Fifth edition, 2015

Medical eligibility criteria for contraceptive use

A WHO family planning cornerstone

COCs Barrier methods IUDs Fertility awareness-based methods Lactational amenorrhoea Patch Female surgical sterilization Intrauterine devices CICs Coitus interruptus Copper IUD for emergency contraception POCs Patch Male surgical sterilization Ring ECPs
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Abbreviations

ART	antiretroviral therapy
ARV	antiretroviral (medication)
ß-hCG	beta-human chorionic gonadotropin
BF	breastfeeding
BMD	bone mineral density
BMI	body mass index
C	continuation
CD4	cluster of differentiation 4
CDC	United States Centers for Disease Control and Prevention
CHC	combined hormonal contraception
CI	coitus interruptus
CIC	combined injectable contraceptive
CIRE	Continuous Identification of Research Evidence
COC	combined oral contraceptive (pill)
CRPD	United Nations Convention on the Rights of Persons with Disabilities
Cu-IUD	copper-bearing intrauterine device
CVR	combined contraceptive vaginal ring
CYP3A4	cytochrome P450 3A4 enzyme
DMPA	depot medroxyprogesterone acetate
DMPA-IM	depot medroxyprogesterone acetate – intramuscular
DMPA-SC	depot medroxyprogesterone acetate – subcutaneous
DVT	deep vein thrombosis
ECP	emergency contraceptive pill
EE	ethinyl estradiol
E-IUD	emergency intrauterine device
EMA	European Medicines Agency
ETG	etonogestrel
FAB	fertility awareness-based methods
FDA	United States Food and Drug Administration
GDG	Guideline Development Group
GRADE	Grading Recommendations, Assessment, Development and Evaluation
GRC	Guidelines Review Committee
GSG	Guideline Steering Group
HbA1c	glycated haemoglobin
HDL	high-density lipoprotein
I	initiation
ICPD	International Conference on Population and Development
IUD	intrauterine device
LAM	lactational amenorrhoea method
LDL	low-density lipoprotein
LNG	levonorgestrel
LNG-IUD	levonorgestrel-releasing intrauterine device
MEC	*Medical eligibility criteria for contraceptive use* (WHO publication)
MI	myocardial infarction
NA	not applicable
NET-EN	norethisterone enanthate
NIH	National Institutes of Health (United States of America)
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside/nucleotide reverse transcriptase inhibitor
OC	oral contraceptive (pill)
P	combined contraceptive patch
PE	pulmonary embolism
PI	protease inhibitor
PID	pelvic inflammatory disease
PICO	population, intervention, comparator, outcome
POC	progestogen-only contraceptive
POI	progestogen-only injectable
POP	progestogen-only pill
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PVR	progesterone-releasing vaginal ring
RCT	randomized controlled trial
SI (I)/SI (II)	Sino-implant (I) / Sino-implant (II)
SLE	systemic lupus erythematosus
SPR	*Selected practice recommendations for contraceptive use* (WHO publication)
STER	sterilization (male and female)
STI	sexually transmitted infection
SVT	superficial venous thrombosis
UN	United Nations
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UPA	ulipristal acetate
USAID	United States Agency for International Development
VTE	venous thromboembolism
WHO	World Health Organization

Executive summary

Introduction

This document is part of the process for improving the quality of care in family planning. *Medical eligibility criteria for contraceptive use* (MEC), the first edition of which was published in 1996, presents current World Health Organization (WHO) guidance on the safety of various contraceptive methods for use in the context of specific health conditions and characteristics. This is the fifth edition of the MEC – the latest in the series of periodic updates.

In the MEC, the safety of each contraceptive method is determined by several considerations in the context of the medical condition or medically relevant characterstics; primarily, whether the contraceptive method worsens the medical condition or creates additional health risks, and secondarily, whether the medical circumstance makes the contraceptive method less effective. The safety of the method should be weighed along with the benefits of preventing unintended pregnancy.

This fifth edition of the MEC is divided into two parts. Part I describes how the recommendations were developed and Part II contains the recommendations and describes how to use them. The recommendations contained within this document are based on the latest clinical and epidemiological data. Several tools and job aids are available from WHO and other sources to help providers use these recommendations in practice.

This document covers the following family planning methods: low-dose (≤ 35 mcg ethinyl estradiol) combined[1] oral contraceptives (COCs), combined patch (P), combined vaginal ring (CVR), combined injectable contraceptives (CICs), progestogen-only pills (POPs), depot medroxyprogesterone acetate (DMPA), norethisterone enanthate (NET-EN), levonorgestrel (LNG) and etonogestrel (ETG) implants, emergency contraceptive pills (ECPs), copper-bearing intrauterine devices (Cu-IUDs), levonorgestrel-releasing IUDs (LNG-IUDs), copper-IUD for emergency contraception (E-IUD), progesterone-releasing vaginal ring (PVR), barrier methods (BARR), fertility awareness-based methods (FAB), lactational amenorrhoea method (LAM), coitus interruptus (CI), and female and male sterilization (STER).

For each medical condition or medically relevant characteristic, contraceptive methods are placed into one of four numbered categories. Depending upon the individual, more than one condition may need to be considered together to determine contraceptive eligibility. These conditions and characteristics include, among others: age, weeks/months postpartum, breastfeeding status, venous thromboembolism, superficial venous disorders, dyslipidaemias, puerperal sepsis, past ectopic pregnancy, history of severe cardiovascular disease, migraines, severe liver disease, use of CYP3A4 inducer, repeat use of ECPs, rape, obesity, increased risk of sexually transmitted infections, high risk of HIV infection, living with HIV, use of antiretroviral therapy.

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

Target audience

The intended audience for this publication includes policy-makers, family planning programme managers and the scientific community. The MEC 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.

1 "Combined" refers to a combination of ethinyl estradiol and a progestogen.

Guideline development methods

The Guideline Development Group (GDG), convened by WHO on 14–15 May 2013, 9–12 March 2014 and 24–25 September 2014, consisted of 68 individuals representing a wide range of stakeholders. Their mandate was to review and, where appropriate, revise the guidance in the fourth edition of the MEC to develop the fifth edition.

For this revision process, the GDG prioritized the review of: (a) six topics identified as important to the field and/or those topics with new evidence that may warrant a change in the existing recommendation; (b) two topics for which interim guidance was issued following the publication of the fourth edition; (c) contraceptive eligibility recommendations for the inclusion of four new contraceptive methods in the fifth edition; and (d) two topics to provide greater clarity for the recommendations in the fourth edition relating to these topics, at the request of the Guidelines Review Committee. Therefore, recommendations for a total of 14 topics were reviewed for the fifth edition of the MEC.

The GDG considered the overall quality of the available scientific evidence, paying particular attention to the strength and consistency of the data, according to the Grading Recommendations, Assessment, Development and Evaluation (GRADE) approach to evidence review.[2] To formulate recommendations using the four MEC categories for contraceptive eligibility, the GDG considered potential harms related to contraceptive use, the GRADE evidence profiles, the benefits of preventing unintended pregnancy, and applied an approach towards values and preferences that prioritized the availability of a wide range of contraceptive options. The GDG reached its decisions through consensus, which entailed discussion, debate and consultation with experts to reconcile any disagreements. For certain recommendations, the GDG added clarification statements to provide further explanation or guidance on interpretation of the numerical classification. For each contraceptive method, the GDG considered the potential benefits and risks of its use with respect to each of the medical conditions or medically relevant physiologic or personal characteristics assessed (such as age, breastfeeding, smoking status).

Updated evidence. In many instances, either no new evidence has been identified since the publication of the fourth edition of the MEC (2009), or evidence emerging since that publication confirms previous research findings. Therefore, in many cases the recommendations that were published in the fourth edition have been reviewed and confirmed by the GDG with no changes made. For such recommendations that remained unchanged, the WHO Secretariat updated the evidence statements, references and citations that appear in the contraceptive method tables in Part II.

WHO will initiate a review of the recommendations in this document in four years. In the interim, WHO will continue to monitor the body of evidence informing these recommendations and will convene additional consultations, as needed, should new evidence necessitate reconsideration of existing recommendations. Such updates may be particularly warranted for issues where the evidence base may change rapidly. These interim recommendations will be made available on the WHO's web pages for sexual and reproductive health. WHO encourages research to address key unresolved issues related to establishing medical eligibility criteria for contraceptive use. WHO also invites comments and suggestions for improving this guidance.

Summary of reviewed recommendations

Fourteen topics (encompassing over 575 recommendations) were reviewed by the GDG during the 2014 revision of the MEC (see Table 1). The GRADE approach was applied to assess the quality of the available evidence, and this provided the basis for the formulation of recommendations (see central column). For some topics, multiple outcomes of interest and/or contraceptive methods were examined. For these topics, GRADE assessments of the quality of evidence are presented, either a single assessment or a range (see final column). An explanation of the process followed to select and prioritize these topics is included in Part I of the document, section 1.2: Methods, pp. 3–7 (Table 1.1). Other than the recommendations shown in Table 1, all other recommendations were confirmed by the GDG and did not undergo formal review for the updated fifth edition of the MEC. A summary of the changes between the fourth and fifth editions of this document is available in Part II, section 2.6, pp. 93–96.

