study. Am J Hypertens. 1995;8:249–53.

185. Siritho S, Thrift AG, McNeil JJ, You RX, Davis SM, Donnan GA, et al. Risk of ischemic stroke among users of the oral contraceptive pill: The Melbourne Risk Factor Study (MERFS) Group. Stroke. 2003;34:1575–80.

186. Lubianca JN, Moreira LB, Gus M, Fuchs FD. Stopping oral contraceptives: an effective blood pressure-lowering intervention in women with hypertension. J Hum Hypertens. 2005;19:451–5.

187. Aberg H, Karlsson L, Melander S. Studies on toxaemia of pregnancy with special reference to blood pressure. II. Results after 6–11 years' follow-up. Upsala J Med Sci. 1978;83:97–102.

188. Carmichael SM, Taylor MM, Ayers CR. Oral contraceptives, hypertension, and toxemia. Obstet Gynecol. 1970;35:371–6.

189. Meinel H, Ihle R, Laschinski M. [Effect of hormonal contraceptives on blood pressure following pregnancy-induced hypertension] Zentralblatt fur Gynakologie. 1987;109:527–31 (in German).

190. Pritchard JA, Pritchard SA. Blood pressure response to estrogen-porgestin oral contraceptive after pregnancy-induced hypertension. Am J Obstet Gynecol. 1977;129:733–9.

191. Sibai BM, Taslimi MM, el-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. Obstet Gynecol. 1986;155:501–9.

192. Sibai BM, Ramadan MK, Chari RS, Friedman SA. Pregnancies complicated by HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): subsequent pregnancy outcome and long-term prognosis. Am J Obstet Gynecol. 1995;172:125–9.

193. Anderson BS, Olsen J, Nielsen GL, Steffensen FH, Sørensen HT, Baech J, et al. Third generation oral contraceptives and heritable thrombophilia as risk factors of non-fatal venous thromboembolism. Thromb Haemost. 1998;79:28–31.

194. Aznar J, Mira Y, Vaya A, Corella D, Ferrando F, Villa P, et al. Factor V Leiden and prothrombin G20210A mutations in young adults with cryptogenic ischemic stroke. Thromb Haemost. 2004;91:1031–4.

195. Bennet L, Odeberg H. Resistance to activated protein C, highly prevalent amongst users of oral contraceptives with venous thromboembolism. J Intern Med. 1998;244:27–32.

196. Bloemenkamp KW, Rosendaal FR, Helmerhorst FM, Vandenbroucke JP. Higher risk of venous thrombosis during early use of oral contraceptives in women with inherited clotting defects [comment]. Arch Intern Med. 2000;160:49–52.

197. de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of cerebral sinu thrombosis in oral contraceptive users and in [correction of who are] carriers of heriditary prothrombotic conditions. The Cerebral Venous Sinus Thrombosis Study Group. BMJ. 1998;316:589–92.

198. Emmerich J, Rosendaal FR, Cattaneo M, Margaglione M, De Stefano V, Cumming T, et al. Combined effect of factor V Leiden and prothrombin 20210A on the risk of venous thromboembolism – pooled analysis of 8 case-control studies including 2310 cases and 3204 controls. Study Group for Pooled-Analysis in Venous Thromboembolism. Thromb Haemost. 2001;86:809–16.

199. Gadelha T, Andre C, Juca AA, Nucci M. Prothrombin 20210A and oral contraceptive use as risk factors for cerebral venous thrombosis. Cerebrovasc Dis. 2005;19:49–52.

200. Legnani C, Palareti G, Guazzaloca G, Cosmi B, Lunghi B, Bernardi F, et al. Venous thromboembolism in young women: role of thrombophilic mutations and oral contraceptive use. Eur Heart J. 2002;23:984–90.

201. Martinelli I, Battaglia C, Burgo I, Di Domenico S, Mannucci PM. Oral contraceptive use, thrombophilia and their interaction in young women with ischemic stroke. Haematologica. 2006;91:844–7.

202. Martinelli I, Battaglioli T, Bucciarelli P, Passamonti SM, Mannucci PM. Risk factors and recurrence rate of primary deep vein thrombosis of the upper extremities. Circulation. 2004;110:566–70.

203. Martinelli I, Sacchi E, Landi G, Taioli E, Duca F, Mannucci PM. High risk of cerebral-vein thrombosis in carriers of a prothrombin-gene mutation and in users of oral contraceptives. [comment]. N Engl J Med. 1998;338:1793–7.

204. Martinelli I, Taioli E, Bucciarelli P, Akhavan S, Mannucci PM. Interaction between the G20210A mutation of the prothrombin gene and oral contraceptive use in deep vein thrombosis. Arterioscler Thromb Vasc Biol. 1999;19:700–3.

205. Middeldorp S, Meinardi JR, Koopman MM, van Pampus EC, Hamulyák K, van Der Meer J, et al. A prospective study of asymptomatic carriers of the factor V Leiden mutation to determine the incidence of venous thromboembolism. [comment]. Ann Intern Med. 2001;135:322–7.

206. Pabinger I, Schneider B. Thrombotic risk of women with hereditary antithrombin III-, protein C- and protein S-deficiency taking oral contraceptive medication. The GTH Study Group on Natural Inhibitors. Thromb Haemost. 1994;71:548–52.

207. Pezzini A, Grassi M, Iacoviello L, Del Zotto E, Archetti S, Giossi A, et al. Inherited thrombophilia and stratification of ischaemic stroke risk among users of oral contraceptives. J Neurol Neurosurg Psychiatry. 2007;78:271–6.

208. Santamaria A, Mateo J, Oliver A, Menéndez B, Souto JC, Borrell M, et al. Risk of thrombosis associated with oral contraceptives of women from 97 families with inherited thrombophilia: high risk of thrombosis in carriers of the G20210A mutation of the prothrombin gene. Haematologica. 2001;86:965–71.

209. Slooter AJ, Rosendaal FR, Tanis BC, Kemmeren JM, van der Graaf Y, Algra A. Prothrombotic conditions, oral contraceptives, and the risk of ischemic stroke. Journal of Thromb Haemost. 2005;3:1213–7.

210. Spannagl M, Heinemann LA, Schramm W. Are factor V Leiden carriers who use oral contraceptives at extreme risk of venous thromboembolism? Eur J Contracept Reprod Health Care. 2000;5:105–12.

211. van Boven HH, Vandenbroucke JP, Briët E, Rosendaal FR. Gene-gene and gene-environment interactions determine risk of thrombosis in families with inherited antithrombin deficiency. Blood. 1999;94:2590–4.

212. van Vlijmen EF, Brouwer JL, Veeger NJ, Eskes TK, de Graeff PA, van der Meer J. Oral contraceptives and the absolute risk of venous thromboembolism in women with single or multiple thrombophilic defects: results from a retrospective family cohort study. Arch Intern Med. 2007;167:282–9.

213. Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation. [comment]. Lancet. 1994;344:1453–7.

214. Vaya AM. Prothrombin G20210A mutation and oral contraceptive use increase upper-extremity deep vein thrombotic risk. Thromb Haemost. 2003;89:452–7.

215. Oral contraceptives, venous thrombosis, and varicose veins. Royal College of General Practitioners' Oral Contraception Study. J R Coll Gen Pract. 1978;28(192):393–9.

216. Roach RE, Lijfering WM, van Hylckama Vlieg A, Helmerhorst FM, Rosendaal FR, Cannegieter SC. The risk of venous thrombosis in individuals with a history of superficial vein thrombosis and acquired venous thrombotic risk factors. Blood. 2013;122(26):4264–9.

217. Tanis BC, van den Bosch MA, Kemmeren JM, Cats VM, Helmerhorst FM, Algra A, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med. 2001;345(25):1787–93.

218. Runnebaum B, Grunwald K, Rabe T. The efficacy and tolerability of norgestimate/ethinyl estradiol (250 micrograms of norgestimate/35 micrograms of ethinyl estradiol): results of an open, multicenter study of 59,701 women. Am J Obstet Gynecol. 1992;166(6 Pt 2):1963–8.

219. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol. 2002;29:2531–6.

220. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol. 2005;193:1361–3.

221. Sarabi ZS, Chang E, Bobba R, Ibanez D, Gladman D, Urowitz M, et al. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum. 2005;53:609–12.

222. Sanchez-Guerrero J, Uribe AG, Jimenez-Santana L, Mestanza-Peralta M, Lara-Reyes P, Seuc AH, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2539–49.

223. Petri M, Kim MY, Kalunian KC, Grossman J, Hahn BH, Sammaritano LR, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2550–8.

224. Petri M. Lupus in Baltimore: evidence-based 'clinical perarls' from the Hopkins Lupus Cohort. Lupus. 2005;14:970–3.

225. Mintz G, Gutierrez G, Delezé M, Rodríguez E. Contraception with progestogens in systemic lupus erythematosus. Contraception. 1984;30:29–38.

226. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis. 1992;51:56–60.

227. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephristis in systemic lupus erythematosus. Ann Rheum Dis. 1993;52:720–4.

228. Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, Jansen-McWilliams L, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145:408–15.

229. Jungers P, Dougados M, Pelissier C, Kuttenn F, Tron F, Lesavre P, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum. 1982;25:618–23.

230. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol. 1993;32:227–30.

231. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol. 1991;20:427–33.

232. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, du Berger R, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum. 2001;44:2331–7.

233. Chopra N, Koren S, Greer WL, Fortin PR, Rauch J, Fortin I, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol. 2002;29:1683–8.

234. Bernatsky S, Ramsey-Goldman R, Gordon C, Joseph L, Boivin JF, Rajan R, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1386–9.

235. Bernatsky S, Clarke A, Ramsey-Goldman R, Joseph L, Boivin JF, Rajan R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1178–81.

236. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res. 1995;8:137–45.

237. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol. 2008;27(3):345–51.

238. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. Am J Med. 1976;60:221–5.

239. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus – a meta-analysis. Lupus. 1997;6:467–73.

240. Carolei A, Marini C, De Matteis G. History of migraine and risk of cerebral ischaemia in young adults. The Italian National Research Council Study Group on Stroke in the Young. Lancet. 1996;347(9014):1503–6.

241. Chang CL, Donaghy M, Poulter N. Migraine and stroke in young women: case-control study. The World Health Organisation Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. BMJ. 1999;318(7175):13–8.

242. Tzourio C, Tehindrazanarivelo A, Iglesias S, Alperovitch A, Chedru F, nglejan-Chatillon J, et al. Case-control study of migraine and risk of ischaemic stroke in young women. BMJ. 1995;310(6983):830–3.

243. Oral contraceptives and stroke in young women. Associated risk factors. JAMA. 1975;231(7):718–22.

244. Etminan M, Takkouche B, Isorna FC, Samii A. Risk of ischaemic stroke in people with migraine: systematic review and meta-analysis of observational studies. BMJ. 2005;330(7482):63.

245. Lidegaard O. Oral contraceptives, pregnancy, and the risk of cerebral thromboembolism: the influence of diabetes, hypertension, migraine and previous thrombotic disease. (Letter). Br J Obstet Gynaecol. 1996;103:94.

246. Nightingale AL, Farmer RD. Ischemic stroke in young women: a nested case-control study using the UK General Practice Research Database. Stroke. 2004;35(7):1574–8.

247. Cromer BA, Smith RD, Blair JM, Dwyer J, Brown RT. A prospective study of adolescents who choose among levonorgestrel implant (Norplant), medroxyprogesterone acetate (Depo-Provera), or the combined oral contraceptive pill as contraception. Pediatrics. 1994;94(5):687–94.

248. Deijen JB, Duyn KJ, Jansen WA, Klitsie JW. Use of a monophasic, low-dose oral contraceptive in relation to mental functioning. Contraception. 1992;46(4):359–67.

249. Duke JM, Sibbritt DW, Young AF. Is there an association between the use of oral contraception and depressive symptoms in young Australian women? Contraception. 2007;75(1):27–31.

250. Gupta N, O'Brien R, Jacobsen LJ, Davis A, Zuckerman A, Supran S, et al. Mood changes in adolescents using depo-medroxyprogesterone acetate for contraception: a prospective study.
Am J Obstet Gynecol. 2001;14(2):71–6.

251. Herzberg BN, Draper KC, Johnson AL, Nicol GC. Oral contraceptives, depression, and libido. Br Med J. 1971;3(773):495–500.

252. Koke SC, Brown EB, Miner CM. Safety and efficacy of fluoxetine in patients who receive oral contraceptive therapy. Am J Obstet Gynecol. 2002;187:551–5.

253. O'Connell K, Davis AR, Kerns J. Oral contraceptives: side effects and depression in adolescent girls. Contraception. 2007;75(4):299–304.

254. Westoff C, Truman C, Kalmuss D, Cushman L, Davidson A, Rulin M, et al. Depressive symptoms and Depo-Provera. Contraception. 1998;57(4):237–40.

255. Westoff C, Truman C, Kalmuss D, Cushman L, Rulin M, Heartwell S, et al. Depressive symptoms and Norplant contraceptive implants. Contraception. 1998;57(4):241–5.

256. Young EA, Kornstein SG, Harvey AT, Wisniewski SR, Barkin J, Fava M, et al. Influences of hormone-based contraception on depressive symptoms in premenopausal women with major depression. Psychoneuroendocrinology. 32(7):843–53.

257. Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. Cochrane Database Syst Rev. 2000;(2):CD000154.

258. Davis L, Kennedy SS, Moore J, Prentice A. Modern combined oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev. 2007;(3):CD001019.

259. Hendrix SL, Alexander NJ. Primary dysmenorrhea treatment with a desogestrel-containing low-dose oral contraceptive. Contraception. 2002;66:393–9.

260. Proctor ML, Roberts H, Farquhar CM. Combined oral contraceptive pill (OCP) as treatment for primary dysmenorrhoea. Cochrane Database Syst Rev. 2001;CD002120.

261. Adewole IF, Oladokun A, Fawole AO, Olawuyi JF, Adeleye JA. Fertility regulatory methods and development of complications after evacuation of complete hydatidiform mole. J Obstet Gynecol. 2000;20:68–9.

262. Berkowitz RS, Goldstein DP, Marean AR, Bernstein M. Oral contraceptives and post-molar trophoblastic disease. Obstet Gynecol. 1981;58:474–7.

263. Curry SL, Schlaerth JB, Kohorn EI, Boyce JB, Gore H, Twiggs LB, et al. Hormonal contraception and trophoblastic sequelae after hydatidiform mole (a Gynecologic Oncology Group Study). Am J Obstet Gynecol. 1989;160:805–9.

264. Deicas RE, Miller DS, Rademaker AW, Lurain JR. The role of contraception in the development of postmolar trophoblastic tumour. Obstet Gynecol. 1991;78:221–6.

265. Goldberg GL, Cloete K, Bloch B, Wiswedel K, Altaras MM. Medroxyprogesterone acetate in non-metastatic gestational trophoblastic disease. Br J Obstet Gynaecol. 1987;94:22–5.

266. Ho Yuen B, Burch P. Relationship of oral contraceptives and the intrauterine contraceptive devices to the regression of concentration of the beta subunit of human chorionic gonadotropin and invasive complications after molar pregnancy. Am J Obstet Gynecol. 1983;145:214–7.

267. Morrow P, Nakamura R, Schlaerth J, Gaddis O, Eddy G. The influence of oral contraceptives on the postmolar human chorionic gonadotropin regression curve. Am J Obstet Gynecol. 1985;151:906–14.

268. Gaffield ME, Kapp N, Curtis KM. Combined oral contraceptive and intrauterine device use among women with gestational trophoblastic disease. Contraception. 2009;80(4):363–71.

269. Eddy GL, Schlaerth JB, Natlick RH, Gaddis O, Nakamura RM, Morrow CP. Postmolar trophoblastic disease in women using hormonal contraception with and without estrogen. Obstet Gynecol. 1983;62:736–40.

270. Smith JS. Cervical cancer and use of hormonal contraceptives: a systematic review. Lancet. 2003;361:1159–67.

271. Black MM, Barclay THC, Polednak A, Kwon CS, Leis HP, Pilnik S. Family history, oral contraceptive useage, and breast cancer. Cancer. 1983;51:2147–51.

272. Brinton LA, Hoover R, Szklo M, Fraumeni JF. Oral contraceptives and breast cancer. Int J Epidemiol. 1982;11(4):316–22.

273. Brohet RM, Goldgar DE, Easton DF, Antoniou A, Andrieu N, Chang-Claude J, et al. Oral contraceptives and breast cancer risk in the International BRCA1/2 Carrier Cohort Study: a report from EMBRACE, GENEPSO, GEO-HEBON, and the IBCCS Collaborating Group. J Clin Oncol. 2007;25(25):3831–6.

274. Claus EB, Stowe M, Carter D. Oral contraceptives and the risk of ductal breast carcinoma in situ. Breast Cancer Research and Treatment. 2003;81:129–36.

275. Grabrick DM, Hartmann LC, Cerhan JR, Vierkant PA, Therneau TM, Vachon CM, et al. Risk of breast cancer with oral contraceptive use in women with a family history of breast cancer [comment]. JAMA. 2000;284:1791–8.

276. Gronwald J, Byrski T, Huzarski T, Cybulski C, Sun P, Tulman A, et al. Influence of selected lifestyle factors on breast and ovarian cancer risk in BRCA1 mutation carriers from Poland. Breast Cancer Res Treat. 2006;95:105–9.

277. Haile RW, Thomas DC, McGuire V, Felberg A, John EM, Milne RL, et al. BRCA1 and BRCA2 mutation carriers, oral contraceptive use, and breast cancer before age 50. Cancer Epidemiol Biomarkers Prev. 2006;15(10):1863–70.

278. Harris NV, Weiss NS, Francis AM, Polissar L. Breast cancer in relation to patterns of oral contraceptive use. Am J Epidemiol. 1982;116:643–51.

279. Hennekens CH, Speizer FE, Lipnick RJ, Rosner BA, Bain C, Belanger C, et al. A case-control study of oral contraceptive use and breast cancer. J Natl Cancer Inst. 1984;72(1):39–42.

280. Jernstrom H, Loman N, Johannsson OT, Borg A, Olsson H. Impact of teenage oral contraceptive use in a population-based series of early-onset breast cancer cases who have undergone BRCA mutation testing. Eur J Cancer. 2005;41:2312–20.

281. Marchbanks PA, McDonald JA, Wilson HG, Folger SG, Mandel MG, Daling JR, et al. Oral contraceptives and the risk of breast cancer. N Engl J Med. 2002;346:2025–32.

282. Milne RL, Knight JA, John EM, Dite GS, Balbuena R, Ziogas A, et al. Oral contraceptive use and risk of early-onset breast cancer in carriers and noncarriers of BRCA1 and BRCA2 mutations. Cancer Epidemiol Biomarkers Prev. 2005;14(2):350–6.

283. Narod S, Dube MP, Klijn J, Lubinski J, Lynch HT, Ghadirian P, et al. Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst. 2002;94(23):1773–9.

284. Rosenberg L, Palmer JR, Rao RS, Zauber AG, Stom BL, Warshauer ME, et al. Case-control study of oral contraceptive use and risk of breast cancer. Am J Epidemiol. 1996;143:25–37.

285. Silvera SAN, Miller AB, Rohan TE. Oral contraceptive use and risk of breast cancer among women with a family history of breast cancer: a prospective cohort study. Cancer Causes Control. 2005;16:1059–63.

286. Ursin G, Henderson BE, Haile RW, Pike MC, Zhou N, Diep A, et al. Does oral contraceptive use increase the risk of breast cancer in women with BRCA1/BRCA2 mutations more than in other women? Cancer Res. 1997;57:3678–81.

287. Ursin G, Ross RK, Sullivan-Halley J, Hanisch R, Henderson B, Bernstein L. Use of oral contraceptives and risk of breast cancer in young women. Breast Cancer Res Treat. 1998;50:175–84.

288. Gaffield ME, Culwell KR, Ravi A. Oral contraceptives and family history of breast cancer. Contraception. 2009;80(4):372–80.

289. The Italian MEGIC Group. Determinants of cervical *Chlamydia trachomatis* infection in Italy. Genitourin Med. 1993;69(2):123–5.

290. Ackers JP, Lumsden WH, Catterall RD, Coyle R. Antitrichomonal antibody in the vaginal secretions of women infected with *T. vaginalis*. Br J Ven Dis. 1975;51(5):319–23.

291. Acosta-Cazares B, Ruiz-Maya L, Escobedo de la Pena J. Prevalence and risk factors for *Chlamydia trachomatis* infection in low-income rural and suburban populations of Mexico. Sex Transm Dis. 1996;23(4):283–8.

292. Addiss DG, Vaughn ML, Holzhueter MA, Bakken LL, Davis JP. Selective screening for *Chlamydia trachomatis* infection in nonurban family planning clinics in Wisconsin. Fam Plann Perspect. 1987;19(6):252–6.

293. Arya OP, Mallinson H, Goddard AD. Epidemiological and clinical correlates of chlamydial infection of the cervix. Br J Ven Dis. 1981;57(2):118–24.

294. Green J, de Gonzalez A, Smith JS, Franceschi S, Appleby P, Plummer M, et al. Human papillomavirus infection and use of oral contraceptives. Br J Cancer. 2003;88(11):1713–20.

295. Gertig DM, Kapiga SH, Shao JF, Hunter DJ. Risk factors for sexually transmitted diseases among women attending family planning clinics in Dar-es-Salaam, Tanzania. Genitourin Med. 1997;73(1):39–43.

296. Fraser JJ, Jr., Rettig PJ, Kaplan DW. Prevalence of cervical *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female adolescents. Pediatrics. 1983;71(3):333–6.

297. Fouts AC, Kraus SJ. *Trichomonas vaginalis*: reevaluation of its clinical presentation and laboratory diagnosis. J Infect Dis. 1980;141(2):137–43.

298. Fish AN, Fairweather DV, Oriel JD, Ridgway GL. *Chlamydia trachomatis* infection in a gynaecology clinic population: identification of high-risk groups and the value of contact tracing. Eur J Obstet Gynecol Reprod Biol. 1989;31(1):67–74.

299. Evans DL, Demetriou E, Shalaby H, Waner JL. Detection of *Chlamydia trachomatis* in adolescent females using direct immunofluorescence. Clin Pediatr. 1988;27(5):223–8.

300. Evans BA, Kell PD, Bond RA, MacRae KD, Slomka MJ, Brown DW. Predictors of seropositivity to herpes simplex virus type 2 in women. Int J STD AIDS. 2003;14(1):30–6.

301. Edwards D, Phillips D, Stancombe S. *Chlamydia trachomatis* infection at a family planning clinic. N Z Med J. 1985;98(778):333–5.

302. Crowley T, Horner P, Hughes A, Berry J, Paul I, Caul O. Hormonal factors and the laboratory detection of *Chlamydia trachomatis* in women: implications for screening? Int J STD AIDS. 1997;8(1):25–31.

303. Cottingham J, Hunter D. *Chlamydia trachomatis* and oral contraceptive use: a quantitative review. Genitourin Med. 1992;68(4):209–16.

304. Chacko M, Lovchik J. *Chlamydia trachomatis* infection in sexually active adolescents: prevalence and risk factors. Pediatrics. 1984;73(6):836–40.

305. Ceruti M, Canestrelli M, Condemi V, Piantelli G, De Paolis P, Amone F, et al. Methods of contraception and rates of genital infections. Clin Exp Obstet Gynecol. 1994;21(2):119–23.

306. Burns DC, Darougar S, Thin RN, Lothian L, Nicol CS. Isolation of Chlamydia from women attending a clinic for sexually transmitted disease. Br J Ven Dis. 1975;51(5):314–8.

307. Bro F, Juul S. Predictors of *Chlamydia trachomatis* infection in women in general practice. Fam Pract. 1990;7(2):138–43.

308. Bramley M, Kinghorn G. Do oral contraceptives inhibit *Trichomonas vaginalis*? Sex Transm Dis. 1979;6(4):261–3.

309. Bontis J, Vavilis D, Panidis D, Theodoridis T, Konstantinidis T, Sidiropoulou A. Detection of *Chlamydia trachomatis* in asymptomatic women: relationship to history, contraception, and cervicitis. Adv Contracept. 1994;10(4):309–15.

310. Blum M, Pery J, Kitai E. The link between contraceptive methods and *Chlamydia trachomatis* infection. Adv Contracept. 1988;4(3):233–9.

311. Bhattacharyya MN, Jephcott AE. Diagnosis of gonorrhea in women – Influence of the contraceptive pill. J Am Ven Dis Assoc. 1976;2(3):21–4.

312. Berger GS, Keith L, Moss W. Prevalence of gonorrhoea among women using various methods of contraception. Br J Ven Dis. 1975;51(5):307–9.

313. Barnes RC, Katz BP, Rolfs RT, Batteiger B, Caine V, Jones RB. Quantitative culture of endocervical *Chlamydia trachomatis*. J Clin Microbiol. 1990;28(4):774–80.

314. Barbone F, Austin H, Louv WC, Alexander WJ. A follow-up study of methods of contraception, sexual activity, and rates of trichomoniasis, candidiasis, and bacterial vaginosis. Am J Obstet Gynecol. 1990;163(2):510–4.

315. Baeten JM, Nyange PM, Richardson BA, Lavreys L, Chohan B, Martin HL, Jr., et al. Hormonal contraception and risk of sexually transmitted disease acquisition: results from a prospective study. Am J Obstet Gynecol. 2001;185(2):380–5.

316. Avonts D, Sercu M, Heyerick P, Vandermeeren I, Meheus A, Piot P. Incidence of uncomplicated genital infections in women using oral contraception or an intrauterine device: a prospective study. Sex Transm Dis. 1990;17(1):23–9.

317. Austin H, Louv WC, Alexander WJ. A case-control study of spermicides and gonorrhea. JAMA. 1984;251(21):2822–4.

318. Masse R, Laperriere H, Rousseau H, Lefebvre J, Remis RS. *Chlamydia trachomatis* cervical infection: prevalence and determinants among women presenting for routine gynecologic examination. CMAJ. 1991;145(8):953–61.

319. Magder LS, Klontz KC, Bush LH, Barnes RC. Effect of patient characteristics on performance of an enzyme immunoassay for detecting cervical *Chlamydia trachomatis* infection. J Clin Microbiol. 1990;28(4):781–4.

320. Magder LS, Harrison HR, Ehret JM, Anderson TS, Judson FN. Factors related to genital *Chlamydia trachomatis* and its diagnosis by culture in a sexually transmitted disease clinic. Am J Epidemiol. 1988;128(2):298–308.

321. Macaulay ME, Riordan T, James JM, Leventhall PA, Morris EM, Neal BR, et al. A prospective study of genital infections in a family-planning clinic. 2. Chlamydia infection – the identification of a high-risk group. Epidemiol Infect. 1990;104(1):55–61.

322. Lycke E, Lowhagen GB, Hallhagen G, Johannisson G, Ramstedt K. The risk of transmission of genital *Chlamydia trachomatis* infection is less than that of genital *Neisseria gonorrhoeae* infection. Sex Transm Dis. 1980;7(1):6–10.

323. Lowe TL, Kraus SJ. Quantitation of *Neisseria gonorrhoeae* from women with gonorrhea. J Infect Dis. 1976;133(6):621–6.

324. Louv WC, Austin H, Perlman J, Alexander WJ. Oral contraceptive use and the risk of chlamydial and gonococcal infections. Am J Obstet Gynecol. 1989;160(2):396–402.

325. Lefevre JC, Averous S, Bauriaud R, Blanc C, Bertrand MA, Lareng MB. Lower genital tract infections in women: comparison of clinical and epidemiologic findings with microbiology. Sex Transm Dis. 1988;15(2):110–3.

326. Lavreys L, Chohan B, Ashley R, Richardson BA, Corey L, Mandaliya K, et al. Human herpesvirus 8: seroprevalence and correlates in prostitutes in Mombasa, Kenya. J Infect Dis. 2003;187(3):359–63.

327. Kinghorn GR, Waugh MA. Oral contraceptive use and prevalence of infection with *Chlamydia trachomatis* in women. Br J Ven Dis. 1981;57(3):187–90.

328. Keith L, Berer GS, Moss W. Cervical gonorrhea in women using different methods of contraception. J Am Ven Dis Assoc. 1976;3(1):17–9.

329. Johannisson G, Karamustafa A, Brorson J. Influence of copper salts on gonococci. Br J Ven Dis. 1976;52(3):176–7.

330. Jick H, Hannan MT, Stergachis A, Heidrich F, Perera DR, Rothman KJ. Vaginal spermicides and gonorrhea. JAMA. 1982;248(13):1619–21.

331. Jaffe LR, Siqueira LM, Diamond SB, Diaz A, Spielsinger NA. *Chlamydia trachomatis* detection in adolescents: a comparison of direct specimen and tissue culture methods. J Adol Health Care. 1986;7(6):401–4.

332. Jacobson DL, Peralta L, Farmer M, Graham NM, Gaydos C, Zenilman J. Relationship of hormonal contraception and cervical ectopy as measured by computerized planimetry to chlamydial infection in adolescents. Sex Transm Dis. 2000;27(6):313–9.

333. Hiltunen-Back E, Haikala O, Kautiainen H, Paavonen J, Reunala T. A nationwide sentinel clinic survey of *Chlamydia trachomatis* infection in Finland. Sex Transm Dis. 2001;28(5):252–8.

334. Hilton AL, Richmond SJ, Milne JD, Hindley F, Clarke SK. Chlamydia A in the female genital tract. Br J Ven Dis. 1974;50(1):1–10.

335. Hewitt AB. Oral contraception among special clinic patients. With particular reference to the diagnosis of gonorrhoea. Br J Ven Dis. 1970;46(2):106–7.

336. Herrmann B, Espinoza F, Villegas RR, Smith GD, Ramos A, Egger M. Genital chlamydial infection among women in Nicaragua: validity of direct fluorescent antibody testing, prevalence, risk factors and clinical manifestations. Genitourin Med. 1996;72(1):20–6.

337. Hart G. Factors associated with genital chlamydial and gonococcal infection in females. Genitourin Med. 1992;68(4):217–20.

338. Harrison HR, Costin M, Meder JB, Bownds LM, Sim DA, Lewis M, et al. Cervical *Chlamydia trachomatis* infection in university women: relationship to history, contraception, ectopy, and cervicitis. Am J Obstet Gynecol. 1985;153(3):244–51.

339. Hanna NF, Taylor-Robinson D, Kalodiki-Karamanoli M, Harris JR, McFadyen IR. The relation between vaginal pH and the microbiological status in vaginitis. Br J Obstet Gynaecol. 1985;92(12):1267–71.

340. Handsfield HH, Jasman LL, Roberts PL, Hanson VW, Kothenbeutel RL, Stamm WE. Criteria for selective screening for *Chlamydia trachomatis* infection in women attending family planning clinics. JAMA. 1986;255(13):1730–4.

341. Han Y, Morse DL, Lawrence CE, Murphy D, Hipp S. Risk profile for Chlamydia infection in women from public health clinics in New York State. J Community Health. 1993;18(1):1–9.

342. Griffiths M, Hindley D. Gonococcal pelvic inflammatory disease, oral contraceptives, and cervical mucus. Genitourin Med. 1985;61(1):67.

343. Ruijs GJ, Kauer FM, van Gijssel PM, Schirm J, Schroder FP. Direct immunofluorescence for *Chlamydia trachomatis* on urogenital smears for epidemiological purposes. Eur J Obstet Gynecol Reprod Biol. 1988;27(4):289–97.

344. Ripa KT, Svensson L, Mardh PA, Westrom L. *Chlamydia trachomatis* cervicitis in gynecologic outpatients. Obstet Gynecol. 1978;52(6):698–702.

345. Reed BD, Huck W, Zazove P. Differentiation of *Gardnerella vaginalis*, *Candida albicans*, and *Trichomonas vaginalis* infections of the vagina. J Fam Pract. 1989;28(6):673–80.

346. Rahm VA, Odlind V, Pettersson R. *Chlamydia trachomatis* in sexually active teenage girls. Factors related to genital chlamydial infection: a prospective study. Genitourin Med. 1991;67(4):317–21.

347. Pereira LH, Embil JA, Haase DA, Manley KM. Cytomegalovirus infection among women attending a sexually transmitted disease clinic: association with clinical symptoms and other sexually transmitted diseases. Am J Epidemiol. 1990;131(4):683–92.

348. Park BJ, Stergachis A, Scholes D, Heidrich FE, Holmes KK, Stamm WE. Contraceptive methods and the risk of *Chlamydia trachomatis* infection in young women. Am J Epidemiol. 1995;142(7):771–8.

349. Paavonen J, Vesterinen E. *Chlamydia trachomatis* in cervicitis and urethritis in women. Scand J Infect Dis Suppl. 1982;32:45–54.

350. Oriel JD, Powis PA, Reeve P, Miller A, Nicol CS. Chlamydial infections of the cervix. Br J Ven Dis. 1974;50(1):11–6.

351. Oriel JD, Johnson AL, Barlow D, Thomas BJ, Nayyar K, Reeve P. Infection of the uterine cervix with *Chlamydia trachomatis*. J Infect Dis. 1978;137(4):443–51.

352. Oh MK, Feinstein RA, Soileau EJ, Cloud GA, Pass RF. *Chlamydia trachomatis* cervical infection and oral contraceptive use among adolescent girls. J Adol Health Care. 1989;10(5):376–81.

353. Nayyar KC, O'Neill JJ, Hambling MH, Waugh MA. Isolation of *Chlamydia trachomatis* from women attending a clinic for sexually transmitted diseases. Br J Ven Dis. 1976;52(6):396–8.

354. Morrison CS, Bright P, Wong EL, Kwok C, Yacobson I, Gaydos CA, et al. Hormonal contraceptive use, cervical ectopy, and the acquisition of cervical infections. Sex Transm Dis. 2004;31(9):561–7.

355. McCormack WM, Reynolds GH. Effect of menstrual cycle and method of contraception on recovery of *Neisseria gonorrhoeae*. JAMA. 1982;247(9):1292–4.

356. Woolfitt JM, Watt L. Chlamydial infection of the urogenital tract in promiscuous and non-promiscuous women. Br J Ven Dis. 1977;53(2):93–5.

357. Wolinska WH, Melamed MR. Herpes genitalis in women attending Planned Parenthood of New York City. Acta Cytol. 1970;14(5):239–42.

358. Winter L, Goldy AS, Baer C. Prevalence and epidemiologic correlates of *Chlamydia trachomatis* in rural and urban populations. Sex Transm Dis. 1990;17(1):30–6.

359. Winer RL, Lee SK, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. Am J Epidemiol. 2003;157(3):218–26.

360. Willmott FE, Mair HJ. Genital herpesvirus infection in women attending a venereal diseases clinic. Br J Vener Dis. 1978;54(5):341–3.