2 Further information is available at the website of the GRADE working group: http://www.gradeworkinggroup.org/index.htm

Table 1. Topics reviewed for the *Medical eligibility criteria for contraceptive use* (MEC), fifth edition

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
1. Recommendations for combined hormonal contraceptive (CHC) use by age group (CHCs include combined oral contraceptives, combined injectable contraceptives, combined patch and combined vaginal ring)		
< 40 years	Women from menarche through 40 years of age can use CHCs without restriction (MEC Category 1).	Range: Low to very low
≥ 40 years	Women 40 years and older can generally use CHCs (MEC Category 2).	
2. Recommendations for CHC use among breastfeeding women		
< 6 weeks postpartum	Breastfeeding women < 6 weeks postpartum should not use CHCs (MEC Category 4).	Range: Low to very low
≥ 6 weeks to <6 months postpartum	Breastfeeding women ≥ 6 weeks to < 6 months postpartum (primarily breastfeeding) generally should not use CHCs (MEC Category 3).	
≥ 6 months postpartum	Breastfeeding women ≥ 6 months postpartum can generally can use CHCs (MEC Category 2).	
3. Recommendations for CHC use among postpartum women		
< 21 days postpartum without other risk factors for venous thromboembolism (VTE)	Women who are < 21 days postpartum and do not have other risk factors for VTE generally should not use CHCs (MEC Category 3).	Range: Low to very low
< 21 days postpartum with other risk factors for VTE	Women who are < 21 days postpartum with other risk factors for VTE should not use CHCs (MEC Category 4).	
≥ 21 days to 42 days postpartum without other risk factors for VTE	Women who are ≥ 21 days to 42 days postpartum without other risk factors for VTE can generally use CHCs (MEC Category 2).	
≥ 21 days to 42 days postpartum with other risk factors for VTE	Women who are ≥ 21 days to 42 days postpartum with other risk factors for VTE generally should not use CHCs (MEC Category 3).	
> 42 days postpartum	Women who are > 42 days postpartum can use CHCs without restriction (MEC Category 1).	
4. Recommendations for CHC use among women with superficial venous disorders		
Varicose veins	Women with varicose veins can use CHCs without restriction (MEC Category 1).	Very low
Superficial venous thrombosis (SVT)	Women with SVT can generally use CHCs (MEC Category 2).	

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
5. Recommendations for CHC use among women with known dyslipidaemias		
Known dyslipidaemias without other known cardiovascular risk factors	Women with known dyslipidaemias without other known cardiovascular risk factors can generally use CHCs (MEC Category 2).	Very low; reviewed for clarity as requested by the GRC
6. Recommendations for progestogen-only contraceptive (POC) and levonorgestrel-releasing intrauterine device (LNG-IUD) use among breastfeeding women		
6a. POC use among breastfeeding women (POCs include progestogen-only pills, implants and injectables)		
< 6 weeks postpartum	Breastfeeding women who are < 6 weeks postpartum can generally use progestogen-only pills (POPs) and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 2). Breastfeeding women who are < 6 weeks postpartum generally should not use progestogen-only injectables (POIs) (DMPA or NET-EN) (MEC Category 3).	Range: Low to very low
≥ 6 weeks to < 6 months postpartum	Breastfeeding women who are ≥ 6 weeks to < 6 months months postpartum can use POPs, POIs, and LNG and ETG implants without restriction (MEC Category 1).	
≥ 6 months postpartum	Breastfeeding women who are ≥ 6 months postpartum can use POPs, POIs, and LNG and ETG implants without restriction (MEC Category 1).	
6b. LNG-IUD use among breastfeeding women		
< 48 hours postpartum	Breastfeeding women who are < 48 hours postpartum can generally use LNG-IUDs (MEC Category 2).	Very low
≥ 48 hours to < 4 weeks postpartum	Breastfeeding women who are ≥ 48 hours to < 4 weeks postpartum generally should not have an LNG-IUD inserted (MEC Category 3).	
≥ 4 weeks postpartum	Breastfeeding women who are ≥ 4 weeks postpartum can use an LNG-IUD without restriction (MEC Category 1).	
Puerperal sepsis	Breastfeeding (and non-breastfeeding) women with puerperal sepsis should not have an LNG-IUD inserted (MEC Category 4).	
7. Recommendations for use of subcutaneously-administered depot medroxyprogesterone acetate (DMPA-SC) – new method added to the guideline		
All recommendations	Recommendations for DMPA-SC will follow the current recommendations for DMPA-IM (intramuscular).	Very low
8. Recommendations for Sino-implant (II) – new method added to the guideline		
All recommendations	Recommendations for Sino-implant (II) will follow the current recommendations for LNG implants.	Range: Moderate to very low

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
9. Recommendations for emergency contraceptive pills (ECPs) – ulipristal acetate (UPA) as a new method added to the guideline and obesity as a new condition for ECP use		
Pregnancy	For pregnant women, ECP use is not applicable.	Very low
Breastfeeding	Breastfeeding women can use combined oral contraceptive pills (COCs) or LNG for ECPs without restriction (MEC Category 1). Women who are breastfeeding can generally use UPA for ECPs (MEC Category 2).	
Past ectopic pregnancies	Women who have experienced past ectopic pregnancies can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1).	
History of severe cardiovascular disease	Women with history of severe cardiovascular disease, including ischaemic heart disease, cerebrovascular attack or other thromboembolic conditions, can generally use COCs, LNG or UPA for ECPs (MEC Category 2).	
Migraines	Women with migraines can generally use COCs, LNG or UPA for ECPs (MEC Category 2).	
Severe liver disease	Women with severe liver disease, including jaundice (a personal characteristic and sign of liver disease prior to diagnosis), can generally use COCs, LNG or UPA for ECPs (MEC Category 2).	
Use of CYP3A4 inducer	Women using CYP3A4 inducers can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1).	
Repeat use of ECP	There are no restrictions on repeated use for COCs, LNG or UPA for ECPs (MEC Category 1).	
Rape	There are no restrictions for use of COCs, LNG or UPA for ECPs in cases of rape (MEC Category 1).	
Obesity	Women who are obese can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1).	Moderate
10. Intrauterine device (IUD) use for women with increased risk of sexually transmitted infections (STIs)		
IUD initiation	Many women with increased risk of STIs can generally undergo either copper-bearing IUD (Cu-IUD) or LNG-IUD initiation (MEC Category 2). Some women at increased risk (very high individual likelihood) of STIs generally should not have an IUD inserted until appropriate testing and treatment occur (MEC Category 3).	No new evidence identified, so quality of evidence not evaluated using GRADE process; reviewed for clarity as requested by the GRC
IUD continuation	Women at increased risk of STIs can generally continue use of either Cu-IUD or LNG-IUD (MEC Category 2).	

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
11. Recommendations for use of progesterone-releasing vaginal ring – new method added to the guideline		
Breastfeeding and ≥ 4 weeks postpartum	Women who are actively breastfeeding and are ≥ 4 weeks postpartum can use the progesterone-releasing vaginal ring without restrictions (MEC Category 1).	Low
12. Recommendations for use of hormonal contraception for women at high risk of HIV infection, women living with HIV, and women living with HIV using antiretroviral therapy (ART)		
12a. Women at high risk of HIV infection	Women at high risk of acquiring HIV can use the following hormonal contraceptive methods without restriction: COCs, combined injectable contraceptives (CICs), combined contraceptive patches and rings, POPs, POIs (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1). Women at high risk of acquiring HIV can generally use LNG-IUDs (MEC Category 2).	Range: Moderate to very low
12b. Women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2)	Women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) can use the following hormonal contraceptive methods without restriction: COCs, CICs, combined contraceptive patches and rings, POPs, POIs (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1). Women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) can generally use the LNG-IUD (MEC Category 2).	Range: Moderate to very low
12c. Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4)	Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) can use the following hormonal contraceptive methods without restriction: COCs, CICs, combined contraceptive patches and rings, POPs, POIs (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) generally should not initiate use of the LNG-IUD (MEC Category 3) until their illness has improved to asymptomatic or mild HIV clinical disease (WHO stage 1 or 2). Women who already have an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation).	

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
12d. Women living with HIV using antiretroviral therapy (ART)		Range: Low to very Low
Nucleoside/nucleotide reverse transcriptase inhibitor (NRTI)	Women taking any NRTI can use all hormonal contraceptive methods without restriction: COCs, CICs, combined contraceptive patches and rings, POPs, POIs (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1). Women taking any NRTI can generally use the LNG-IUD (MEC Category 2), provided that their HIV clinical disease is asymptomatic or mild (WHO Stage 1 or 2). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) and taking any NRTI generally should not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease. Women taking any NRTI who already have had an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation).	
Non-nucleoside/ nucleotide reverse transcriptase inhibitors (NNRTIs) containing efavirenz or nevirapine-containing ART	Women using NNRTIs containing either efavirenz or nevirapine can generally use COCs, CICs, combined contraceptive patches and rings, POPs, NET-EN, and LNG and ETG implants (MEC Category 2). Women using efavirenz or nevirapine can use DMPA without restriction (MEC Category 1). Women taking any NNRTI can generally use the LNG-IUD (MEC Category 2), provided that their HIV clinical disease is asymptomatic or mild (WHO Stage 1 or 2). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) and taking any NNRTI generally should not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease. Women taking any NNRTI who already have had an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation).	
NNRTIs containing etravirine and rilpivirine	Women using the newer NNRTIs containing etravirine and rilpivirine can use all hormonal contraceptive methods without restriction (MEC Category 1).	

ART: antiretroviral therapy; ARV: antiretroviral (medication); CHC: combined hormonal contraceptive; CIC: combined injectable contraceptive; COC: combined oral contraceptive; Cu-IUD: copper-bearing IUD; DMPA: depot medroxyprogesterone acetate; ETG: etonogestrel; GRADE: Grading Recommendations, Assessment, Development and Evaluation; GRC: Guidelines Review Committee; IM: intramuscular; IUD: intrauterine device; LNG: levonorgestrel; NET-EN: norethisterone enanthate; POC: progesterone-only contraceptive; NRTI: nucleoside/nucleotide reverse transcriptase inhibitor; NNRTI: non-nucleoside/nucleotide reverse transcriptase inhibitor; POI: progresterone-only injectable; POP: progesterone-only pill; SC: subcutaneous; SVT: superficial venous thrombosis; VTE: venous thromboembolism.

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

TOPIC	MEC RECOMMENDATION	GRADE ASSESSMENT OF QUALITY OF EVIDENCE[a]
12d. Women living with HIV using antiretroviral therapy (ART) (continued)		Range: Low to very Low
Protease inhibitors (e.g. ritonavir and ARVs boosted with ritonavir)	Women using protease inhibitors (e.g. ritonavir and ARVs boosted with ritonavir) can generally use COCs, CICs, combined contraceptive patches and rings, POPs, NET-EN, and LNG and ETG implants (MEC Category 2). Women using protease inhibitors (e.g. ritonavir and ARVs boosted with ritonavir) can use DMPA without restriction (MEC Category 1). Women taking any PI can generally use the LNG-IUD (MEC Category 2), provided that their HIV clinical disease is asymptomatic or mild (WHO Stage 1 or 2). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) and taking any PI generally should not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease. Women taking any PI who already have had an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation).	
Raltegravir (integrase inhibitor)	Women using the integrase inhibitor raltegravir can use all hormonal contraceptive methods without restriction (MEC Category 1). Women taking an RI can generally use the LNG-IUD (MEC Category 2), provided that their HIV clinical disease is asymptomatic or mild (WHO Stage 1 or 2). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) and taking an RI generally should not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease. Women taking an RI who already have had an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation).	

ART: antiretroviral therapy; ARV: antiretroviral (medication); CHC: combined hormonal contraceptive; CIC: combined injectable contraceptive; COC: combined oral contraceptive; Cu-IUD: copper-bearing IUD; DMPA: depot medroxyprogesterone acetate; ETG: etonogestrel; GRADE: Grading Recommendations, Assessment, Development and Evaluation; GRC: Guidelines Review Committee; IM: intramuscular; IUD: intrauterine device; LNG: levonorgestrel; NET-EN: norethisterone enanthate; NNRTI: non-nucleoside/nucleotide reverse transcriptase inhibitor; NRTI: nucleoside/nucleotide reverse transcriptase inhibitor; POC: progesterone-only contraceptive; POI: progresterone-only injectable; POP: progesterone-only pill; SC: subcutaneous; SVT: superficial venous thrombosis; VTE: venous thromboembolism.

[a] GRADE assessment includes the quality categories of very low, low, moderate and high. When a range is presented, the range reflects the GRADE quality assessment across important outcomes and/or across contraceptive methods. See the specific GRADE table in Part I, section 1.4: Reviewed recommendations (p. 8–82) for outcomes explored.

Part I

Development of the
Medical eligibility criteria for contraceptive use,
fifth edition

1.1 Background

1.1.1 Overview and scope of the guidelines

Over the past 40 years, there have been significant advances in the development of new contraceptive technologies, including changes in formulations and dosing, schedules for administration and novel delivery systems. However, current policies and health-care practices in some countries are based on scientific studies of contraceptive products that are no longer in wide use, on long-standing theoretical concerns that have never been substantiated or on the personal preference or bias of service providers. These outdated policies or practices often result in limitations to both the quality of, and the access to, family planning services for clients.

The goal of this 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 medical eligibility criteria used in the provision of 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 given 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 characteristics (e.g. age).

Because country situations and programme environments vary so greatly, it is inappropriate to set firm international guidelines on criteria for contraceptive use. However, it is expected that national programmes will use these recommendations for updating or developing their own contraceptive eligibility guidelines according to national health policies, needs, priorities and resources, while reflecting upon local values and preferences.

There are a total of four WHO guidance documents (cornerstones) pertaining to contraception; two that focus on evidence-based recommendations (primarily targeted towards policy-makers and programme managers) and two that focus on application of the recommendations (primarily targeted towards health-care providers). All four cornerstones are best interpreted and used in a broader context of reproductive and sexual health care. These four documents, listed below, are updated periodically to reflect changes in the medical and scientific knowledge.

Evidence-based recommendations for provision of contraception:

1. *Medical eligibility criteria for contraceptive use* (MEC) – provides guidance regarding "who" can use contraceptive methods safely; and

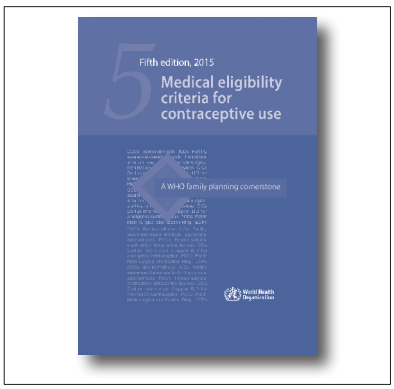
2. *Selected practice recommendations for contraceptive use* (SPR) – provides guidance regarding "how" to use contraceptive methods safely and effectively.

Practical tools for front-line providers of contraceptive counselling and services:

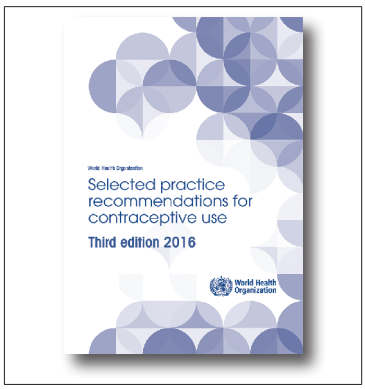
3. *Decision-making tool for family planning clients and providers* – counselling tool that supports both provider and client in the process of choosing a contraceptive method; and

4. *Family planning: a global handbook for providers* – offers evidence-based information on service delivery, method by method.

Figure 1. The four cornerstones of family planning guidance



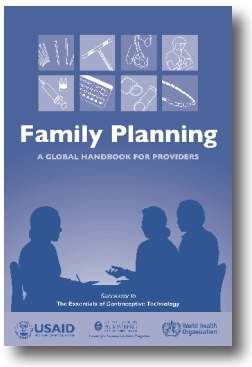
Medical eligibility criteria for contraceptive use



Selected practice recommendations for contraceptive use

These are evidence-based guidance and consensus-driven guidelines. They provide recommendations made by expert working groups based on an appraisal of relevant evidence. They are reviewed and updated in a timely manner.

Decision-making tool for family planning clients and providers



Family planning: a global handbook for providers

These are tools that incorporate the *Medical eligibility criteria*, the *Selected practice recommendations* and other consensus recommendations on how to meet the needs of the family planning client. They will be updated as the guidelines are updated or as other evidence warrants.

Process for assuring that the guidelines remain current:

1. Identify new, relevant evidence as soon as it becomes available through an ongoing comprehensive bibliographic search.
2. Critically appraise the new evidence.
3. Evaluate the new evidence in light of prior evidence.
4. Determine whether the newly synthesized evidence is sufficient to warrant an update of existing recommendations.
5. Provide electronic updates on WHO's reproductive health web site (www.who.int/reproductivehealth) as appropriate and determine the need to convene an expert working group to reassess guidelines formally.

1.2 Methods

1.2.1 Development of earlier editions of the *Medical eligibility criteria for contraceptive use*

This document builds on a process initiated in 1994 to develop the first edition. The initial process involved comparing the eligibility criteria used by different agencies for various contraceptives, preparing summaries of published medical and epidemiological literature relevant to medical eligibility criteria, and preparing a draft classification for review by a larger group of experts and agencies. Two expert Working Group meetings were organized by WHO, in March 1994 and May 1995, to review the background classifications and to formulate recommendations; publication of the document followed in 1996.

Since the publication of the first edition of the MEC, the guideline has been revised and updated three times. With each revision, a Working Group of multidisciplinary experts was assembled to review newly published evidence pertaining to the topics addressed in the guideline. Moreover, with each revision, the Working Group used the opportunity to consider inclusion of new medical conditions and new contraceptive methods, as appropriate.

The second edition of the MEC was based on the recommendations of an expert Working Group meeting held at WHO on 8–10 March 2000, which brought together 32 participants from 17 countries, including representatives of many agencies and organizations. The Working Group reviewed new evidence since the last meetings in 1994 and 1995, primarily obtained from systematic reviews of the most recent literature.

The third edition of the MEC, was based on the recommendations of an expert Working Group meeting held at WHO on 21–24 October 2003, which gathered 36 participants from 18 countries, including representatives of many agencies and organizations. Systematic reviews of the evidence were prepared on topics with newly published evidence since the meeting in 2000; they were presented to the Working Group and provided the basis for their decision-making. A Guideline Steering Group (GSG), comprising seven external members, was established for this edition. The GSG was formed to advise WHO on behalf of the larger expert Working Group on matters related to emerging published evidence on topics covered by the guideline during interim periods between expert Working Group meetings.

The fourth edition of the MEC was based on the recommendations of an expert Working Group meeting held at WHO on 1–4 April 2008, which brought together 43 participants from 23 countries, including nine agency representatives. Eighty-six new recommendations were developed and 165 recommendations were revised for the fourth edition. All members of the expert Working Group were asked to declare any conflict of interest and three of the experts declared conflicts of interest relevant to the subject matter of the meeting. These conflicts of interest were determined not to be sufficient to preclude the experts from participating in the deliberations and development of recommendations and thus they were not asked to withdraw from this process.