361. Vaccarella S, Herrero R, Dai M, Snijders PJ, Meijer CJ, Thomas JO, et al. Reproductive factors, oral contraceptive use, and human papillomavirus infection: pooled analysis of the IARC HPV prevalence surveys. Cancer Epidemiol Biomarkers Prev. 2006;15(11):2148–53.

362. Tait IA, Rees E, Hobson D, Byng RE, Tweedie MC. Chlamydial infection of the cervix in contacts of men with nongonococcal urethritis. Br J Ven Dis. 1980;56(1):37–45.

363. Svensson L, Westrom L, Mardh PA. *Chlamydia trachomatis* in women attending a gynaecological outpatient clinic with lower genital tract infection. Br J Ven Dis. 1981;57(4):259–62.

364. Staerfelt F, Gundersen TJ, Halsos AM, Barlinn C, Johansen AG, Norregaard KM, et al. A survey of genital infections in patients attending a clinic for sexually transmitted diseases. Scand J Infect Dis Suppl. 1983;40:53–7.

365. Smith JS, Herrero R, Munoz N, Eluf-Neto J, Ngelangel C, Bosch FX, et al. Prevalence and risk factors for herpes simplex virus type 2 infection among middle-age women in Brazil and the Philippines. Sex Transm Dis. 2001;28(4):187–94.

366. Shafer MA, Beck A, Blain B, Dole P, Irwin CE, Jr., Sweet R, et al. *Chlamydia trachomatis*: important relationships to race, contraception, lower genital tract infection, and Papanicolaou smear. J Pediatr. 1984;104(1):141–6.

367. Sessa R, Latino MA, Magliano EM, Nicosia R, Pustorino R, Santino I, et al. Epidemiology of urogenital infections caused by *Chlamydia trachomatis* and outline of characteristic features of patients at risk. J Med Microbiol. 1994;41(3):168–72.

368. Sellors JW, Karwalajtys TL, Kaczorowski J, Mahony JB, Lytwyn A, Chong S, et al. Incidence, clearance and predictors of human papillomavirus infection in women. CMAJ. 2003;168(4):421–5.

369. Schachter J, Stoner E, Moncada J. Screening for chlamydial infections in women attending family planning clinics. West J Med. 1983;138(3):375–9.

370. Polis CB, Phillips SJ, Curtis KM, Westreich DJ, Steyn PS, Raymond E, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception. 2014;90(4):360–90.

371. Wand H, Ramjee G. The effects of injectable hormonal contraceptives on HIV seroconversion and on sexually transmitted infections. AIDS. 2012;26(3):375–80.

372. Reid SE, Dai JY, Wang J, Sichalwe BN, Akpomiemie G, Cowan FM, et al. Pregnancy, contraceptive use, and HIV acquisition in HPTN 039: relevance for HIV prevention trials among African women. J Acquir Immune Defic Syndr. 2010;53(5):606–13.

373. Myer L, Denny L, Wright TC, Kuhn L. Prospective study of hormonal contraception and women's risk of HIV infection in South Africa. Int J Epidemiol. 2007;36(1):166–74.

374. Morrison CS, Skoler-Karpoff S, Kwok C, Chen PL, van de Wijgert J, Gehret-Plagianos M, et al. Hormonal contraception and the risk of HIV acquisition among women in South Africa. AIDS. 2012;26(4):497–504.

375. Morrison CS, Richardson BA, Mmiro F, Chipato T, Celentano DD, Luoto J, et al. Hormonal contraception and the risk of HIV acquisition. AIDS. 2007;21(1):85–95.

376. Morrison CS, Chen PL, Kwok C, Richardson BA, Chipato T, Mugerwa R, et al. Hormonal contraception and HIV acquisition: reanalysis using marginal structural modeling. AIDS. 2010;24(11):1778–81.

377. McCoy SI, Zheng W, Montgomery ET, Blanchard K, van der Straten A, de Bruyn G, et al. Oral and injectable contraception use and risk of HIV acquisition among women in sub-Saharan Africa. AIDS. 2013;27(6):1001–9.

378. Heffron R, Donnell D, Rees H, Celum C, Mugo N, Were E, et al. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. Lancet Infect Dis. 2012;12(1):19–26.

379. Baeten JM, Benki S, Chohan V, Lavreys L, McClelland RS, Mandaliya K, et al. Hormonal contraceptive use, herpes simplex virus infection, and risk of HIV-1 acquisition among Kenyan women. AIDS. 2007;21(13):1771–7.

380. Stringer EM, Giganti M, Carter RJ, El-Sadr W, Abrams EJ, Stringer JS. Hormonal contraception and HIV disease progression: a multicountry cohort analysis of the MTCT-Plus Initiative. AIDS. 2009;23 Suppl 1:S69–77.

381. Polis CB, Wawer MJ, Kiwanuka N, Laeyendecker O, Kagaayi J, Lutalo T, et al. Effect of hormonal contraceptive use on HIV progression in female HIV seroconverters in Rakai, Uganda. AIDS. 2010;24(12):1937–44.

382. Morrison CS, Chen PL, Nankya I, Rinaldi A, Van Der Pol B, Ma YR, et al. Hormonal contraceptive use and HIV disease progression among women in Uganda and Zimbabwe. J Acquir Immune Defic Syndr. 2011;57(2):157–64.

383. Kilmarx PH, Limpakarnjanarat K, Kaewkungwal J, Srismith R, Saisorn S, Uthaivoravit W, et al. Disease progression and survival with human immunodeficiency virus type 1 subtype E infection among female sex workers in Thailand. J Infect Dis. 2000;181(5):1598–606.

384. Heffron R, Mugo N, Ngure K, Celum C, Donnell D, Were E, et al. Hormonal contraceptive use and risk of HIV-1 disease progression. AIDS. 2013;27(2):261–7.

385. Allen S, Stephenson R, Weiss H, Karita E, Priddy F, Fuller L, et al. Pregnancy, hormonal contraceptive use, and HIV-related death in Rwanda. J Womens Health (Larchmt). 2007;16(7):1017–27.

386. Survival and progression of HIV disease in women attending GUM/HIV clinics in Britain and Ireland. Study Group for the MRC Collaborative Study of HIV Infection in Women. Sex Transm Infect. 1999;75(4):247–52.

387. Stringer EM, Levy J, Sinkala M, Chi BH, Matongo I, Chintu N, et al. HIV disease progression by hormonal contraceptive method: secondary analysis of a randomized trial. AIDS. 2009;23(11):1377–82.

388. Stringer EM, Kaseba C, Levy J, Sinkala M, Goldenberg RL, Chi BH, et al. A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol. 2007;197(2):144–8.

389. Lutalo T, Musoke R, Kong X, Makumbi F, Serwadda D, Nalugoda F, et al. Effects of hormonal contraceptive use on HIV acquisition and transmission among HIV-discordant couples. AIDS. 2013;27 Suppl 1:S27–34.

390. Richardson BA, Otieno PA, Mbori-Ngacha D, Overbaugh J, Farquhar C, John-Stewart GC. Hormonal contraception and HIV-1 disease progression among postpartum Kenyan women. AIDS. 2007;21(6):749–53.

391. Kreiss J, Willerford DM, Hensel M, Emonyi W, Plummer F, Ndinya-Achola J, et al. Association between cervical inflammation and cervical shedding of human immunodeficiency virus DNA. J Infect Dis. 1994;170(6):1597–601.

392. Graham SM, Masese L, Gitau R, Jalalian-Lechak Z, Richardson BA, Peshu N, et al. Antiretroviral adherence and development of drug resistance are the strongest predictors of genital HIV-1 shedding among women initiating treatment. J Infect Dis. 2010;202(10):1538–42.

393. Clemetson DB, Moss GB, Willerford DM, Hensel M, Emonyi W, Holmes KK, et al. Detection of HIV DNA in cervical and vaginal secretions. Prevalence and correlates among women in Nairobi, Kenya. JAMA. 1993;269(22):2860–4.

394. Clark RA, Theall KP, Amedee AM, Dumestre J, Wenthold L, Kissinger PJ. Lack of association between genital tract HIV-1 RNA shedding and hormonal contraceptive use in a cohort of Louisiana women. Sex Transm Dis. 2007;34(11):870–2.

395. Cejtin HE, Jacobson L, Springer G, Watts DH, Levine A, Greenblatt R, et al. Effect of hormonal contraceptive use on plasma HIV-1-RNA levels among HIV-infected women. AIDS. 2003;17(11):1702–4.

396. Kovacs A, Wasserman SS, Burns D, Wright DJ, Cohn J, Landay A, et al. Determinants of HIV-1 shedding in the genital tract of women. Lancet. 2001;358:1593–601.

397. Kumwenda JJ, Makanani B, Taulo F, Nkhoma C, Kafulafula G, Li Q, et al. Natural history and risk factors associated with early and established HIV type 1 infection among reproductive-age women in Malawi. Clin Infect Dis. 2008;46(12):1913–20.

398. Lavreys L, Baeten JM, Kreiss JK, Richardson BA, Chohan BH, Hassan W, et al. Injectable contraceptive use and genital ulcer disease during the early phase of HIV-1 infection increase plasma virus load in women. J Infect Dis. 2004;189(2):303–11.

399. Morrison CS, Demers K, Kwok C, Bulime S, Rinaldi A, Munjoma M, et al. Plasma and cervical viral loads among Ugandan and Zimbabwean women during acute and early HIV-1 infection. AIDS. 2010;24(4):573–82.

400. Mostad SB, Overbaugh J, DeVange DM, Welch MJ, Chohan B, Mandaliya K, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet. 1997;350:922–7.

401. Roccio M, Gardella B, Maserati R, Zara F, Iacobone D, Spinillo A. Low-dose combined oral contraceptive and cervicovaginal shedding of human immunodeficiency virus. Contraception. 2011;83(6):564–70.

402. Sagar M, Lavreys L, Baeten JM, Richardson BA, Mandaliya K, Ndinya-Achola JO, et al. Identification of modifiable factors that affect the genetic diversity of the transmitted HIV-1 population. AIDS. 2004;18(4):615–9.

403. Seck K, Samb N, Tempesta S, Mulanga-Kabeya C, Henzel D, Sow PS, et al. Prevalence and risk factors of cervicovaginal HIV shedding among HIV-1 and HIV-2 infected women in Dakar, Senegal. Sex Transm Infect. 2001;77(3):190–3.

404. Tanton C, Weiss HA, Le Goff J, Changalucha J, Rusizoka M, Baisley K, et al. Correlates of HIV-1 genital shedding in Tanzanian women. PLoS One. 2011;6(3):e17480.

405. Tagy AH, Saker ME, Moussa AA, Kolgah A. The effect of low-dose combined oral contraceptive pills versus injectable contraceptive (Depot Provera) on liver function tests of women with compensated bilharzial liver fibrosis. Contraception. 2001;64:173–6.

406. Sy FS, Osteria TS, Opiniano V, Gler S. Effect of oral contraceptive on liver function tests of women with schistosomiasis in the Philippines. Contraception. 1986;34:283–94.

407. Shaaban MM, Ghaneimah SA, Mohamed MA, Abdel-Chani S, Mostafa SA. Effective of oral contraception on serum bile acid. Int J Gynaecol Obstet. 1984;22:111–5.

408. Shaaban MM, Hammad WA, Falthalla MF, Ghaneimah SA, El-Sharkawy MM, Salim TH, et al. Effects of oral contraception on liver function tests and serum proteins in women with active schistosomiasis. Contraception. 1982;26:75–82.

409. Gad-el-Mawla N, el-Roubi O, Sabet S, Abdallah A. Plasma lipids and lipoproteins in bilharzial females during oral contraceptive therapy. J Egypt Med Assoc. 1972;55:137–47.

410. Gad-el-Mawla N, Abdallah A. Liver function in bilharzial females receiving contraceptive pills. Acta Hepato-Splenol. 1969;16:308–10.

411. el Raghy I, Back DJ, Osman F, Orme ML, Fathalla M. Contraceptive steroid concentrations in women with early active schistosomiasis: lack of effect of antischistosomal drugs. Contraception. 1986;33:373–7.

412. Beck P, Wells SA. Comparison of the mechanisms underlying carbohydrate intolerance in subclinical diabetic women during pregnancy and during post-partum oral contraceptive steroid treatment. J Clin Endocrinol Metab. 1969;29(6):807–18.

413. Kjos SL, Peters RK, Xiang A, Thomas D, Schaefer U, Buchanan TA. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. JAMA. 1998;280(6):533–8.

414. Kung AW, Ma JT, Wong VC, Li DF, Ng MM, Wang CC, et al. Glucose and lipid metabolism with triphasic oral contraceptives in women with history of gestational diabetes. Contraception. 1987;35(3):257–69.

415. Radberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in gestational diabetic women during contraceptive treatment: effects on glucose tolerance and fatty acid composition of serum lipids. Gynecol Obstet Invest. 1982;13(1):17–29.

416. Skouby SO, Andersen O, Saurbrey N, Kuhl C. Oral contraception and insulin sensitivity: in vivo assessment in normal women and women with previous gestational diabetes. J Clin Endocrinol Metab. 1987;64(3):519–23.

417. Skouby SO, Molsted-Pedersen L, Kuhl C. Low dosage oral contraception in women with previous gestational diabetes. Obstet Gynecol. 1982;59(3):325–8.

418. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA. Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. Diabetes Care. 2006;29(3):613–7.

419. Skouby SO, Andersen O, Kuhl C. Oral contraceptives and insulin receptor binding in normal women and those with previous gestational diabetes. Am J Obstet Gynecol. 1986;155(4):802–7.

420. Kjos SL, Shoupe D, Douyan S, Friedman RL, Bernstein GS, Mestman JH, et al. Effect of low-dose oral contraceptives on carbohydrate and lipid metabolism in women with recent gestational diabetes: results of a controlled, randomized, prospective study. Am J Obstet Gynecol. 1990;163(6 Pt 1):1822–7.

421. Radberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in women with previous gestational diabetes during contraceptive treatment: effects on serum lipids and high density lipoproteins. Acta Endocrinol (Copenh). 1982;101(1):134–9.

422. Skouby SO, Kuhl C, Molsted-Pedersen L, Petersen K, Christensen MS. Triphasic oral contraception: metabolic effects in normal women and those with previous gestational diabetes. Am J Obstet Gynecol. 1985;153(5):495–500.

423. Beck P, Arnett DM, Alsever RN, Eaton RP. Effect of contraceptive steroids on arginine-stimulated glucagon and insulin secretion in women. II. Carbohydrate and lipid phsiology in insulin-dependent diabetics. Metabolism. 1976;25(1):23–31.

424. Diab KM, Zaki MM. Contraception in diabetic women: comparative metabolic study of norplant, depot medroxyprogesterone acetate, low dose oral contraceptive pill and CuT380A. J Obstet Gynecol Res. 2000;26(1):17–26.

425. Garg SK, Chase P, Marshall G, Hoops SL, Holmes DL, Jackson WE. Oral contraceptives and renal and retinal complications in young women with insulin-dependent diabetes mellitus. JAMA. 1994;271(14):1099–102.

426. Grigoryan OR, Grodnitskaya EE, Andreeva EN, Shestakova MV, Melnichenko GA, Dedov II. Contraception in perimenopausal women with diabetes mellitus. Gynecol Endocrinol. 2006;22(4):198–206.

427. Margolis KL, Adami H-O, Luo J, Ye W, Weiderpass E. A prospective study of oral contraceptive use and risk of myocardial infarction among Swedish women. Fertil Steril. 2007;88(2):310–6.

428. Petersen KR, Skouby SO, Jespersen J. Balance of coagulation activity with fibrinolysis during use of oral contraceptives in women with insulin-dependent diabetes millitus. Int J Fertil. 1995;40(Suppl 2):105–11.

429. Radberg T, Gustafson A, Skryten A, Karlsson K. Oral contraception in diabetic women. A cross-over study on seum and high density lipoprotein (HDL) lipids and diabetes control during progestogen and combined estrogen/progestogen contraception. Horm Metab Res. 1982;14:61–5.

430. Petersen KR, Skouby SO, Sidelmann J, Jespersen J. Assessment of endothelial function during oral contraception on women with insulin-dependent diabetes mellitus. Metabolism. 1994;43(11):1379–83.

431. Di Martino V, Lebray P, Myers RP, Pannier E, Paradis V, Charlotte F, et al. Progression of liver fibrosis in women infected with hepatitis C: long-term benefit of estrogen exposure. Hepatology. 2004;40(6):1426–33.

432. Libbrecht L, Craninx M, Nevens F, Desmet V, Roskams T. Predictive value of liver cell dysplasia for development of hepatocellular carcinoma in patients with non-cirrhotic and cirrhotic chronic viral hepatitis. Histopathology. 2001;39(1):66–73.

433. Eisalo A, Konttinen A, Hietala O. Oral contraceptives after liver disease. Br Med J. 1971;3(5774):561–2.

434. Wang P, Lai Z, Tang J, Xu W, Mi X, Ma F. Safety of hormonal steroid contraceptive use for hepatitis B virus carrier women. Pharmacoepidemiol Drug Saf. 2000;9(3):245–6.

435. Schweitzer IL, Weiner JM, McPeak CM, Thursby MW. Oral contraceptives in acute viral hepatitis. JAMA. 1975;233(9):979–80.

436. Kapp N, Tilley IB, Curtis KM. The effects of hormonal contraceptive use among women with viral hepatitis or cirrhosis of the liver: a systematic review. Contraception. 2009;80(4):381–6.

437. Mathieu D, Kobeiter H, Maison P, Rahmouni A, Cherqui D, Zafrani ES, et al. Oral contraceptive use and focal nodular hyperplasia of the liver. Gastroenterology. 2000;118(3):560–4.

438. Kapp N, Curtis KM. Hormonal contraceptive use among women with liver tumors: a systematic review. Contraception. 2009;80(4):387–90.

439. D'halluin V, Vilgrain V, Pelletier G, Rocher L, Belghiti J, Erlinger S, et al. [Natural history of focal nodular hyperplasia. A retrospective study of 44 cases]. Gastroenterol Clin Biol. 2001;25(11):1008–10 (in French).

440. Aweeka FT, Rosenkranz SL, Segal Y, Coombs RW, Bardeguez A, Thevanayagam L, et al. The impact of sex and contraceptive therapy on the plasma and intracellular pharmacokinetics of zidovudine. AIDS. 2006;20(14):1833–41.

441. Kearney BP, Mathias A. Lack of effect of tenofovir disoproxil fumarate on pharmacokinetics of hormonal contraceptives. Pharmacotherapy. 2009;29(8):924–9.

442. Stuart GS, Moses A, Corbett A, Phiri G, Kumwenda W, Mkandawire N, et al. Combined oral contraceptives and antiretroviral PK/PD in Malawian women: pharmacokinetics and pharmacodynamics of a combined oral contraceptive and a generic combined formulation antiretroviral in Malawi. J Acquir Immune Defic Syndr. 2011;58(2):e40–3.

443. Nanda K, Delany-Moretlwe S, Dube K, Lendvay A, Kwok C, Molife L, et al. Nevirapine-based antiretroviral therapy does not reduce oral contraceptive effectiveness. AIDS. 2013;27 Suppl 1:S17–25.

444. Mildvan D, Yarrish R, Marshak A, Hutman HW, McDonough M, Lamson M, et al. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. J Acquir Immune Defic Syndr. 2002;29(5):471–7.

445. Landolt NK, Phanuphak N, Ubolyam S, Pinyakorn S, Kriengsinyot R, Ahluwalia J, et al. Efavirenz, in contrast to nevirapine, is associated with unfavorable progesterone and antiretroviral levels when coadministered with combined oral contraceptives. J Acquir Immune Defic Syndr. 2013;62(5):534–9.

446. Sevinsky H, Eley T, Persson A, Garner D, Yones C, Nettles R, et al. The effect of efavirenz on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy HIV-negative women. Antivir Ther. 2011;16(2):149–56.

447. Carten ML, Kiser JJ, Kwara A, Mawhinney S, Cu-Uvin S. Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and Efavirenz. Infect Dis Obstet Gynecol. 2012;2012:137192.

448. Scholler-Gyure M, Kakuda TN, Woodfall B, Aharchi F, Peeters M, Vandermeulen K, et al. Effect of steady-state etravirine on the pharmacokinetics and pharmacodynamics of ethinylestradiol and norethindrone. Contraception. 2009;80(1):44–52.

449. Crauwels HM, van Heeswijk RP, Buelens A, Stevens M, Hoetelmans RM. Lack of an effect of rilpivirine on the pharmacokinetics of ethinylestradiol and norethindrone in healthy volunteers. Int J Clin Pharmacol Ther. 2014;52(2):118–28.

450. Sekar VJ, Lefebvre E, Guzman SS, Felicione E, De Pauw M, Vangeneugden T, et al. Pharmacokinetic interaction between ethinyl estradiol, norethindrone and darunavir with low-dose ritonavir in healthy women. Antivir Ther. 2008;13(4):563–9.

451. Kasserra C, Li J, March B, O'Mara E. Effect of vicriviroc with or without ritonavir on oral contraceptive pharmacokinetics: a randomized, open-label, parallel-group, fixed-sequence crossover trial in healthy women. Clin Ther. 2011;33(10):1503–14.

452. Vogler MA, Patterson K, Kamemoto L, Park JG, Watts H, Aweeka F, et al. Contraceptive efficacy of oral and transdermal hormones when co-administered with protease inhibitors in HIV-1-infected women: pharmacokinetic results of ACTG trial A5188. J Acquir Immune Defic Syndr. 2010;55(4):473–82.

453. Atrio J, Stanczyk FZ, Neely M, Cherala G, Kovacs A, Mishell DR, Jr. Effect of protease inhibitors on steady-state pharmacokinetics of oral norethindrone contraception in HIV-infected women. J Acquir Immune Defic Syndr. 2014;65(1):72–7.

454. Song I, Mark S, Borland J, Chen S, Wajima T, Peppercorn A, et al. Dolutegravir has no effect on the pharmacokinetics of methadone or oral contraceptives with norgestimate and ethinyl estradiol. Atlanta (GA): 20th Conference on Retroviruses and Opportunistic Infections; 3–6 March 2013.

455. Anderson MS, Hanley WD, Moreau AR, Jin B, Bieberdorf FA, Kost JT, et al. Effect of raltegravir on estradiol and norgestimate plasma pharmacokinetics following oral contraceptive administration in healthy women. Br J Clin Pharmacol. 2011;71(4):616–20.

456. Rosenfeld WE, Doose DR, Walker SA, Nayak RK. Effect of topiramate on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in patients with epilepsy. Epilepsia. 1997;38:317–23.

457. Fattore C, Cipolla G, Gatti G, Limido GL, Sturm Y, Bernasconi C, et al. Induction of ethinylestradiol and levonorgestrel metabolism by oxcarbazepine in healthy women. Epilepsia. 1999;40:783–7.

458. Doose DR, Wang S, Padmanabhan M, Schwabe S, Jacobs D, Bialer M. Effects of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in healthy obese and nonobese female subjects. Epilepsia. 2003;44:540–9.

459. Back DJ, Bates M, Bowden A, Breckenridge AM, Hall MJ, Jones H, et al. The interaction of Phenobarbital and other anticonvulsants with oral contraceptive steroid therapy. Contraception. 1980;22:495–503.

460. Sabers A, Ohman I, Christensen J, Tomson T. Oral contraceptives reduce lamotrigine plasma levels. Neurology. 2003;61:570–1.

461. Sabers A, Buchholt JM, Uldall P, Hansen EL. Lamotrigine plasma levels reduced by oral contraceptives. Epilepsy Research. 2001;47:151–4.

462. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia. 2005;46(9):1414–7.

463. Contin M, Albani F, Ambrosetto G, Avoni P, Bisulli F, Riva R, et al. Variation in lamotrigine plasma concentrations with hormonal contraceptive monthly cycles in partiens with epilepsy. Epilepsia. 2006;47(9):1573–5.

464. Christensen J, Petrenaite V, Atterman J, Sidenius P, Ohman I, Tomson T, et al. Oral contraceptives induce lamotrigine metabolism: evidence from a double-blind, placebo-controlled trial. Epilepsia. 2007;48(3):484–9.

465. Bainton R. Interaction between antibiotic therapy and contraceptive medication. Oral Surg Oral Med Oral Pathol. 1986;61:453–5.

466. Bacon JF, Shenfield GM. Pregnancy attributable to interaction between tetracycline and oral contraceptives. Br Med J. 1980;280:293.

467. Back DJ, Tjia J, Martin C, Millar E, Mant T, Morrison P, et al. The lack of interaction between temafloxacin and combined oral contraceptive steroids. Contraception. 1991;43:317–23.

468. Back DJ, Grimmer SF, Orme ML, Proudlove C, Mann RD, Breckenridge AM. Evaluation of the Committee on Safety of Medicines yellow card reports on oral contraceptive-drug interactions with anticonvulsants and antibiotics. Br J Clin Pharmacol. 1988;25:527–32.

469. Back DJ, Breckenridge AM, MacIver M, Orme ML, Rowe PH, Staiger C, et al. The effects of ampicillin on oral contraceptive steroids in women. Br J Clin Pharmacol. 1982;14:43–8.

470. Bollen M. Use of antibiotics when taking the oral contraceptive pill. [comment]. Aust Fam Physician. 1995;24:928–9.

471. Kakouris H, Kovacs GT. Pill failure and nonuse of secondary precautions. Br J Fam Plann. 1992;18:41–4.

472. Joshi JV, Joshi UM, Sankholi GM, Krishna U, Mandlekar A, Chowdhury V, et al. A study of interaction of low-dose combination oral contraceptive with ampicillin and metronidazole. Contraception. 1980;22:643–52.

473. Hughes BR, Cunliffe WJ. Interactions between the oral contraceptive pill and antibiotics. [comment]. Br J Dermatol. 1990;122:717–8.

474. Hetenyi G. Possible interactions between antibiotics and oral contraceptives. Therapia Hungarica (English edition). 1989;37:86–9.

475. Hempel E, Zorn C, Graf K. [Effect of chemotherapy agents and antibiotics on hormonal contraception]. Zeitschrift fur Arztliche Forbildung (Jena). 1978;72:924–6 (in German).

476. Hempel E, Bohm W, Carol W, Klinger G. [Enzyme induction by drugs and hormonal contraception]. Zentralblatt fur Gynakologie. 1973;95:1451–7 (in German).

477. Helms SE, Bredle DL, Zajic J, Jarjoura D, Brodell RT, Krishnarao I. Oral contraceptive failure rates and oral antibiotics. J Am Acad Dermatol. 1997;36:705–10.

478. Grimmer SF, Allen WL, Back DJ, Breckenridge AM, Orme ML, Tjia J. The effect of cotrimoxazole on oral contraceptive steroids in women. Contraception. 1983;28:53–9.

479. Friedman CI, Huneke AL, Kim MH, Powell J. The effect of ampicillin on oral contraceptive effectiveness. Obstet Gynecol. 1980;55:33–7.

480. Donley TG, Smith RF, Roy B. Reduced oral contraceptive effectiveness with concurrent antibiotic use: a protocol for prescribing antibiotics to women of childbearing age. Compendium. 1990;11:392–6.

481. DeSano EA Jr, Hurley SC. Possible interactions of antihistamines and antibiotics with oral contraceptive effectiveness. Fertil Steril. 1982;37:853–4.

482. de Groot AC, Eshuis H, Stricker BH. [Inefficiency of oral contraception during use of minocycline]. Nederlands Tijedschrift voor Geneeskunde. 1990;134:1227–9 (in Dutch).

483. Csemiczky G, Alvendal C, Landgren BM. Risk for ovulation in women taking a low-dose oral contraceptive (Microgynon) when receiving antibacterial treatment with a fluoroquinoline (ofloxacin). Adv Contracept. 1996;12:101–9.

484. Cote J. Interaction of griseofulvin and oral contraceptives. [comment]. J Am Acad Dermatol. 1990;22:124–5.

485. Bromham DR. Knowledge and use of secondary contraception among patients requesting termination of pregnancy. BMJ. 1993;306:556–7.

486. Young LK, Farquhar C, McCowan LM, Roberts HE, Taylor J. The contraceptive practices of women seeking termination of pregnancy in an Auckland clinic. N Z Med J. 1994;107:189–92.

487. Wermeling DP, Chandler MH, Sides GD, Collins D, Muse KN. Dirithromycin increases ethinyl estradiol clearance without allowing ovulation. Obstet Gynecol. 1995;86:78–84.

488. van Dijke CP, Weber JC. Interaction between oral contraceptives and griseofulvin. Br Med J (Clin Res Ed). 1984;288:1125–6.

489. Sparrow MJ. Pill method failures in women seeking abortion – fourteen years experience. N Z Med J. 1998;111:386–8.

490. Sparrow MJ. Pregnancies in reliable pill takers. N Z Med J. 1989;102:575–7.

491. Sparrow MJ. Pill method failures. N Z Med J. 1987;100:102–5.

492. Silber TJ. Apparent oral contraceptive failure associated with antibiotic administration. J Adol Health Care. 1983;4:287–9.

493. Scholten PC, Droppert RM, Zwinkels MG, Moesker HL, Nauta JJ, Hoepelman IM. No interaction between ciprofloxacin and an oral contraceptive. Antimicrob Agents Chemother. 1998;42:3266–8.

494. Pillans PI, Sparrow MJ. Pregnancy associated with a combined oral contraceptive and itraconazole. [comment]. N Z Med J. 1993;106:436.

495. Neely JL, Abate M, Swinker M, D'Angio R. The effect of doxycycline on serum levels of ethinyl estradiol, noretindrone, and endogenous progesterone. Obstet Gynecol. 1991;77:416–20.

496. Murphy AA, Zacur HA, Charache P, Burkman RT. The effect of tetracycline on levels of oral contraceptives. Am J Obstet Gynecol. 1991;164:28–33.

497. Maggiolo F, Puricelli G, Dottorini M, Caprioloi S, Bianchi W, Suter F. The effects of ciprofloxacin on oral contraceptive steroid treatments. Drugs Exp Clin Res. 1991;17:451–4.

498. London BM, Lookingbill DP. Frequency of pregnancy in acne patients taking oral antibiotics and oral contraceptives. Arch Dermatol. 1994;130:392–3.

499. Lequeux A. [Pregnancy under oral contraceptives after treatment with tetracycline]. Louvain Medical. 1980;99:413–4 (in French).

500. Kovacs GT, Riddoch G, Duncombe P, Welberry L, Chick P, Weisberg E, et al. Inadvertent pregnancies in oral contraceptive users. Med J Aust. 1989;150:549–51.

501. Kakouris H, Kovacs GT. How common are predisposing factors to pill failure among pill users? Br J Fam Plann. 1994;20:33–5.

502. Abrams LS, Skee D, Natarajan J, Wong FA. Pharmocokinetic overview of Ortho Evra/Evra. Fertil Steril. 2002;77(supplement 2):s3–s12.

503. Dogterom P, van den Heuvel MW, Thomsen T. Absence of pharmacokinetic interactions of the combined contraceptive vaginal ring NuvaRing with oral amoxicillin or doxycycline in two randomized trials. Clin Pharmacokinet. 2005;44:429–38.

504. van Puijenbroek EP, Feenstra J, Meyboom RH. [Pill cycle disturbance in simultaneous use of itraconazole and oral contraceptives]. Ned Tijdschr Geneeskd. 1998;142:146–9 (in Dutch).

505. Sinofsky FE, Pasquale SA. The effect of fluconazole on circulating ethinyl estradiol levels in women taking oral contraceptives. Am J Obstet Gynecol. 1998;178:300–4.

506. Rieth H, Sauerbrey N. [Interaction studies with fluconazole, a new tirazole antifungal drug]. Wiener Medizinische Wochenschrift. 1989;139:370–4 (in German).

507. Meyboom RH, van Puijenbroek EP, Vinks MH, Lastdrager CJ. Disturbance of withdrawal bledding during concomitant use of itraconazole and oral contraceptives. N Z Med J. 1997;110:300.

508. McDaniel PA, Cladroney RD. Oral contraceptives and griseofulvin interactions. DICP. 1986;20:384.

509. Lunell NO, Pschera H, Zador G, Carlstrom K. Evaluation of the possible interaction of the antifungal triazole SCH 39304 with oral contraceptives in normal health women. Gynecol Obstet Invest. 1991;32:91–7.

510. Kovacs I, Somos P, Hamori M. Examination of the potential interaction between ketoconazole (Nizoral) and oral contraceptives with special regard to products of low hormone content (Rigevidon, anteovin). Therapia Hungarica (English edition). 1986;34:167–70.

511. Hilbert J, Messig M, Kuye O. Evaluation of interaction between fluconazole and an oral contraceptive in healthy women. Obstet Gynecol. 2001;98:218–23.

512. Devenport MH, Crook D, Wynn V, Lees LJ. Metabolic effects of low-dose fluconazole in healthy female users and non-users of oral contraceptives. Br J Clin Pharmacol. 1989;27:851–9.

513. van Puijenbroek EP, Egberts ACG, Meyboom RHB, Leufkens HGM. Signalling possible drug-drug interactions in a spontaneous reporting system: delay of withdrawal bleeding during concomitant use of oral contraceptives and itraconazole. Br J Clin Pharmacol. 1999;47:689–93.

514. Verhoeven CH, van den Heuvel MW, Mulders TM, Dieben TO. The contraceptive vaginal ring, NuvaRing, and antimycotic co-medication. Contraception. 2004;69:129–32.

515. Wanwimolruk S, Kaewvichit S, Tanthayaphinant O, Suwannarach C, Oranratnachai A. Lack of effect of oral contraceptive use on the pharmacokinetics of quinine. Br J Clin Pharmacol. 1991;31:179–81.

516. McGready R, Stepniewska K, Seaton E, Cho T, Cho D, Ginsberg A, et al. Pregnancy and use of oral contaceptives reduces the biotransformation of proguanil to cycloguanil. Eur J Clin Pharmacol. 2003;59:553–7.

517. Karbwang J, Looareesuwan S, Back DJ, Migasana S, Bunnag D. Effect of oral contraceptive steroids on the clinical course of malaria infection and on the pharmacokinetics of mefloquine in Thai women. Bull World Health Organ. 1988;66:763–7.

518. Croft AM, Herxheimer A. Adverse effects of the antimalaria drug, mefloquine: due to primary liver damage with secondary thyroid involvement? BMC Public Health. 2002;2:6.

519. Back DJ, Breckenridge AM, Grimmer SF, Orme ML, Purba HS. Pharmacokinetics of oral contraceptive steroids following the administration of the antimalarial drugs primaquine and chloroquine. Contraception. 1984;30:289–95.

520. Gupta KC, Ali MY. Failure of oral contraceptive with rifampicin. Med J Zambia. 1981;15:23.

521. Bolt HM, Bolt M, Kappus H. Interaction of rifampicin treatment with pharmacokinetics and metabolism of ethinyloestradiol in man. Acta Endocrinol (Copenh). 1977;85:189–97.