The Guidelines Review Committee (GRC) was established by the Director-General of WHO in 2007 to ensure that WHO guidelines are of a high methodological quality and are developed through a transparent, evidence-based decision-making process. The fourth edition of the MEC was reviewed by the newly established GRC and was approved on 16 September 2009.

To assure that the guidelines remain current between guideline meetings, new evidence is identified through an ongoing comprehensive bibiliographic search (the Continuous Identification of Research Evidence, or CIRE system)[1]. This evidence is synthesized and reviewed. In circumstances where new evidence warrants further evaluation, the GSG is tasked with evaluating such evidence and issuing interim guidance if necessary. Since the release of the fourth edition of the MEC, interim guidance has been issued twice. At the request of the GSG, WHO first convened a technical consultation on 26 January 2010 via teleconference to review new evidence regarding the risk of venous thromboembolism (VTE) in postpartum women. The teleconference brought together members of the GSG and three experts on VTE during the postpartum period. All participants in the consultation were asked to declare any conflict of interest; two participants declared a conflict of interest relevant to the subject matter, but they were not asked to withdraw from the process of recommendation formulation because the WHO Secretariat and GSG did not find these conflicts of interest sufficient to preclude them from participating in the deliberations and development of recommendations. The GRC approved the updated recommendations on 21 April 2010.

1 Mohllajee AP, Curtis KM, Flanagan RG, Rinehart W, Gaffield ML, Peterson HB. Keeping up with evidence: a new system for WHO's evidence-based family planning guidance. Am J Prev Med. 2005;28(5):483–90.

Following new findings of epidemiological studies regarding the use of hormonal contraception and HIV acquisition, progression and transmission, a second technical consultation was convened by WHO during 31 January – 1 February 2012. The meeting involved 75 individuals representing a wide range of stakeholders. Through a consensus-driven process, the group considered whether recommendations in the MEC pertaining to hormonal contraceptive use among women at high risk of HIV or women living with HIV should be changed in light of the accumulating evidence. All participants in the consultation were asked to declare any conflict of interest; 13 participants declared an academic conflict of interest relevant to the subject matter of the meeting. These conflicts of interest were determined not to be sufficient to preclude them from participating in the deliberations and development of recommendations and so they were not asked to withdraw from this process. The GRC approved the technical statement presenting the conclusions and updated recommendations of the meeting on 15 February 2012.

1.2.2 Development of the *Medical eligibility for criteria for contraceptive use, fifth edition*

In preparation for the fifth edition of the document, both approval for the planning and ultimately the final document were obtained from the GRC. Several key aspects of the updating process were adjusted to be in closer alignment with requirements set forth in the *WHO handbook for guideline development,* authored by the GRC Secretariat.[2] Specifically, these alterations included:

- creation of groups with varying roles to undertake the revision;
- convening an additional consultation to define the scope of the revision, giving priority to controversial topics and those for which new evidence had emerged, including topics addressed in interim guidance, clarifying recommendations with a Category 2/3 classification, and drafting questions relating to population, intervention, comparator and outcome (PICO questions) to guide the preparation of systematic reviews; and
- applying the Grading Recommendations, Assessment, Development and Evaluation (GRADE) approach to evidence review and recommendation formulation.[3]

The groups responsible for the development of the fifth edition of the MEC included: a WHO Secretariat; an Evidence Secretariat including a GRADE methodologist; a Guideline Steering Group (GSG); and a Guideline Development Group (GDG), which was formerly called the expert Working Group for the earlier MEC editions. The GSG, which has served as an external advisory group to WHO on family planning guidelines since 2003, was part of the larger GDG, to be compliant with WHO requirements for guideline development and to gain input from a larger advisory group. For a summary of the members of the WHO Secretariat, the Evidence Secretariat and the GDG, see the Acknowledgements at the beginning of this document.

1.2.3 Prioritization of topics for the revision process

On 14–15 May 2013, the first GDG meeting convened in Ferney Voltaire, France, to initiate the revision process for the development of the fifth edition of the MEC. Prior to the meeting, the CIRE system[1] was used to identify recommendations from the fourth edition of the MEC for which new evidence was available.

To further inform decision-making with respect to clinical questions and priorities, the WHO Secretariat reached out to a broad group of stakeholders with expertise in family planning and familiarity with the guideline, including individuals from a number of implementing agencies, professional societies, and WHO regional and country offices, as well as the Ministry of Health in each of the Member States. They were asked to voluntarily complete an electronic 24-question anonymous survey available in English, French and Spanish, and to forward the link for the survey to others in their professional communities familiar with family planning and the MEC during the period 2 March – 2 May 2013. The respondents were asked to rank the importance of various outcomes pertaining to topics that had been identified as priority questions for the current revision, as well as to suggest other outcomes and clinical questions of importance, and to give input regarding the format of the guidance. More than 250 individuals submitted completed surveys; these results were presented to the GDG during the meeting to inform the prioritization process.

At the meeting, the WHO Secretariat presented brief summaries of new evidence to the GDG to determine whether the existing recommendation remained consistent or had become inconsistent with the updated body of evidence. Recommendations considered to be possibly inconsistent with the updated body of evidence were selected for presentation and discussion at a larger meeting convened in March 2014. Recommendations considered to be consistent with the updated body of evidence, and recommendations for which no new evidence had been identified through CIRE were

2 The first edition was published in 2012, the second edition in 2014.

3 For further information on GRADE, see: www.gradeworkinggroup.org/index.htm

determined by the GDG to need no further review during the revision process.

Also at this first GDG meeting, the members were asked to consider whether WHO should include several new conditions, contraceptive methods and/or formulations of methods, based upon their global relevance and availability in multiple countries. Participants were also asked to review the two interim guidance documents released since the fourth edition. Further, during this meeting the GDG was asked to address current recommendations which were classified as category "2/3" in the fourth edition, as earlier reviews by the GRC noted that these recommendations may be confusing to users of the document.

Thus, topics were prioritized for review and consideration by the GDG at the second meeting in March 2014 based on meeting one or more of the following criteria: topics identified as controversial or of particular importance to the field; topics with new evidence, for which the existing recommendation was potentially inconsistent with the updated body of evidence; topics with interim guidance issued by WHO since the MEC fourth edition; newly introduced contraceptive methods; or recommendations from the MEC fourth edition that were determined to lack clarity by the GRC. All existing recommendations that did not fall into one of these categories were reaffirmed by the GRC and thus were not reviewed.

Table 1.1 Medical eligibility criteria for contraceptive use, fifth edition: selection of topics for 2014 revision

Prioritized topics reviewed by the Guideline Development Group (GDG) using the GRADE process in 2014:
1. **Topics identified as important to the field and/or topics with new, potentially inconsistent evidence identified (6 topics):** • progesterone-only contraceptive (POC) use among breastfeeding women • combined hormonal contraceptive (CHC) use among breastfeeding women • CHC use among women with superficial venous disorders • CHC use by age group • hormonal contraceptive use among women using antiretroviral therapy • emergency contraceptive pill (ECP) use among women with obesity (new condition added to ECP recommendations).
2. **Interim guidance issued by WHO since the MEC fourth edition (2 topics):** • CHC use during the postpartum period (guidance updated in 2010) • hormonal contraceptive use among women at high risk of HIV acquisition and women living with HIV (guidance reaffirmed in 2012).
3. **New contraceptive methods added to the MEC for the fifth edition (4 methods):** • subcutaneously-administered depot medroxyprogesterone acetate (DMPA) 104 mg • 2-rod levonorgestrel (LNG)-containing implant with 75 mg LNG/rod, approved for 4 years of use, i.e. Sino-implant (II) • progesterone-releasing vaginal ring (PVR) • ulipristal acetate (UPA) for emergency contraception.
4. **Recommendations reviewed by the GDG for clarity, as required by the Guidelines Review Committee (GRC) (2 topics):** • intrauterine device (IUD) use among women with increased risk of sexually transmitted infections (STIs) (no new evidence identified since 2008 systematic review) • CHC use among women with known dyslipidaemias.
All other existing recommendations from the MEC fourth edition (approximately 2000 recommendations):[a] • reaffirmed by the GDG in March 2014.

CIRE: Continuous Identification of Research Evidence; GRADE: Grading Recommendations, Assessment, Development and Evaluation.

[a] Evidence continuously monitored using CIRE system. Topics not prioritized for 2014 update.

For the topics outlined in Table 1.1, the GDG developed questions using the PICO format (i.e. questions with specified populations, interventions, comparators and outcomes) to serve as the framework for the systematic reviews and GRADE evidence tables. In order to inform the MEC recommendations, PICO questions generally guide the systematic review to focus on studies of populations with the condition or characteristic of interest using a specific contraceptive method compared with the same population not using the method, reporting on critical safety outcomes. PICO questions were also crafted to also identify relevant indirect evidence that may have included comparator populations without the condition or characteristic of interest using the same method, or reporting on surrogate outcomes. These systematic reviews, therefore, assessed the safety risks of using a given method among women with a particular medical condition or characteristic. The remainder of the existing recommendations were determined to be consistent with the body of published evidence and did not need to be formally reviewed for this revision.