522. Barditch-Crovo P, Trapnell CB, Ette E, Zacur HA, Coresh J, Rocco LE, et al. The effects of rifampicin and rifabutin on the pharmacokinetics and pharmacodynamics of a combination oral contraceptive. Clin Pharmacol Ther. 1999;65:428–38.

523. Back DJ, Breckenridge AM, Crawford FE, Hall JM, MacIver M, Orme ML, et al. The effect of rifampicin on the pharmacokinetics of ethynylestradiol in women. Contraception. 1980;21:135–43.

524. Back DJ, Breckenridge AM, Crawford FE, MacIver M, Orme ML, Park BK, et al. The effect of rifampicin on norethisterone pharmacokinetics. Eur J Clin Pharmacol. 1979;15:193–7.

525. Joshi JV, Joshi UM, Sankholi GM, Gupta K, Rao AP, Hazari K, et al. A study of interaction of a low-dose combination oral contraceptive with anti-tubercular drugs. Contraception. 1980;21:617–29.

526. Hirsch A, Tillement JP, Chretien J. *Effets contrariants de la rifampicine sur les contraceptifs oraux: a propos de trois grossesses non desiree chez trois malades.* Revue française des maladies respiratoires. 1975;2:174–82 (in French).

527. Hirsch A. [Letter: Sleeping pills]. La Nouvelle presse médicale. 1973;2:2957 (in French).

528. Kropp R. [Rifampicin and oral contraceptives (author's transl)]. Praxis der Pneumologie vereinigt mit Der Tuberkulosearzt. 1974;28:270–2 (in German).

529. Szoka PR, Edgren RA. Drug interactions with oral contraceptives: compilation and analysis of an adverse experience report database. Fertil Steril. 1988;49:s31–s8.

530. Skolnick JL, Stoler BS, Katz DB, Anderson WH. Rifampicin, oral contraceptives, and pregnancy. JAMA. 1976;236:1382.

531. Reimers D, Jezek A. [the simultaneous use of rifampicin and other antitubercular agents with oral contraceptives]. Praxis der Pneumologie vereinigt mit Der Tuberkulosearzt. 1971;25:255–62 (in German).

532. Piguet B, Muglioni JF, Chaline G. [Letter: Oral contraception and rifampicin]. La Nouvelle presse médicale. 1975;4:115–6 (in French).

533. Nocke-Finke L, Breuer H, Reimers D. [Effects of rifampicin on the menstrual cycle and on oestrogen excretion in patients taking oral contraceptives]. Deutsche medizinische Wochenschrift. 1973;98:1521–3 (in German).

534. Meyer B, Muller F, Wessels P, Maree J. A model to detect interactions between roxithromycin and oral contraceptives. Clin Pharmacol Ther. 1990;47:671–4.

535. LeBel M, Masson E, Guilbert E, Colborn D, Paquet F, Allard S, et al. Effects of rifabutin and rifampicin on the pharmacokinetics of ethinylestradiol and norethindrone. J Clin Pharmacol. 1998;38:1042–50.

2.7.2 Progestogen-only contraceptives (POCs)

PROGESTOGEN-ONLY PILLS (POPs)

POPs contain only a progestogen and no estrogen.

PROGESTOGEN-ONLY INJECTABLES (POIs)

These injectables include depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN).

There are three formulations considered here:

1. DMPA-IM = 150 mg of DMPA given intramuscularly
2. DMPA-SC = 104 mg of DMPA given subcutaneously
3. NET-EN = 200 mg of NET-EN given intramuscularly

Identified evidence for the conditions of age, obesity, endometriosis and HIV among DMPA-SC users appear consistent with existing recommendations for DMPA-IM *(1–12)*. Further, DMPA-SC and DMPA-IM appear to be therapeutically equivalent, with similar safety profiles when used by healthy women *(3, 5, 11)*. Pending further evidence, the Guideline Development Group (GDG) concluded that the evidence available for DMPA-IM applies to DMPA-SC and, therefore, DMPA-SC should have the same categories as DMPA-IM; the assigned recommendations should be considered a preliminary best judgement, which will be re-evaluated as new data become available.

PROGESTOGEN-ONLY IMPLANTS

Progestogen-only implants are a type of long-acting, reversible contraception. The various types of implants that are considered here are the following:

1. Levonorgestrel (LNG): The LNG-containing implants are Norplant®, Jadelle® and Sino-implant (II)®.
   a. Norplant® is a 6-rod implant, each rod containing 36 mg of LNG (no longer in production).
   b. Jadelle® is a 2-rod implant, each rod containing 75 mg of LNG
   c. Sino-implant (II) ® is a 2-rod implant, each rod containing 75 mg of LNG
2. Etonogestrel (ETG): The ETG-containing implants are Implanon® and Nexplanon®. Both consist of a single-rod implant containing 68 mg of ETG.

No studies were identified that provided direct evidence on the use of the Sino-implant (II) among women with medical conditions in the MEC and included a comparison group. Evidence from three studies of healthy women demonstrate that Sino-implant (II) has a similar safety and pharmacokinetic profile to that of other LNG implants, with no significant differences in serious adverse events, such as ectopic pregnancy or discontinuation due to medical problems *(13–15)*. Therefore, safety data from studies of other LNG implants among women with medical conditions were used due to the similarity of Sino-implant (II) and other LNG implants in hormone formulation, quality profile and daily release rates. The GDG assigned the same recommendations for Sino-implant (II) as for the other LNG implants.

PROGESTOGEN-ONLY CONTRACEPTIVES (POCs)

POCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation			CLARIFICATIONS/EVIDENCE
	POP	DMPA/ NET-EN	LNG/ETG	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**POP** = progestogen-only pill **LNG/ETG** = levonorgestrel and etonogestrel (implants) **DMPA** = depot medroxyprogesterone acetate (injectable) **NET-EN** = norethisterone enanthate (injectable)			
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY				
PREGNANCY	NA	NA	NA	NA = not applicable **Clarification**: Use of POCs is not required. There is no known harm to the woman, the course of her pregnancy, or the fetus if POCs are accidentally used during pregnancy. However, the relationship between DMPA use during pregnancy and its effects on the fetus remains unclear.
AGE a) Menarche to < 18 years b) 18 to 45 years c) > 45 years	 1 1 1	 2 1 2	 1 1 1	**Evidence**: Most studies have found that women lose bone mineral density (BMD) during DMPA use, but recover BMD after discontinuation. Limited evidence shows a weak association with fracture, although 1 large study suggests that women who choose DMPA may be at higher risk for fracture even prior to initiation of the method *(16)*. It is unclear whether adult women with long durations of DMPA use can regain BMD to baseline levels before entering menopause and whether adolescents can reach peak bone mass after discontinuation of DMPA. The relationship between these changes in BMD during the reproductive years and future fracture risk is unknown. Studies generally find no effect of POCs other than DMPA on BMD *(5, 12, 16–60)*.
PARITY a) Nulliparous b) Parous	 1 1	 1 1	 1 1	

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BREASTFEEDING†				**Clarification:** There is theoretical concern about the potential exposure of the neonate to DMPA/NET-EN during the first 6 weeks postpartum. In many settings, however, pregnancy-related morbidity and mortality risks are high, and access to services is limited. In such settings, DMPA/NET-EN may be among the few methods widely available and accessible to breastfeeding women immediately postpartum. **Evidence:** Direct evidence demonstrates no harmful effect of POCs on breastfeeding performance (61–109) and generally demonstrates no harmful effects on infant growth, health or development *(74, 76, 89, 99)*; however, these studies have been inadequately designed to determine whether a risk of long-term effects exists. Animal data suggest an effect of progesterone on the developing brain; whether similar effects occur following progestogen exposure in humans is unclear *(110–112)*.
a) < 6 weeks postpartum	2	3	2	
b) ≥ 6 weeks to < 6 months postpartum (primarily breastfeeding)	1	1	1	
c) ≥ 6 months postpartum	1	1	1	
POSTPARTUM (NON-BREASTFEEDING WOMEN)				
a) < 21 days	1	1	1	
b) ≥ 21 days	1	1	1	
POST-ABORTION				**Clarification**: POCs may be started immediately post-abortion. **Evidence**: Limited evidence suggests that there are no adverse side-effects when an LNG implant or NET-EN are initiated after first-trimester abortion *(113–116)*.
a) First trimester	1	1	1	
b) Second trimester	1	1	1	
c) Immediate post-septic abortion	1	1	1	
PAST ECTOPIC PREGNANCY*	2	1	1	
HISTORY OF PELVIC SURGERY	1	1	1	
SMOKING				
a) Age < 35 years	1	1	1	
b) Age ≥ 35 years				
i) < 15 cigarettes/day	1	1	1	
ii) ≥ 15 cigarettes/day	1	1	1	

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OBESITY a) ≥ 30 kg/m^2 BMI b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	 1 1	 1 2	 1 1	**Clarification**: There is evidence for differential weight gain among normal-weight and obese adolescents who use DMPA, but not among those using NET-EN. However, NET-EN is Category 2 due to evidence regarding potential effects of NET-EN on BMD among adolescents (see row: Age). **Evidence**: Among adult women, there is generally no association between baseline weight and weight gain among DMPA users compared with non-users. Evidence is mixed for adolescent DMPA users, with some studies observing greater weight gain among obese compared with normal-weight users, but other studies showing no association. Methodological differences across studies may account for the differences in findings. Data on other POC methods and other adverse outcomes are limited *(10, 117–133)*.
BLOOD PRESSURE MEASUREMENT UNAVAILABLE	NA	NA	NA	NA = not applicable **Clarification**: It is desirable to have blood pressure measurements taken before initiation of POC use. However, in some settings blood pressure measurements are unavailable. In many of these settings, pregnancy-related morbidity and mortality risks are high, and POCs are among the few methods widely available. In such settings, women should not be denied use of POCs simply because their blood pressure cannot be measured.
CARDIOVASCULAR DISEASE				
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (such as older age, smoking, diabetes, hypertension and known dyslipidaemias)	2	3	2	**Clarification**: When multiple major risk factors exist, the risk of cardiovascular disease may increase substantially. Some POCs may increase the risk of thrombosis, although this increase is substantially less than with combined oral contraceptives (COCs). The effects of DMPA and NET-EN may persist for some time after discontinuation.

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HYPERTENSION* For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, the risk of cardiovascular disease may increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive.				
a) History of hypertension, where blood pressure CANNOT be evaluated (including hypertension in pregnancy)	2	2	2	**Clarification**: It is desirable to have blood pressure measurements taken before initiation of POC use. However, in some settings blood pressure measurements are unavailable. In many of these settings, pregnancy-related morbidity and mortality risks are high, and POCs are among the few types of methods widely available. In such settings, women should not be denied the use of POCs simply because their blood pressure cannot be measured.
b) Adequately controlled hypertension, where blood pressure CAN be evaluated	1	2	1	**Clarification**: Women adequately treated for hypertension are at reduced risk of acute myocardial infarction (MI) and stroke as compared with untreated women. Although there are no data, POC users with adequately controlled and monitored hypertension should be at reduced risk of acute MI and stroke compared with untreated hypertensive POC users.
c) Elevated blood pressure levels (properly taken measurements)				**Evidence**: Limited evidence suggests that among women with hypertension, those who used POPs or progestogen-only injectables (POIs) had a small increased risk of cardiovascular events compared with women who did not use these methods *(134)*.
i) systolic 140–159 or diastolic 90–99 mm Hg	1	2	1	
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	2	3	2	
d) Vascular disease	2	3	2	
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	1	1	1	

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DEEP VEIN THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)*				
a) History of DVT/PE	2	2	2	
b) Acute DVT/PE	3	3	3	**Evidence**: There is no direct evidence on the use of POCs among women with DVT/PE on anticoagulant therapy. Although evidence on the risk of venous thrombosis with the use of POCs is inconsistent in otherwise healthy women, any small increased risk is substantially less than that with COCs *(134–136)*.
c) DVT/PE and established on anticoagulant therapy	2	2	2	**Evidence**: There is no direct evidence on the use of POCs among women with DVT/PE on anticoagulant therapy. Although evidence on the risk of venous thrombosis with the use of POCs is inconsistent in otherwise healthy women, any small increased risk is substantially less than that with COCs *(134–136)*. Limited evidence indicates that intramuscular injections of DMPA in women on chronic anticoagulation therapy does not pose a significant risk of haematoma at the injection site or increase the risk of heavy or irregular vaginal bleeding *(137, 138)*.
d) Family history (first-degree relatives)	1	1	1	
e) Major surgery				
i) with prolonged immobilization	2	2	2	
ii) without prolonged immobilization	1	1	1	
f) Minor surgery without immobilization	1	1	1	
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	2	2	2	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.

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SUPERFICIAL VENOUS DISORDERS						
a) Varicose veins	1		1	1		
b) Superficial venous thrombosis	1		1	1		
CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE*	I	C		I	C	
	2	3	3	2	3	
STROKE* (HISTORY OF CEREBROVASCULAR ACCIDENT)	I	C		I	C	
	2	3	3	2	3	
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS	2		2	2		**Clarification**: Routine screening is not appropriate because of the rarity of the condition and the high cost of screening.
VALVULAR HEART DISEASE						
a) Uncomplicated	1		1	1		
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	1		1	1		
RHEUMATIC DISEASES						
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)*						
People with SLE are at increased risk of ischaemic heart disease, stroke and venous thromboembolism. Categories assigned to such conditions in the *Medical eligibility criteria for contraceptive use* should be the same for women with SLE who present with these conditions. For all categories of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Available evidence indicates that many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives *(139–156)*.						
		I	C			
a) Positive (or unknown) antiphospholipid antibodies	3	3	3	3		**Evidence**: Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis *(157–159)*.
b) Severe thrombocytopenia	2	3	2	2		
c) Immunosuppressive treatment	2	2	2	2		
d) None of the above	2	2	2	2		

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NEUROLOGIC CONDITIONS							
HEADACHES*	I	C	I	C	I	C	
a) Non-migrainous (mild or severe)	1	1	1	1	1	1	**Clarification**: Classification depends on accurate diagnosis of those severe headaches that are migrainous and those that are not. Any new headaches or marked changes in headaches should be evaluated. Classification is for women without any other risk factors for stroke. Risk of stroke increases with age, hypertension and smoking.
b) Migraine							
i) without aura							
age < 35 years	1	2	2	2	2	2	
age ≥ 35 years	1	2	2	2	2	2	
ii) with aura, at any age	2	3	2	3	2	3	
EPILEPSY	1		1		1		**Clarification**: If a woman is taking anticonvulsants, refer to the last section of this table, on drug interactions. Certain anticonvulsants lower POC effectiveness.
DEPRESSIVE DISORDERS							
DEPRESSIVE DISORDERS	1		1		1		**Clarification**: The classification is based on data for women with selected depressive disorders. No data on bipolar disorder or postpartum depression were available. There is a potential for drug interactions between certain antidepressant medications and hormonal contraceptives. **Evidence**: POC use did not increase depressive symptoms in women with depression compared with baseline *(160–163)*.
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS							
VAGINAL BLEEDING PATTERNS*							
a) Irregular pattern without heavy bleeding	2		2		2		
b) Heavy or prolonged bleeding (includes regular and irregular patterns)	2		2		2		**Clarification**: Unusually heavy bleeding should raise the suspicion of a serious underlying condition.

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UNEXPLAINED VAGINAL BLEEDING* (suspicious for serious condition) Before evaluation	2	3	3	**Clarification**: If pregnancy or an underlying pathological condition (such as pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation.
ENDOMETRIOSIS	1	1	1	
BENIGN OVARIAN TUMOURS (including cysts)	1	1	1	
SEVERE DYSMENORRHOEA	1	1	1	
GESTATIONAL TROPHOBLASTIC DISEASE				
a) Decreasing or undetectable β-hCG levels	1	1	1	
b) Persistently elevated β-hCG levels or malignant disease	1	1	1	
CERVICAL ECTROPION	1	1	1	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)	1	2	2	**Evidence**: Among women with persistent human papillomavirus (HPV) infection, long-term DMPA use (≥ 5 years) may increase the risk of carcinoma in situ and invasive carcinoma *(164)*.
CERVICAL CANCER* (awaiting treatment)	1	2	2	
BREAST DISEASE*				
a) Undiagnosed mass	2	2	2	**Clarification**: Evaluation should be pursued as early as possible.
b) Benign breast disease	1	1	1	
c) Family history of cancer	1	1	1	
d) Breast cancer				
i) current	4	4	4	
ii) past and no evidence of current disease for 5 years	3	3	3	
ENDOMETRIAL CANCER*	1	1	1	
OVARIAN CANCER*	1	1	1	

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UTERINE FIBROIDS*				
a) Without distortion of the uterine cavity	1	1	1	
b) With distortion of the uterine cavity	1	1	1	
PELVIC INFLAMMATORY DISEASE (PID)*				
a) Past PID (assuming no current risk factors for STIs)				
i) with subsequent pregnancy	1	1	1	
ii) without subsequent pregnancy	1	1	1	
b) PID – current	1	1	1	
STIs				
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	
b) Other STIs (excluding HIV and hepatitis)	1	1	1	
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	
d) Increased risk of STIs	1	1	1	**Evidence**: Evidence suggests that there may be an increased risk of chlamydial cervicitis among DMPA users at high risk of STIs. For other STIs, there is either evidence of no association between DMPA use and STI acquisition or too limited evidence to draw any conclusions. There is no evidence for other POCs *(165–172)*.

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HIV/AIDS				
HIGH RISK OF HIV	1	1	1	See below for Clarification/Evidence

Clarification for high risk of HIV:

Women at high risk of HIV who are using progestogen-only injectables (POIs) should be informed that available studies on the association between POI contraception and HIV acquisition have important methodological limitations hindering interpretation. Some studies suggest that women using POI contraception may be at increased risk of HIV acquisition; other studies have not found this association. The public health impact of any such association would depend upon the local context, including rates of injectable contraceptive use, maternal mortality and HIV prevalence. This must be considered when adapting guidelines to local contexts. WHO expert groups continue to actively monitor any emerging evidence. At the meeting in 2014, as at the 2012 technical consultation, it was agreed that the epidemiological data did not warrant a change to the MEC. Given the importance of this issue, women at high risk of HIV infection should be informed that POIs may or may not increase their risk of HIV acquisition. Women and couples at high risk of HIV acquisition considering POIs should also be informed about and have access to HIV preventive measures, including male and female condoms.

Evidence for high risk of HIV:

Five studies assessed the use of NET-EN injectables and were considered to be "informative but with important limitations" *(73)*. Four of them reported no statistically significant association with HIV acquisition *(174–177)*, while one did *(178)*.

Nine studies assessed DMPA, or, if a DMPA-specific result was unavailable, assessed non-specified injectables; these studies were considered to be "informative but with important limitations" *(173)*. The results were mixed: three of the studies showed a significant increase in risk *(178–180)*, one showed a significant increase in risk using one statistical model but this association was not statistically significant using another statistical model *(181, 182)*, and five showed no significant increase in risk *(174–177, 183)*.

Two studies assessed implants, one of which was classified as "unlikely to inform the primary question" *(173, 184)*. Neither of these studies reported a statistically significant increased risk of HIV acquisition, but confidence intervals were wide *(184, 185)*.

PROGESTOGEN-ONLY CONTRACEPTIVES (POCs)

POCs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation			CLARIFICATIONS/EVIDENCE
	POP	DMPA/ NET-EN	LNG/ETG	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	**POP** = progestogen-only pill **LNG/ETG** = levonorgestrel and etonogestrel (implants) **DMPA** = depot medroxyprogesterone acetate (injectable) **NET-EN** = norethisterone enanthate (injectable)			
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	1	1	1	**Clarification for asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) and severe or advanced HIV clinical disease (WHO stage 3 or 4)**: Because there may be drug interactions between hormonal contraceptives and ARV therapy, refer to the last section of this table, on drug interactions. **Evidence for asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) and severe or advanced HIV clinical disease (WHO stage 3 or 4):** Out of 6 available studies, 5 suggest no association between use of POIs and progression of HIV, as measured by CD4 count < 200 cells/mm3, initiation of antiretroviral therapy (ART), or mortality (186–190). One randomized trial found an increased risk of a composite outcome of declining CD4 count or death among oral contraceptive users (COCs and POPs) when compared with users of copper-bearing IUDs; this study, however, had significant loss to follow-up and method switching among groups, limiting its interpretation (188, 191). One study found no difference in ART initiation or CD4 count between users and non-users of the LNG-IUD (192). Two prospective observational studies directly assessed the effects of different hormonal contraceptive methods on female-to-male HIV transmission by measuring seroconversions in male partners of women living with HIV and known to be using hormonal contraceptives. One study reported a statistically significant association between use of POIs and female-to-male transmission of HIV (180), while another study did not find a statistically significant association between use of DMPA and female-to-male HIV transmission (184). The findings of studies indirectly assessing the effects of various hormonal contraceptive methods on female-to-male HIV transmission by measuring genital viral shedding as a proxy for infectivity have been mixed. Most of indirect studies measuring whether various hormonal contraceptive methods affect plasma HIV viral load have found no effect (189, 193–207).
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	1	1	1	

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OTHER INFECTIONS				
SCHISTOSOMIASIS				
a) Uncomplicated	1	1	1	**Evidence**: Among women with uncomplicated schistosomiasis, limited evidence showed that DMPA use had no adverse effects on liver function *(208)*.
b) Fibrosis of the liver (if severe, see cirrhosis)	1	1	1	
TUBERCULOSIS				
a) Non-pelvic	1	1	1	**Clarification**: If a woman is taking rifampicin, refer to the last section of this table, on drug interactions. Rifampicin is likely to decrease the effectiveness of some POCs.
b) Pelvic	1	1	1	
MALARIA	1	1	1	
ENDOCRINE CONDITIONS				
DIABETES*				
a) History of gestational disease	1	1	1	**Evidence**: POCs had no adverse effects on serum lipid levels in women with a history of gestational diabetes in 2 small studies *(209, 210)*. There is only limited and inconsistent evidence regarding the development of non-insulin-dependent diabetes among users of POCs with a history of gestational diabetes *(211–214)*.
b) Non-vascular disease				**Evidence**: Among women with insulin- or non-insulin-dependent diabetes, limited evidence on the use of progestogen-only methods (POPs, DMPA injectable, LNG implant) suggests that these methods have little effect on short-term or long-term diabetes control (e.g. HbA1c levels), haemostatic markers or lipid profile *(215–218)*.
i) non-insulin dependent	2	2	2	
ii) insulin dependent	2	2	2	
c) Nephropathy/retinopathy/ neuropathy	2	3	2	
d) Other vascular disease or diabetes of > 20 years' duration	2	3	2	

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THYROID DISORDERS				
a) Simple goitre	1	1	1	
b) Hyperthyroid	1	1	1	
c) Hypothyroid	1	1	1	
GASTROINTESTINAL CONDITIONS				
GALL BLADDER DISEASE				
a) Symptomatic				
i) treated by cholecystectomy	2	2	2	
ii) medically treated	2	2	2	
iii) current	2	2	2	
b) Asymptomatic	2	2	2	
HISTORY OF CHOLESTASIS*				
a) Pregnancy-related	1	1	1	
b) Past-COC related	2	2	2	
VIRAL HEPATITIS				
a) Acute or flare	1	1	1	
b) Carrier	1	1	1	
c) Chronic	1	1	1	
CIRRHOSIS				
a) Mild (compensated)	1	1	1	
b) Severe (decompensated)	3	3	3	
LIVER TUMOURS*				
a) Benign				
i) focal nodular hyperplasia	2	2	2	**Evidence**: There is limited, direct evidence that hormonal contraceptive use does not influence either progression or regression of liver lesions among women with focal nodular hyperplasia *(219–221)*.
ii) hepatocellular adenoma	3	3	3	
b) Malignant (hepatoma)	3	3	3	

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ANAEMIAS				
THALASSAEMIA	1	1	1	
SICKLE CELL DISEASE	1	1	1	**Evidence**: Among women with sickle cell disease, POC use did not have adverse effects on haematological parameters and, in some studies, was beneficial with respect to clinical symptoms *(222–229)*.
IRON-DEFICIENCY ANAEMIA*	1	1	1	
DRUG INTERACTIONS				
ANTIRETROVIRAL THERAPY (ART)				
a) Nucleoside reverse transcriptase inhibitors (NRTIs)				**Evidence**: NRTIs do not appear to have significant risk of interactions with hormonal contraceptive methods *(230, 231)*.
Abacavir (ABC)	1	1	1	
Tenofovir (TDF)	1	1	1	
Zidovudine (AZT)	1	1	1	
Lamivudine (3TC)	1	1	1	
Didanosine (DDI)	1	1	1	
Emtricitabine (FTC)	1	1	1	
Stavudine (D4T)	1	1	1	
b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)				**Clarification**: Antiretroviral drugs have the potential to either decrease or increase the levels of steroid hormones in women using hormonal contraceptives. Pharmacokinetic data suggest potential drug interactions between some antiretroviral drugs (particularly some NNRTIs and ritonavir-boosted PIs) and some hormonal contraceptives. These interactions may reduce the effectiveness of the hormonal contraceptive. **Evidence**: One retrospective chart review of women using efavirenz-containing ART showed increased contraceptive failure rates for women using LNG implants *(232)*. Based primarily on pharmacokinetic data, the effectiveness of DMPA is likely not affected by NNRTIs, and vice versa *(233, 234)*.
Efavirenz (EFV)	2	DMPA=1 NET-EN=2	2	
Etravirine (ETR)	1	1	1	
Nevirapine (NVP)	2	DMPA=1 NET-EN=2	2	
Rilpivirine (RPV)	1	1	1	

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c) Protease inhibitors (PIs)				**Clarification**: Antiretroviral drugs have the potential to either decrease or increase the levels of steroid hormones in women using hormonal contraceptives. Pharmacokinetic data suggest potential drug interactions between some antiretroviral drugs (particularly some NNRTIs and ritonavir-boosted PIs) and some hormonal contraceptives. These interactions may reduce the effectiveness of the hormonal contraceptive. **Evidence**: One study found higher progestogen levels with concurrent PI use in users of POPs *(238)*. Based primarily on pharmacokinetic data, the effectiveness of DMPA is likely not affected by PIs, and vice versa *(233, 234)*.
Ritonavir-boosted atazanavir (ATV/r)	2	DMPA=1 NET-EN=2	2	
Ritonavir-boosted lopinavir (LPV/r)	2	DMPA=1 NET-EN=2	2	
Ritonavir-boosted darunavir (DRV/r)	2	DMPA=1 NET-EN=2	2	
Ritonavir (RTV)	2	DMPA=1 NET-EN=2	2	
d) Integrase inhibitors				Evidence: The integrase inhibitor raltegravir does not appear to interact with norgestimate-containing COCs *(239, 240)*.
Raltegravir (RAL)	1	1	1	
ANTICONVULSANT THERAPY				
a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	3	DMPA=1 NET-EN=2	2	**Clarification**: Although the interaction of certain anticonvulsants with POPs, NET-EN and LNG/ETG implants is not harmful to women, it is likely to reduce the effectiveness of POPs, NET-EN and LNG/ETG implants. Whether increasing the hormone dose of POPs alleviates this concern remains unclear. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. Use of DMPA is Category 1 because its effectiveness is not decreased by the use of certain anticonvulsants. **Evidence**: Use of certain anticonvulsants may decrease the effectiveness of POCs *(241–243)*.
b) Lamotrigine	1	1	1	**Evidence**: No drug interactions have been reported among women with epilepsy taking lamotrigine and using POCs *(244)*.

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ANTIMICROBIAL THERAPY				
a) Broad-spectrum antibiotics	1	1	1	
b) Antifungals	1	1	1	
c) Antiparasitics	1	1	1	
d) Rifampicin or rifabutin therapy	3	DMPA=1 NET-EN=2	2	**Clarification**: Although the interaction of rifampicin or rifabutin with POPs, NET-EN and LNG/ETG implants is not harmful to women, it is likely to reduce the effectiveness of POPs, NET-EN and LNG/ETG implants. Whether increasing the hormone dose of POPs alleviates this concern remains unclear. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. Use of DMPA is Category 1 because its effectiveness is not decreased by the use of rifampicin or rifabutin.

RECOMMENDATIONS REVIEWED FOR FIFTH EDITION

These recommendations were reviewed according to WHO requirements for guideline development, as part of the preparation of the *Medical eligibility criteria for contraceptive use, fifth edition*. The Population, Intervention, Comparator, Outcome (PICO) questions developed by the Guideline Development Group (GDG) and the databases searched to retrieve the evidence, which guided the preparation of systematic reviews, are described in greater detail in Part I of this document. Additionally, GRADE evidence profiles, the overall GRADE assessment of the quality of the evidence, summaries of the evidence supporting the recommendation(s), and other supplementary remarks from the GDG regarding the recommendations, are available in Part I.

ADDITIONAL COMMENTS

PAST ECTOPIC PREGNANCY

POPs have a higher absolute rate of ectopic pregnancy compared with other POCs, but still less than using no method. The 75 µg desogestrel-containing pill inhibits ovulation in most cycles, which suggests a low risk of ectopic pregnancy.

HYPERTENSION

Vascular disease: There is concern regarding hypo-estrogenic effects and reduced high-density lipoprotein (HDL) levels, particularly among users of DMPA and NET-EN. However, there is little concern about these effects with regard to POPs or LNG/ETG implants. The effects of DMPA and NET-EN may persist for some time after discontinuation.

DEEP VEIN THROMBOSIS/PULMONARY EMBOLISM

Women on anticoagulation therapy who have a history of haemorrhagic ovarian cysts may benefit from DMPA use.

CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE

There is concern regarding hypo-estrogenic effects and reduced HDL levels, particularly among users of DMPA and NET-EN. However, there is little concern about these effects with regard to POPs or LNG/ETG implants. The effects of DMPA and NET-EN may persist for some time after discontinuation.

STROKE

There is concern regarding hypo-estrogenic effects and reduced HDL levels, particularly among users of DMPA and NET-EN. However, there is little concern about these effects with regard to POPs or LNG/ETG implants. The effects of DMPA and NET-EN may persist for some time after discontinuation.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Severe thrombocytopenia increases the risk of bleeding. POCs may be useful in the treatment of menorrhagia in women with severe thrombocytopenia. However, given the increased or erratic bleeding that may be seen on initiation of DMPA and its irreversibility for 11–13 weeks after administration, initiation of this method in women with severe thrombocytopenia should be done with caution.

HEADACHES

Aura is a specific focal neurologic symptom. For more information on this and other diagnostic criteria, see: Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. Cephalalgia. 2004;24(Suppl 1):1–150.[13]

There is concern that severe headaches may increase with use of NET-EN, DMPA and implants. The effects of NET-EN and DMPA may persist for some time after discontinuation.

VAGINAL BLEEDING PATTERNS

Irregular menstrual bleeding patterns are common among healthy women. POC use frequently induces an irregular bleeding pattern. Implant use may induce irregular bleeding patterns, especially during the first 3–6 months, but these patterns may persist longer. ETG users are more likely than LNG users to develop amenorrhoea.

UNEXPLAINED VAGINAL BLEEDING

POCs may cause irregular bleeding patterns, which may mask symptoms of underlying pathology. The effects of DMPA and NET-EN may persist for some time after discontinuation.

13 Available at: http://ihs-classification.org/en/02_klassifikation

CERVICAL CANCER (AWAITING TREATMENT)

There is some theoretical concern that POC use may affect prognosis of the existing disease. While awaiting treatment, women may use POCs. In general, treatment of this condition renders a woman sterile.

BREAST DISEASE

Breast cancer: Breast cancer is a hormonally sensitive tumour, and the prognosis of women with current or recent breast cancer may worsen with POC use.

ENDOMETRIAL CANCER

While awaiting treatment, women may use POCs. In general, treatment of this condition renders a woman sterile.

OVARIAN CANCER

While awaiting treatment, women may use POCs. In general, treatment of this condition renders a woman sterile.

UTERINE FIBROIDS

POCs do not appear to cause growth of uterine fibroids.

PELVIC INFLAMMATORY DISEASE (PID)

Whether POCs, like COCs, reduce the risk of PID among women with STIs is unknown, but they do not protect against HIV or lower genital tract STIs.

DIABETES

Nephropathy/retinopathy/neuropathy, other vascular disease, or diabetes of > 20 years' duration: There is concern regarding hypo-estrogenic effects and reduced HDL levels, particularly among users of DMPA and NET-EN. The effects of DMPA and NET-EN may persist for some time after discontinuation. Some POCs may increase the risk of thrombosis, although this increase is substantially less than with COCs.

HISTORY OF CHOLESTASIS

Theoretically, a history of COC-related cholestasis may predict subsequent cholestasis with POC use. However, this has not been documented.

LIVER TUMOURS

There is no evidence regarding hormonal contraceptive use among women with hepatocellular adenoma.

Given that COC use in healthy women is associated with development and growth of hepatocellular adenoma, it is not known whether other hormonal contraceptives have similar effects.

IRON-DEFICIENCY ANAEMIA

Changes in the menstrual pattern associated with POC use have little effect on haemoglobin levels.

References

1. Arias RD, Jain JK, Brucker C, Ross D, Ray A. Changes in bleeding patterns with depot medroxyprogesterone acetate subcutaneous injection 104 mg. Contraception. 2006;74(3):234–8.
2. Crosignani PG, Luciano A, Ray A, Bergqvist A. Subcutaneous depot medroxyprogesterone acetate versus leuprolide acetate in the treatment of endometriosis-associated pain. Hum Reprod. 2006;21(1):248–56.
3. Goldstein J, Cushman M, Badger GJ, Johnson JV. Effect of depomedroxyprogesterone acetate on coagulation parameter: a pilot study. Fertil Steril. 2007;87(6):1267–70.
4. Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. Contraception. 2004;70(4):269–75.
5. Kaunitz AM, Darney PD, Ross D, Wolter KD, Speroff L. Subcutaneous DMPA vs. intramuscular DMPA: a 2-year randomized study of contraceptive efficacy and bone mineral density. Contraception. 2009;80(1):7–17.
6. Polis CB, Nakigozi GF, Nakawooya H, Mondo G, Makumbi F, Gray RH, et al. Preference for Sayana(R) Press versus intramuscular Depo-Provera among HIV-positive women in Rakai, Uganda: a randomized crossover trial. Contraception. 2013;89(5) 385–95.
7. Schlaff WD, Carson SA, Luciano A, Ross D, Bergqvist A. Subcutaneous injection of depot medroxyprogesterone acetate compared with leuprolide acetate in the treatment of endometriosis-associated pain. Fertil Steril. 2006;85(2):314–25.
8. Segall-Gutierrez P, Du J, Niu C, Ge M, Tilley I, Mizraji K, et al. Effect of subcutaneous depo-medroxyprogesterone acetate (DMPA-SC) on serum androgen markers in normal-weight, obese, and extremely obese women. Contraception. 2012;86(6):739–45.
9. Segall-Gutierrez P, Taylor D, Liu X, Stanzcyk F, Azen S, Mishell DR, Jr. Follicular development and ovulation in extremely obese women receiving depo-medroxyprogesterone acetate subcutaneously. Contraception. 2010;81(6):487–95.
10. Segall-Gutierrez P, Xiang AH, Watanabe RM, Trigo E, Stanczyk FZ, Liu X, et al. Deterioration in cardiometabolic risk markers in obese women during depot medroxyprogesterone acetate use. Contraception. 2012;85(1):36–41.
11. Westhoff C, Jain JK, Milsom I, Ray A. Changes in weight with depot medroxyprogesterone acetate subcutaneous injection 104 mg/0.65 mL. Contraception. 2007;75(4):261–7.
12. Segall-Gutierrez P, Agarwal R, Ge M, Lopez C, Hernandez G, Stanczyk FZ. A pilot study examining short-term changes in bone mineral density among class 3 obese users of depot-medroxyprogesterone acetate. Eur J Contracept Reprod Health Care. 2013;18(3):199–205.
13. Fan H, Han L, Jiang J, Wu M, Chen B, Meng F, et al. A Multicenter Comparative Clinical Study of Sino-Levonorgestrel-Releasing Implants – No. I and No. II with Norplant. J Reprod Contracept. 2004;15(2):101–7.
14. Fang K, Guan Y, Fan H, Gao E, Yang D, Xue L, et al. A multicentre study of CLa implant and Sino-implant: expanded application (two-year follow-up). Reprod Contracept. 1997;8(2):101–10.
15. Qi L, Liu J, Yu L, Ye L, Sun L, Liu K. Multicenter clinical study of two Sino-subdermal implants. Chinese J Fam Plann. 2002;5(79).
16. Lanza LL, McQuay LJ, Rothman KJ, Bone HG, Kaunitz AM, Harel Z, et al. Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture. Obstet Gynecol. 2013;121(3):593–600.
17. Bahamondes L, Monteiro-Dantas C, Espejo-Arce X, Dos Santos Fernandes AM, Lui-Filho JF, Perrotti M, et al. A prospective study of the forearm bone density of users of etonorgestrel- and levonorgestrel-releasing contraceptive implants. Hum Reprod. 2006;21(2):466–70.
18. Bahamondes MV, Monteiro I, Castro S, Espejo-Arce X, Bahamondes L. Prospective study of the forearm bone mineral density of long-term users of the levonorgestrel-releasing intrauterine system. Hum Reprod. 2010;25(5):1158–64.
19. Banks E, Berrington A, Casabonne D. Overview of the relationship between use of progestogen-only contraceptives and bone mineral density. BJOG. 2001;108(12):1214–21.
20. Beerthuizen R, van Beek A, Massai R, Makarainen L, Hout J, Bennink HC. Bone mineral density during long-term use of the progestagen contraceptive implant Implanon compared to a non-hormonal method of contraception. Hum Reprod. 2000;15(1):118–22.
21. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in adolescents using norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives for contraception. Contraception. 2007;75(6):438–43.
22. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in a cohort of adolescents during use of norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives and after discontinuation of norethisterone enanthate. Contraception. 2009;79(5):345–9.
23. Berenson AB, Breitkopf CR, Grady JJ. Effects of hormonal contraception on bone mineral density after 24 months of use. Obstet Gynecol. 2004;103:899–906.

24. Berenson AB, Rahman M, Breitkopf CR, Bi LX. Effects of depot medroxyprogesterone acetate and 20-microgram oral contraceptives on bone mineral density. Obstet Gynecol. 2008;112(4):788–99.

25. Busen NH, Britt RB, Rianon N. Bone mineral density in a cohort of adolescent women using depot medroxyprogesterone acetate for one to two years. J Adolesc Health. 2003;32(4):257–9.

26. Caird LE, Reid-Thomas V, Hannan WJ. Oral progestogen-only contraception may protect against loss of bone mass in breast-feeding women. Clin Endocrinol (Oxf). 1994;41:739–45.

27. Clark MK, Sowers M, Levy B, Nichols S. Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. Fertil Steril. 2006;86(5):1466–74.

28. Cromer BA, Lazebnik R, Rome E. Double-blinded randomized controlled trial of estrogen supplementation in adolescent girls who receive depot medroxyprogesterone acetate for contraception. Am J Obstet Gynecol. 2005;192:42–7.

29. Cromer BA, Blair JM, Mahan JD, Zibners L, Naumovski Z. A prospective comparison of bone density in adolescent girls receiving depot medroxyprogesterone acetate (Depo-Provera), levonorgestrel (Norplant), or oral contraceptives. J Pediatr. 1996;129(5):671–6.

30. Cromer BA, Bonny AE, Stager M, Lazebnik R, Rome E, Ziegler J, et al. Bone mineral density in adolescent females using injectable or oral contraceptives: a 24-month prospective study. Fertil Steril. 2008;90(6):2060–7.

31. Cromer BA, Stager M, Bonny A, Lazebnik R, Rome E, Ziegler J, et al. Depot medroxyprogesterone acetate, oral contraceptives and bone mineral density in a cohort of adolescent girls. J Adolesc Health. 2004;35(6):434–41.

32. Cundy T, Cornish J, Evans MC. Recovery of bone density in women who stop using medroxyprogesterone acetate. BMJ Case Rep. 1994;308:247–8.

33. Cundy T, Ames R, Horne A, Clearwater J, Roberts H, Gamble G, et al. A randomized controlled trial of estrogen replacement therapy in long-term users of depot medroxyprogesterone acetate. J Clin Endocrinol Metab. 2003;88(1):78–81.

34. Cundy T, Cornish J, Roberts H, Reid IR. Menopausal bone loss in long-term users of depot medroxyprogesterone acetate contraception. Am J Obstet Gynecol. 2002;186(5):978–83.

35. Di X, Li Y, Zhang C, Jiang J, Gu S. Effects of levonorgestrel-releasing subdermal contraceptive implants on bone density and bone metabolism. Contraception. 1999;60(3):161–6.

36. Diaz S, Reyes MV, Zepeda A. Norplant((R)) implants and progesterone vaginal rings do not affect maternal bone turnover and density during lactation and after weaning. Hum Reprod. 1999;14:2499–505.

37. Gai L, Zhang J, Zhang H, Gai P, Zhou L, Liu Y. The effect of depot medroxyprogesterone acetate (DMPA) on bone mineral density (BMD) and evaluating changes in BMD after discontinuation of DMPA in Chinese women of reproductive age. Contraception. 2011;83(3):218–22.

38. Harel Z, Johnson CC, Gold MA, Cromer B, Peterson E, Burkman R, et al. Recovery of bone mineral density in adolescents following the use of depot medroxyprogesterone acetate contraceptive injections. Contraception. 2010;81(4):281–91.

39. Kaunitz AM, Miller PD, Rice VM. Bone mineral density in women aged 25–35 years receiving depot medroxyprogesterone acetate: recovery following discontinuation. Contraception. 2006;74:90–9.

40. Kaunitz AM, Arias R, McClung M. Bone density recovery after depot medroxyprogesterone acetate injectable contraception use. Contraception. 2008;77(2):67–76.

41. Lappe JM, Stegman MR, Recker RR. The impact of lifestyle factors on stress fractures in female Army recruits. Osteoporos Int. 2001;12:35–42.

42. Lara-Torre E, Edwards CP, Perlman S. Bone mineral density in adolescent females using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol. 2004;17:17–21.

43. Lopez LM, Chen M, Mullins S, Curtis KM, Helmerhorst FM. Steroidal contraceptives and bone fractures in women: evidence from observational studies. Cochrane Database Syst Rev. 2012;8:CD009849.

44. Lopez LM, Grimes DA, Schulz KF, Curtis KM. Steroidal contraceptives: effect on bone fractures in women. Cochrane Database Syst Rev. 2011;(7):CD006033.

45. Meier C, Brauchli YB, Jick SS, Kraenzlin ME, Meier CR. Use of depot medroxyprogesterone acetate and fracture risk. J Clin Endocrinol Metab. 2010;95(11):4909–16.

46. Merki-Feld GS, Neff M, Keller PJ. A 2-year prospective study on the effects of depot medroxyprogesterone acetate on bone mass-response to estrogen and calcium therapy in individual users. Contraception. 2003;67(2):79–86.

47. Monteiro-Dantas C, Espejo-Arce X, Lui-Filho JF, Fernandes AM, Monteiro I, Bahamondes L. A three-year longitudinal evaluation of the forearm bone density of users of etonogestrel- and levonorgestrel-releasing contraceptive implants. Reprod Health. 2007;4:11.

48. Naessen T, Olsson SE, Gudmundson J. Differential effects on bone density of progestogen-only methods for contraception in premenopausal women. Contraception. 1995;52:35–9.

49. Pitts SA, Feldman HA, Dorale A, Gordon CM. Bone mineral density, fracture, and vitamin D in adolescents and young women using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol. 2012;25(1):23–6.

50. Sanches L, Marchi NM, Castro S, Juliato CT, Villarroel M, Bahamondes L. Forearm bone mineral density in postmenopausal former users of depot medroxyprogesterone acetate. Contraception. 2008;78(5):365–9.

51. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Injectable hormone contraception and bone density: results from a prospective study. Epidemiology. 2002;13(5):581–7.

52. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. Arch Pediatr Adolesc Med. 2005;159(2):139–44.

53. Tang OS, Tang G, Yip PS, Li B. Further evaluation on long-term depot-medroxyprogesterone acetate use and bone mineral density: a longitudinal cohort study. Contraception. 2000;62(4):161–4.

54. Vestergaard P, Rejnmark L, Mosekilde L. The effects of depot medroxyprogesterone acetate and intrauterine device use on fracture risk in Danish women. Contraception. 2008;78(6):459–64.

55. Viola AS, Castro S, Marchi NM, Bahamondes MV, Viola CF, Bahamondes L. Long-term assessment of forearm bone mineral density in postmenopausal former users of depot medroxyprogesterone acetate. Contraception. 2011;84(2):122–7.

56. Walsh JS, Eastell R, Peel NF. Depot medroxyprogesterone acetate use after peak bone mass is associated with increased bone turnover but no decrease in bone mineral density. Fertil Steril. 2010;93(3):697–701.

57. Wetmore CM, Ichikawa L, LaCroix AZ, Ott SM, Scholes D. Association between caffeine intake and bone mass among young women: potential effect modification by depot medroxyprogesterone acetate use. Osteoporos Int. 2008;19(4):519–27.

58. Wong AY, Tang LC, Chin RK. Levonorgestrel-releasing intrauterine system (Mirena) and Depot medroxyprogesterone acetate (Depoprovera) as long-term maintenance therapy for patients with moderate and severe endometriosis: a randomised controlled trial. Aust N Z J Obstet Gynaecol. 2010;50(3):273–9.

59. Yang KY, Kim YS, Ji YI, Jung MH. Changes in bone mineral density of users of the levonorgestrel-releasing intrauterine system. J Nippon Med Sch. 2012;79(3):190–4.

60. Zhang MH, Zhang W, Zhang AD, Yang Y, Gai L. Effect of depot medroxyprogesterone acetate on bone mineral density in adolescent women. Chin Med J (Engl). 2013;126(21):4043–7.

61. Progestogen-only contraceptives during lactation: I. Infant growth. World Health Organization Task force for Epidemiological Research on Reproductive Health; Special Programme of Research, Development and Research Training in Human Reproduction. Contraception. 1994;50(1):35–53.

62. Abdel-Aleem H, Abol-Oyoun el SM, Shaaban MM, el-Saeed M, Shoukry M, Makhlouf A, et al. The use of nomegestrol acetate subdermal contraceptive implant, uniplant, during lactation. Contraception. 1996;54(5):281–6.

63. Abdulla KA, Elwan SI, Salem HS, Shaaban MM. Effect of early postpartum use of the contraceptive implants, NORPLANT, on the serum levels of immunoglobulins of the mothers and their breastfed infants. Contraception. 1985;32(3):261–6.

64. Affandi B, Karmadibrata S, Prihartono J, Lubis F, Samil RS. Effect of Norplant on mothers and infants in the postpartum period. Adv Contracept. 1986;2(4):371–80.

65. Bahamondes L, Bahamondes MV, Modesto W, Tilley IB, Magalhaes A, Pinto e Silva JL, et al. Effect of hormonal contraceptives during breastfeeding on infant's milk ingestion and growth. Fertil Steril. 2013;100(2):445–50.

66. Baheiraei A, Ardsetani N, Ghazizadeh S. Effects of progestogen-only contraceptives on breast-feeding and infant growth. Int J Gynaecol Obstet. 2001;74(2):203–5.

67. Bjarnadottir RI, Gottfredsdottir H, Sigurdardottir K, Geirsson RT, Dieben TO. Comparative study of the effects of a progestogen-only pill containing desogestrel and an intrauterine contraceptive device in lactating women. BJOG. 2001;108(11):1174–80.

68. Brito MB, Ferriani RA, Quintana SM, Yazlle ME, Silva de S· MF, Vieira CS. Safety of the etonogestrel-releasing implant during the immediate postpartum period: a pilot study. Contraception. 2009;80(6):519–26.

69. Brownell EA, Fernandez ID, Fisher SG, Howard CR, Ternullo SR, Lawrence RA, et al. The effect of immediate postpartum depot medroxyprogesterone on early breastfeeding cessation. Contraception. 2013;87(6):836–43.

70. Chen BA, Reeves MF, Creinin MD, Schwarz EB. Postplacental or delayed levonorgestrel intrauterine device insertion and breast-feeding duration. Contraception. 2011;84(5):499–504.

71. Costa ML, Cecatti JG, Krupa FG, Rehder PM, Sousa MH, Costa-Paiva L. Progestin-only contraception prevents bone loss in postpartum breastfeeding women. Contraception. 2012;85(4):374–80.

72. Coutinho EM, Athayde C, Dantas C, Hirsch C, Barbosa I. Use of a single implant of elcometrine (ST-1435), a nonorally active progestin, as a long acting contraceptive for postpartum nursing women. Contraception. 1999;59(2):115–22.

73. Croxatto HB, Dìaz S, Peralta O, Juez G, Casado ME, Salvatierra AM, et al. Fertility regulation in nursing women. II. Comparative performance of progesterone implants versus placebo and copper T. Am J Obstet Gynecol. 1982;144(2):201–8.

74. Dahlberg K. Some effects of depo-medroxyprogesterone acetate (DMPA): observations in the nursing infant and in the long-term user. Int J Gynaecol Obstet. 1982;20(1):43–8.

75. Diaz S, Herreros C, Juez G, Casado ME, Salvatierra AM, Miranda P, et al. Fertility regulation in nursing women: VII. Influence of NORPLANT levonorgestrel implants upon lactation and infant growth. Contraception. 1985;32(1):53–74.

76. Dìaz S, Peralta O, Juez G, Herreros C, Casado ME, Salvatierra AM, et al. Fertility regulation in nursing women. VI. Contraceptive effectiveness of a subdermal progesterone implant. Contraception. 1984;30(4):311–25.

77. Diaz S, Reyes MV, Zepeda A, Gonzalez GB, Lopez JM, Campino C, et al. Norplant((R)) implants and progesterone vaginal rings do not affect maternal bone turnover and density during lactation and after weaning. Hum Reprod. 1999;14(10):2499–505.

78. Diaz S, Zepeda A, Maturana X, Reyes MV, Miranda P, Casado ME, et al. Fertility regulation in nursing women. IX. Contraceptive performance, duration of lactation, infant growth, and bleeding patterns during use of progesterone vaginal rings, progestin-only pills, Norplant implants, and Copper T 380-A intrauterine devices. Contraception. 1997;56(4):223–32.

79. Espey E, Ogburn T, Leeman L, Singh R, Ostrom K, Schrader R. Effect of progestin compared with combined oral contraceptive pills on lactation: a randomized controlled trial. Obstet Gynecol. 2012;119(1):5–13.

80. Giner Velazquez J, Cortes Gallegos V, Sotelo Lopez A, Bondani G. [Effect of daily oral administration of 0.350 mg of norethindrone on lactation and on the composition of milk]. Ginecol Obstet Mex. 1976;40(237):31–9.

81. Guiloff E, Ibarra-Polo A, ZaÒartu J, Toscanini C, Mischler TW, GÛmez-Rogers C. Effect of contraception on lactation. Am J Obstet Gynecol. 1974;118(1):42–5.

82. Gurtcheff SE, Turok DK, Stoddard G, Murphy PA, Gibson M, Jones KP. Lactogenesis after early postpartum use of the contraceptive implant: a randomized controlled trial. Obstet Gynecol. 2011;117(5):1114–21.

83. 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):1250–8.

84. Hannon PR, Duggan AK, Serwint JR, Vogelhut JW, Witter F, DeAngelis C. The influence of medroxyprogesterone on the duration of breast-feeding in mothers in an urban community. Arch Pediatr Adolesc Med. 1997;151(5):490–6.

85. Heikkila M, Luukkainen T. Duration of breast-feeding and development of children after insertion of a levonorgestrel-releasing intrauterine contraceptive device. Contraception. 1982;25(3):279–92.

86. Jimenez J, Ochoa M, Soler MP, Portales P. Long-term follow-up of children breast-fed by mothers receiving depot-medroxyprogesterone acetate. Contraception. 1984;30(6):523–33.

87. Kamal I, Hefnawi F, Ghoneim M, Abdallah M, Abdel Razek S. Clinical, biochemical, and experimental studies on lactation. V. Clinical effects of steroids on the initiation of lactation. Am J Obstet Gynecol. 1970;108(4):655–8.

88. Kamal I, Hefnawi F, Ghoneim M, Talaat M, Younis N, Tagui A, et al. Clinical, biochemical, and experimental studies on lactation. II. Clinical effects of gestagens on lactation. Am J Obstet Gynecol. 1969;105(3):324–34.

89. Karim M, Ammar R, el-Mahgoub S, el-Ganzoury B, Fikri F, Abdou I. Injected progestogen and lactation. Br Med J. 1971;1(5742):200–3.

90. Massai MR, Dìaz S, Quinteros E, Reyes MV, Herreros C, Zepeda A, et al. Contraceptive efficacy and clinical performance of Nestorone implants in postpartum women. Contraception. 2001;64(6):369–76.

91. Matias SL. In: Phillips SJ, editor. 2014.

92. Matias SL, Nommsen-Rivers LA, Dewey KG. Determinants of exclusive breastfeeding in a cohort of primiparous periurban peruvian mothers. J Hum Lact. 2012;28(1):45–54.

93. McCann MF, Moggia AV, Higgins JE, Potts M, Becker C. The effects of a progestin-only oral contraceptive (levonorgestrel 0.03 mg) on breast-feeding. Contraception. 1989;40(6):635–48.

94. McEwan JA, Joyce DN, Tothill AU, Hawkins DF. Early experience in contraception with a new progestogen. Contraception. 1977;16(4):339–50.

95. Moggia AV, Harris GS, Dunson TR, Diaz R, Moggia MS, Ferrer MA, et al. A comparative study of a progestin-only oral contraceptive versus non-hormonal methods in lactating women in Buenos Aires, Argentina. Contraception. 1991;44(1):31–43.

96. Pardthaisong T, Yenchit C, Gray R. The long-term growth and development of children exposed to Depo-Provera during pregnancy or lactation. Contraception. 1992;45:313–24.

97. Reinprayoon D, Taneepanichskul S, Bunyavejchevin S, Thaithumyanon P, Punnahitananda S, Tosukhowong P, et al. Effects of the etonogestrel-releasing contraceptive implant (Implanon on parameters of breastfeeding compared to those of an intrauterine device. Contraception. 2000;62:239–46.

98. Schiappacasse V, Diaz S, Zepeda A, Alvarado R, Herreros C. Health and growth of infants breastfed by Norplant contraceptive implants users: a six-year follow-up study. Contraception. 2002;66(1):57–65.

99. Seth U, Yadava HS, Agarwal N, Laumas KR, Hingorani V. Effect of a subdermal silastic implant containing norethindrone acetate on human lactation. Contraception. 1977;16(4):383–98.

100. Shaaban MM. Contraception with progestogens and progesterone during lactation. J Steroid Biochem Mol Biol. 1991;40(4–6):705–10.

101. Shaaban MM, Salem HT, Abdullah KA. Influence of levonorgestrel contraceptive implants, NORPLANT, initiated early postpartum upon lactation and infant growth. Contraception. 1985;32(6):623–35.

102. Shaamash AH, Sayed GH, Hussien MM, Shaaban MM. A comparative study of the levonorgestrel-releasing intrauterine system Mirena versus the Copper T380A intrauterine device during lactation: breast-feeding performance, infant growth and infant development. Contraception. 2005;72:346–51.

103. Shikary ZK, Betrabet SS, Toddywala WS, Patel DM, Datey S, Saxena BN. Pharmacodynamic effects of levonorgestrel (LNG) administered either orally or subdermally to early postpartum lactating mothers on the urinary levels of follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (T) in their breast-fed male infants. Contraception. 1986;34(4):403–12.

104. Taneepanichskul S, Reinprayoon D, Thaithumyanon P, Praisuwanna P, Tosukhowong P, Dieben T. Effects of the etonogestrel-releasing implant Implanon and a nonmedicated intrauterine device on the growth of breast-fed infants. Contraception. 2006;73(4):368–71.

105. Tankeyoon M, Dusitsin N, Chalapati S, Koetsawang S, Saibiang S, Sas M, et al. Effects of hormonal contraceptives on milk volume and infant growth. WHO Special Programme of Research, Development and Research Training in Human Reproduction Task force on oral contraceptives. Contraception. 1984;30(6):505–22.

106. West CP. The acceptability of a progestagen-only contraceptive during breast-feeding. Contraception. 1983;27(6):563–9.

107. Zacharias S, Aguilera E, Assenzo JR, Zanartu J. Effects of hormonal and nonhormonal contraceptives on lactation and incidence of pregnancy. Contraception. 1986;33(3):203–13.

108. Zanartu J, Aguilera E, Munoz G, Peliowsky H. Effect of a long-acting contraceptive progestogen on lactation. Obstet Gynecol. 1976;47(2):174–6.

109. Zanartu J, Aguilera E, Munoz-Pinto G. Maintenance of lactation by means of continuous low-dose progestogen given post-partum as a contraceptive. Contraception. 1976;13(3):313–8.

110. Quadros PS, Pfau JL, Wagner CK. Distribution of progesterone receptor immunoreactivity in the fetal and neonatal rat forebrain. J Comp Neurol. 2007;504(1):42–56.

111. Wagner CK. The many faces of progesterone: a role in adult and developing male brain. Front Neuroendocrinol. 2006;27(3):340–59.

112. Wagner CK. Progesterone receptors and neural development: a gap between bench and bedside? Endocrinology. 2008;149(6):2743–9.

113. Kurunmaki H. Contraception with levonorgestrel-releasing subdermal capsules, Norplant, after pregnancy termination. Contraception. 1983;27:473–82.

114. Kurunmaki H, Toivonen J, Lähteenmäki PL, Luukkainen T. Immediate postabortal contraception with Norplant: levonorgestrel, gonadotropin, estradiol, and progesterone levels over two postaboral months and return of fertility after removal of Norplant capsules. Contraception. 1984;30:431–42.

115. Lahteenmake P, Toivonen J, Lahteenmaki PL. Postabortal contraception with norethisterone enanthate injections. Contraception. 1983;27:553–62.

116. Ortayli N, Bulut A, Sahin T, Sivin I. Immediate postabortal contraception with the levonorgestrel intrauterine device, Norplant, and traditional methods. Contraception. 2001;63:309–14.

117. Beksinska ME, Smit JA, Kleinschmidt I, Milford C, Farley TM. Prospective study of weight change in new adolescent users of DMPA, NET-EN, COCs, nonusers and discontinuers of hormonal contraception. Contraception. 2010;81(1):30–4.

118. Bender NM, Segall-Gutierrez P, Najera SO, Stanczyk FZ, Montoro M, Mishell DR, Jr. Effects of progestin-only long-acting contraception on metabolic markers in obese women. Contraception. 2013;88(3):418–25.

119. 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):329–8.

120. Bonny AE, Secic M, Cromer B. Early weight gain related to later weight gain in adolescents on depot medroxyprogesterone acetate. Obstet Gynecol. 2011;117(4):793–7.

121. Bonny AE, Ziegler J, Harvey R, Debanne SM, Secic M, Cromer BA. Weight gain in obese and nonobese adolescent girls initiating depot medroxyprogesterone, oral contraceptive pills, or no hormonal contraceptive method. Arch Pediatr Adolesc Med. 2006;160(1):40–5.

122. Clark MK, Dillon JS, Sowers M, Nichols S. Weight, fat mass, and central distribution of fat increase when women use depot-medroxyprogesterone acetate for contraception. Int J Obes (Lond). 2005;29(10):1252–8.

123. Gerlach LS, Saldana SN, Wang Y, Nick TG, Spigarelli MG. Retrospective review of the relationship between weight change and demographic factors following initial depot medroxyprogesterone acetate injection in adolescents. Clin Ther. 2011;33(2):182–7.

124. Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. Contraception. 2004;70(4):269–75.

125. Kozlowski KJ, Rickert VI, Hendon A, Davis P. Adolescents and Norplant: preliminary findings of side effects. J Adolesc Health. 1995;16(5):373–8.

126. Le YC, Rahman M, Berenson AB. Early weight gain predicting later weight gain among depot medroxyprogesterone acetate users. Obstet Gynecol. 2009;114(2 Pt 1):279–84.

127. Leiman G. Depo-medroxyprogesterone acetate as a contraceptive agent: its effect on weight and blood pressure. Am J Obstet Gynecol. 1972;114(1):97–102.

128. Lopez LM, Grimes DA, Chen M, Otterness C, Westhoff C, Edelman A, et al. Hormonal contraceptives for contraception in overweight or obese women. Cochrane Database Syst Rev. 2013;4:CD008452.

129. Mangan SA, Larsen PG, Hudson S. Overweight teens at increased risk for weight gain while using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol. 2002;15(2):79–82.

130. Nyirati CM, Habash DL, Shaffer LE. Weight and body fat changes in postpartum depot-medroxyprogesterone acetate users. Contraception. 2013;88(1):169–76.

131. Pantoja M, Medeiros T, Baccarin MC, Morais SS, Bahamondes L, Fernandes AM. Variations in body mass index of users of depot-medroxyprogesterone acetate as a contraceptive. Contraception. 2010;81(2):107–11.

132. Risser WL, Gefter LR, Barratt MS, Risser JM. Weight change in adolescents who used hormonal contraception. J Adolesc Health. 1999;24(6):433–6.

133. Westhoff C, Jain JK, Milsom I, Ray A. Changes in weight with depot medroxyprogesterone acetate subcutaneous injection 104 mg/0.65 mL. Contraception. 2007;75(4):261–7.

134. World Health Organization. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. Contraception. 1998;57:315–24.

135. Heinemann LA, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the health of Young Women. Eur J Contracept Reprod Health Care. 1999;4:67–73.

136. Vasilakis C, Jick H, Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestogens alone. Lancet. 1999;354:1610–1.

137. Sonmezer M, Atabekoglu C, Cengiz B, Dökmeci F, Cengiz SD. Depot-medroxyprogesterone acetate in anticoagulated patients with previous hemorrhagic corpus luteum. Eur J Contracept Reprod Health Care. 2005;10:9–14.

138. Culwell KR, Curtis KM. Use of contraceptive methods by women with current venous thrombosis on anticoagulant therapy: a systematic review. Contraception. 2009;80(4):337–45.

139. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol. 2002;29:2531–6.

140. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol. 2005;193:1361–3.

141. Sarabi ZS, Chang E, Bobba R, Ibanez D, Gladman D, Urowitz M, et al. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum. 2005;53:609–12.

142. Sanchez-Guerrero J, Uribe AG, Jimenez-Santana L, Mestanza-Peralta M, Lara-Reyes P, Seuc AH, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2539–49.

143. Petri M, Kim MY, Kalunian KC, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2550–8.

144. Petri M. Lupus in Baltimore: evidence-based 'clinical perarls' from the Hopkins Lupus Cohort. Lupus. 2005;14:970–3.

145. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res. 1995;8:137–45.

146. Mintz G, Gutierrez G, Delezé M, Rodríguez E. Contraception with progestogens in systemic lupus erythematosus. Contraception. 1984;30:29–38.

147. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis. 1992;51:56–60.

148. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephristis in systemic lupus erythematosus. Ann Rheum Dis. 1993;52:720–4.

149. Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, Jansen-McWilliams L, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145:408–15.

150. Jungers P, Dougados M, Pelissier C, Kuttenn F, Tron F, Lesavre P, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum. 1982;25:618–23.

151. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol. 1993;32:227–30.

152. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol. 1991;20:427–33.

153. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, du Berger R, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum. 2001;44:2331–7.

154. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol. 2002;29:1683–8.

155. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1386–9.

156. Bernatsky S, Clarke A, Ramsey-Goldman R, Joseph L, Boivin JF, Rajan R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1178–81.

157. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol. 2008;27(3):345–51.

158. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus – a meta-analysis. Lupus. 1997;6:467–73.

159. Culwell KR, Curtis KM, del Carmen Cravioto M. Safety of contraceptive method use among women with systemic lupus erythematosus: a systematic review. Obstet Gynecol. 2009;114(2 Pt 1):341–53.

160. Cromer BA, Blair JM, Mahan JD, Zibners L, Naumovski Z. A prospective comparison of bone density in adolescent girls receiving depot medroxyprogesterone acetate (Depo-Provera), levonorgestrel (Norplant), or oral contraceptives. J Pediatr. 1996;129(5):671–6.

161. Gupta N, O'Brien R, Jacobsen LJ, Davis A, Zuckerman A, Supran S, et al. Mood changes in adolescents using depo-medroxyprogesterone acetate for contraception: a prospective study. Am J Obstet Gynecol. 2001;14(2):71–6.

162. Westoff C, Truman C. Depressive symptoms and Depo-Provera. Contraception. 1998;57(4):237–40.

163. Westoff C, Truman C, Kalmuss D, Cushman L, Rulin M, Heartwell S, et al. Depressive symptoms and Norplant contraceptive implants. Contraception. 1998;57(4):241–5.

164. Smith JS. Cervical cancer and use of hormonal conraceptives: a systematic review. Lancet. 2003;361:1159–67.

165. Baeten JM, Nyange PM, Richardson BA, Lavreys L, Chohan B, Martin HL, Jr., et al. Hormonal contraception and risk of sexually transmitted disease acquisition: results from a prospective study. Am J Obstet Gynecol. 2001;185(2):380–5.

166. Giuliano AR, Papenfuss M, Abrahamsen M, Denman C, de Zapien JG, Henze JL, et al. Human papillomavirus infection at the United States-Mexico border: implications for cervical cancer prevention and control. Cancer Epidemiol Biomarkers Prev. 2001;10(11):1129–36.

167. Jacobson DL, Peralta L, Farmer M, Graham NM, Gaydos C, Zenilman J. Relationship of hormonal contraception and cervical ectopy as measured by computerized planimetry to chlamydial infection in adolescents. Sex Transm Dis. 2000;27(6):313–9.

168. Lavreys L, Chohan B, Ashley R, Richardson BA, Corey L, Mandaliya K, et al. Human herpesvirus 8: seroprevalence and correlates in prostitutes in Mombasa, Kenya. J Infect Dis. 2003;187(3):359–63.

169. Morrison CS, Bright P, Wong EL, Kwok C, Yacobson I, Gaydos CA, et al. Hormonal contraceptive use, cervical ectopy, and the acquisition of cervical infections. Sex Transm Dis. 2004;31(9):561–7.

170. Moscicki AB, Hills N, Shiboski S, Powell K, Jay N, Hanson E, et al. Risks for incident human papillomavirus infection and low-grade squamous intraepithelial lesion development in young females. JAMA. 2001;285(23):2995–3002.

171. Nsofor BI, Bello CS, Ekwempu CC. Sexually transmitted disease among women attending a family planning clinic in Zaria, Nigeria. Int J Gynaecol Obstet. 1989;28(4):365–7.

172. Ruijs GJ, Kauer FM, van Gijssel PM, Schirm J, Schroder FP. Direct immunofluorescence for Chlamydia trachomatis on urogenital smears for epidemiological purposes. Eur J Obstet Gynecol Reprod Biol. 1988;27(4):289–97.

173. Polis CB, Phillips SJ, Curtis KM, Westreich DJ, Steyn PS, Raymond E, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception. 2014;90(4):360–90.

174. Kleinschmidt I, Rees H, Delany S, Smith D, Dinat N, Nkala B, et al. Injectable progestin contraceptive use and risk of HIV infection in a South African family planning cohort. Contraception. 2007;75(6):461–7.

175. McCoy SI, Zheng W, Montgomery ET, Blanchard K, van der Straten A, de Bruyn G, et al. Oral and injectable contraception use and risk of HIV acquisition among women in sub-Saharan Africa. AIDS. 2013;27(6):1001–9.

176. Morrison CS, Skoler-Karpoff S, Kwok C, Chen PL, van de Wijgert J, Gehret-Plagianos M, et al. Hormonal contraception and the risk of HIV acquisition among women in South Africa. AIDS. 2012;26(4):497–504.

177. Myer L, Denny L, Wright TC, Kuhn L. Prospective study of hormonal contraception and women's risk of HIV infection in South Africa. Int J Epidemiol. 2007;36(1):166–74.

178. Wand H, Ramjee G. The effects of injectable hormonal contraceptives on HIV seroconversion and on sexually transmitted infections. AIDS. 2012;26(3):375–80.

179. Baeten JM, Benki S, Chohan V, Lavreys L, McClelland RS, Mandaliya K, et al. Hormonal contraceptive use, herpes simplex virus infection, and risk of HIV-1 acquisition among Kenyan women. AIDS. 2007;21(13):1771–7.

180. Heffron R, Donnell D, Rees H, Celum C, Mugo N, Were E, et al. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. Lancet Infect Dis. 2012;12(1):19–26.

181. Morrison CS, Chen PL, Kwok C, Richardson BA, Chipato T, Mugerwa R, et al. Hormonal contraception and HIV acquisition: reanalysis using marginal structural modeling. AIDS. 2010;24(11):1778–81.

182. Morrison CS, Richardson BA, Mmiro F, Chipato T, Celentano DD, Luoto J, et al. Hormonal contraception and the risk of HIV acquisition. AIDS. 2007;21(1):85–95.

183. Reid SE, Dai JY, Wang J, Sichalwe BN, Akpomiemie G, Cowan FM, et al. Pregnancy, contraceptive use, and HIV acquisition in HPTN 039: relevance for HIV prevention trials among African women. J Acquir Immune Defic Syndr. 2010;53(5):606–13.