1.2.4 Evidence identification and synthesis

For each of the priority topics listed in Table 1.1, systematic reviews were conducted in accordance with PRISMA guidelines to answer PICO-formatted questions regarding safety outcomes.[4] The systematic reviews may be accessed in Annex 2. In general, the PubMed and Cochrane databases were searched for studies published in any language in a peer-reviewed journal up to 15 January 2014, to inform the systematic reviews. Reference lists and direct contact with experts in the field were also used to identify other studies, including those in press; neither grey literature nor conference abstracts were included in these reviews. Due to heterogeneity of study designs, contraceptive formulations and outcome measures, meta-analyses were generally not performed. The quality of evidence presented in individual studies within a systematic review was assessed by review authors using the United States Preventive Services Task Force system.[5] GRADE evidence profiles were then prepared by a GRADE methodologist to assess the quality of the summarized evidence and include the range of the estimates of effect for each clinical outcome assessed. GRADE evidence profiles were prepared for each PICO question for which evidence was found and clinical outcomes were reported. The systematic reviews that resulted from this process were peer-reviewed by selected members of the GDG, and final drafts were made electronically available to all GDG members prior to the consultations. Printed copies of GRADE evidence profiles for each topic were also given to each GDG member during the March 2014 GDG meeting. The written and orally presented systematic reviews and GRADE evidence profiles served as the basis for the GDG's deliberations.

1.2.5 Decision-making during the Guideline Development Group meetings

During 9–12 March 2014 and 24–25 September 2014, WHO convened a series of GDG meetings to review the evidence for the priority topics and, where appropriate, revise specific recommendations in the MEC. Members of the GDG and members of the External Peer Review Group (who did not participate in the GDG meeting) submitted Declaration of Interest forms to the WHO Secretariat: 14 individuals declared an academic conflict of interest relevant to the MEC guidance. The WHO Secretariat and the GDG reviewed all declarations of interest and, with the exception of two members (Dr Glasier and Dr Sitruk-Ware), found no conflicts of interest sufficient to preclude anyone from participating in the deliberations or development of recommendations. In the case of the two exceptions, the WHO Secretariat and the GDG agreed that their disclosed academic conflicts of interest were sufficient to preclude them from participating in the deliberations and development of recommendations relevant to ulipristal acetate (Dr Glasier) and the progesterone-releasing vaginal ring (Dr Sitruk-Ware). For details of the declared academic interests see Annex 1.

The GDG considered the overall quality of the safety evidence, paying particular attention to the strength and consistency of the data, according to the GRADE approach to evidence review. In most cases, the quality of evidence pertaining to each recommendation was low or very low and only addressed potential harms related to contraceptive use. To arrive at a category designation, within the range 1–4, the GDG considered these potential harms, the GRADE evidence profiles, the benefits of preventing unintended pregnancy, as well as the other GRADE constructs of values and preferences.

The GDG endorsed an approach to patient preferences and values that prioritized the availability of a wide range of contraceptive options, as women vary in their preferences regarding contraceptive selection and in the value they place

4 Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. PLoS Med. 2009;6(6):e1000097.

5 Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20(3 Suppl):21–35.

on different beneficial and harmful outcomes.[6 7] In addition, the availability of a range of contraceptive options is critical because a woman's contraceptive choices are made at a particular time and in a particular societal and cultural context, and these choices are complex, multifactorial and subject to change.[8 9] Decision-making for contraceptive methods usually requires making trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Owing to the focus of this guidance on the safety of specific contraceptive methods for women with medical conditions or personal characteristics, opportunity costs were not formally assessed during the formulation of these recommendations since costs may vary widely throughout different regions.[10]

Since publication of the first edition of the MEC in 1996, the 1–4 scale has been used to categorize medical eligibility for contraceptive use. These categories are well known by health-care providers, professional organizations, training institutions and ministries of health as the basis for determining contraceptive eligibility for women with medical conditions or characteristics. As a result, to avoid confusion and retain consistency, it was determined that recommendations would not be defined as "strong" or "weak" according to GRADE methodology and would instead retain the 1–4 scale reflecting eligibility for contraceptive use.

Through consensus, the GDG arrived at new and revised recommendations, as well as upholding the majority of the existing recommendations using the categories 1–4. For the topics they reviewed in 2014 (see Box 1.1), the GDG considered the potential benefits and risks of contraceptive method use with respect to each of the medical conditions or personal characteristics assessed.

Owing to the public health importance of recommendations on hormonal contraceptive use for women at risk of HIV and women living with HIV, and based on encouragement from the GDG, WHO issued its contraceptive eligibility guidance for women living with HIV or at high risk of acquiring the infection in advance of the entire guideline revision. The document, *Hormonal contraceptive methods for women at high risk of HIV and living with HIV: 2014 guidance statement* was approved by the WHO Guidelines Review Committee (GRC) on 7 July 2014. The statement was released on 24 July 2014, at the 20th International AIDS Conference.

A draft version of the entire MEC document was sent to the External Peer Review Group, comprising eight experts who did not participate in the GDG meeting. Comments received from these reviewers were addressed and incorporated into this guidance by the WHO Secretariat as appropriate. The final version of this document was approved by the GRC on 18 March 2015.

1.3 Dissemination and evaluation of the *Medical eligibility criteria for contraceptive use, fifth edition*

The recommendations in the *Medical eligibility criteria for contraceptive use, fifth edition* guidance were released during a global live Facebook Chat on 1 June 2015. A comprehensive dissemination and evaluation plan will be implemented, which will include widespread dissemination through the WHO regional and country offices, WHO Member States, the United Nations (UN) agency cosponsors of the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) within the WHO Department of Reproductive Health and Research (i.e. UNDP, UNFPA, UNICEF, WHO and the World Bank), WHO collaborating centres, professional organizations, governmental and nongovernmental partner organizations working in the area of sexual and reproductive health, and civil society groups engaged in sexual and reproductive health projects The WHO Secretariat will work closely with sexual and reproductive health points of contact in the WHO regional offices to conduct a series of regional events during 2015–2016. In addition, special panel sessions will be organized during the summer and autumn of 2015 at international conferences convened by the International Society of Obstetricians and Gynaecologists (FIGO), the International Council of Nurses (ICN) and the International

6 Madden T, Secura GM, Nease RF, Politi MC, Peipert JF. The role of contraceptive attributes in women's contraceptive decision making. Am J Obstet Gynecol. 2015;pii: S0002-9378(15)00107–6. [Epub ahead of print]

7 Hooper DJ. Attitudes, awareness, compliance and preferences among hormonal contraception users: a global, cross-sectional, self-administered, online survey. Clin Drug Investig. 2010;30(11):749–63.

8 d'Arcangues CM, Ba-Thike K, Say L. Expanding contraceptive choice in the developing world: lessons from the Lao People's Republic and the Republic of Zambia. Eur J Contracept Reprod Health Care. 2013;18:421–34.

9 Blanc A, Tsui AO, Croft TN, Trevitt JL. Patterns and trends in adolescents' contraceptive use and discontinuation in developing countries and comparisons with adult women. Int Perspect Sex Reprod Health. 2009;35(2):63–71.

10 Singh S, Darroch JE. Adding it up: costs and benefits of contraceptive services – estimates for 2012. New York (NY): Guttmacher Institute and United Nations Population Fund (UNFPA); 2012 (https://www.guttmacher.org/pubs/AIU-2012-estimates.pdf, accessed 24 March 2015).

Confederation of Midwives (ICM) to update the membership of these societies about the revised recommendations. Once translations of the document in other official languages of the UN become available, opportunities to ensure effective dissemination will be actively sought. An evaluation survey targeting ministries of health, WHO offices and partners, professional organizations and civil society will be fielded to assess the extent and effectiveness of the dissemination, evaluate the level of implementation of the guidance into national policies, and identify areas for further refinement and research gaps in contraceptive eligibility criteria.

1.4 Reviewed recommendations

The Guideline Development Group (GDG) determined priority topics to be addressed as part of the revision process for the fifth edition (see Table 1.1).

Information on using the recommendations in practice, as well as recommendations in the fifth edition (new, revised and confirmed) are presented in Part II, sections 2.3 and 2.7, starting on p. 91. A summary of changes between the fourth edition of the MEC and the updated fifth edition is available in Part II (see section 2.6 and Tables 2.4–2.6, pp. 93–96).

1. Recommendations for combined hormonal contraceptives by age group

Question 1: Are women who use combined hormonal contraceptives (CHCs) at increased risk for fracture compared with women who do not use CHCs? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women of reproductive age
Intervention	CHC use
Comparator	Non-use of CHCs
Outcome	Fracture
Databases searched	PubMed and Cochrane Library

Question 2: Are women who use combined hormonal contraceptives (CHCs) at increased risk for decreased bone mineral density compared with women who do not use CHCs, with a specific focus on adolescents? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women of reproductive age (with a specific focus on adolescents)
Intervention	CHC use
Comparator	Non-use of CHCs
Outcome	Decreased bone mineral density
Databases searched	PubMed and Cochrane Library

Recommendations

- Women from menarche to < 40 years of age can use combined hormonal contraceptives (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) without restriction (MEC Category 1).
- Women 40 years and older can generally use combined hormonal contraceptive methods (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 2).

Remarks

- In 2014, the GDG focused specifically on the evidence pertaining to fracture risk among women of all ages, and the evidence for combined hormonal contraceptives (CHCs) and potential for decreased bone mineral density (BMD) among adolescents. BMD is a surrogate marker for fracture risk that may not be valid for premenopausal women, and therefore may not accurately predict current or future (postmenopausal) fracture risk *(1–3)*. The risk of cardiovascular disease increases with age and may also increase with CHC use. In the absence of other adverse clinical conditions, CHC can be used until menopause.
- Due to heterogeneity of study designs, contraceptive formulations and outcome measures a meta-analysis was not performed.
- 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, male or female, is recommended.

- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Evidence is inconsistent on the question of whether CHC use affects fracture risk *(4–15)*, although three recent studies show no effect *(4, 5, 15)*. CHC use may decrease BMD in adolescents, especially in those choosing very-low-dose formulations (< 30 µg ethinylestradiol-containing combined oral contraceptives) (16–29). CHC use has little to no effect on BMD in premenopausal women *(30–44)*, and may preserve bone mass in those who are perimenopausal *(45-54)*.

Quality of the evidence

(intervention versus comparator; outcome)

CHC use versus non-use of CHC; fracture risk (direct):	low
COC use versus non-use in adolescents; bone mineral density (indirect):	low
Combined contraceptive patch use versus non-use in adolescents; bone mineral density (indirect):	very low

GRADE table 1 (Question 1): Are women who use combined hormonal contraceptives (CHCs) at increased risk for fracture compared with women who do not use CHCs? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Oral combined hormonal contraceptive use vs non-use								
Fracture	3 cohort studies (n=128 255); 7 case-control studies (n=84 695 cases)	Serious limitations (1 good, 6 fair, 3 poor)	Serious inconsistency	No serious imprecision	Serious indirectness (no study specifically evaluated CHC use during adolescence)	No duration-response effect observed	Low	7 studies showed no association between CHC use and fracture risk, including 1 good-quality study (OR 1.05, 95% CI 0.86–1.29); 3 studies found a statistically significant but weak association (risk estimate range 1.07–1.3)[a]

CI: confidence interval; OR: odds ratio.
a Six studies evaluated any fracture, two studies hip fracture, two studies forearm fracture.

GRADE table 2 (Question 2): Are women who use combined hormonal contraceptives (CHCs) at increased risk for decreased bone mineral density compared with women who do not use CHCs, with a specific focus on adolescents? (Indirect evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Oral combined hormonal contraceptive use vs non-use in adolescent women								
Bone mass density (BMD)	1 RCT (n=83), 1 non-randomized trial (n=84); 11 cohort studies (n=3242)	Serious limitations (2 good, 5 fair, 6 poor)	Serious inconsistency	No serious imprecision	Serious indirectness (intermediate outcome)	1 study showed duration-response effect; variability in duration of follow-up	Low	9 studies showed oral CHC use associated with less BMD gain (or greater loss) than non-use, including the 2 good-quality studies; 4 studies showed no difference[a]
Patch use vs non-use in adolescent women								
BMD	1 non-randomized trial (n=10)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	Serious indirectness (intermediate outcome)	None	Very low	1 study found no effect of patch on BMD vs non-use

RCT: randomized controlled trial.
a Eight studies evaluated 30–35mcg ethinyl estradiol (EE) formulation (one 30–40mcg EE), six studies 15–20mcg EE, two not specified.

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2. Recommendations for combined hormonal contraceptives among breastfeeding women

Question 1: Among breastfeeding women, does initiation of combined hormonal contraceptives (CHCs) at < 6 weeks postpartum have negative effects on breastfeeding outcomes or infant outcomes, compared with no contraception or non-hormonal contraception? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Breastfeeding women
Intervention	Use of CHCs
Comparator	No contraception or use of non-hormonal contraception
Outcome	Breastfeeding outcomes (duration, exclusivity, supplementation) Infant outcomes (growth, health, development)
Databases searched	PubMed and Cochrane Library

Question 2: Among breastfeeding women, does initiation of combined hormonal contraceptives (CHCs) at ≥ 6 weeks postpartum have negative effects on breastfeeding outcomes or infant outcomes, compared with no contraception or non-hormonal contraception? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Breastfeeding women
Intervention	Use of CHCs
Comparator	No contraception or non-hormonal contraception
Outcome	Breastfeeding outcomes (duration, exclusivity, supplementation) Infant outcomes (growth, health, development)
Databases searched	PubMed and Cochrane Library

Recommendations

- Breastfeeding women < 6 weeks postpartum should not use combined hormonal contraceptives (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 4).
- Breastfeeding women ≥ 6 weeks to < 6 months postpartum (primarily breastfeeding) generally should not use CHCs (MEC Category 3).
- Breastfeeding women ≥ 6 months postpartum can generally use CHCs (MEC Category 2).

Remarks

- Due to heterogeneity of study designs, contraceptive formulations and outcome measures, a meta-analysis was not performed.
- Combined hormonal contraceptives (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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to combined oral contraceptives (COCs) during lactation. No consistent effects on infant growth or illness have been reported *(1–6)*. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs 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.

Quality of the evidence
< 6 weeks postpartum:
(method; outcome)

For COCs compared with progestogen-only pills (POPs), breastfeeding and infant outcomes:	low
For COCs compared with non-hormonal or non-use, breastfeeding continuation:	very low
For COCs compared with non-hormonal or non-use, breastfeeding duration:	very low
For COCs compared with non-hormonal or non-use, supplementation:	low
For COCs compared with non-hormonal or non-use, infant outcomes:	very low
For patch, ring, combined injectable contraceptives (CICs):	no evidence

≥ 6 weeks postpartum:
(method; outcome)

For COCs, breastfeeding continuation:	low
For COCs, breastfeeding duration:	very low
For COCs, breastfeeding episodes:	very low
For COCs, supplementation:	low
For COCs, infant outcomes:	low
For patch, ring, CICs:	no evidence

GRADE table 1 (Question 1): Among breastfeeding women, does initiation of combined hormonal contraceptives (CHCs) at < 6 weeks postpartum have negative effects on breastfeeding outcomes or infant outcomes, compared with no contraception or non-hormonal contraception? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Combined oral contraceptives (COCs) vs progestogen-only pills initiated at < 6 weeks postpartum								
Breastfeeding continuation	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Not applicable	Low	Ethinyl estradiol (EE) vs POP (1 RCT): 64% vs 64%, RR 1.0 (95% CI 0.78–1.3) at 8 weeks; 44% vs 41%, RR 1.1 (95% CI 0.71–1.6) at 6 months
Use of supplementation	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Not applicable	Low	EE vs POP (1 RCT): no difference at 8 weeks (data not provided)
Infant growth	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Not applicable	Low	EE vs POP (1 RCT): no difference in percent change in weight ($P = 0.56$), length ($P = 0.41$), or head circumference ($P = 0.79$) from weeks 2–8
COCs initiated at < 6 weeks postpartum vs non-hormonal or non-use								
Breastfeeding continuation	1 RCT; 2 non-randomized studies (n=550)	Very serious limitations (1 fair-quality RCT; 2 poor-quality studies)	Serious inconsistency	No serious imprecision	Serious indirectness (older COC formulations with mestranol)	Variability in outcomes assessed and duration of follow-up	Very low	1 RCT found EE COC associated with lower likelihood of breastfeeding continuation vs placebo or Cu-IUD at 6 months (84% vs 91% vs 95%, RR 0.92 [95% CI 0.82–1.0] vs placebo and 0.88 [95% CI 0.79–0.97] vs IUD) but no difference at 12 months (61% vs 59% vs 65%); 1 poor-quality study of various COCs found no difference in breastfeeding continuation at 6 weeks; 1 poor-quality study found initiation of mestranol at 2 weeks associated with lower likelihood vs initiation at 6 weeks (RR 0.40, 95% CI 0.17–0.96) or non-use (RR 0.29, 95% CI 0.13–0.64)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Breastfeeding duration	1 cohort study (n=696)	Very serious limitations (1 poor)	Cannot determine (1 study)	No serious imprecision	Serious indirectness (older estrogen component of COC formulations)	None	Very low	Various COCs (quinestrol, EE or mestranol) vs no COC (1 study): 2.5 to 4.6 vs 5.3 months, $P = 0.01$ for quinestrol and mestranol vs no COC
Use of supplementation	2 RCTs (n=727)	Serious limitations (1 fair, 1 poor)	No serious inconsistency	Serious imprecision	Serious indirectness (largest study [n=451] evaluated mestranol COC)	Variability in duration of follow-up	Low	1 fair-quality RCT found EE COC associated with increased likelihood of supplementation vs injectable placebo (19.4% vs 7.8%, RR 2.5 [95% CI 1.1–5.4]) or oral placebo (19.4% vs 8.0%, RR 2.4 [95% CI 1.0–5.8]) at day 91; 1 poor-quality RCT found mestranol COC associated with increased likelihood (12.3% vs 3.4%, RR 3.6 [95% CI 1.7–8.1]) at day 8
Infant growth	3 RCTs (n=712); 3 observational studies (n=100)	Very serious limitations (1 fair-quality RCT; 5 poor-quality studies)	Serious inconsistency	No serious imprecision	Serious indirectness (most studies evaluated mestranol COC)	Variability in outcomes assessed and duration of follow-up	Very low	1 fair-quality RCT found EE COC associated with lower infant weight at 6 months (7864 vs 8333) and 1 year (9938 vs 10 746) vs placebo; 4 poor-quality studies of mestranol COC reported conflicting results vs placebo or no COC (1 study no difference, 1 study growth greater with COC, and 2 studies less weight gain with COC)

CI: confidence interval; COC: combined oral contraceptive; EE: ethinyl estradiol; IUD: intrauterine device; POP: progestogen-only pill; RCT: randomized, controlled trial; RR: relative risk.