184. Lutalo T, Musoke R, Kong X, Makumbi F, Serwadda D, Nalugoda F, et al. Effects of hormonal contraceptive use on HIV acquisition and transmission among HIV-discordant couples. AIDS. 2013;27 Suppl 1:S27–34.

185. Lavreys L, Baeten JM, Martin HL, Jr., Overbaugh J, Mandaliya K, Ndinya-Achola J, et al. Hormonal contraception and risk of HIV-1 acquisition: results of a 10-year prospective study. AIDS. 2004;18(4):695–7.

186. Kilmarx PH, Limpakarnjanarat K, Kaewkungwal J, Srismith R, Saisorn S, Uthaivoravit W, et al. Disease progression and survival with human immunodeficiency virus type 1 subtype E infection among female sex workers in Thailand. J Infect Dis. 2000;181(5):1598–606.

187. Allen S, Stephenson R, Weiss H, Karita E, Priddy F, Fuller L, et al. Pregnancy, hormonal contraceptive use, and HIV-related death in Rwanda. J Womens Health (Larchmt). 2007;16(7):1017–27.

188. Stringer EM, Kaseba C, Levy J, Sinkala M, Goldenberg RL, Chi BH, et al. A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol. 2007;197(2):144–8.

189. Polis CB, Wawer MJ, Kiwanuka N, Laeyendecker O, Kagaayi J, Lutalo T, et al. Effect of hormonal contraceptive use on HIV progression in female HIV seroconverters in Rakai, Uganda. AIDS. 2010;24(12):1937–44.

190. Morrison CS, Chen PL, Nankya I, Rinaldi A, Van Der Pol B, Ma YR, et al. Hormonal contraceptive use and HIV disease progression among women in Uganda and Zimbabwe. J Acquir Immune Defic Syndr. 2011;57(2):157–64.

191. Stringer EM, Giganti M, Carter RJ, El-Sadr W, Abrams EJ, Stringer JS. Hormonal contraception and HIV disease progression: a multicountry cohort analysis of the MTCT-Plus Initiative. AIDS. 2009;23 Suppl 1:S69–77.

192. Heikinheimo O, Lehtovirta P, Suni J, Paavonen J. The levonorgestrel-releasing intrauterine system (LNG-IUS) in HIV-infected women – effects on bleeding patterns, ovarian function and genital shedding of HIV. Human Reproduction. 2006;21:2857–61.

193. Clemetson DB, Moss GB, Willerford DM, Hensel M, Emonyi W, Holmes KK, et al. Detection of HIV DNA in cervical and vaginal secretions. Prevalence and correlates among women in Nairobi, Kenya. JAMA. 1993;269(22):2860–4.

194. Cejtin HE, Jacobson L, Springer G, Watts DH, Levine A, Greenblatt R, et al. Effect of hormonal contraceptive use on plasma HIV-1-RNA levels among HIV-infected women. AIDS. 2003;17(11):1702–4.

195. Clark RA, Theall KP, Amedee AM, Dumestre J, Wenthold L, Kissinger PJ. Lack of association between genital tract HIV-1 RNA shedding and hormonal contraceptive use in a cohort of Louisiana women. Sex Transm Dis. 2007;34(11):870–2.

196. Richardson BA, Otieno PA, Mbori-Ngacha D, Overbaugh J, Farquhar C, John-Stewart GC. Hormonal contraception and HIV-1 disease progression among postpartum Kenyan women. AIDS. 2007;21(6):749–53.

197. Graham SM, Masese L, Gitau R, Jalalian-Lechak Z, Richardson BA, Peshu N, et al. Antiretroviral adherence and development of drug resistance are the strongest predictors of genital HIV-1 shedding among women initiating treatment. J Infect Dis. 2010;202(10):1538–42.

198. Kovacs A, Wasserman SS, Burns D, Wright DJ, Cohn J, Landay A, et al. Determinants of HIV-1 shedding in the genital tract of women. Lancet. 2001;358:1593–601.

199. Kreiss J, Willerford DM, Hensel M, Emonyi W, Plummer F, Ndinya-Achola J, et al. Association between cervical inflammation and cervical shedding of human immunodeficiency virus DNA. J Infect Dis. 1994;170(6):1597–601.

200. Kumwenda JJ, Makanani B, Taulo F, Nkhoma C, Kafulafula G, Li Q, et al. Natural history and risk factors associated with early and established HIV type 1 infection among reproductive-age women in Malawi. Clin Infect Dis. 2008;46(12):1913–20.

201. Lavreys L, Baeten JM, Kreiss JK, Richardson BA, Chohan BH, Hassan W, et al. Injectable contraceptive use and genital ulcer disease during the early phase of HIV-1 infection increase plasma virus load in women. J Infect Dis. 2004;189(2):303–11.

202. Morrison CS, Demers K, Kwok C, Bulime S, Rinaldi A, Munjoma M, et al. Plasma and cervical viral loads among Ugandan and Zimbabwean women during acute and early HIV-1 infection. AIDS. 2010;24(4):573–82.

203. Mostad SB, Overbaugh J, DeVange DM, Welch MJ, Chohan B, Mandaliya K, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet. 1997;350:922–7.

204. Roccio M, Gardella B, Maserati R, Zara F, Iacobone D, Spinillo A. Low-dose combined oral contraceptive and cervicovaginal shedding of human immunodeficiency virus. Contraception. 2011;83(6):564–70.

205. Sagar M, Lavreys L, Baeten JM, Richardson BA, Mandaliya K, Ndinya-Achola JO, et al. Identification of modifiable factors that affect the genetic diversity of the transmitted HIV-1 population. AIDS. 2004;18(4):615–9.

206. Seck K, Samb N, Tempesta S, Mulanga-Kabeya C, Henzel D, Sow PS, et al. Prevalence and risk factors of cervicovaginal HIV shedding among HIV-1 and HIV-2 infected women in Dakar, Senegal. Sex Transm Infect. 2001;77(3):190–3.

207. Tanton C, Weiss HA, Le Goff J, Changalucha J, Rusizoka M, Baisley K, et al. Correlates of HIV-1 genital shedding in Tanzanian women. PLoS One. 2011;6(3):e17480.

208. Tagy AH, Saker ME, Moussa AA, Kolgah A. The effect of low-dose combined oral contraceptive pills versus injectable contraceptive (Depot Provera) on liver function tests of women with compensated bilharzial liver fibrosis. Contraception. 2001;64:173–6.

209. Pyorala T, Vahapassi J, Huhtala M. The effect of lynestrenol and norethindrone on the carbohydrate and lipid metabolism in subjects with gestational diabetes. Ann Chir Gynaecol. 1979;68(2):69–74.

210. Radberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in women with previous gestational diabetes during contraceptive treatment: effects on serum lipids and high density lipoproteins. Acta Endocrinol (Copenh). 1982;101(1):134–9.

211. Kjos SL, Peters RK, Xiang A, Thomas D, Schaefer U, Buchanan TA. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. JAMA. 1998;280(6):533–8.

212. Nelson AL, Le MH, Musherraf Z, Vanberckelaer A. Intermediate-term glucose tolerance in women with a history of gestational diabetes: natural history and potential associations with breastfeeding and contraception. Am J Obstet Gynecol. 2008;198:699.e1–.e8.

213. Xiang AH, Kawakubo M, Buchanan TA, Kjos SL. A longitudinal study of lipids and blood pressure in relation to method of contraception in Latino women with prior gestational diabetes mellitus. Diabetes Care. 2007;30(8):1952–8.

214. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA. Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. Diabetes Care. 2006;29(3):613–7.

215. Diab KM, Zaki MM. Contraception in diabetic women: comparative metabolic study of norplant, depot medroxyprogesterone acetate, low dose oral contraceptive pill and CuT380A. J Obstet Gynecol Res. 2000;26(1):17–26.

216. Lunt H, Brown LJ. Self-reported changes in capillary glucose and insulin requirements during the menstrual cycle. Diabet Med. 1995;13:525–30.

217. Radberg T, Gustafson A, Skryten A, Karlsson K. Oral contraception in diabetic women. A cross-over study on seum and high density lipoprotein (HDL) lipids and diabetes control during progestogen and combined estrogen/progestogen contraception. Horm Metab Res. 1982;14:61–5.

218. Skouby SO, Molsted-Petersen L, Kuhl C, Bennet P. Oral contraceptives in diabetic womne: metabolic effects of four compounds with different estrogen/progestogen profiles. Fertil Steril. 1986;46:858–64.

219. D'halluin V, Vilgrain V, Pelletier G, Rocher L, Belghiti J, Erlinger S, et al. [Natural history of focal nodular hyperplasia. A retrospective study of 44 cases]. Gastroenterol Clin Biol. 2001;25(11):1008–10.

220. Mathieu D, Kobeiter H, Maison P, Rahmouni A, Cherqui D, Zafrani ES, et al. Oral contraceptive use and focal nodular hyperplasia of the liver. Gastroenterology. 2000;118(3):560–4.

221. Kapp N, Curtis KM. Hormonal contraceptive use among women with liver tumors: a systematic review. Contraception. 2009;80(4):387–90.

222. Adadevoh BK, Isaacs WA. The effect of megestrol acetate on sickling. Am J Med Sci. 1973;265:367–70.

223. Barbosa IC, Ladipo OA, Nascimento ML, Athayde C, Hirsch C, Lopes R, et al. Carbohydrate metabolism in sickle cell patients using subdermal implant containing nomegesterol acetate (Uniplant). Contraception. 2001;63:263–5.

224. de Abood M, de Castillo Z, Guerrero F, Espino M, Austin KL. Effects of Depo-Provera or Microgynon on the painful crises of sickle cell anemia patients. Contraception. 1997;56:313–6.

225. De Ceulaer K, Gruber C, Hayes R, Serjeant GR. Medroxyprogesterone acetate and homozygous sickle-cell disease. Lancet. 1982;2:229–31.

226. Howard RJ, Lillis C, Tuck SM. Contraceptives, counseling, and pregnancy in women with sickle cell disease. BMJ. 1993;306:1735–7.

227. Ladipo OA, Falusi AG, Feldblum PJ, Osotimehin BO, Otolorin EO, Ojengbede OA. Norplant use by women with sickle cell disease. Int J Gynaecol Obstet. 1993;41:85–7.

228. Nascimento ML, Ladipo OA, Coutinho E. Nomogestrol acetate contraceptive implant use by women with sickle cell disease. Clin Pharmacol Ther. 1998;64:433–8.

229. Yoong WC, Tuck SM, Yardumian A. Red cell deformability in oral contraceptive pill users with sickle cell anaemia. Br J Haematol. 1999;104:868–70.

230. Aweeka FT, Rosenkranz SL, Segal Y, Coombs RW, Bardeguez A, Thevanayagam L, et al. The impact of sex and contraceptive therapy on the plasma and intracellular pharmacokinetics of zidovudine. AIDS. 2006;20(14):1833–41.

231. Kearney BP, Mathias A. Lack of effect of tenofovir disoproxil fumarate on pharmacokinetics of hormonal contraceptives. Pharmacotherapy. 2009;29(8):924–9.

232. Perry SH, Swamy P, Preidis GA, Mwanyumba A, Motsa N, Sarero HN. Implementing the Jadelle implant for women living with HIV in a resource-limited setting: concerns for drug interactions leading to unintended pregnancies. AIDS. 2014;28(5):791–3.

233. Cohn SE, Park JG, Watts DH, Stek A, Hitti J, Clax PA, et al. Depo-medroxyprogesterone in women on antiretroviral therapy: effective contraception and lack of clinically significant interactions. Clin Pharmacol Ther. 2007;81(2):222–7.

234. Nanda K, Amaral E, Hays M, Viscola MA, Mehta N, Bahamondes L. Pharmacokinetic interactions between depot medroxyprogesterone acetate and combination antiretroviral therapy. Fertil Steril. 2008;90(4):965–71.

235. Sekar VJ, Lefebvre E, Guzman SS, Felicione E, De Pauw M, Vangeneugden T, et al. Pharmacokinetic interaction between ethinyl estradiol, norethindrone and darunavir with low-dose ritonavir in healthy women. Antivir Ther. 2008;13(4):563–9.

236. Kasserra C, Li J, March B, O'Mara E. Effect of vicriviroc with or without ritonavir on oral contraceptive pharmacokinetics: a randomized, open-label, parallel-group, fixed-sequence crossover trial in healthy women. Clin Ther. 2011;33(10):1503–14.

237. Vogler MA, Patterson K, Kamemoto L, Park JG, Watts H, Aweeka F, et al. Contraceptive efficacy of oral and transdermal hormones when co-administered with protease inhibitors in HIV-1-infected women: pharmacokinetic results of ACTG trial A5188. J Acquir Immune Defic Syndr. 2010;55(4):473–82.

238. Atrio J, Stanczyk FZ, Neely M, Cherala G, Kovacs A, Mishell DR, Jr. Effect of protease inhibitors on steady-state pharmacokinetics of oral norethindrone contraception in HIV-infected women. J Acquir Immune Defic Syndr. 2014;65(1):72–7.

239. Anderson MS, Hanley WD, Moreau AR, Jin B, Bieberdorf FA, Kost JT, et al. Effect of raltegravir on estradiol and norgestimate plasma pharmacokinetics following oral contraceptive administration in healthy women. Br J Clin Pharmacol. 2011;71(4):616–20.

240. Song I, Mark S, Borland J, Chen S, Wajima T, Peppercorn A, et al. Dolutegravir has no effect on the pharmacokinetics of methadone or oral contraceptives with norgestimate and ethinyl estradiol. Atlanta (GA): 20th Conference on Retroviruses and Opportunistic Infections; 3–6 March 2013.

241. Odlind V, Olsson SE. Enhanced metabolism of levonorgestrel during phenytoin treatment in a woman with Norplant implants. Contraception. 1986;33:257–61.

242. Schindlbeck C, Janni W, Friese K. Failure of Implanon contraception in a patient taking carbamazepine for epilepsia. Arch Gynecol Obstet. 2006;273(4):255–6.

243. Shane-McWhorter L, Cerven JD, MacFarlane LL, Osborn C. Enhanced metabolism of levonorgestrel during phenobarbital treatment and resultant pregnancy. Pharmacotherapy. 1998;18:1360–4.

244. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia. 2005;46(9):1414–7.

2.7.3 Emergency contraceptive pills (ECPs)

EMERGENCY CONTRACEPTIVE PILLS (ECPs)				
ECPs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.				
CONDITION	**CATEGORY**			**CLARIFICATIONS/EVIDENCE**
	COC	**LNG**	**UPA†**	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	COC = combined oral contraceptive LNG = levonorgestrel contraceptive UPA = ulipristal acetate			
PREGNANCY	NA	NA	NA	NA = not applicable **Clarification**: Although this method is not indicated for a woman with a known or suspected pregnancy, there is no known harm to the woman, the course of her pregnancy, or the fetus if ECPs are accidentally used.
BREASTFEEDING	1	1	2	**Clarification**: Breastfeeding is not recommended for 1 week after taking UPA since it is excreted in breast-milk. Breast-milk should be expressed and discarded during that time *(1)*.
PAST ECTOPIC PREGNANCY	1	1	1	
OBESITY†	1	1	1	**Clarification**: ECPs may be less effective among women with BMI ≥ 30 kg/m^2 than among women with BMI < 25 kg/m^2. Despite this, there are no safety concerns. **Evidence**: There is limited evidence from 1 study that suggests obese women with BMI ≥ 30 kg/m^2 experience an increased risk of pregnancy after use of LNG compared with women with BMI < 25 kg/m^2 *(2)*. Two studies suggest obese women may also experience an increased risk of pregnancy after use of UPA compared with non-obese women, though this increase was not significant in 1 study *(2, 3)*.
HISTORY OF SEVERE CARDIOVASCULAR DISEASE* (ischaemic heart disease, cerebrovascular attack, or other thromboembolic conditions)	2	2	2	
MIGRAINE*	2	2	2	
SEVERE LIVER DISEASE* (INCLUDING JAUNDICE)	2	2	2	

EMERGENCY CONTRACEPTIVE PILLS (ECPs)

ECPs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY			CLARIFICATIONS/EVIDENCE
	COC	LNG	UPA†	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	COC = combined oral contraceptive LNG = levonorgestrel contraceptive UPA = ulipristal acetate			
CYP3A4 INDUCERS† (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, efavirenz, fosphenytoin, nevirapine, oxcarbazepine, primidone, rifabutin, St John's wort/hypericum perforatum)	1	1	1	**Clarification**: Strong CYP3A4 inducers may reduce the effectiveness of ECPs. **Evidence**: According to labelling information, rifampicin markedly decreases UPA levels by 90% or more which may decrease its efficacy *(1, 4)*. Theoretical concerns therefore extend to use of other CYP3A4 inducers as well as to COC and LNG ECPs, which have similar metabolic pathways to UPA. A small pharmacokinetic study found that concomitant efavirenz use decreased LNG levels in women taking LNG ECP (0.75 mg) by 56% compared with LNG ECP alone *(5)*.
REPEATED ECP USE	1	1	1	**Clarification**: Repeated ECP use is an indication that the woman requires further counselling on other contraceptive options. Frequently repeated ECP use may be harmful for women with conditions classified as Category 2, 3 or 4 for combined hormonal contraception (CHC) or POC use.
RAPE*	1	1	1	

RECOMMENDATIONS REVIEWED FOR FIFTH EDITION

These recommendations were reviewed according to WHO requirements for guideline development, as part of the preparation of the *Medical eligibility criteria for contraceptive use, fifth edition*. The population, intervention, comparator, outcome (PICO) questions developed by the Guideline Development Group (GDG) and the databases searched to retrieve the evidence, which guided the preparation of systematic reviews, are described in greater detail in Part I of this document. Additionally, GRADE evidence profiles, the overall GRADE assessment of the quality of the evidence, summaries of the evidence supporting the recommendation(s), and other supplementary remarks from the GDG regarding the recommendations, are available in Part I.

ADDITIONAL COMMENTS

History of severe cardiovascular disease, migraine, and severe liver disease (including jaundice)

The duration of use of ECPs is less than that of regular use of COCs or POPs and thus would be expected to have a lower risk for adverse health outcomes.

Rape

There are no restrictions for the use of ECPs in cases of rape.

References

1. ellaOne® ulipristal acetate. Abbreviated prescribing information (UK). London: HRA Pharma UK & Ireland Ltd; 2013 (http://www.ellaone.co.uk/hcp/abbreviated-prescribing-information-uk, accessed 23 October 2014).
2. Glasier A, Cameron ST, Blithe D, Scherrer B, Mathe H, Levy 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(4):363–7.
3. Moreau C, Trussell J. Results from pooled Phase III studies of ulipristal acetate for emergency contraception. Contraception. 2012;86(6):673–80.
4. Full prescribing information: ELLA (ulipristal acetate) tablet. Charleston (SC): Afaxys, Inc.; updated June 2014 (http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022474s004lbl.pdf, accessed 9 March 2015).
5. Carten ML, Kiser JJ, Kwara A, Mawhinney S, Cu-Uvin S. Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and Efavirenz. Infect Dis Obstet Gynecol. 2012;2012:137192.

2.7.4 Intrauterine devices (IUDs)

INTRAUTERINE DEVICES (IUDs)			
IUDs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.			
CONDITION	**CATEGORY** **I = initiation, C = continuation**		**CLARIFICATIONS/EVIDENCE**
	Cu-IUD	**LNG-IUD**	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	Cu-IUD = copper-bearing IUD LNG-IUD = levonorgestrel-releasing IUD (20 µg/24 hours)		
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY			
PREGNANCY	4	4	**Clarification**: The IUD is not indicated during pregnancy and should not be used because of the risk of serious pelvic infection and septic spontaneous abortion.
AGE			**Evidence**: Risks of pregnancy, infection and perforation are low among IUD users of any age. Heavy bleeding or removals for bleeding do not seem to be associated with age. Young women using Cu-IUDs may have an increased risk of expulsion compared with older Cu-IUD users *(1–15)*.
a) Menarche to < 20 years	2	2	
b) ≥ 20 years	1	1	
PARITY			**Evidence**: Risks of pregnancy, infection, perforation and expulsion are low among all IUD users, and differences by parity may not be clinically meaningful. Data do not suggest an increased delay in return to fertility for nulliparous IUD users *(1, 3, 7–10)*.
a) Nulliparous	2	2	
b) Parous	1	1	

INTRAUTERINE DEVICES (IUDs)

IUDs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation		CLARIFICATIONS/EVIDENCE
	Cu-IUD	LNG-IUD	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	Cu-IUD = copper-bearing IUD LNG-IUD = levonorgestrel-releasing IUD (20 µg/24 hours)		
POSTPARTUM † (breastfeeding or non-breastfeeding women, including caesarean section)			
a) < 48 hours including insertion immediately after delivery of the placenta			**Evidence:** Immediate postpartum Cu-IUD insertion, particularly when insertion occurs immediately after delivery of the placenta, is associated with lower expulsion rates than delayed postpartum insertion. Additionally, post-placental placement at the time of caesarean section has lower expulsion rates than post-placental vaginal insertions. Insertion complications of perforation and infection are not increased by IUD placement at any time during the postpartum period *(16–29)*. One randomized controlled trial found that immediate insertion of the LNG-IUD was associated with decreased breastfeeding duration compared with delayed insertion *(30)*. Two other randomized controlled trials assessing early vs delayed initiation of progestogen-only contraceptives failed to show a difference in breastfeeding outcomes *(31, 32)*. In other studies, initiation of LNG-IUD at 4 weeks postpartum or later demonstrated no detrimental effect on breastfeeding outcomes *(33–35)*.
i) breastfeeding	1	2	
ii) non-breastfeeding	1	1	
b) ≥ 48 hours to < 4 weeks	3	3	
c) ≥ 4 weeks	1	1	
d) Puerperal sepsis	4	4	

INTRAUTERINE DEVICES (IUDs)

IUDs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY I = initiation, C = continuation		CLARIFICATIONS/EVIDENCE
	Cu-IUD	LNG-IUD	
† recommendations reviewed for the MEC 5th edition, further details after this table * additional comments after this table	Cu-IUD = copper-bearing IUD LNG-IUD = levonorgestrel-releasing IUD (20 µg/24 hours)		
POST-ABORTION*			
a) First trimester	1	1	**Clarification**: IUDs can be inserted immediately after first-trimester, spontaneous or induced abortion. **Evidence**: There was no difference in risk of complications for immediate vs delayed insertion of an IUD after abortion. Expulsion was greater when an IUD was inserted following a second-trimester abortion vs a first-trimester abortion. There were no differences in safety or expulsions for post-abortion insertion of an LNG-IUD compared with a Cu-IUD *(36–48)*.
b) Second trimester	2	2	
c) Immediate post-septic abortion	4	4	
PAST ECTOPIC PREGNANCY*	1	1	
HISTORY OF PELVIC SURGERY (see postpartum, including caesarean section)	1	1	
SMOKING			
a) Age < 35 years	1	1	
b) Age ≥ 35 years			
i) < 15 cigarettes/day	1	1	
ii) ≥ 15 cigarettes/day	1	1	
OBESITY			
a) ≥ 30 kg/m^2 BMI	1	1	
b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	1	1	
BLOOD PRESSURE MEASUREMENT UNAVAILABLE	NA	NA	**NA = not applicable** **Clarification**: While a blood pressure measurement may be appropriate for good preventive health care, it is not materially related to safe and effective IUD use. Women should not be denied use of IUDs simply because their blood pressure cannot be measured.

INTRAUTERINE DEVICES (IUDs)			
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CONDITION	**CATEGORY** **I = initiation, C = continuation**		**CLARIFICATIONS/EVIDENCE**
	Cu-IUD	**LNG-IUD**	
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CARDIOVASCULAR DISEASE			
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (such as older age, smoking, diabetes, hypertension and known dyslipidaemias)	1	2	
HYPERTENSION* For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, the risk of cardiovascular disease may increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive.			
a) History of hypertension, where blood pressure CANNOT be evaluated (including hypertension in pregnancy)	1	2	
b) Adequately controlled hypertension, where blood pressure CAN be evaluated	1	1	
c) Elevated blood pressure levels (properly taken measurements)			
i) systolic 140–159 or diastolic 90–99 mm Hg	1	1	
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	1	2	
d) Vascular disease	1	2	
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	1	1	

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DEEP VEIN THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)*			
a) History of DVT/PE	1	2	
b) Acute DVT/PE	1	3	**Evidence**: Although evidence on the risk of venous thrombosis with the use of progestogen-only contraceptives (POCs) is inconsistent, any small increased risk is substantially less than that with combined oral contraceptives (COCs) *(49–51)*.
c) DVT/PE and established on anticoagulant therapy	1	2	**Evidence**: Although evidence on the risk of venous thrombosis with the use of POCs is inconsistent, any small increased risk is substantially less than that with COCs *(49–51)*. Limited evidence indicates that insertion of the LNG-IUD does not pose major bleeding risks in women on chronic anticoagulant therapy *(52–54)*.
d) Family history (first-degree relatives)	1	1	
e) Major surgery			
i) with prolonged immobilization	1	2	
ii) without prolonged immobilization	1	1	
f) Minor surgery without immobilization	1	1	
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	1	2	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.
SUPERFICIAL VENOUS DISORDERS			
a) Varicose veins	1	1	
b) Superficial venous thrombosis	1	1	

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CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE*	1	I 2	C 3	
STROKE* (history of cerebrovascular accident)	1	2		
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS	1	2		**Clarification**: Routine screening is not appropriate because of the rarity of the condition and the high cost of screening.
VALVULAR HEART DISEASE				
a) Uncomplicated	1	1		
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	2	2		**Clarification**: Prophylactic antibiotics to prevent endocarditis are advised for insertion.
RHEUMATIC DISEASES				
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) People with SLE are at increased risk of ischaemic heart disease, stroke and venous thromboembolism. Categories assigned to such conditions in the Medical eligibility criteria for contraceptive use should be the same for women with SLE who present with these conditions. For all categories of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Available evidence indicates that many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives *(54–71)*.				
a) Positive (or unknown) antiphospholipid antibodies	I 1	C 1	3	**Evidence**: Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis *(72, 73)*.
b) Severe thrombocytopenia	3	2	2	**Clarification**: Severe thrombocytopenia increases the risk of bleeding. The category should be assessed according to the severity of the thrombocytopenia and its clinical manifestations. In women with very severe thrombocytopenia who are at risk for spontaneous bleeding, consultation with a specialist and certain pretreatments may be warranted. **Evidence**: The LNG-IUD may be a useful treatment for menorrhagia in women with severe thrombocytopenia *(54)*.

INTRAUTERINE DEVICES (IUDs)

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c) Immunosuppressive treatment	2	1	2		
d) None of the above	1	1	2		
NEUROLOGIC CONDITIONS					
HEADACHES*			I	C	**Clarification**: Any new headaches or marked changes in headaches should be evaluated.
a) Non-migrainous (mild or severe)	1		1	1	
b) Migraine					
i) without aura					
age < 35 years	1		2	2	
age > 35 years	1		2	2	
ii) with aura, at any age	1		2	3	
EPILEPSY	1		1		
DEPRESSIVE DISORDERS					
DEPRESSIVE DISORDERS	1		1		**Clarification**: The classification is based on data for women with selected depressive disorders. No data on bipolar disorder or postpartum depression were available. There is a potential for drug interactions between certain antidepressant medications and hormonal contraceptives.
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS					
VAGINAL BLEEDING PATTERNS			I	C	
a) Irregular pattern without heavy bleeding	1		1	1	
b) Heavy or prolonged bleeding (includes regular and irregular patterns)	2		1	2	Clarification: Unusually heavy bleeding should raise the suspicion of a serious underlying condition. Evidence: Evidence from studies examining the treatment effects of the LNG-IUD among women with heavy or prolonged bleeding reported no increase in adverse effects and found the LNG-IUD to be beneficial in the treatment of menorrhagia *(74–81)*.

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UNEXPLAINED VAGINAL BLEEDING (suspicious for serious condition)	I	C	I	C	**Clarification**: If pregnancy or an underlying pathological condition (such as pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation. There is no need to remove the IUD before evaluation.
Before evaluation	4	2	4	2	
ENDOMETRIOSIS	2		1		Evidence: LNG-IUD use among women with endometriosis decreased dysmenorrhoea, pelvic pain and dyspareunia *(82–86)*.
BENIGN OVARIAN TUMOURS (including cysts)	1		1		
SEVERE DYSMENORRHOEA*	2		1		
GESTATIONAL C TROPHOBLASTIC DISEASE					**Evidence**: Limited evidence suggests that women using an IUD following uterine evacuation for a molar pregnancy are not at increased risk of developing post-molar trophoblastic disease when compared to women using other methods of contraception *(87–90)*.
a) Decreasing or undetectable β-hCG levels	3		3		
b) Persistently elevated β-hCG levels or malignant disease	4		4		
CERVICAL ECTROPION	1		1		
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)*	1		2		
CERVICAL CANCER* (awaiting treatment)	I	C	I	C	
	4	2	4	2	
BREAST DISEASE*					
a) Undiagnosed mass	1		2		
b) Benign breast disease	1		1		
c) Family history of cancer	1		1		
d) Breast cancer					
i) current	1		4		
ii) past and no evidence of current disease for 5 years	1		3		
ENDOMETRIAL CANCER*	I	C	I	C	
	4	2	4	2	

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	I	C	I	C	
OVARIAN CANCER*	3	2	3	2	
UTERINE FIBROIDS*					**Evidence**: Among women with fibroids, there were no adverse health events with LNG-IUD use, and there was a decrease in symptoms and size of fibroids for some women *(91–97)*.
a) Without distortion of the uterine cavity	1		1		
b) With distortion of the uterine cavity	4		4		
ANATOMICAL ABNORMALITIES*					
a) Distorted uterine cavity (any congenital or acquired uterine abnormality distorting the uterine cavity in a manner that is incompatible with IUD insertion)	4		4		
b) Other abnormalities (including cervical stenosis or cervical lacerations) not distorting the uterine cavity or interfering with IUD insertion	2		2		
PELVIC INFLAMMATORY DISEASE (PID)*					
a) Past PID (assuming no current risk factors for STIs)	I	C	I	C	
i) with subsequent pregnancy	1	1	1	1	
ii) without subsequent pregnancy	2	2	2	2	
b) PID – current	4	2	4	2	**Clarification for continuation:** Treat the PID using appropriate antibiotics. There is usually no need for removal of the IUD if the client wishes to continue its use (see WHO publication *Selected practice recommendations for contraceptive use*) Continued use of an IUD depends on the woman's informed choice and her current risk factors for STIs and PID. **Evidence**: Among IUD users treated for PID, there was no difference in clinical course if the IUD was removed or left in place *(98–100)*.

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STIs †	I	C	I	C	
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	4	2	4	2	**Clarification for continuation:** Treat the STI using appropriate antibiotics. There is usually no need for removal of the IUD if the client wishes to continue its use. Continued use of an IUD depends on the woman's informed choice and her current risk factors for STIs and PID. **Evidence:** There is no evidence regarding whether IUD insertion among women with STIs increases the risk of PID compared with no IUD insertion. Among women who have an IUD inserted, the absolute risk of subsequent PID was low among women with STI at the time of insertion but greater than among women with no STI at the time of IUD insertion *(101–108)*.
b) Other STIs (excluding HIV and hepatitis)	2	2	2	2	
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	2	2	2	2	
d) Increased risk of STIs	2/3	2	2/3	2	**Clarification:** IUD insertion may further increase the risk of PID among women at increased risk of STIs, although limited evidence suggests that this risk is low. Current algorithms for determining increased risk of STIs have poor predictive value. Risk of STIs varies by individual behaviour and local STI prevalence. Therefore, while many women at increased risk of STIs can generally have an IUD inserted, some women at increased risk (very high individual likelihood) of STIs should generally not have an IUD inserted until appropriate testing and treatment occur. **Evidence:** Using an algorithm to classify STI risk status among IUD users, 1 study reported that 11% of high-STI-risk women experienced IUD-related complications compared with 5% of those not classified as high risk *(104)*. In another small study, the incidence of PID after IUD insertion was low (2.2%) in a cohort of women considered to be high-risk based on high background rates of STIs in the general population *(109)*.