GRADE table 2 (Questions 2): Among breastfeeding women, does initiation of combined hormonal contraceptives (CHCs) at > 6 weeks postpartum have negative effects on breastfeeding outcomes or infant outcomes, compared with no contraception or non-hormonal contraception? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Combined oral contraceptive (COC) initiated at ≥ 6 weeks postpartum vs non-hormonal or non-use								
Breastfeeding continuation	2 non-randomized studies (n=339)	Serious limitations (2 fair)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	2 non-randomized studies found no difference between ethinyl estradiol (EE) COC vs non-COC (various) in breastfeeding continuation rates at 6 or 12 months (RR 0.96–0.99 in both studies)
Duration of breastfeeding	1 cohort study (n=96)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	1 cohort study found a difference between EE COC vs no oral contraceptives in duration of breastfeeding (3.7 vs 4.6 months, $P < 0.05$)
Breastfeeding episodes	1 cohort study (n=20)	Serious limitations (1 fair)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	1 small study found EE COC associated with more breastfeeding episodes than IUD on 7 of 21 days from postpartum day 42 to day 63 with no differences on other days
Use of supplementation	3 non-randomized studies; 1 cohort study (n=359 plus 1 study with < 50 women)	Serious limitations (3 fair, 1 poor)	Serious inconsistency	Serious imprecision	No indirectness	None	Low	2 fair-quality non-randomized studies found EE COC associated with increased likelihood of use of supplementation vs non-COC (various) at 3–12 months (differences ranged from 10–25% at various time points); 1 cohort study found no difference; 1 study found no difference between mestranol COC and IUD in age at supplementation
Infant growth	2 non-randomized studies; 3 cohort studies (n=455 plus 1 study with < 50 women)	Serious limitations (3 fair, 1 poor)	Serious inconsistency	Serious imprecision	No indirectness	None	Low	1 cohort study found EE COC associated with lower infant growth vs non-COC (various) from 3–4 months (599 vs 708 g) but not at 5–6 months and no difference in mean weight at 1 year; 1 non-randomized study found no difference in change in weight at 12–16 or 20–24 weeks; 1 non-randomized study found mestranol COC 0.1 mg with more infant growth than 0.075 mg or IUD; 1 cohort study found no difference in infant growth through 8 years; 1 cohort study showed no difference between EE COC and IUD from day 42 to 63

COC: combined oral contraceptive; EE: ethinyl estradiol; IUD: intrauterine device; RR: relative risk.

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3. Recommendations for combined hormonal contraceptives among postpartum women

Question 1: Among postpartum women, does combined hormonal contraceptive (CHC) use increase risk of venous thromboembolism (VTE) compared with no CHC use? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Postpartum women
Intervention	CHC use
Comparator	Non-use of CHCs
Outcome	VTE
Databases searched	PubMed and Cochrane Library

Question 2: Among women of reproductive age, do postpartum women have increased risk of venous thromboembolism (VTE) compared with non-postpartum, non-pregnant women? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women of reproductive age
Intervention	Postpartum
Comparator	Non-postpartum, non-pregnant
Outcome	VTE
Databases searched	PubMed and Cochrane Library

Recommendations

- Women who are < 21 days postpartum and do not have other risk factors for venous thromboembolism (VTE) generally should not use combined hormonal contraceptives (CHCs) (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 3).
- Women who are < 21 days postpartum with other risk factors for VTE should not use CHCs (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 4). For women ≤ 42 days 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.
- Women who are 21–42 days postpartum and do not have other risk factors for VTE can generally use CHCs (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 2). Women who are 21–42 days postpartum with other risk factors for VTE generally should not use CHC methods (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 3). For women ≤ 42 days 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.
- Women who are > 42 days postpartum can use CHC methods (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) without restriction (MEC Category 1).

Remarks

- The Guideline Development Group (GDG) considered the balance of benefits and harms for CHC use among postpartum women, at different time points postpartum, and with and without other risk factors for VTE, including the risk of VTE in the postpartum period, the risks associated with rapid repeat pregnancy, the benefits of preventing rapid repeat pregnancy, and the availability of other contraceptive methods that are safe for use by postpartum women. The GDG also considered that risk of pregnancy during the first 21 days postpartum is very low, but increases after that time in non-breastfeeding women; ovulation before first menses is common *(1).*
- Due to heterogeneity of study designs, contraceptive formulations and outcome measures, a meta-analysis was not performed.
- 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the

right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the 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 *(2)*. 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 *(3–7)*.

Quality of the evidence
(intervention versus comparator; outcome)

CHC use versus non-CHC use postpartum; VTE (direct):	very low
First 6 weeks postpartum versus non-pregnant, non-postpartum; VTE (indirect):	low

GRADE table 1 (Question 1): Among postpartum women, does combined hormonal contraceptive (CHC) use increase risk of venous thromboembolism (VTE) compared with no CHC use? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
CHC use vs non-use in postpartum period								
Venous thromboembolism (VTE)	1 cohort study (773 017 person-years)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	VTE (1 study): rate ratio 1.3 (95% CI 0.3–5.2) in weeks 0–6 for CHC use vs non-use; incidence 4.9 (95% CI 0.6–18) vs 3.5 (95% CI 3.1–3.9) per 1000 person-years in weeks 0–6 and 0.7 (95% CI 0.3–1.6) vs 0.3 (95% CI 0.2–0.5) per 1000 person-years in weeks 7–13

CI: confidence interval.

GRADE table 2 (Question 2): Among women of reproductive age, do postpartum women have increased risk of venous thromboembolism (VTE) compared with non-postpartum, non-pregnant women? (Indirect evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
First 6 weeks postpartum vs non-pregnant, non-postpartum								
Venous thromboembolism (VTE)	4 cohort studies (n=3 365 650); 1 case-control study (285 cases)	Serious limitations (1 good, 4 fair)	No serious inconsistency (direction consistent; variability in magnitude)	No serious imprecision	Serious indirectness (not women using CHC vs not using CHC)	Duration-response effect in first 6 weeks, first 1–3 weeks associated with highest risk;[a] weeks 0–6 associated with higher risk than after week 7[b]	Low	Any VTE (2 studies): rate ratio 21.5 (CI not available) and 22 (95% CI 18–27) and OR 84 (95% CI 32–223) and 12 (95% CI 7.9–18.6) DVT (1 study): incidence ratio 15 (95% CI 13–18) Pulmonary embolism (1 study): incidence ratio 9.2 (95% CI 6.5–13)

CI: confidence interval; OR: odds ratio.
a Based on 5 studies, 4 of which reported incidence by week and 1 of which reported the proportion of VTE events by week.
b Based on 6 studies.

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4. Recommendations for combined hormonal contraceptives among women with superficial venous disorders

The disease nomenclature has been updated to reflect current recognized standard terminology and more accurately describe the condition and sub-conditions. The overall name of the condition has been changed to "superficial venous disorders". The subcondition "superficial thrombophlebitis" has been changed to "superficial venous thrombosis" (SVT).

Question 1: Among women with varicose veins, does use of combined hormonal contraceptives (CHCs) increase the risk of venous thromboembolism (VTE) or superficial venous thrombosis (SVT) compared with non-use of CHCs? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women with varicose veins
Intervention	Use of CHCs
Comparator	Non-use of CHCs
Outcome	VTE or SVT
Databases searched	PubMed and Cochrane Library

Question 2: Among women with superficial venous thrombosis (SVT), does use of combined hormonal contraceptives (CHCs) increase the risk of venous thromboembolism (VTE) compared with non-use of CHCs? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women with SVT
Intervention	Use of CHCs
Comparator	Non-use of CHCs
Outcome	VTE
Databases searched	PubMed and Cochrane Library

Recommendations

- Women with varicose veins can use combined hormonal contraceptives (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) without restriction (MEC Category 1).
- Women with superficial venous thrombosis (SVT) can generally use combined hormonal contraceptives (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 2). SVT may be associated with an increased risk of venous thromboembolism (VTE).

Remarks

- Due to heterogeneity of study designs, contraceptive formulations and outcome measures, a meta-analysis was not performed.
- 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

One study suggested that among women with varicose veins, the rate of VTE and SVT was higher in oral contraceptive users compared with non-users; however, statistical significance was not reported and the number of events was small *(1)*. One study demonstrated that among women with SVT, the risk of VTE was higher in oral contraceptive users compared with non-users *(2)*.

Quality of the evidence

Women with varicose veins:
(intervention versus comparator; outcome)

Use of CHCs versus non-use of CHCs; risk of VTE:	very low
Use of CHCs versus non-use of CHCs; risk of SVT:	very low

Women with superficial venous thrombosis:
(intervention versus comparator; outcome)

Use of CHCs versus non-use of CHCs; risk of VTE:	very low

GRADE table 1 (Question 1): Among women with varicose veins, does use of combined hormonal contraceptives (CHCs) increase the risk of venous thromboembolism (VTE) or superficial venous thrombosis (SVT) compared with non-use of CHCs? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Use of oral contraceptives vs non-use in women with varicose veins								
Deep vein thrombosis (DVT)	1 cohort study (96 335 women-years)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	IRR 5.97 in women with history of varicose veins; 4.42 in women with no history of varicose veins
Superficial venous thrombosis (SVT)	1 cohort (96 335 women-years)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	IRR 1.40 in women with history of varicose veins; 2.45 in women with no history of varicose veins

IRR: incidence rate ratio.

GRADE table 2 (Question 2): Among women with superficial venous thrombosis (SVT), does use of combined hormonal contraceptives (CHCs) increase the risk of venous thromboembolism (VTE) compared with non-use of CHCs? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Use of oral contraceptives vs non-use in women with superficial venous thrombosis								
Venous thromboembolism (VTE)	1 case-control study (1445 cases)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	OR 4.0 (95% CI 3.3–4.7) for OC use vs non-use with no history of SVT; OR 8.4 for OC use vs non-use with history of SVT (based on OR of 5.1 (95% CI 2.8–9.5) for no OC use and 43.0 (95% CI 15.5–119.3) OC use, reference no SVT history/no OC use)[a]

CI: confidence interval; OC: oral contraceptive; OR: odds ratio.
a Adjusted for age, BMI, smoking and family history of VTE; similar pattern observed for DVT, DVT + PE, and PE.