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HIV/AIDS †					
HIGH RISK OF HIV	I	C	I	C	**Evidence**: Among women at risk for HIV, Cu-IUD use did not increase risk of HIV acquisition *(110–120)*.
	2	2	2	2	
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	2	2	2	2	**Evidence**: Among IUD users, limited evidence shows no increased risk of overall complications or infectious complications when comparing women living with HIV to women not living with HIV. IUD use did not adversely affect progression of HIV when compared to hormonal contraceptive use among women living with HIV. Furthermore, IUD use among women living with HIV was not associated with increased risk of sexual transmission from female to male partners *(121–128)*. One study found no difference in initiation of antiretroviral therapy (ART) or CD4 count between users and non-users of the LNG-IUD *(129)*.
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	3	2	3	2	**Clarification for continuation**: IUD users with severe or advanced HIV clinical disease should be closely monitored for pelvic infection. **Evidence**: One study found no difference in ART initiation or CD4 count between users and non-users of the LNG-IUD *(129)*.
OTHER INFECTIONS					
SCHISTOSOMIASIS					
a) Uncomplicated	1		1		
b) Fibrosis of the liver (if severe, see cirrhosis)	1		1		
TUBERCULOSIS*	I	C	I	C	
a) Non-pelvic	1	1	1	1	
a) Pelvic	4	3	4	3	
MALARIA	1		1		

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ENDOCRINE CONDITIONS			
DIABETES			
a) History of gestational disease	1	1	
b) Non-vascular disease			
i) non-insulin-dependent	1	2	**Evidence**: Limited evidence on the use of the LNG-IUD among women with insulin- or non-insulin-dependent diabetes suggests that these methods have little effect on short-term or long-term diabetes control (e.g. HbA1c levels), haemostatic markers or lipid profile *(130, 131)*.
ii) insulin-dependent	1	2	
c) Nephropathy/retinopathy/ neuropathy	1	2	
d) Other vascular disease or diabetes of > 20 years' duration	1	2	
THYROID DISORDERS			
a) Simple goitre	1	1	
b) Hyperthyroid	1	1	
c) Hypothyroid	1	1	
GASTROINTESTINAL CONDITIONS			
GALL BLADDER DISEASE			
a) Symptomatic			
i) treated by cholecystectomy	1	2	
ii) medically treated	1	2	
iii) current	1	2	
b) Asymptomatic	1	2	
HISTORY OF CHOLESTASIS*			
a) Pregnancy-related	1	1	
b) Past-COC related	1	2	

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VIRAL HEPATITIS					
a) Acute or flare	1		1		
b) Carrier	1		1		
c) Chronic	1		1		
CIRRHOSIS					
a) Mild (compensated)	1		1		
b) Severe (decompensated)	1		3		
LIVER TUMOURS*					
a) Benign					
i) focal nodular hyperplasia	1		2		
ii) hepatocellular adenoma	1		3		
b) Malignant (hepatoma)	1		3		
ANAEMIAS					
THALASSAEMIA*	2		1		
SICKLE CELL DISEASE*	2		1		
IRON-DEFICIENCY ANAEMIA*	2		1		
DRUG INTERACTIONS					
ANTIRETROVIRAL THERAPY (ART)					**Clarification**: There is no known interaction between ART and IUD use. However, severe or advanced HIV clinical disease (WHO stage 3 or 4) as a condition is classified as Category 3 for initiation and Category 2 for continuation. Asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) is classified as Category 2 for both initiation and continuation.
a) Nucleoside reverse transcriptase inhibitors (NRTIs)	I	C	I	C	
Abacavir (ABC)	2/3	2	2/3	2	
Tenofovir (TDF)	2/3	2	2/3	2	
Zidovudine (AZT)	2/3	2	2/3	2	
Lamivudine (3TC)	2/3	2	2/3	2	
Didanosine (DDI)	2/3	2	2/3	2	
Emtricitabine (FTC)	2/3	2	2/3	2	
Stavudine (D4T)	2/3	2	2/3	2	

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b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	I	C	I	C	
Efavirenz (EFV)	2/3	2	2/3	2	
Etravirine (ETR)	2/3	2	2/3	2	
Nevirapine (NVP)	2/3	2	2/3	2	
Rilpivirine (RPV)	2/3	2	2/3	2	
c) Protease inhibitors (PIs)					
Ritonavir-boosted atazanavir (ATV/r)	2/3	2	2/3	2	
Ritonavir-boosted lopinavir (LPV/r)	2/3	2	2/3	2	
Ritonavir-boosted darunavir (DRV/r)	2/3	2	2/3	2	
Ritonavir (RTV)	2/3	2	2/3	2	
d) Integrase inhibitors					
Raltegravir (RAL)	2/3	2	2/3	2	
ANTICONVULSANT THERAPY					
a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	1		1		**Evidence**: Limited evidence suggests that use of certain anticonvulsants does not interfere with the contraceptive effectiveness of the LNG-IUD *(132)*.
b) Lamotrigine	1		1		**Evidence**: No drug interactions have been reported among women with epilepsy taking lamotrigine and using the LNG-IUD *(133)*.
ANTIMICROBIAL THERAPY					
a) Broad-spectrum antibiotics	1		1		
b) Antifungals	1		1		
c) Antiparasitics	1		1		
d) Rifampicin or rifabutin therapy	1		1		**Evidence**: One cross-sectional survey found that rifabutin had no impact on the effectiveness of LNG-IUD *(132)*.

RECOMMENDATIONS REVIEWED FOR FIFTH EDITION

These recommendations were reviewed according to WHO requirements for guideline development, as part of the preparation of the *Medical eligibility criteria for contraceptive use, fifth edition*. The population, intervention, comparator, outcome (PICO) questions developed by the Guideline Development Group (GDG) and the databases searched to retrieve the evidence, which guided the preparation of systematic reviews, are described in greater detail in Part I of this document. Additionally, GRADE evidence profiles, the overall GRADE assessment of the quality of the evidence, summaries of the evidence supporting the recommendation(s), and other supplementary remarks from the GDG regarding the recommendations, are available in Part I.

ADDITIONAL COMMENTS

Puerperal sepsis

Insertion of an iud may substantially worsen the condition.

Post-abortion

Immediate post-septic abortion: insertion of an iud may substantially worsen the condition.

Past ectopic pregnancy

The absolute risk of ectopic pregnancy is extremely low due to the high effectiveness of iuds. However, when a woman becomes pregnant during iud use, the relative likelihood of ectopic pregnancy is greatly increased.

Hypertension

There is theoretical concern about the effect of levonorgestrel (LNG) on lipids. There is no restriction for copper-bearing IUDs (Cu-IUDs).

Deep vein thrombosis/pulmonary embolism

The LNG-IUD may be a useful treatment for menorrhagia in women on chronic anticoagulation therapy.

Current and history of ischaemic heart disease

There is theoretical concern about the effect of LNG on lipids. There is no restriction for Cu-IUDs.

Stroke

There is theoretical concern about the effect of LNG on lipids. There is no restriction for Cu-IUDs.

Headaches

Aura is a specific focal neurologic symptom. For more information on this and other diagnostic criteria, see: headache classification subcommittee of the international headache society. The international classification of headache dis-orders, 2nd edition. Cephalalgia. 2004;24(Suppl 1):1–150.[14]

Severe dysmenorrhoea

Dysmenorrhoea may intensify with Cu-IUD use. LNG-IUD use has been associated with reduction of dysmenorrhoea.

Cervial intraepithelial neoplasia (CIN)

There is some theoretical concern that LNG-IUDs may hasten the progression of CIN.

Cervical cancer (awaiting treatment)

There is concern about the increased risk of infection and bleeding at insertion. The IUD will likely need to be removed at the time of treatment but, until then, the woman is at risk of pregnancy.

Breast disease

Breast cancer: breast cancer is a hormonally sensitive tumour. Concerns about progression of the disease may be less with lng-iuds than with combined oral contraceptives (cocs) or higher-dose progestogen-only contraceptives (POCs).

Endometrial cancer

There is concern about the increased risk of infection, perforation and bleeding at insertion. The iud will likely need to be removed at the time of treatment but, until then, the woman is at risk of pregnancy.

Ovarian cancer

The IUD will likely need to be removed at the time of treatment but, until then, the woman is at risk of pregnancy.

14 Available at: http://ihs-classification.org/en/02_klassifikation

Uterine fibroids

Without distortion of the uterine cavity: Women with heavy or prolonged bleeding should be assigned the category for that condition.

With distortion of the uterine cavity: Pre-existing uterine fibroids that distort the uterine cavity may be incompatible with insertion and proper placement of the IUD.

Anatomical abnormalities

Distorted uterine cavity: In the presence of an anatomic abnormality that distorts the uterine cavity, proper IUD placement may not be possible.

Pelvic inflammatory disease (PID)

IUDs do not protect against STI/HIV/PID. In women at low risk of STIs, IUD insertion poses little risk of PID. Current risk of STIs and desire for future pregnancy are relevant considerations.

Tuberculosis

Pelvic: Insertion of an IUD may substantially worsen the condition.

History of cholestasis

There is concern that a history of cholestasis related to combined hormonal contraceptives (CHCs) may predict subsequent cholestasis with LNG use. Whether there is any risk with use of an LNG-IUD is unclear.

Liver tumours

There is no evidence regarding hormonal contraceptive use among women with hepatocellular adenoma. Given that COC use in healthy women is associated with development and growth of hepatocellular adenoma, it is not known whether other hormonal contraceptives have similar effects.

Thalassaemia, sickle cell disease, iron-deficiency anaemia

There is concern about a risk of increased blood loss with Cu-IUDs.

References

1. Albert A, Carrasco F, Duenas JL, Navarro J. Analisis de las complicaciones menores surgidas durante el uso de DIU con cobre [Analysis of minor complications in copper IUD wearers]. Clin Invest Ginecol Obstet. 1983;10(1):16–22 (in Spanish).
2. Allonen H, Luukkainen T, Nielsen NC, Nygren KG, Pyorala T. Two-year rates for Nova T and Copper T in a comparative study. Contraception. 1980;21(4):321–34.
3. Allonen H, Luukkainen T, Nielsen NC, Nygren KG, Pyorala T. Factors affecting the clinical performance of Nova T and Copper T 200. Obstet Gynecol. 1984;64(4):524–9.
4. Alton TM, Brock GN, Yang D, Wilking DA, Hertweck SP, Loveless MB. Retrospective review of intrauterine device in adolescent and young women. J Pediatr Adolesc Gynecol. 2012;25(3):195–200.
5. Behringer T, Reeves MF, Rossiter B, Chen BA, Schwarz EB. Duration of use of a levonorgestrel IUS amongst nulliparous and adolescent women. Contraception. 2011;84(5):e5–e10.
6. Berenson AB, Tan A, Hirth JM, Wilkinson GS. Complications and continuation of intrauterine device use among commercially insured teenagers. Obstet Gynecol. 2013;121(5):951–8.
7. Luukkainen T, Allonen H, Nielsen NC, Nygren KG, Pyorala T. Five years' experience of intrauterine contraception with the Nova-T and the Copper-T-200. Am J Obstet Gynecol. 1983;147(8):885–92.
8. Luukkainen T, Nielsen NC, Nygren KG, Pyorala T. Nulliparous women, IUD and pelvic infection. Ann Clin Res. 1979;11(4):121–4.
9. Luukkainen T, Nielsen NC, Nygren KG, Pyorala T, Allonen H. Combined and national experience of postmenstrual IUD insertions of Nova-T and Copper-T in a randomized study. Contraception. 1979;19(1):11–20.
10. Nygren KG, Nielsen NC, Pyorala T, Allonen H, Luukkainen T. Intrauterine contraception with Nova-T and copper-T-200 during three years. Contraception. 1981;24(5):529–42.
11. Osser S, Gullberg B, Liedholm P, Sjoberg NO. Risk of pelvic inflammatory disease among intrauterine-device users irrespective of previous pregnancy. Lancet. 1980;1(8165):386–8.
12. Rasheed SM, Abdelmonem AM. Complications among adolescents using copper intrauterine contraceptive devices. Int J Gynaecol Obstet. 2011;115(3):269–72.
13. Skajaa K, Dorup I, Skajaa T. [Complications caused by intrauterine contraceptive devices]. Ugeskr Laeger. 1990;152(41):3002–6 (in Danish).
14. Suhonen S, Haukkamaa M, Jakobsson T, Rauramo I. Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: a comparative study. Contraception. 2004;69(5):407–12.
15. Zhang J, Feldblum PJ, Chi IC, Farr MG. Risk factors for copper T IUD expulsion: an epidemiologic analysis. Contraception. 1992;46(5):427–33.
16. Bonilla Rosales F, Aguilar Zamudio ME, Cazares Montero Mde L, Hernandez Ortiz ME, Luna Ruiz MA. [Factors for expulsion of intrauterine device Tcu380A applied immediately postpartum and after a delayed period]. Rev Med Inst Mex Seguro Soc. 2005;43(1):5–10 (in Spanish).
17. Brenner PF. A clinical trial of the Delta-T intrauterine device: immediate postpartum insertion. Contraception. 1983;28(2):135–47.
18. Celen S, Moroy P, Sucak A, Aktulay A, Danisman N. Clinical outcomes of early postplacental insertion of intrauterine contraceptive devices. Contraception. 2004;69(4):279–82.
19. Chi IC, Wilkens L, Rogers S. Expulsions in immediate postpartum insertions of Lippes Loop D and Copper T IUDs and their counterpart Delta devices – an epidemiological analysis. Contraception. 1985;32(2):119–34.
20. Eroglu K, Akkuzu G, Vural G, Dilbaz B, Akin A, Taskin L, et al. Comparison of efficacy and complications of IUD insertion in immediate postplacental/early postpartum period with interval period: 1 year follow-up. Contraception. 2006;74(5):376–81.
21. Kapp N, Curtis KM. Intrauterine device insertion during the postpartum period: a systematic review. Contraception. 2009;80(4):327–36.
22. Lara R, Sanchez RA, Aznar R. Aplicacion del dispositivo intrauterino a traves de la incision de la cesarea [Application of intrauterine device through the incision of the cesarean section]. Ginecol Obstet Mex. 1989;57:23–7 (in Spanish).
23. Letti Muller AL, Lopes Ramos JG, Martins-Costa SH, Palma Dias RS, Valerio EG, Hammes LS, et al. Transvaginal ultrasonographic assessment of the expulsion rate of intrauterine devices inserted in the immediate postpartum period: a pilot study. Contraception. 2005;72(3):192–5.
24. Mishell DR, Jr., Roy S. Copper intrauterine contraceptive device event rates following insertion 4 to 8 weeks post partum. Am J Obstet Gynecol. 1982;143(1):29–35.
25. Morrison C, Waszak C, Katz K, Diabate F, Mate EM. Clinical outcomes of two early postpartum IUD insertion programs in Africa. Contraception. 1996;53(1):17–21.

26. Thiery M, van Kets H, van der Pas H, van Os W, Dombrowicz N. The ML Cu250; clinical experience in Belgium and The Netherlands. Br J Obstet Gynaecol. 1982;89(Suppl 4):51–3.

27. Van Der Pas MT, Delbeke L, Van Dets H. Comparative performance of two copper-wired IUDs (ML Cu 250 and T Cu 200: immediate postpartum and interval insertion. Contracept Deliv Syst. 1980;1(1):27–35.

28. Welkovic S, Costa LO, Faundes A, de Alencar Ximenes R, Costa CF. Post-partum bleeding and infection after post-placental IUD insertion. Contraception. 2001;63(3):155–8.

29. Zhou SW, Chi IC. Immediate postpartum IUD insertions in a Chinese hospital – a two year follow-up. Int J Gynaecol Obstet. 1991;35(2):157–64.

30. Chen BA, Reeves MF, Creinin MD, Schwarz EB. Postplacental or delayed levonorgestrel intrauterine device insertion and breast-feeding duration. Contraception. 2011;84(5):499–504.

31. Brito MB, Ferriani RA, Quintana SM, Yazlle ME, Silva de Sá MF, Vieira CS. Safety of the etonogestrel-releasing implant during the immediate postpartum period: a pilot study. Contraception. 2009;80(6):519–26.

32. Gurtcheff SE, Turok DK, Stoddard G, Murphy PA, Gibson M, Jones KP. Lactogenesis after early postpartum use of the contraceptive implant: a randomized controlled trial. Obstet Gynecol. 2011;117(5):1114–21.

33. Bahamondes L, Bahamondes MV, Modesto W, Tilley IB, Magalhaes A, Pinto e Silva JL, et al. Effect of hormonal contraceptives during breastfeeding on infant's milk ingestion and growth. Fertil Steril. 2013;100(2):445–50.

34. Costa ML, Cecatti JG, Krupa FG, Rehder PM, Sousa MH, Costa-Paiva L. Progestin-only contraception prevents bone loss in postpartum breastfeeding women. Contraception. 2012;85(4):374–80.

35. Shaamash AH, Sayed GH, Hussien MM, Shaaban MM. A comparative study of the levonorgestrel-releasing intrauterine system Mirena versus the Copper T380A intrauterine device during lactation: breast-feeding performance, infant growth and infant development. Contraception. 2005;72(5):346–51.

36. Zhang PZ. Five years experience with the copper T 200 in Shanghai - 856 cases. Contraception. 1980;22:561–71.

37. Timonen H, Luukkainen T. Immediate postabortion insertion of the copper-T (TCu-200) with eighteen months follow-up. Contraception. 1974;9:153–60.

38. The World Health Organization's Special Programme of Research Development and Research Training in Human Reproduction. Task Force on Intrauterine Devices for Fertility Regulation. The Alza T IPCS 52, a longer acting progesterone IUD: safety and efficacy compared to the TCu220C and multiload 250 in two randomized multicentre trials. Clin Reprod Fertil. 1983;2:113–28.

39. The World Health Organization's Special Programme of Research Development and Research Training in Human Reproduction. Task Force on Intrauterine Devices for Fertility Regulation. IUD insertion following termination of pregnancy: a clinical trial of the TCu 220C, Lippes loop D, and copper 7. Stud Fam Plann. 1983;14:99–108.

40. The World Health Organization's Special Programme of Research Development and Research Training in Human Reproduction. Task Force on Intrauterine Devices for Fertility Regulation. IUD insertion following spontaneous abortion: a clinical trial of the TCu 220C, Lippes loop D, and copper 7. Stud Fam Plann. 1983;14:109–14.

41. Suvisaari J, Lahteenmaki P. Detailed analysis of menstrual bleeding patterns after postmensstrual and postabortal insertion of a copper IUD or a levonorgestrel-releasing intrauterine system. Contraception. 1996;54:201–8.

42. Stanwood NL, Grimes DA, Schulz KF. Insertion of an intrauterine contraceptive device after induced or spontaneous abortion: a review of the evidence. BJOG. 2001;108:1168–73.

43. Pakarinen P, Toivonen J, Luukkainen T. Randomized comparison of levonorgestrel- and copper-releasing intrauterine systems immediately after abortion, with 5 years' follow-up. Contraception. 2003;68:31–4.

44. Moussa A. Evaluation of postabortion IUD insertion in Egyptian women. Contraception. 2001;63:315–7.

45. Gupta I, Devi PK. Studies on immediate post-abortion copper 'T' device. Indian J Med Res. 1975;63:736–9.

46. Grimes D, Schulz K, Stanwood N. Immediate postabortal insertion of intrauterine devices. [update of Cochrane Database Syst Rev. 2000;(2):CD001777]. Cochrane Database Syst Rev. 2002;CD001777.

47. Gillett PG, Lee NH, Yuzpe AA, Cerskus I. A comparison of the efficacy and acceptability of the Copper-7 intrauterine device following immediate or delayed insertion after first-trimester therapeutic abortion. Fertil Steril. 1980;34:121–4.

48. El Tagy A, Sakr E, Sokal DC, Issa AH. Safety and acceptability of post-abortal IUD insertion and the importance of counseling. Contraception. 2003;67:229–34.

49. Vasilakis C, Jick H, Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestogens alone. Lancet. 1999;354:1610–1.

50. Heinemann L, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the health of Young Women. Eur J Contracep Repr. 1999;4:67–73.

51. World Health Organization. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. Contraception. 1998;57:315–24.

52. Kingman CE, Kadir RA, Lee CA, Economides DL. The use of the levonorgestrel-releasing intrauterine system for treatment of menorrhagia in women with inherited bleeding disorders. BJOG. 2004;111:1425–8.

53. 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;15:877–80.

54. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol. 2005;193:1361–3.

55. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol. 2002;29:2531–6.

56. Sarabi ZS, Chang E, Bobba R, al e. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum. 2005;53:609–12.

57. Sanchez-Guerrero J, Uribe AG, Jimenez-Santana L, Mestanza-Peralta M, Lara-Reyes P, Seuc AH, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2539–49.

58. Petri M, Kim MY, Kalunian KC, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med. 2005;353:2550–8.

59. Petri M. Lupus in Baltimore: evidence-based 'clinical perarls' from the Hopkins Lupus Cohort. Lupus. 2005;14:970–3.

60. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res. 1995;8:137–45.

61. Mintz G, Gutierrez G, Delezé M, Rodríguez E. Contraception with progestogens in systemic lupus erythematosus. Contraception. 1984;30:29–38.

62. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis. 1992;51:56–60.

63. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephristis in systemic lupus erythematosus. Ann Rheum Dis. 1993;52:720–4.

64. Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, Jansen-McWilliams L, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145:408–15.

65. Jungers P, Dougados M, Pelissier C, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum. 1982;25:618–23.

66. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol. 1993;32:227–30.

67. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol. 1991;20:427–33.

68. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, du Berger R, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum. 2001;44:2331–7.

69. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol. 2002;29:1683–8.

70. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1386–9.

71. Bernatsky S, Clarke A, Ramsey-Goldman R, Joseph L, Boivin JF, Rajan R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1178–81.

72. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus – a meta-analysis. Lupus. 1997;6:467–73.

73. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol. 2008;27(3):345–51.

74. Barrington JW, Arunkalaivanan AS, bdel-Fattah M. Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia. Eur J Obstet Gynecol Repr Biol. 2003;108(1):72–4.

75. Gupta B, Mittal S, Misra R, Deka D, Dadhwal V. Levonorgestrel-releasing intrauterine system vs. transcervical endometrial resection for dysfunctional uterine bleeding. Int J Gynaecol Obstet. 2006;95(3):261–6.

76. Hurskainen R, Teperi J, Rissanen P, Aalto AM, Grenman S, Kivela A, et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. Lancet. 2001;357(9252):273–7.

77. Istre O, Trolle B. Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection. Fertil Steril. 2001;76(2):304–9.

78. Koh SC, Singh K. The effect of levonorgestrel-releasing intrauterine system use on menstrual blood loss and the hemostatic, fibrinolytic/inhibitor systems in women with menorrhagia. J Thromb Haemost. 2007;5(1):133–8.

79. Lethaby AE, Cooke I, Rees M. Progesterone/progestogen releasing intrauterine systems versus either placebo or any other medication for heavy menstrual bleeding. Cochrane Database Syst Rev. 2000;(2):CD002126.

80. Magalhaes J, Aldrighi JM, de Lima GR. Uterine volume and menstrual patterns in users of the levonorgestrel-releasing intrauterine system with idiopathic menorrhagia or menorrhagia due to leiomyomas. Contraception. 2007;75(3):193–8.

81. Stewart A, Cummins C, Gold L, Jordan R, Phillips W. The effectiveness of the levonorgestrel-releasing intrauterine system in menorrhagia: a systematic review. Br J Obstet Gynaecol. 2001;108(1):74–86.

82. Fedele L, Bianchi S, Zanconato G, Portuese A, Raffaelli R. Use of a levonorgestrel-releasing intrauterine device in the treatment of rectovaginal endometriosis. Fertil Steril. 2001;75(3):485–8.

83. Lockhat FBE. The effect of a levonorgestrel intrauterine system (LNG-IUS) on symptomatic endometriosis. Fertil Steril. 2002;77 Suppl 1:S24.

84. Petta CA, Ferriani RA, Abrao MS, Hassan D, Rosa E Silva JC, Podgaec S, et al. Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis. Hum Reprod. 2005;20(7):1993–8.

85. Vercellini P, Aimi G, Panazza S, De Giorgi O, Pesole A, Crosignani PG. A levonorgestrel-releasing intrauterine system for the treatment of dysmenorrhea associated with endometriosis: a pilot study. Fertil Steril. 1999;72(3):505–8.

86. Vercellini P, Frontino G, De GO, Aimi G, Zaina B, Crosignani PG. Comparison of a levonorgestrel-releasing intrauterine device versus expectant management after conservative surgery for symptomatic endometriosis: a pilot study. Fertil Steril. 2003;80(2):305–9.

87. Gaffield ME, Kapp N, Curtis KM. Combined oral contraceptive and intrauterine device use among women with gestational trophoblastic disease. Contraception. 2009;80(4):363–71.

88. Adewole IF, Oladokun A, Fawole AO, Olawuyi JF, Adeleye JA. Fertility regulatory methods and development of complications after evacuation of complete hydatidiform mole. J Obstet Gynecol. 2000;20:68–9.

89. Deicas RE, Miller DS, Rademaker AW, Lurain JR. The role of contraception in the development of postmolar trophoblastic tumour. Obstet Gynecol. 1991;78:221–6.

90. Ho Yuen B, Burch P. Relationship of oral contraceptives and the intrauterine contraceptive devices to the regression of concentration of the beta subunit of human chorionic gonadotropin and invasive complications after molar pregnancy. Am J Obstet Gynecol. 1983;145:214–7.

91. Fedele L, Bianchi S, Raffaelli R, Portuese A, Dorta M. Treatment of adenomyosis-associated menorrhagia with a levonorgestrel-releasing intrauterine device. Fertil Steril. 1997;68:426–9.

92. Grigorieva V, Chen-Mok M, Tarasova M, Mikhailov A. Use of a levonorgestrel-releasing intrauterine system to treat bledding related to uterine leiomyomas. Fertil Steril. 2003;79:1194–8.

93. Wildemeersch D, Schacht E. The effect on menstrual blood loss in women with uterine fibroids of a novel 'frameless' intrauterine levonorgestrel-releasing drug delivery system: a pilot study. Eur J Obstet Gynecol Repr Biol. 2002;102:74–9.

94. Wildemeersch D, Schacht E, Wildemeersch P. Treatment of primary and secondary dysmenorrhea with a novel 'frameless' intrauterine levonorgestrel-releasing drug delivery system: a pilot study. Eur J Contracept Reprod Health Care. 2001;6:192–8.

95. Wildemeersch D, Schacht E, Wildemeersch P. Contraception and treatment in the perimenopause with a novel 'frameless' intrauterine levonorgestrel-releasing drug delivery system: an extended pilot study. Contraception. 2002;66:93–9.

96. Wildemeersch D, Schacht E, Wildemeersch P. Performance and acceptability of intrauterine release of levonorgestrel with a miniature delivery system for hormonal substitution therapy, contraception and treatment in peri and postmenopausal women. Maturitas. 2003;44:237–45.

97. Mercoria F, De Simone R, Di Spiezio Sardo A, Cerrota G, Bifulco G, Vanacore F, et al. The effect of a levonorgestrel-releasing intrauterine device in the treatment of myoma-related menorrhagia. Contraception. 2003;67:277–80.

98. Larsson B, Wennergren M. Investigation of a copper-intrauterine device (Cu-IUD) for possible effect on frequency and healing of pelvic inflammatory disease. Contraception. 1977;15:143–9.

99. Soderberg G, Lindgren S. Influence of an intrauterine device on the course of an acute pelvic inflammatory disease. Contraception. 1981;24:137–43.

100. Teisala K. Removal of an intrauterine device and the treatment of acute pelvic inflammatory disease. Ann Med. 1989;21:63–5.

101. Faundes A, Telles E, Cristofoletti ML, Faundes D, Castro S, Hardy E. The risk of inadvertent intrauterine device insertion in women carriers of endocervical Chlamydia trachomatis. Contraception. 1998;58(2):105–9.

102. Ferraz do Lago R, Simoes JA, Bahamondes L, Camargo RP, Perrotti M, Monteiro I. Follow-up of users of intrauterine device with and without bacterial vaginosis and other cervicovaginal infections. Contraception. 2003;68(2):105–9.

103. 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.

104. Morrison CS, Sekadde-Kigondu C, Miller WC, Weiner DH, Sinei SK. Use of sexually transmitted disease risk assessment algorithms for selection of intrauterine device candidates. Contraception. 1999;59(2):97–106.

105. Pap-Akeson M, Solheim F, Thorbert G, Akerlund M. Genital tract infections associated with the intrauterine contraceptive device can be reduced by inserting the threads into the uterine cavity. Br J Obstet Gynaecol. 1992;99(8):676–9.

106. Sinei SK, Schulz KF, Lamptey PR, Grimes DA, Mati JK, Rosenthal SM, et al. Preventing IUCD-related pelvic infection: the efficacy of prophylactic doxycycline at insertion. Br J Obstet Gynaecol. 1990;97(5):412–9.

107. Skjeldestad FE, Halvorsen LE, Kahn H, Nordbo SA, Saake K. IUD users in Norway are at low risk for genital C. trachomatis infection. Contraception. 1996;54(4):209–12.

108. Walsh TL, Bernstein GS, Grimes DA, Frezieres R, Bernstein L, Coulson AH. Effect of prophylactic antibiotics on morbidity associated with IUD insertion: results of a pilot randomized controlled trial. IUD Study Group. Contraception. 1994;50(4):319–27.

109. Cropsey KL, Matthews C, Campbel S, Ivey S, Adawadkar S. Long-term, reversible contraception use among high-risk women treated in a university-based gynecology clinic: comparison between IUD and depo-provera. J Womens Health (Larchmt). 2010;19(2):349–53.

110. Carael M, Van de Perre PH, Lepage PH, Allen S, Nsengumuremyi F, Van Goethem C, et al. Human immunodeficiency virus transmission among heterosexual couples in Central Africa. AIDS. 1988;2(3):201–5.

111. European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. BMJ. 1992;304(6830):809–13.

112. Mann JM, Nzilambi N, Piot P, Bosenge N, Kalala M, Francis H, et al. HIV infection and associated risk factors in female prostitutes in Kinshasa, Zaire. AIDS. 1998;2:249–54.

113. Kapiga SH, Lyamuya EF, Lwihula GK, Hunter DJ. The incidence of HIV infection among women using family planning methods in Dar es Salaam, Tanzania. AIDS. 1998;12(1):75–84.

114. Kapiga SH, Shao JF, Lwihula GK, Hunter DJ. Risk factors for HIV infection among women in Dar-es-Salaam, Tanzania. J Acquir Immune Defic Syndr. 1994;7(3):301–9.

115. Martin HL, Jr., Nyange PM, Richardson BA, Lavreys L, Mandaliya K, Jackson DJ, et al. Hormonal contraception, sexually transmitted diseases, and risk of heterosexual transmission of human immunodeficiency virus type 1. J Infect Dis. 1998;178(4):1053–9.

116. Mati JK, Hunter DJ, Maggwa BN, Tukei PM. Contraceptive use and the risk of HIV infection in Nairobi, Kenya. Int J Gynaecol Obstet. 1995;48(1):61–7.

117. Nicolosi A, Correa Leite ML, Musicco M, Arici C, Gavazzeni G, Lazzarin A. The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: a study of 730 stable couples. Italian Study Group on HIV Heterosexual Transmission [comment]. Epidemiology. 1994;5(6):570–5.

118. Plourde PJ, Plummer FA, Pepin J, Agoki E, Moss G, Ombette J, et al. Human immunodeficiency virus type 1 infection in women attending a sexually transmitted diseases clinic in Kenya [comment]. J Infect Dis. 1992;166(1):86–92.

119. Sinei SK, Fortney JA, Kigondu CS, Feldblum PJ, Kuyoh M, Allen MY, et al. Contraceptive use and HIV infection in Kenyan family planning clinic attenders. Int J STD AIDS. 1996;7(1):65–70.

120. Spence MR, Robbins SM, Polansky M, Schable CA. Seroprevalence of human immunodeficiency virus type I (HIV-1) antibodies in a family-planning population. Sex Transm Dis. 1991;18(3):143–5.

121. Mostad SB, Overbaugh J, DeVange DM, Welch MJ, Chohan B, Mandaliya K, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet. 1997;350:922–7.

122. Sinei SK, Morrison CS, Sekadde-Kigondu C, Allen M, Kokonya D. Complications of use of intrauterine devices among HIV-1 infected women. Lancet. 1998;351:1238–41.

123. Richardson BA, Morrison CS, Sekadde-Kigondu C, Sinei SK, Overbaugh J, Panteleeff DD, et al. Effect of intrauterine device use on cervical shedding of HIV-1 DNA. AIDS. 1999;13:2091–7.

124. Kovacs A, Wasserman SS, Burns D, Wright DJ, Cohn J, Landay A, et al. Determinants of HIV-1 shedding in the genital tract of women. Lancet. 2001;358:1593–601.

125. Morrison CS, Sekadde-Kigondu C, Sinei SK, Weiner DH, Kwok C, Kokonya D. Is the intrauterine device appropriate contraception for HIV-1 infected women? BJOG. 2001;108:784–90.

126. Heikinheimo O, Lehtovirta P, Suni J, Paavonen J. The levonorgestrel-releasing intrauterine system (LNG-IUS) in HIV-infected women – effects on bleeding patterns, ovarian function and genital shedding of HIV. Hum Reprod. 2006;21:2857–61.

127. Stringer EM, Kaseba C, Levy J, Sinkala M, Goldenberg RL, Chi BH, et al. A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol. 2007;197:144.e1–8.

128. Lehtovirta P, Paavonen J, Heikinheimo O. Experience with the levonorgestrel-releasing intrauterine system among HIV-infected women. Contraception. 2007;75:37–9.

129. World Health Organization, Task Force for Epidemiological Research on Reproductive Health; Special Programme of Research, Development, and Research Training in Human Reproduction. Progestogen-only contraceptives during lactation: II. Infant development. Contraception. 1994;50(1):55–68.

130. Rogovskaya S, Rivera R, Grimes DA, Chen P-L, Pierre-Louis B, Prilepskaya V, et al. Effect of a levonorgestrel intrauterine system on women with type 1 diabetes: a randomized trial. Obstet Gynecol. 2005;105:811–5.

131. Grigoryan OR, Grodnitskaya EE, Andreeva EN, Shestakova MV, Melnichenko GA, Dedov II. Contraception in perimenopausal women with diabetes mellitus. Gynecol Endocrinol. 2006;22(4):198–206.

132. Bounds W, Guillebaud J. Observational series on women using the contraceptive Mirena concurrently with anti-epileptic and other enzyme-inducing drugs. J Fam Plann Reprod Health Care. 2002;28:78–80.

133. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia. 2005;46(9):1414–7.

2.7.5 Copper-bearing IUD for emergency contraception (E-IUD)

Use of a copper-bearing IUD (Cu-IUD) for emergency contraception (E-IUD) is highly effective for preventing pregnancy. For this purpose, a Cu-IUD can be inserted within five days of unprotected intercourse. However, when the time of ovulation can be estimated, the Cu-IUD can be inserted beyond five days after intercourse, if necessary, as long as the insertion does not occur more than five days after ovulation.

The eligibility criteria for general Cu-IUD insertion also apply for the insertion of E-IUDs (see section 2.7.4 on IUDs, pp. 189–204).

COPPER IUD FOR EMERGENCY CONTRACEPTION (E-IUD)

IUDs for emergency contraception do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY	CLARIFICATIONS/EVIDENCE
PREGNANCY	4	**Clarification**: The IUD is not indicated during pregnancy and should not be used because of the risk of serious pelvic infection and septic spontaneous abortion.
RAPE*		
a) High risk of STI	3	
b) Low risk of STI	1	

ADDITIONAL COMMENTS

Rape

IUDs do not protect against STI/HIV or pelvic inflammatory disease (PID). Among women with chlamydial infection or gonorrhoea, the potential increased risk of PID with IUD insertion should be avoided. The concern is less for other STIs.

2.7.6 Progesterone-releasing vaginal ring (PVR) for breastfeeding women

The progesterone-releasing vaginal ring (PVR) is a contraceptive method for women who are actively breastfeeding at least four times a day. It consists of a flexible ring that releases 10 mg/day of progesterone. During use, average plasma concentrations of 20 nmol/L are achieved, which are similar to those detected in the average luteal phase in normal fertile women. The PVR is worn continuously for three-month periods (approximately 90 days) and can be initiated at six weeks after childbirth. Use of the PVR during breastfeeding requires replacing the used ring with a new ring at three-month intervals (± two weeks). The mechanism of contraceptive action of the PVR is through the inhibition of ovulation *(1, 2)*.

PROGESTERONE-RELEASING VAGINAL RING FOR BREASTFEEDING WOMEN		
PVRs do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION **† recommendations reviewed for the MEC 5th edition, further details after this table**	**CATEGORY**	**CLARIFICATIONS/EVIDENCE**
PREGNANCY	NA	NA = not applicable **Clarification**: Use of PVRs is not required. There is no known harm to the woman, the course of her pregnancy, or the fetus if PVRs are accidentally used during pregnancy.
BREASTFEEDING ≥ 4 WEEKS POSTPARTUM †	1	**Clarification**: The woman must be actively breastfeeding (i.e. at least 4 breastfeeding episodes per day) during PVR use to maintain efficacy. **Evidence**: No differences were observed between various measures of breastfeeding performance among PVR users compared with users of non-hormonal or progestogen-only (synthetic progesterone) contraceptives during 12 months of observation *(3–8)*. No statistically significant differences in infant weight gain were observed among PVR users compared with women using a non-hormonal or progestogen-only contraceptives *(5, 7, 9)*, and similar patterns of infant weight gain were observed in another study that compared PVR and IUD users *(8)*. One study reported no significant difference in infant health *(8)*.

RECOMMENDATIONS REVIEWED FOR FIFTH EDITION

These recommendations were reviewed according to WHO requirements for guideline development, as part of the preparation of the *Medical eligibility criteria for contraceptive use, fifth edition*. The population, intervention, comparator, outcome (PICO) questions developed by the Guideline Development Group (GDG) and the databases searched to retrieve the evidence, which guided the preparation of systematic reviews, are described in greater detail in Part I of this document. Additionally, GRADE evidence profiles, the overall GRADE assessment of the quality of the evidence, summaries of the evidence supporting the recommendation(s), and other supplementary remarks from the GDG regarding the recommendations, are available in Part I.

References

1. Diaz S, Aravena R, Cardenas H, Casado ME, Miranda P, Schiappacasse V, et al. Contraceptive efficacy of lactational amenorrhea in urban Chilean women. Contraception. 1991;43(4):335–52.
2. Nath A, Sitruk-Ware R. Progesterone vaginal ring for contraceptive use during lactation. Contraception. 2010;82(5):428–34.
3. Diaz S, Jackanicz TM, Herreros C, Juez G, Peralta O, Miranda P, et al. Fertility regulation in nursing women: VIII. Progesterone plasma levels and contraceptive efficacy of a progesterone-releasing vaginal ring. Contraception. 1985;32(6):603–22.
4. Diaz S, Reyes MV, Zepeda A, Gonzalez GB, Lopez JM, Campino C, et al. Norplant® implants and progesterone vaginal rings do not affect maternal bone turnover and density during lactation and after weaning. Human reproduction (Oxford, England). 1999;14(10):2499–505.
5. Diaz S, Zepeda A, Maturana X, Reyes MV, Miranda P, Casado ME, et al. Fertility regulation in nursing women. IX. Contraceptive performance, duration of lactation, infant growth, and bleeding patterns during use of progesterone vaginal rings, progestin-only pills, Norplant implants, and Copper T 380-A intrauterine devices. Contraception. 1997;56(4):223–32.
6. Massai R, Miranda P, Valdes P, Lavin P, Zepeda A, Casado ME, et al. Preregistration study on the safety and contraceptive efficacy of a progesterone-releasing vaginal ring in Chilean nursing women. Contraception. 1999;60(1):9–14.
7. Shaaban MM. Contraception with progestogens and progesterone during lactation. J Steroid Biochem Mol Biol. 1991;40(4–6):705–10.
8. Sivin I, Diaz S, Croxatto HB, Miranda P, Shaaban M, Sayed EH, et al. Contraceptives for lactating women: a comparative trial of a progesterone-releasing vaginal ring and the copper T 380A IUD. Contraception. 1997;55(4):225–32.
9. Chen JH, Wu SC, Shao WQ, Zou MH, Hu J, Cong L, et al. The comparative trial of TCu 380A IUD and progesterone-releasing vaginal ring used by lactating women. Contraception. 1998;57(6):371–9.

2.7.7 Barrier methods (BARR)

BARRIER METHODS (BARR)				
If there is a risk of sexually transmitted infections (STIs), including HIV, then the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.				
CONDITION * additional comments after this table	**CATEGORY** I = initiation, C = continuation			**CLARIFICATIONS/EVIDENCE**
	Condom	**Spermicide**	**Diaphragm**	
Condoms = male latex condoms, male polyurethane condoms, female condoms **Diaphragm = diaphragm (with spermicide), cervical cap**				
Women with conditions that make pregnancy an unacceptable risk should be advised that barrier methods for pregnancy prevention may not be appropriate for those who cannot use them consistently and correctly because of their relatively higher typical-use failure rates.				
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY				
PREGNANCY	NA	NA	NA	NA = not applicable **Clarification**: None of these methods are relevant for contraception during known pregnancy. However, for women who continue to be at risk of STI/HIV during pregnancy, the correct and consistent use of condoms is recommended.
AGE				
a) Menarche to < 40 years	1	1	1	
b) ≥ 40 years	1	1	1	
PARITY				
a) Nulliparous	1	1	1	
b) Parous	1	1	2	**Clarification**: There is a higher risk of cervical cap failure in parous women than in nulliparous women.
POSTPARTUM				
a) < 6 weeks postpartum	1	1	NA	**Clarification**: The diaphragm and cap are unsuitable until uterine involution is complete.
b) ≥ 6 weeks postpartum	1	1	1	
POST-ABORTION				
a) First trimester	1	1	1	
b) Second trimester	1	1	1	**Clarification**: The diaphragm and cap are unsuitable until 6 weeks after second-trimester abortion.
c) Immediate post-septic abortion	1	1	1	
PAST ECTOPIC PREGNANCY	1	1	1	
HISTORY OF PELVIC SURGERY	1	1	1	

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SMOKING				
a) Age < 35 years	1	1	1	
b) Age > 35 years				
i) < 15 cigarettes/day	1	1	1	
ii) ≥ 15 cigarettes/day	1	1	1	
OBESITY*				
a) ≥ 30 kg/m^2 BMI	1	1	1	
b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	1	1	1	
BLOOD PRESSURE MEASUREMENT UNAVAILABLE	NA	NA	NA	**Clarification**: While a blood pressure measurement may be appropriate for good preventive health care, it is not required for safe and effective barrier method use. Women should not be denied the use of barrier methods simply because their blood pressure cannot be measured.
CARDIOVASCULAR DISEASE				
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (such as older age, smoking, diabetes, hypertension and known dyslipidaemias)	1	1	1	
HYPERTENSION				
a) History of hypertension, where blood pressure CANNOT be evaluated (including hypertension in pregnancy)	1	1	1	
b) Adequately controlled hypertension, where blood pressure CAN be evaluated	1	1	1	

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c) Elevated blood pressure levels (properly taken measurements)				
i) systolic 140–159 or diastolic 90–99 mm Hg	1	1	1	
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	1	1	1	
d) Vascular disease	1	1	1	
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	1	1	1	
DEEP VEIN THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)				
a) History of DVT/PE	1	1	1	
b) Acute DVT/PE	1	1	1	
c) DVT/PE and established on anticoagulant therapy	1	1	1	
d) Family history (first-degree relatives)	1	1	1	
e) Major surgery				
i) with prolonged immobilization	1	1	1	
ii) without prolonged immobilization	1	1	1	
f) Minor surgery without immobilization	1	1	1	
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	1	1	1	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.

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SUPERFICIAL VENOUS DISORDERS				
a) Varicose veins	1	1	1	
b) Superficial venous thrombosis	1	1	1	
CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE	1	1	1	
STROKE (history of cerebrovascular accident)	1	1	1	
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS	1	1	1	**Clarification**: Routine screening is not appropriate because of the rarity of the condition and the high cost of screening.
VALVULAR HEART DISEASE*				
a) Uncomplicated	1	1	1	
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	1	1	2	
RHEUMATIC DISEASES				
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)				
a) Positive (or unknown) antiphospholipid antibodies	1	1	1	
b) Severe thrombocytopenia	1	1	1	
c) Immunosuppressive treatment	1	1	1	
d) None of the above	1	1	1	

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NEUROLOGIC CONDITIONS				
HEADACHES				
a) Non-migrainous (mild or severe)	1	1	1	
b) Migraine				
i) without aura				
age < 35 years	1	1	1	
age ≥ 35 years	1	1	1	
ii) with aura, at any age	1	1	1	
EPILEPSY	1	1	1	
DEPRESSIVE DISORDERS				
DEPRESSIVE DISORDERS	1	1	1	
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS				
UNEXPLAINED VAGINAL BLEEDING (suspicious for serious condition) Before evaluation	1	1	1	**Clarification**: If pregnancy or an underlying pathological condition (such as pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation.
ENDOMETRIOSIS	1	1	1	
BENIGN OVARIAN TUMOURS (including cysts)	1	1	1	
SEVERE DYSMENORRHOEA	1	1	1	

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GESTATIONAL TROPHOBLASTIC DISEASE				
a) Decreasing or undetectable β-hCG levels	1	1	1	
b) Persistently elevated β-hCG levels or malignant disease	1	1	1	
CERVICAL ECTROPION	1	1	1	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)	1	1	1	**Clarification**: The cap should not be used. There is no restriction for diaphragm use.
CERVICAL CANCER* (AWAITING TREATMENT)	1	2	1	**Clarification**: The cap should not be used. There is no restriction for diaphragm use.
BREAST DISEASE				
a) Undiagnosed mass	1	1	1	
b) Benign breast disease	1	1	1	
c) Family history of cancer	1	1	1	
d) Breast cancer				
i) current	1	1	1	
ii) past and no evidence of current disease for 5 years	1	1	1	
ENDOMETRIAL CANCER	1	1	1	
OVARIAN CANCER	1	1	1	
UTERINE FIBROIDS				
a) Without distortion of the uterine cavity	1	1	1	
b) With distortion of the uterine cavity	1	1	1	

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ANATOMICAL ABNORMALITIES	1	1	NA	**NA = not applicable** **Clarification**: The diaphragm cannot be used in certain cases of prolapse. Cap use is not appropriate for a client with a markedly distorted cervical anatomy.
PELVIC INFLAMMATORY DISEASE (PID)				
a) Past PID (assuming no current risk factors for STIs)				
i) with subsequent pregnancy	1	1	1	
ii) without subsequent pregnancy	1	1	1	
b) PID – current	1	1	1	
STIS				
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	
b) Other STIs (excluding HIV and hepatitis)	1	1	1	
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	
d) Increased risk of STIs	1	1	1	
HIV/AIDS				
HIGH RISK OF HIV*	1	4	4	**Evidence:** Repeated and high-dose use of the spermicide nonoxynol-9 was associated with increased risk of genital lesions, which may increase the risk of acquiring HIV *(1)*.
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)*	1	3	3	

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SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)*	1	3	3	
OTHER INFECTIONS				
SCHISTOSOMIASIS				
a) Uncomplicated	1	1	1	
b) Fibrosis of the liver	1	1	1	
TUBERCULOSIS				
a) Non-pelvic	1	1	1	
a) Pelvic	1	1	1	
MALARIA	1	1	1	
HISTORY OF TOXIC SHOCK SYNDROME*	1	1	3	
URINARY TRACT INFECTION*	1	1	2	
ENDOCRINE CONDITIONS				
DIABETES				
a) History of gestational disease	1	1	1	
b) Non-vascular disease				
i) non-insulin-dependent	1	1	1	
ii) insulin-dependent	1	1	1	
c) Nephropathy/retinopathy/ neuropathy	1	1	1	
d) Other vascular disease or diabetes of > 20 years' duration	1	1	1	
THYROID DISORDERS				
a) Simple goitre	1	1	1	
b) Hyperthyroid	1	1	1	
c) Hypothyroid	1	1	1	

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GASTROINTESTINAL CONDITIONS				
GALL BLADDER DISEASE				
a) Symptomatic				
i) treated by cholecystectomy	1	1	1	
ii) medically treated	1	1	1	
iii) current	1	1	1	
b) Asymptomatic	1	1	1	
HISTORY OF CHOLESTASIS				
a) Pregnancy-related	1	1	1	
b) Past-COC-related	1	1	1	
VIRAL HEPATITIS				
a) Acute or flare	1	1	1	
b) Carrier	1	1	1	
c) Chronic	1	1	1	
CIRRHOSIS				
a) Mild (compensated)	1	1	1	
b) Severe (decompensated)	1	1	1	
LIVER TUMOURS				
a) Benign				
i) focal nodular hyperplasia	1	1	1	
ii) hepatocellular adenoma	1	1	1	
b) Malignant (hepatoma)	1	1	1	
ANAEMIAS				
THALASSAEMIA	1	1	1	
SICKLE CELL DISEASE	1	1	1	
IRON-DEFICIENCY ANAEMIA	1	1	1	

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DRUG INTERACTIONS				
ANTIRETROVIRAL THERAPY (ART)				
a) Nucleoside reverse transcriptase inhibitors (NRTIs)				**Clarification**: There is no known drug interaction between ART and barrier method use. However, HIV clinical disease WHO stages 1 through 4 as conditions are classified as Category 3 for spermicides and diaphragms (see HIV conditions above).
Abacavir (ABC)	1	3	3	
Tenofovir (TDF)	1	3	3	
Zidovudine (AZT)	1	3	3	
Lamivudine (3TC)	1	3	3	
Didanosine (DDI)	1	3	3	
Emtricitabine (FTC)	1	3	3	
Stavudine (D4T)	1	3	3	
b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)				
Efavirenz (EFV)	1	3	3	
Etravirine (ETR)	1	3	3	
Nevirapine (NVP)	1	3	3	
Rilpivirine (RPV)	1	3	3	
c) Protease inhibitors (PIs)				
Ritonavir-boosted atazanavir (ATV/r)	1	3	3	
Ritonavir-boosted lopinavir (LPV/r)	1	3	3	
Ritonavir-boosted darunavir (DRV/r)	1	3	3	
Ritonavir (RTV)	1	3	3	

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d) Integrase inhibitors Raltegravir (RAL)	1	3	3	
ANTICONVULSANT THERAPY a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	1	1	1	
b) Lamotrigine	1	1	1	
ANTIMICROBIAL THERAPY a) Broad-spectrum antibiotics	1	1	1	
b) Antifungals	1	1	1	
c) Antiparasitics	1	1	1	
d) Rifampicin or rifabutin therapy	1	1	1	
ALLERGY TO LATEX	3	1	3	**Clarification**: This does not apply to plastic condoms/diaphragm.

ß-hCG: beta-human chorionic gonadotropin; BMI: body mass index; COC: combined oral contraceptive; PID: pelvic inflammatory disease; STI: sexually transmitted infections.

ADDITIONAL COMMENTS

Obesity

Severe obesity may make diaphragm and cap placement difficult.

Valvular heart disease

Risk of urinary tract infection with the diaphragm may increase in a client with subacute bacterial endocarditis.

Cervical cancer (awaiting treatment)

Repeated and high-dose use of nonoxynol-9 can cause vaginal and cervical irritation or abrasions.

High risk of HIV

Category 4 for diaphragm use is assigned due to concerns about the spermicide, not the diaphragm.

Asymptomatic or mild HIV clinical disease (WHO stage 1 or 2)

Use of spermicides and/or diaphragms (with spermicide) can disrupt the cervical mucosa, which may lead to increased viral shedding and HIV transmission to uninfected sexual partners.

Severe or advanced hiv clinical disease (WHO stage 3 or 4)

Use of spermicides and/or diaphragms (with spermicide) can disrupt the cervical mucosa, which may lead to increased viral shedding and HIV transmission to uninfected sexual partners.

History of toxic shock syndrome

Toxic shock syndrome has been reported in association with diaphragm use.

Urinary tract infection

There is a potential increased risk of urinary tract infection with diaphragms and spermicides.

References

1. Wilkinson D, Ramjee G, Tholandi M, Rutherford G. Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men. Cochrane Database Syst Rev. 2002;4(CD003936).

2.7.8 Fertility awareness-based (FAB) methods

Fertility awareness-based (FAB) methods of family planning involve identification of the fertile days of the menstrual cycle, whether by observing fertility signs such as cervical secretions and basal body temperature (i.e. symptoms-based methods) or by monitoring cycle days (calendar-based methods).

Symptom-based methods

Symptoms-based methods include the cervical mucus method (also called the ovulation method) and the TwoDay Method, which are both based on the evaluation of cervical mucus, and the sympto-thermal method, which is a double-check method based on evaluation of cervical mucus to determine the first fertile day and evaluation of cervical mucus and temperature to determine the last fertile day.

Calendar-based methods

Calendar-based methods include the Calendar Rhythm Method and the Standard Days Method, which avoids intercourse on cycle days 8–19.

FAB methods can be used in combination with abstinence or barrier methods during the fertile time. If barrier methods are used, refer to section 2.7.7 on barrier methods (BARR), see pp. 200–211.

There are no medical conditions that become worse because of use of FAB methods. In general, these methods can be provided without concern for health effects to people who choose them; therefore, the 1–4 recommendation categories do not apply to these methods. However, there are a number of conditions that make their use more complex. The existence of these conditions suggests that (i) use of FAB methods should be delayed until the condition is corrected or resolved, or (ii) use of FAB methods will require special counselling for the client, and a more highly trained provider is generally necessary to ensure correct use. The need for caution or delay in the use of these FAB methods is noted in the categories assigned in the table, per condition.

FERTILITY AWARENESS-BASED (FAB) METHODS			
Fertility awareness-based (FAB) methods do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.			
CONDITION	CATEGORY[a] A = accept, C = caution, D = delay		CLARIFICATIONS/EVIDENCE
	SYM	CAL	
* additional comments after this table	SYM = symptoms-based method CAL = calendar-based method		
Women with conditions that make pregnancy an unacceptable risk should be advised that FAB methods for pregnancy prevention may not be appropriate for them because of their relatively higher typical-use failure rates.			
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY			
PREGNANCY	NA	NA	**NA = not applicable** **Clarification**: FAB methods are not relevant during pregnancy.
LIFE STAGE			**Clarification**: Menstrual irregularities are common in post-menarche and perimenopause and may complicate the use of FAB methods.
a) Post-menarche	C	C	
b) Perimenopause	C	C	

FERTILITY AWARENESS-BASED (FAB) METHODS

Fertility awareness-based (FAB) methods do not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION	CATEGORY[a] A = accept, C = caution, D = delay		CLARIFICATIONS/EVIDENCE
	SYM	CAL	
* additional comments after this table	SYM = symptoms-based method CAL = calendar-based method		
BREASTFEEDING*			
a) < 6 weeks postpartum	D	D	
b) ≥ 6 weeks	C	D	
c) After menses begins	C	C	
POSTPARTUM* (in non-breastfeeding women)			
a) < 4 weeks	D	D	
b) ≥ 4 weeks	A	D	
POST-ABORTION*	C	D	
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS			
IRREGULAR VAGINAL BLEEDING*	D	D	
VAGINAL DISCHARGE*	D	A	
OTHER			
USE OF DRUGS THAT AFFECT CYCLE REGULARITY, HORMONES AND/OR FERTILITY SIGNS*	C/D	C/D	
DISEASES THAT ELEVATE BODY TEMPERATURE*			
a) Chronic diseases	C	A	
b) Acute diseases	D	A	

a Further explanation of A, C and D categories:

A = accept: There is no medical reason to deny the particular FAB method to a woman in this circumstance.

C = caution: The method is normally provided in a routine setting, but with extra preparation and precautions. For FAB methods, this usually means that special counselling may be needed to ensure correct use of the method by a woman in this circumstance.

D = delay: Use of this method should be delayed until the condition is evaluated or corrected. Alternative temporary methods of contraception should be offered.

ADDITIONAL COMMENTS

Breastfeeding

Fertility awareness-based (FAB) methods during breastfeeding may be less effective than when not breastfeeding.

< 6 weeks postpartum: Women who are exclusively breastfeeding and are amenorrhoeic are unlikely to have sufficient ovarian function to produce detectable fertility signs and hormonal changes during the first six weeks postpartum. However, the likelihood of resumption of fertility increases with time postpartum and with substitution of breast-milk by other foods.

After menses begin: When the woman notices fertility signs (particularly cervical secretions), she can use a symptoms-based method. First postpartum menstrual cycles in breastfeeding women vary significantly in length. It takes several cycles for the return to regularity. When she has had at least three postpartum menses and her cycles are regular again, she can use the Calendar Rhythm Method. When she has had at least four postpartum menses and her most recent cycle was 26–32 days long, she can use the Standard Days Method. Prior to that time, a barrier method should be offered if the woman plans to use a FAB method later.

Postpartum

< 4 weeks: Non-breastfeeding woman are not likely to have sufficient ovarian function to either require a FAB method or have detectable fertility signs or hormonal changes prior to four weeks postpartum. Although the risk of pregnancy is low, a method that is appropriate for the postpartum period should be offered.

≥ 4 weeks: Non-breastfeeding women are likely to have sufficient ovarian function to produce detectable fertility signs and/or hormonal changes at this time; the likelihood increases rapidly with time postpartum. A woman can use calendar-based methods as soon as she has completed at least three postpartum menses and her cycles are regular again. A woman can use the Standard Days Method when she has had at least four postpartum menses and her most recent cycle was 26–32 days long. Methods appropriate for the postpartum period should be offered prior to that time.

Post-abortion

Post-abortion women are likely to have sufficient ovarian function to produce detectable fertility signs and/or hormonal changes; the likelihood increases with time post-abortion. A woman can start using calendar-based methods after she has had at least one post-abortion menses; if most of her cycles prior to this pregnancy were 26–32 days long, she can use the Standard Days Method. Methods appropriate for the post-abortion period should be offered prior to that time.

2.7.9 Lactational amenorrhoea method (LAM)

The lactational amenorrhoea method (LAM) does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

Women with conditions that make pregnancy an unacceptable risk should be advised that the LAM may not be appropriate for them because of its relatively higher typical-use failure rates.

The Bellagio Consensus provided the scientific basis for defining the conditions under which breastfeeding can be used safely and effectively for birth-spacing purposes, and programmatic guidelines were developed for the use of the LAM in family planning. These guidelines include the following three criteria, all of which must be met to ensure adequate protection from an unplanned pregnancy:

1. amenorrhoea
2. fully or nearly fully breastfeeding
3. less than six months postpartum.

The main indications for breastfeeding remain the need to provide an ideal food for the infant and to protect it against disease. There are no medical conditions in which the use of the LAM is restricted and there is no documented evidence of its negative impact on maternal health. However, certain conditions or obstacles which affect breastfeeding may also affect the duration of amenorrhoea, making this a less useful choice for family planning purposes. These include:

HIV

Breastfeeding should be promoted, protected and supported in all populations, for all women who are HIV-negative or of unknown HIV status. A woman living with HIV, however, can transmit the virus to her child through breastfeeding. Yet breastfeeding, and especially early and exclusive breastfeeding, is one of the most critical factors for improving child survival. Breastfeeding also confers many other benefits in addition to reducing the risk of death.

There is now strong evidence that giving antiretroviral medications (ARVs) to either the HIV-positive mother or the HIV-exposed infant or both can significantly reduce the risk of transmitting HIV through breastfeeding.[15] This transforms the landscape in which decisions should be made by national health authorities and individual mothers. In the presence of ARVs – either lifelong antiretroviral therapy (ART) to the mother or other ARV interventions to the mother or infant – the infant can receive all the benefits of breastfeeding with little risk of acquiring HIV. In some well-resourced countries with low infant and child mortality rates, avoidance of all breastfeeding will still be appropriate.

Mothers living with HIV should receive the appropriate ARV interventions and should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and should continue breastfeeding their infants for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast-milk can be provided. When mothers decide to stop breastfeeding, they should stop gradually within one month and infants should be provided with safe and adequate replacement feeds to enable normal growth and development.

If the infant is HIV-negative or of unknown HIV status:

A mother known to be living with HIV should only give commercial infant formula milk as a replacement feed to this infant when all of the following specific conditions are met:

1. safe water and sanitation are assured at the household level and in the community, and
2. the mother or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant, and
3. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition, and
4. the mother or caregiver can, in the first six months, exclusively give infant formula milk, and
5. the family is supportive of this practice, and
6. the mother or caregiver can access health care that offers comprehensive child health services.

15 Further information: http://www.who.int/hiv/topics/mtct

If the infant is known to be HIV-positive:

The mother is strongly encouraged to exclusively breastfeed for the first six months of the infant's life and to continue breastfeeding as per the recommendations for the general population, that is up to two years or beyond.

Women who are living with HIV should receive skilled counselling to help them. They should also have access to follow-up care and support, including family planning and nutritional support.

Medication used during breastfeeding

In order to protect infant health, breastfeeding is not recommended for women using such drugs as: anti-metabolites, bromocriptine, certain anticoagulants, corticosteroids (high doses), ciclosporin, ergotamine, lithium, mood-altering drugs, radioactive drugs and reserpine.

Conditions affecting the newborn

Congenital deformities of the mouth, jaw or palate; newborns who are small-for-date or premature and needing intensive neonatal care; and certain metabolic disorders of the infant can all make breastfeeding difficult.

2.7.10 Coitus interruptus (CI)

Coitus interruptus (CI) does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

Women with conditions that make pregnancy an unacceptable risk should be advised that CI may not be appropriate for them because of its relatively higher typical-use failure rates.

Coitus interruptus (CI), also known as withdrawal, is a traditional family planning method in which the man completely removes his penis from the vagina, and away from the external genitalia of the female partner, before he ejaculates. CI prevents sperm from entering the woman's vagina, thereby preventing contact between spermatozoa and the ovum.

This method may be appropriate for couples:

- who are highly motivated and able to use this method effectively;
- with religious or philosophical reasons for not using other methods of contraception;
- who need contraception immediately and have entered into a sexual act without alternative methods available;
- who need a temporary method while awaiting the start of another method;
- who have intercourse infrequently.

Some benefits of CI are that the method, if used correctly, does not affect breastfeeding and is always available for primary use or use as a back-up method. In addition, CI involves no economic cost or use of chemicals. There are no health risks associated directly with CI.

Men and women who are at high risk of STI/HIV infection should use a condom with each act of intercourse.

CI is unforgiving of incorrect use, and its effectiveness depends on the willingness and ability of the couple to use withdrawal with every act of intercourse.

2.7.11 Surgical sterilization procedures (STER)

Given that sterilization is a surgical procedure that is intended to be permanent, special care must be taken to assure that every client makes a voluntary, informed choice of the method. Particular attention must be given in the case of young people, nulliparous women, men who have not yet been fathers and clients with mental health problems, including depressive conditions. All clients should be carefully counselled about the intended permanence of sterilization and the availability of alternative, long-term, highly effective methods. This is of extra concern for young people. The national laws and existing norms for the delivery of sterilization procedures must be considered in the decision process.

Transcervical methods of female sterilization are not addressed in these recommendations.

There is no medical condition that would absolutely restrict a person's eligibility for sterilization, although some conditions and circumstances will require that certain precautions are taken, including those where the recommendation is assigned as Category C (caution), D (delay) or S (special). For some of these conditions and circumstances, the theoretical or proven risks may outweigh the advantages of undergoing sterilization, particularly female sterilization. Where the risks of sterilization outweigh the benefits, long-term, highly effective contraceptive methods are a preferable alternative. Decisions in this regard will have to be made on an individual basis, considering the risks and benefits of sterilization versus the risks of pregnancy, and the availability and acceptability of highly effective, alternative methods.

Sterilization procedures should only be performed by well-trained providers in appropriate clinical settings using proper equipment and supplies. Appropriate service-delivery guidelines, including infection-prevention protocols, should be followed to maximize client safety.

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY		
PREGNANCY	D	
YOUNG AGE	C	**Clarification**: Young women, like all women, should be counselled about the permanency of sterilization and the availability of alternative, long-term, highly effective methods. **Evidence**: Studies show that up to 20% of women sterilized at a young age later regret this decision, and that young age is one of the strongest predictors of regret (including request for referral information and obtaining reversal) that can be identified before sterilization *(1–19)*.
PARITY* a) Nulliparous b) Parous	 A A	
BREASTFEEDING	A	

FEMALE SURGICAL STERILIZATION

Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY[a] A = accept, C = caution, D = delay, S = special	CLARIFICATIONS/EVIDENCE
POSTPARTUM*		
a) < 7 days	A	
7 to < 42 days	D	
≥ 42 days	A	
b) Pre-eclampsia/eclampsia		
i) mild pre-eclampsia	A	
ii) severe pre-eclampsia/ eclampsia	D	
c) Prolonged rupture of membranes, 24 hours or more	D	
d) Puerperal sepsis, intrapartum or puerperal fever	D	
e) Severe antepartum or postpartum haemorrhage	D	
f) Severe trauma to the genital tract (cervical or vaginal tear at time of delivery)	D	
g) Uterine rupture or perforation	S	**Clarification**: If exploratory surgery or laparoscopy is conducted and the patient is stable, repair of the problem and tubal sterilization may be performed concurrently if no additional risk is involved.
POST-ABORTION*		
a) Uncomplicated	A	
b) Post-abortal sepsis or fever	D	
c) Severe post-abortal haemorrhage	D	
d) Severe trauma to the genital tract (cervical or vaginal tear at time of abortion)	D	
e) Uterine perforation	S	**Clarification**: If exploratory surgery or laparoscopy is conducted and the patient is stable, repair of the problem and tubal sterilization may be performed concurrently if no additional risk is involved.
f) Acute haematometra	D	
PAST ECTOPIC PREGNANCY	A	

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
SMOKING		
a) Age < 35 years	A	
b) Age ≥ 35 years		
i) < 15 cigarettes/day	A	
ii) ≥ 15 cigarettes/day	A	
OBESITY		**Clarification**: The procedure may be more difficult. There is an increased risk of wound infection and disruption. Obese women may have limited respiratory function and may be more likely to require general anaesthesia. **Evidence**: Obese women were more likely to have complications when undergoing sterilization *(20–23)*.
a) ≥ 30 kg/m^2 BMI	C	
b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	C	
CARDIOVASCULAR DISEASE		
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE* (such as older age, smoking, diabetes, hypertension and known dyslipidaemias)	S	
HYPERTENSION For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, the risk of cardiovascular disease may increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive.		
a) Hypertension: adequately controlled	C	
b) Elevated blood pressure levels (properly taken measurements)		**Clarification**: Elevated blood pressure should be controlled before surgery. There are increased anaesthesia-related risks and an increased risk of cardiac arrhythmia with uncontrolled hypertension. Careful monitoring of blood pressure intra-operatively is particularly necessary in this situation.
i) systolic 140–159 or diastolic 90–99 mm Hg	C	
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	S	
c) Vascular disease	S	
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	A	

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
DEEP VENOUS THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)		**Clarification**: To reduce the risk of DVT/PE, early ambulation is recommended.
a) History of DVT/PE	A	
b) Acute DVT/PE	D	
c) DVT/PE and established on anticoagulant therapy	S	
d) Family history (first-degree relatives)	A	
e) Major surgery		
i) with prolonged immobilization	D	
ii) without prolonged immobilization	A	
f) Minor surgery without immobilization	A	
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	A	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.
SUPERFICIAL VENOUS DISORDERS		
a) Varicose veins	A	
b) Superficial venous thrombosis	A	
CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE*		
a) Current ischaemic heart disease	D	
b) History of ischaemic heart disease	C	
STROKE (history of cerebrovascular accident)	C	
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS	A	**Clarification**: Routine screening is not appropriate because of the rarity of the condition and the high cost of screening.
VALVULAR HEART DISEASE		
a) Uncomplicated	C	**Clarification**: The woman requires prophylactic antibiotics.
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	S	**Clarification**: The woman is at high risk for complications associated with anaesthesia and surgery. If the woman has atrial fibrillation that has not been successfully managed or current subacute bacterial endocarditis, the procedure should be delayed.

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
RHEUMATIC DISEASES		
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) People with SLE are at increased risk of ischaemic heart disease, stroke and venous thromboembolism. Categories assigned to such conditions in the MEC should be the same for women with SLE who present with these conditions. For all categories of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Available evidence indicates that many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives *(24–42)*.		
a) Positive (or unknown) antiphospholipid antibodies	S	
b) Severe thrombocytopenia	S	
c) Immunosuppressive treatment	S	
d) None of the above	C	
NEUROLOGIC CONDITIONS		
HEADACHES		
a) Non-migrainous (mild or severe)	A	
b) Migraine		
i) without aura		
age < 35 years	A	
age ≥ 35 years	A	
ii) with aura, at any age	A	
EPILEPSY	C	
DEPRESSIVE DISORDERS		
DEPRESSIVE DISORDERS	C	
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS		
VAGINAL BLEEDING PATTERNS		
a) Irregular pattern without heavy bleeding	A	
b) Heavy or prolonged bleeding (includes regular and irregular patterns)	A	
UNEXPLAINED VAGINAL BLEEDING (suspicious for serious condition)		
a) Before evaluation	D	**Clarification**: The condition must be evaluated before the procedure is performed.

FEMALE SURGICAL STERILIZATION

Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY[a] A = accept, C = caution, D = delay, S = special	CLARIFICATIONS/EVIDENCE
ENDOMETRIOSIS	S	
BENIGN OVARIAN TUMOURS (including cysts)	A	
SEVERE DYSMENORRHOEA	A	
GESTATIONAL TROPHOBLASTIC DISEASE		
a) Decreasing or undetectable β-hCG levels	A	
b) Persistently elevated β-hCG levels or malignant disease	D	
CERVICAL ECTROPION	A	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)	A	
CERVICAL CANCER* (awaiting treatment)	D	
BREAST DISEASE		
a) Undiagnosed mass	A	
b) Benign breast disease	A	
c) Family history of cancer	A	
d) Breast cancer		
i) current	C	
ii) past and no evidence of current disease for 5 years	A	
ENDOMETRIAL CANCER*	D	
OVARIAN CANCER*	D	
UTERINE FIBROIDS*		
a) Without distortion of the uterine cavity	C	
b) With distortion of the uterine cavity	C	

FEMALE SURGICAL STERILIZATION

Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY[a] A = accept, C = caution, D = delay, S = special	CLARIFICATIONS/EVIDENCE
PELVIC INFLAMMATORY DISEASE (PID)*		
a) Past PID (assuming no current risk factors for STIs)		**Clarification**: A careful pelvic examination must be performed to rule out recurrent or persistent infection and to determine the mobility of the uterus.
i) with subsequent pregnancy	A	
ii) without subsequent pregnancy	C	
b) PID – current	D	
STIS*		
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	D	**Clarification**: If no symptoms persist following treatment, sterilization may be performed.
b) Other STIs (excluding HIV and hepatitis)	A	
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	A	
d) Increased risk of STIs	A	
HIV/AIDS		
HIGH RISK OF HIV	A	**Clarification**: No routine screening is needed. Appropriate infection prevention procedures, including universal precautions, must be carefully observed with all surgical procedures. The use of condoms is recommended following sterilization.
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	A	**Clarification**: No routine screening is needed. Appropriate infection prevention procedures, including universal precautions, must be carefully observed with all surgical procedures. The use of condoms is recommended following sterilization.
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	S	**Clarification**: The presence of an AIDS-related illness may require that the procedure be delayed.
OTHER INFECTIONS		
SCHISTOSOMIASIS		
a) Uncomplicated	A	
b) Fibrosis of the liver (if severe, see cirrhosis)	C	**Clarification**: Liver function may need to be evaluated.

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
TUBERCULOSIS		
a) Non-pelvic	A	
b) Pelvic	S	
MALARIA	A	
ENDOCRINE CONDITIONS		
DIABETES*		**Clarification:** If blood glucose is not well controlled, referral to a higher-level facility is recommended.
a) History of gestational disease	A	
b) Non-vascular disease		**Clarification:** There is a possible decrease in healing and an increased risk of wound infection. Use of prophylactic antibiotics is recommended.
i) non-insulin-dependent	C	
ii) insulin-dependent	C	
c) Nephropathy/retinopathy/ neuropathy	S	**Evidence**: Diabetic women were more likely to have complications when undergoing sterilization *(20)*.
d) Other vascular disease or diabetes of > 20 years' duration	S	
THYROID DISORDERS*		
a) Simple goitre	A	
b) Hyperthyroid	S	
c) Hypothyroid	C	
GASTROINTESTINAL CONDITIONS		
GALL BLADDER DISEASE		
a) Symptomatic		
i) treated by cholecystectomy	A	
ii) medically treated	A	
iii) current	D	
b) Asymptomatic	A	
HISTORY OF CHOLESTASIS		
a) Pregnancy related	A	
b) Past-COC related	A	

FEMALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY**[a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
VIRAL HEPATITIS*		**Clarification:** Appropriate infection-prevention procedures, including universal precautions, must be carefully observed with all surgical procedures.
a) Acute or flare	D	
b) Carrier	A	
c) Chronic	A	
CIRRHOSIS		**Clarification:** Liver function and clotting might be altered. Liver function should be evaluated.
a) Mild (compensated)	A	
b) Severe (decompensated)	S	
LIVER TUMOURS		**Clarification:** Liver function and clotting might be altered. Liver function should be evaluated.
a) Benign		
i) focal nodular hyperplasia	A	
ii) hepatocellular adenoma	C	
b) Malignant (hepatoma)	C	
ANAEMIAS		
THALASSAEMIA	C	
SICKLE CELL DISEASE*	C	
IRON-DEFICIENCY ANAEMIA		**Clarification**: The underlying disease should be identified. Both preoperative haemoglobin (Hb) level and operative blood loss are important factors in women with anaemia. If peripheral perfusion is inadequate, this may decrease wound healing.
a) Hb < 7 g/dl	D	
a) Hb ≥ 7 to < 10 g/dl	C	
OTHER CONDITIONS RELEVANT ONLY FOR FEMALE SURGICAL STERILIZATION		
LOCAL INFECTION	D	**Clarification**: There is an increased risk of postoperative infection.
COAGULATION DISORDERS*	S	
RESPIRATORY DISEASES		**Clarification**: The procedure should be delayed until the condition is corrected. There are increases in anaesthesia-related and other perioperative risks.
a) Acute (bronchitis, pneumonia)	D	
b) Chronic		
i) asthma	S	
ii) bronchitis	S	
iii) emphysema	S	
iv) lung infection	S	

FEMALE SURGICAL STERILIZATION

Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY[a] A = accept, C = caution, D = delay, S = special	CLARIFICATIONS/EVIDENCE
SYSTEMIC INFECTION OR GASTROENTERITIS*	D	
FIXED UTERUS DUE TO PREVIOUS SURGERY OR INFECTION*	S	
ABDOMINAL WALL OR UMBILICAL HERNIA	S	**Clarification**: Hernia repair and tubal sterilization should be performed concurrently if possible.
DIAPHRAGMATIC HERNIA*	C	
KIDNEY DISEASE*	C	
SEVERE NUTRITIONAL DEFICIENCIES*	C	
PREVIOUS ABDOMINAL OR PELVIC SURGERY	C	**Evidence**: Women with previous abdominal or pelvic surgery were more likely to have complications when undergoing sterilization *(20, 22, 43–45)*.
STERILIZATION CONCURRENT WITH ABDOMINAL SURGERY		
a) Elective	C	
b) Emergency (without previous counselling)	D	
c) Infectious condition	D	
STERILIZATION CONCURRENT WITH CAESAREAN SECTION*	A	

[a] Further explanation of A, C, D and S categories:

A = **accept**: There is no medical reason to deny sterilization to a person with this condition.

C = **caution**: The procedure is normally conducted in a routine setting, but with extra preparation and precautions.

D = **delay**: The procedure is delayed until the condition is evaluated and/or corrected. Alternative temporary methods of contraception should be provided.

S = **special**: The procedure should be undertaken in a setting with an experienced surgeon and staff, equipment needed to provide general anaesthesia, and other back-up medical support. For these conditions, the capacity to decide on the most appropriate procedure and anaesthesia regimen is also needed. Alternative temporary methods of contraception should be provided if referral is required or there is otherwise any delay.

MALE SURGICAL STERILIZATION		
Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.		
CONDITION * additional comments after this table	**CATEGORY** [a] A = accept, C = caution, D = delay, S = special	**CLARIFICATIONS/EVIDENCE**
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY		
YOUNG AGE	C	**Clarification**: Young men, like all men, should be counselled about the permanency of sterilization and the availability of alternative, long-term, highly effective methods. **Evidence**: Men who underwent vasectomy at young ages were more likely to have the procedure reversed than those who underwent vasectomy at older ages *(2)*.
DEPRESSIVE DISORDERS		
DEPRESSIVE DISORDERS	C	
HIV/AIDS		
HIGH RISK OF HIV	A	**Clarification**: No routine screening is needed. Appropriate infection prevention procedures, including universal precautions, must be carefully observed with all surgical procedures. The use of condoms is recommended following sterilization.
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	A	**Clarification**: No routine screening is needed. Appropriate infection prevention procedures, including universal precautions, must be carefully observed with all surgical procedures. The use of condoms is recommended following sterilization.
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	S	**Clarification**: The presence of severe or advanced HIV clinical disease may require that the procedure be delayed.
ENDOCRINE CONDITIONS		
DIABETES*	C	**Clarification:** If blood glucose is not well controlled, referral to a higher-level facility is recommended.
ANAEMIAS		
SICKLE CELL DISEASE*	A	
OTHER CONDITIONS RELEVANT ONLY FOR MALE SURGICAL STERILIZATION		
LOCAL INFECTION*		
a) Scrotal skin infection	D	
b) Active STI	D	
c) Balanitis	D	
d) Epididymitis or orchitis	D	

MALE SURGICAL STERILIZATION

Sterilization does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended. When used correctly and consistently, condoms offer one of the most effective methods of protection against STIs, including HIV. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.

CONDITION * additional comments after this table	CATEGORY [a] A = accept, C = caution, D = delay, S = special	CLARIFICATIONS/EVIDENCE
COAGULATION DISORDERS*	S	
PREVIOUS SCROTAL INJURY	C	
SYSTEMIC INFECTION OR GASTROENTERITIS*	D	
LARGE VARICOCELE*	C	
LARGE HYDROCELE*	C	
FILIARIASIS; ELEPHANTIASIS*	D	
INTRASCROTAL MASS*	D	
CRYPTORCHIDISM	S	
INGUINAL HERNIA*	S	

[a] Further explanation of A, C, D and S categories:

A = **accept**: There is no medical reason to deny sterilization to a person with this condition.

C = **caution**: The procedure is normally conducted in a routine setting, but with extra preparation and precautions.

D = **delay**: The procedure is delayed until the condition is evaluated and/or corrected. Alternative temporary methods of contraception should be provided.

S = **special**: The procedure should be undertaken in a setting with an experienced surgeon and staff, equipment needed to provide general anaesthesia, and other back-up medical support. For these conditions, the capacity to decide on the most appropriate procedure and anaesthesia regimen is also needed. Alternative temporary methods of contraception should be provided if referral is required or there is otherwise any delay.

ADDITIONAL COMMENTS FOR FEMALE STERILIZATION

Parity

Nulliparous women: Like all women, they should be counselled about the permanency of sterilization and the availability of alternative, long-term, highly effective methods.

Postpartum

< 7 days postpartum: Sterilization can be safely performed immediately postpartum.

7 to < 42 days: There is an increased risk of complications when the uterus has not fully involuted.

Pre-eclampsia/eclampsia: There are increased anaesthesia-related risks.

Prolonged rupture of membranes, 24 hours or more: There is an increased risk of postoperative infection.

Puerperal sepsis, intrapartum or puerperal fever: There is an increased risk of postoperative infection.

Severe antepartum or postpartum haemorrhage: The woman may be anaemic and unable to tolerate further blood loss.

Severe trauma to the genital tract (cervical or vaginal tear at the time of delivery): There may have been significant blood loss and anaemia.

Uterine rupture or perforation: There may have been significant blood loss or damage to abdominal contents.

Post-abortion

P*ost-abortal sepsis or fever*: There is an increased risk of postoperative infection.

Severe post-abortal haemorrhage: The woman may be anaemic and unable to tolerate further blood loss.

Severe trauma to the genital tract (cervical or vaginal tear at the time of abortion): The woman may be anaemic and unable to tolerate further blood loss. The procedure may be more painful.

U*terine perforation*: There may have been significant blood loss or damage to abdominal contents.

Acute haematometra: The woman may be anaemic and unable to tolerate further blood loss.

OTHER CONSIDERATIONS

Multiple risk factors for arterial cardiovascular disease

Concurrent presence of multiple risk factors: There may be a high risk of complications associated with anaesthesia and surgery.

Current and history of ischaemic heart disease

There is a high risk of complications associated with anaesthesia and surgery.

Cervical cancer (awaiting treatment), endometrial cancer, ovarian cancer

In general, the treatment renders a woman sterile.

Uterine fibroids

Depending on the size and location of the fibroids, it might be difficult to localize the tubes and mobilize the uterus.

Pelvic inflammatory disease (pid)

PID can lead to an increased risk of post-sterilization infection or adhesions.

STIs

There is an increased risk of postoperative infection.

Diabetes

There is a risk of hypoglycaemia or ketoacidosis when the procedure is performed, particularly if blood sugar is not well controlled before the procedure.

Thyroid disorders

There is a higher risk of complications associated with anaesthesia and surgery.

Viral hepatitis

There is a high risk for complications associated with anaesthesia and surgery.

Sickle cell disease

There is an increased risk of pulmonary, cardiac or neurologic complications and possible increased risk of wound infection.

Coagulation disorders

There is a higher risk of haematologic complications of surgery.

Systemic infection or gastroenteritis

There are increased risks of postoperative infection, complications from dehydration, and anaesthesia-related complications.

Fixed uterus due to previous surgery or infection

Decreased mobility of the uterus, fallopian tubes and bowel may make laparoscopy and minilaparotomy difficult and increase the risk of complications.

Diaphragmatic hernia

For laparoscopy, a woman may experience acute cardiorespiratory complications induced by pneumoperitoneum or the Trendelenburg position.

Kidney disease

Blood clotting may be impaired. There may be an increased risk of infection and hypovolemic shock. Condition may cause baseline anaemia, electrolyte disturbances, and abnormalities in drug metabolism and excretion.

Severe nutritional deficiencies

There may be an increased risk of wound infection and impaired healing.

Sterilization concurrent with caesarean section

There is no increased risk of complications in a surgically stable client.

ADDITIONAL COMMENTS FOR MALE STERILIZATION

Diabetes

Individuals with diabetes are more likely to get postoperative wound infections. If signs of infection appear, treatment with antibiotics needs to be given.

Local infection

There is an increased risk of postoperative infection.

Coagulation disorders

Bleeding disorders lead to an increased risk of postoperative haematoma formation, which, in turn, leads to an increased risk of infection.

Systemic infection or gastroenteritis

There is an increased risk of postoperative infection.

Large varicocele

The vas may be difficult or impossible to locate; a single procedure to repair varicocele and perform a vasectomy decreases the risk of complications.

Large hydrocele

The vas may be difficult or impossible to locate; a single procedure to repair hydrocele and perform a vasectomy decreases the risk of complications.

Filariasis; elephantiasis

If elephantiasis involves the scrotum, it may be impossible to palpate the spermatic cord and testis.

Intrascrotal mass

This may indicate underlying disease.

Inguinal hernia

Vasectomy can be performed concurrent with hernia repair.

Sickle cell disease

There is an increased risk of pulmonary, cardiac or neurologic complications and possible increased risk of wound infection.

References

1. Wilcox LS, Chu SY, Eaker ED, Zeger SL, Peterson HB. Risk factors for regret after tubal sterilization: 5 years of follow-up in a prospective study. Fertil Steril. 1991;55:927–33.
2. Trussell J, Guilbert E, Hedley A. Sterilization failure, sterilization reversal, and pregnancy after sterilization reversal in Quebec. Obstet Gynecol. 2003;101:677–84.
3. Thranov I, Kjersgaard AG, Rasmussen OV, Hertz J. Regret among 547 Danish sterilized women. Scand J Soc Med. 1988;16:41–8.
4. Schmidt JE, Hillis SD, Marchbanks PA, Jeng G, Peterson HB. Requesting information about and obtaining reversal after tubal sterilization: findings from the U.S. Collaborative Review of Sterilization. Fertil Steril. 2000;74:892–8.
5. Ramsay IN, Russell SA. Who requests reversal of female sterilisation? A retrospective study from a Scottish unit. Scot Med J. 1991;36:44–6.
6. Platz-Christensen JJ, Tronstad SE, Johansson O, Carlsson SA. Evaluation of regret after tubal sterilization. Int J Gynaecol Obstet. 1992;38:223–6.
7. Marcil-Gratton N. Sterilization regret among women in metropolitan Montreal. Fam Plann Perspect. 1988;20:222–7.
8. Loaiza E. Sterilization regret in the Dominican Republic: looking for quality-of-care issues. Stud Fam Plann. 1995;26:39–48.
9. Leader A, Galan N, George R, Taylor PJ. A comparison of definable traits in women requesting reversal of sterilization and women satisfied with sterilization. Am J Obstet Gynecol. 1983;145:198–202.
10. Kariminia A, Saunders DM, Chamberlain M. Risk factors for strong regret and subsequent IVF request after having tubal ligation. Aust N Z J Obstet Gynaecol. 2002;42:526–9.
11. Jamieson DJ, Kaufman SC, Costello C, Hillis SD, Marchbanks PA, Peterson HB, et al. A comparison of women's regret after vasectomy versus tubal sterilization. Obstet Gynecol. 2002;99:1073–9.
12. Hillis SD, Marchbanks PA, Tylor LR, Peterson HB. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol. 1999;93:889–95.
13. Henshaw SK, Singh S. Sterilization regret among U.S. couples. Fam Plann Perspect. 1986;18:238–40.
14. Hardy E, Bahamondes L, Osis MJ, Costa RG, Faúndes A. Risk factors for tubal sterilization regret, detectable before surgery. Contraception. 1996;54:159–62.
15. Grubb GS, Peterson HB, Layde PM, Rubin GL. Regret after decision to have a tubal sterilization. Fertil Steril. 1985;44:248–53.
16. Clarkson SE, Gillett WR. Psychological aspects of female sterilisation – assessment of subsequent regret. N Z Med J. 1985;98:748–50.
17. Boring CC, Rochat RW, Becerra J. Sterilization regret among Puerto Rican women. Fertil Steril. 1988;44:973–81.
18. Allyn DP, Leton DA, Westcott NA, Hale RW. Presterilization counseling and women's regret about having been sterilized. J Reprod Med. 1986;31:1027–32.
19. Abraham S, Jansen R, Fraser IS, Kwok CH. The characteristics, perceptions and personalities of women seeking a reversal of their tubal sterilization. Med J Aust. 1986;145:4–7.
20. Jamieson DJ, Hillis SD, Duerr A, Marchbanks PA, Costello C, Peterson HB. Complications of interval laparoscopic tubal sterilization: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol. 2000;96:997–1002.
21. Chi I, Mumford SD, Laufe LE. Technical failures in tubal ring sterilization: incidence, perceived reasons, outcome, and risk factors. Am J Obstet Gynecol. 1980;138:307–12.
22. Chi I, Kennedy KI. Early readmission following elective laparoscopic sterilization: a brief analysis of a rare event. Am J Obstet Gynecol. 1984;148:322–7.
23. White MK, Ory HW, Goldenberg LA. A case-control study of uterine perforations documented at laparoscopy. Am J Obstet Gynecol. 1977;129:623–5.
24. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. Am J Med. 1976;60:221–5.
25. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. Journal of Rheumatology. 2002;29:2531–6.
26. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. American Journal of Obstetrics & Gynecology. 2005;193:1361–3.
27. Sarabi ZS, Chang E, Bobba R, al e. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis and Rheumatism. 2005;53:609–12.
28. Sanchez-Guerrero J, Uribe AG, Jimenez-Santana L, Mestanza-Peralta M, Lara-Reyes P, Seuc AH, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. New England Journal of Medicine. 2005;353:2539–49.

29. Petri M, Kim MY, Kalunian KC, et al. Combined oral contraceptives in women with systemic lupus erythematosus. New England Journal of Medicine. 2005;353:2550–8.

30. Petri M. Lupus in Baltimore: evidence-based 'clinical perarls' from the Hopkins Lupus Cohort. Lupus. 2005;14:970–3.

31. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care and Research. 1995;8:137–45.

32. Mintz G, Gutierrez G, Delezé M, Rodríguez E. Contraception with progestogens in systemic lupus erythematosus. Contraception. 1984;30:29–38.

33. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Annals of Rheumatic Diseases. 1992;51:56–60.

34. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephristis in systemic lupus erythematosus. Annals of Rheumatic Diseases. 1993;52:720–4.

35. Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, Jansen-McWilliams L, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. American Journal of Epidemiology. 1997;145:408–15.

36. Jungers P, Dougados M, Pelissier C, Kuttenn F, Tron F, Lesavre P, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis and Rheumatism. 1982;25:618–23.

37. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. British Journal of Rheumatology. 1993;32:227–30.

38. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scandinavian Journal of Rheumatology. 1991;20:427–33.

39. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, du Berger R, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis and Rheumatism. 2001;44:2331–7.

40. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. Journal of Rheumatology. 2002;29:1683–8.

41. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1386–9.

42. Bernatsky S, Clarke A, Ramsey-Goldman R, Joseph L, Boivin JF, Rajan R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford). 2004;43:1178–81.24.

43. Baggish MS, Lee WK, Miro SJ, Dacko L, Cohen G. Complications of laparoscopic sterlization. Comparison of 2 methods. Obstet Gynecol. 1979;54:54–9.

44. Chi I, Feldblum PJ, Balogh SA. Previous abdominal surgery as a risk factor in interval laparoscopic sterilization. Am J Obstet Gynecol. 1983(841):846.

45. Feldblum PJ, Champion CB, Chi IC, Lamptey P. Technical failures in female sterilization using the tubal ring: a case-control analysis. Contraception. 1986;34:505–12.

2.7.12 Summary table (SUMM)

This summary table highlights the medical eligibility recommendations for combined hormonal contraceptives (COC, CIC, patch [P] and vaginal ring [CVR]), progestogen-only contraceptives (POP, DMPA/NET-EN injectables, and LNG/ETG implants) and intrauterine devices (Cu-IUD and LNG-IUD). For further information about these recommendations, please consult the corresponding method tables. Eligibility recommendations for emergency contraceptive pills (ECPs), IUDs for emergency contraception (E-IUD), progesterone-releasing vaginal rings (PVR), barrier methods (BARR), fertility awareness-based (FAB) methods, lactational amenorrhea method (LAM), coitus interruptus (CI) and surgical sterilization (STER) are presented in their respective sub-sections in this document.

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
PREGNANCY	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
AGE	Menarche to < 40=1 ≥ 40=2	Menarche to < 40=1 ≥ 40=2	Menarche to < 18=1 18-45=1 > 45=1	Menarche to < 18=2 18-45=1 > 45=2	Menarche to < 18=1 18-45=1 > 45=1	Menarche to < 20=2 ≥ 20=1	Menarche to < 20=2 ≥ 20=1
PARITY							
a) Nulliparous	1	1	1	1	1	2	2
b) Parous	1	1	1	1	1	1	1
BREASTFEEDING							
a) < 6 weeks postpartum	4	4	2[a]	3[a]	2[a]		
b) ≥ 6 weeks to < 6 months (primarily breastfeeding)	3	3	1	1	1		
c) ≥ 6 months postpartum	2	2	1	1	1		
POSTPARTUM (non-breastfeeding women)							
a) < 21 days			1	1	1		
i) without other risk factors for venous thromboembolism (VTE)	3[a]	3[a]					
ii) with other risk factors for VTE	4[a]	4[a]					
b) ≥ 21 days to 42 days			1	1	1		
i) without other risk factors for VTE	2[a]	2[a]					
ii) with other risk factors for VTE	3[a]	3[a]					
c) > 42 days	1	1	1	1	1		

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
POSTPARTUM (breastfeeding or non-breastfeeding women, including after caesarean section)							
a) < 48 hours including insertion immediately after delivery of the placenta						1	not BF=1; BF=2
b) ≥ 48 hours to < 4 weeks						3	3
c) ≥ 4 weeks						1	1
d) Puerperal sepsis						4	4
POST-ABORTION							
a) First trimester	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]
b) Second trimester	1[a]	1[a]	1[a]	1[a]	1[a]	2[a]	2[a]
c) Immediate post-septic abortion	1[a]	1[a]	1[a]	1[a]	1[a]	4	4
PAST ECTOPIC PREGNANCY	1	1	2	1	1	1	1
HISTORY OF PELVIC SURGERY (see postpartum, including caesarean section)	1	1	1	1	1	1	1
SMOKING							
a) Age < 35 years	2	2	1	1	1	1	1
b) Age ≥ 35 years							
i) < 15 cigarettes/day	3	2	1	1	1	1	1
ii) ≥ 15 cigarettes/day	4	3	1	1	1	1	1

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
OBESITY							
a) ≥ 30 kg/m^2 BMI	2	2	1	1	1	1	1
b) Menarche to < 18 years and ≥ 30 kg/m^2 BMI	2	2	1	2[a]	1	1	1
BLOOD PRESSURE MEASUREMENT UNAVAILABLE	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
CARDIOVASCULAR DISEASE							
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (such as older age, smoking, diabetes, hypertension and known dyslipidaemias)	3/4[a]	3/4[a]	2[a]	3[a]	2[a]	1	2
HYPERTENSION							
a) History of hypertension where blood pressure CANNOT be evaluated (including hypertension during pregnancy)	3[a]	3[a]	2[a]	2[a]	2[a]	1	2
b) Adequately controlled hypertension, where blood pressure CAN be evaluated	3[a]	3[a]	1[a]	2[a]	1[a]	1	1
c) Elevated blood pressure levels (properly taken measurements)							
i) systolic 140–159 or diastolic 90–99 mm Hg	3	3	1	2	1	1	1
ii) systolic ≥ 160 or diastolic ≥ 100 mm Hg	4	4	2	3	2	1	2
d) Vascular disease	4	4	2	3	2	1	2

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
HISTORY OF HIGH BLOOD PRESSURE DURING PREGNANCY (where current blood pressure is measurable and normal)	2	2	1	1	1	1	1
DEEP VEIN THROMBOSIS (DVT)/ PULMONARY EMBOLISM (PE)							
a) History of DVT/PE	4	4	2	2	2	1	2
b) Acute DVT/PE	4	4	3	3	3	1	3
c) DVT/PE and established on anticoagulant therapy	4	4	2	2	2	1	2
d) Family history (first-degree relatives)	2	2	1	1	1	1	1
e) Major surgery							
i) with prolonged immobilization	4	4	2	2	2	1	2
ii) without prolonged immobilization	2	2	1	1	1	1	1
f) Minor surgery without immobilization	1	1	1	1	1	1	1
KNOWN THROMBOGENIC MUTATIONS (e.g. factor V Leiden; prothrombin mutation; protein S, protein C, and antithrombin deficiencies)	4[a]	4[a]	2[a]	2[a]	2[a]	1[a]	2[a]

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
SUPERFICIAL VENOUS DISORDERS							
a) Varicose veins	1	1	1	1	1	1	1
b) Superficial venous thrombosis	2[a]	2[a]	1	1	1	1	1
CURRENT AND HISTORY OF ISCHAEMIC HEART DISEASE	4	4	I: 2 / C: 3	3	I: 2 / C: 3	1	I: 2 / C: 3
STROKE (history of cerebrovascular accident)	4	4	I: 2 / C: 3	3	I: 2 / C: 3	1	2
KNOWN DYSLIPIDAEMIAS WITHOUT OTHER KNOWN CARDIOVASCULAR RISK FACTORS	2[a]	2[a]	2[a]	2[a]	2[a]	1[a]	2[a]
VALVULAR HEART DISEASE							
a) Uncomplicated	2	2	1	1	1	1	1
b) Complicated (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	4	4	1	1	1	2[a]	2[a]

SUMMARY TABLE														
	COC//P/CVR		CIC		POP		DMPA/NET-EN		LNG/ETG/ IMPLANTS		CU-IUD		LNG-IUD	
RHEUMATIC DISEASES														
SYSTEMIC LUPUS ERYTHEMATOSUS							I	C			I	C		
a) Positive (or unknown) antiphospholipid antibodies	4		4		3		3	3	3		1	1	3	
b) Severe thrombocytopenia	2		2		2		3	2	2		3[a]	2[a]	2[a]	
c) Immunosuppressive treatment	2		2		2		2	2	2		2	1	2	
d) None of the above	2		2		2		2	2	2		1	1	2	
NEUROLOGIC CONDITIONS														
HEADACHES	I	C	I	C	I	C	I	C	I	C			I	C
a) Non-migrainous (mild or severe)	1[a]	2[a]	1[a]	2[a]	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]		1[a]	1[a]
b) Migraine														
i) without aura														
age < 35 years	2[a]	3[a]	2[a]	3[a]	1[a]	2[a]	2[a]	2[a]	2[a]	2[a]	1[a]		2[a]	2[a]
age ≥ 35 years	3[a]	4[a]	3[a]	4[a]	1[a]	2[a]	2[a]	2[a]	2[a]	2[a]	1[a]		2[a]	2[a]
ii) with aura (at any age)	4[a]	4[a]	4[a]	4[a]	2[a]	3[a]	2[a]	3[a]	2[a]	3[a]	1[a]		2[a]	3[a]
EPILEPSY	1[a]		1[a]		1[a]		1[a]		1[a]		1[a]		1[a]	
	If on treatment, see DRUG INTERACTIONS (last section of this table)													
DEPRESSIVE DISORDERS														
DEPRESSIVE DISORDERS	1[a]		1[a]		1[a]		1[a]		1[a]		1[a]		1[a]	

SUMMARY TABLE									
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD		LNG-IUD	
REPRODUCTIVE TRACT INFECTIONS AND DISORDERS									
VAGINAL BLEEDING PATTERNS								I	C
a) Irregular pattern without heavy bleeding	1	1	2	2	2	1		1	1
b) Heavy or prolonged bleeding (includes regular and irregular patterns)	1[a]	1[a]	2[a]	2[a]	2[a]	2[a]		1[a]	2[a]
UNEXPLAINED VAGINAL BLEEDING (suspicious for serious condition)						I	C	I	C
a) Before evaluation	2[a]	2[a]	2[a]	3[a]	3[a]	4[a]	2[a]	4[a]	2[a]
ENDOMETRIOSIS	1	1	1	1	1	2		1	
BENIGN OVARIAN TUMOURS (INCLUDING CYSTS)	1	1	1	1	1	1		1	
SEVERE DYSMENORRHOEA	1	1	1	1	1	2		1	
GESTATIONAL TROPHOBLASTIC DISEASE									
a) Decreasing or undetectable β-hCG levels	1	1	1	1	1	3		3	
b) Persistently elevated β-hCG levels or malignant disease	1	1	1	1	1	4		4	
CERVICAL ECTROPION	1	1	1	1	1	1		1	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)	2	2	1	2	2	1		2	

SUMMARY TABLE									
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD		LNG-IUD	
CERVICAL CANCER (AWAITING TREATMENT)						I	C	I	C
	2	2	1	2	2	4	2	4	2
BREAST DISEASE									
a) Undiagnosed mass	2[a]	2[a]	2[a]	2[a]	2[a]	1		2	
b) Benign breast disease	1	1	1	1	1	1		1	
c) Family history of cancer	1	1	1	1	1	1		1	
d) Breast cancer									
i) current	4	4	4	4	4	1		4	
ii) past and no evidence of current disease for 5 years	3	3	3	3	3	1		3	
ENDOMETRIAL CANCER						I	C	I	C
	1	1	1	1	1	4	2	4	2
OVARIAN CANCER						I	C	I	C
	1	1	1	1	1	3	2	3	2
UTERINE FIBROIDS									
a) Without distortion of the uterine cavity	1	1	1	1	1	1		1	
b) With distortion of the uterine cavity	1	1	1	1	1	4		4	

SUMMARY TABLE									
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD		LNG-IUD	
ANATOMICAL ABNORMALITIES									
a) That distort the uterine cavity						4		4	
b) That do not distort the uterine cavity						2		2	
PELVIC INFLAMMATORY DISEASE (PID)									
a) Past PID (assuming no current risk factors for sexually transmitted infections)						I	C	I	C
i) with subsequent pregnancy	1	1	1	1	1	1	1	1	1
ii) without subsequent pregnancy	1	1	1	1	1	2	2	2	2
b) PID – current	1	1	1	1	1	4	2[a]	4	2[a]
SEXUALLY TRANSMITTED INFECTIONS (STIS)						I	C	I	C
a) Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	1	1	4	2[a]	4	2[a]
b) Other STIs (excluding HIV and hepatitis)	1	1	1	1	1	2	2	2	2
c) Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	1	1	2	2	2	2
d) Increased risk of STIs	1	1	1	1	1	2/3[a]	2	2/3[a]	2

SUMMARY TABLE									
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD		LNG-IUD	
HIV/AIDS						I	C	I	C
HIGH RISK OF HIV	1	1	1	1[a]	1	2	2	2	2
ASYMPTOMATIC OR MILD HIV CLINICAL DISEASE (WHO STAGE 1 OR 2)	1[a]	1[a]	1[a]	1[a]	1[a]	2	2	2	2
SEVERE OR ADVANCED HIV CLINICAL DISEASE (WHO STAGE 3 OR 4)	1[a]	1[a]	1[a]	1[a]	1[a]	3	2[a]	3	2[a]
OTHER INFECTIONS									
SCHISTOSOMIASIS									
a) Uncomplicated	1	1	1	1	1	1		1	
b) Fibrosis of the liver	1	1	1	1	1	1		1	
TUBERCULOSIS						I	C	I	C
a) Non-pelvic	1[a]	1[a]	1[a]	1[a]	1[a]	1	1	1	1
b) Pelvic	1[a]	1[a]	1[a]	1[a]	1[a]	4	3	4	3
MALARIA	1	1	1	1	1	1		1	

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
ENDOCRINE CONDITIONS							
DIABETES							
a) History of gestational disease	1	1	1	1	1	1	1
b) Non-vascular disease							
i) non-insulin-dependent	2	2	2	2	2	1	2
ii) insulin-dependent	2	2	2	2	2	1	2
c) Nephropathy/retinopathy/ neuropathy	3/4[a]	3/4[a]	2	3	2	1	2
d) Other vascular disease or diabetes of > 20 years' duration	3/4[a]	3/4[a]	2	3	2	1	2
THYROID DISORDERS							
a) Simple goitre	1	1	1	1	1	1	1
b) Hyperthyroid	1	1	1	1	1	1	1
c) Hypothyroid	1	1	1	1	1	1	1
GASTROINTESTINAL CONDITIONS							
GALL BLADDER DISEASE							
a) Symptomatic							
i) treated by cholecystectomy	2	2	2	2	2	1	2
ii) medically treated	3	2	2	2	2	1	2
iii) current	3	2	2	2	2	1	2
b) Asymptomatic	2	2	2	2	2	1	2

SUMMARY TABLE								
	COC//P/CVR		CIC		POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
HISTORY OF CHOLESTASIS									
a) Pregnancy-related	2		2		1	1	1	1	1
b) Past-COC-related	3		2		2	2	2	1	2
VIRAL HEPATITIS	I	C	I	C					
a) Acute or flare	3/4[a]	2	3	2	1	1	1	1	1
b) Carrier	1	1	1	1	1	1	1	1	1
c) Chronic	1	1	1	1	1	1	1	1	1
CIRRHOSIS									
a) Mild (compensated)	1		1		1	1	1	1	1
b) Severe (decompensated)	4		3		3	3	3	1	3
LIVER TUMOURS									
a) Benign									
i) focal nodular hyperplasia	2		2		2	2	2	1	2
ii) hepatocellular adenoma	4		3		3	3	3	1	3
b) Malignant (hepatoma)	4		3/4		3	3	3	1	3
ANAEMIAS									
Thalassaemia	1		1		1	1	1	2	1
Sickle cell disease	2		2		1	1	1	2	1
Iron-deficiency anaemia	1		1		1	1	1	2	1

SUMMARY TABLE									
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD		LNG-IUD	
DRUG INTERACTIONS									
ANTIRETROVIRAL THERAPY (ART)									
a) Nucleoside reverse transcriptase inhibitors (NRTIs)						I	C	I	C
Abacavir (ABC)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Tenofovir (TDF)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Zidovudine (AZT)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Lamivudine (3TC)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Didanosine (DDI)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Emtricitabine (FTC)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Stavudine (D4T)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)									
Efavirenz (EFV)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
Etravirine (ETR)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
Nevirapine (NVP)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
Rilpirivine (RPV)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]
c) Protease inhibitors (PIs)									
Ritonavir-boosted atazanavir (ATV/r)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
Ritonavir-boosted lopinavir (LPV/r)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
Ritonavir-boosted darunavir (DRV/r)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
Ritonavir (RTV)	2[a]	2[a]	2[a]	DMPA=1, NET-EN=2[a]	2[a]	2/3[a]	2[a]	2/3[a]	2[a]
d) Integrase inhibitors									
Raltegravir (RAL)	1	1	1	1	1	2/3[a]	2[a]	2/3[a]	2[a]

SUMMARY TABLE							
	COC//P/CVR	CIC	POP	DMPA/NET-EN	LNG/ETG/ IMPLANTS	CU-IUD	LNG-IUD
ANTICONVULSANT THERAPY							
a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	3[a]	2	3[a]	DMPA=1, NET-EN=2[a]	2[a]	1	1
b) Lamotrigine	3[a]	3	1	1	1	1	1
ANTIMICROBIAL THERAPY							
a) Broad-spectrum antibiotics	1	1	1	1	1	1	1
b) Antifungals	1	1	1	1	1	1	
c) Antiparasitics	1	1	1	1	1	1	1
d) Rifampicin or rifabutin therapy	3[a]	2[a]	3[a]	DMPA=1, NET-EN=2[a]	2[a]	1	1

[a] Please consult the tables in the text for a clarification to this classification.