References

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5. Recommendations for combined hormonal contraceptives among women with dyslipidaemias

Question 1: Among women with known dyslipidaemias, without other known cardiovascular risk factors, does combined hormonal contraceptive (CHC) use increase risk of arterial thromboembolism (ATE), venous thromboembolism (VTE) or pancreatitis compared with no CHC use? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort and case-control studies
Population	Women of reproductive age with dyslipidaemia
Intervention	CHC use
Comparator	Non-use of CHCs
Outcome	Arterial thrombotic events (e.g. myocardial infarction or thrombotic stroke), VTE or pancreatitis
Databases searched	PubMed and Cochrane Library

Question 2: Among women of reproductive age using combined hormonal contraception (CHC), are women with known dyslipidaemias without other known cardiovascular risk factors at increased risk for ATE, VTE or pancreatitis compared to women without known dyslipidaemias? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort and case-control studies
Population	Women of reproductive age using CHCs
Intervention	Known dyslipidaemia without other known cardiovascular risk factors
Comparator	No known dyslipidaemia
Outcome	ATE or VTE or pancreatitis
Databases searched	PubMed and Cochrane Library

Question 3: Among women with known dyslipidaemias without other known cardiovascular risk factors, does combined hormonal contraceptive (CHC) use increase risk for worsening of lipid abnormalities compared with no CHC use? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort and case-control studies
Population	Women of reproductive age with dyslipidaemia
Intervention	CHC use
Comparator	Non-use of CHCs
Outcome	Worsening of lipid abnormalities (e.g. increase in total cholesterol, LDL or triglycerides; decrease in HDL)
Databases searched	PubMed and Cochrane Library

Recommendations

- Women with known dyslipidaemias without other known cardiovascular risk factors can generally use combined hormonal contraceptive methods (combined oral contraceptives, combined contraceptive patch, combined contraceptive vaginal ring, combined injectable contraceptives) (MEC Category 2). Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening. Increased levels of total cholesterol, low-density lipoprotein (LDL) and triglycerides, as well as decreased levels of high-density lipoprotein (HDL), are known risk factors for cardiovascular disease. Women with known severe genetic lipid disorders at much higher lifetime risk for cardiovascular disease may warrant further clinical consideration.

Remarks

- The Guideline Development Group (GDG) determined that the existing condition name, “known hyperlipidaemias”, should be changed to “known dyslipidaemias” to better describe the spectrum of clinically important lipid abnormalities. They also specified that the condition should include only women “without other known cardiovascular risk factors” for better clarity.
- The GDG noted that the baseline absolute risk for cardiovascular disease among women of reproductive age is very low. Using available cardiovascular risk prediction

models, even among healthy perimenopausal women with high total cholesterol and normal HDL, 10-year risks for cardiovascular disease remain low. The most recent guidelines from the Fifth Joint Task Force of the European Society of Cardiology, published in 2012, predict that a healthy woman aged 45–49 years with total cholesterol levels greater than 280 mg/dL has < 1% 10-year risk for fatal myocardial infarction (MI) or stroke; similarly, recent guidelines released by the American College of Cardiology and the American Heart Association predict a 1.9% 10-year risk for a non-fatal or fatal first MI or stroke. Further, it was concluded that even if combined oral contraceptive (COC) use increases risk for MI or stroke among women of reproductive age with known dyslipidaemias and no other risk factors for cardiovascular disease, the absolute risk for these serious adverse events remains low.

- Use of combined hormonal contraception (CHC) among women with severe genetic lipid disorders may warrant further clinical consideration given that these women are at much higher lifetime risk for cardiovascular disease.
- The GDG determined that risk for arterial thrombotic events was the main safety concern for women with known dyslipidaemias without other cardiovascular risk factors. Independent of COC use, there does not appear to be a clear association between dyslipidaemia and risk for VTE among women of reproductive age, and indirect evidence from one study identified in our systematic review noted only a slight increased risk for VTE among COC users with the condition compared to users without the condition. No comparative data were available to assess the risk of pancreatitis among women with known dyslipidaemias, and while it is well established that elevated triglyceride levels are associated with acute pancreatitis, severe hypertriglyceridemia is a very rare condition with a risk for pancreatitis associated with triglyceride levels ≥ 1000 mg/dL estimated at approximately 5%.
- Due to heterogeneity of study designs, contraceptive formulations and outcome measures, a meta-analysis was not performed.
- 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

One case-control study suggested an increased risk for MI among COC users with hypercholesterolemia compared to non-users without hypercholesterolemia *(1)*. One retrospective cohort study suggested an increased risk for stroke and VTE among COC users with dyslipidaemia compared to COC users without dyslipidaemia *(2)*. One prospective cohort study suggested no worsening of lipid abnormalities among CHC users with dyslipidaemia compared to non-users with dyslipidaemia *(3)*.

Quality of the evidence

CHC use versus non-use of CHCs; ATE, VTE or pancreatitis (direct):	very low
Know dyslipidaemia versus no known dylipidaemia; ATE, VTE or pancreatitis (indirect):	very low
CHC use versus non-use of CHC; risk of lipid abnormalities (indirect):	very low

GRADE table 1 (Question 1): Among women with known dyslipidaemias without other known cardiovascular risk factors, does combined hormonal contraceptive (CHC) use increase risk of arterial thromboembolism (ATE), venous thromboembolism (VTE) or pancreatitis compared with no CHC use? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Use of combined oral contraceptives (COCs) vs non-use in women with hyperlipidaemia								
Myocardial infarction	1 case-control study (248 cases)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	OR 7.5 for COC use vs no COC use, based on OR 24.7 (95% CI 5.6–108.5) for COC use/ hyperlipidemia and 3.3 (95% CI 1.6–6.8) for no COC use/hyperlipidaemia, reference no COC use/no hyperlipidaemia

CI: confidence interval; OR: odds ratio

GRADE table 2 (Question 2): Among women of reproductive age using combined hormonal contraception (CHC), are women with known dyslipidaemias without other known cardiovascular risk factors at increased risk for ATE, VTE or pancreatitis compared to women without known dyslipidaemias? (Indirect evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Women with hyperlipidaemia vs no hyperlipidaemia prescribed combined oral contraceptives								
Deep vein thrombosis (DVT) and pulmonary embolism (PE)	1 cohort study (n=329 995)	Very serious limitations (1 poor)	Cannot determine (1 study)	No serious imprecision	Serious indirectness (not COC use vs non-use)	None	Very low	8.51 vs 6.14 per 10 000 woman-years, IRR 1.39 (95% CI 1.04–1.85)
Worsening hyperlipidemia in users of combined oral contraceptives vs non-users								
Transient ischemic attacks and cerebrovascular accidents	1 cohort study (n=329 995)	Very serious limitations (1 poor)	Cannot determine (1 study)	No serious imprecision	Serious indirectness (not COC use vs non-use)	None	Very low	10.14 vs 5.76 per 10 000 woman years, IRR 1.76 (95% CI 1.51–2.06)

CI: confidence interval; IRR: incidence rate ratio.

References

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6. Recommendations for progestogen-only contraceptives and levonorgestrel-releasing intrauterine devices among breastfeeding women

Question 1: Among breastfeeding women (and their infants), does the use of progestogen-only contraceptives (POCs) and levonorgestrel-releasing intrauterine devices (LNG-IUDs) have an impact on breastfeeding or infant health outcomes compared with those not using POCs? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Breastfeeding women and their infants
Intervention	Use of POCs or LNG-IUDs
Comparator	Non-use of POCs
Outcome	Breastfeeding continuation and exclusivity/ supplementation; infant growth (as measured by weight, length, head circumference, arm circumference or skin-fold thickness); infant health (as measured by illness and mortality); infant development
Databases searched	PubMed and Cochrane Library

Question 2: Among breastfeeding women (and their infants), does the use of progestogen-only contraceptives (POCs) and levonorgestrel-releasing intrauterine devices (LNG-IUDs) initiated up to 6 weeks postpartum have an impact on breastfeeding or infant health outcomes compared with initiation after 6 weeks postpartum? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Breastfeeding women and their infants
Intervention	Use of POCs or LNG-IUDs initiated ≤ 6 weeks postpartum
Comparator	Use of POCs or LNG-IUDs initiated > 6 weeks postpartum
Outcome	Breastfeeding continuation and exclusivity/ supplementation; infant growth (as measured by weight, length, head circumference, arm circumference or skin-fold thickness); infant health (as measured by illness and mortality); infant development
Databases searched	PubMed and Cochrane Library

6a. Recommendations for use of progestogen-only contraceptives (pills, injectables, implants)

< 6 weeks postpartum

- Breastfeeding women who are < 6 weeks postpartum can generally use progestogen-only pills (POPs), and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 2).
- Breastfeeding women who are < 6 weeks postpartum generally should not use progestogen-only injectables (DMPA/NET-EN) (MEC Category 3). There is theoretical concern about the potential exposure of the neonate to DMPA/NET-EN during the first 6 weeks postpartum. However, in many settings pregnancy-related morbidity and mortality risks are high, and access to services is limited. In such settings, DMPA/NET-EN may be one of the few types of methods widely available and accessible to breastfeeding women immediately postpartum.

≥ 6 weeks to < 6 months postpartum

- Breastfeeding women who are 6 weeks to < 6 months postpartum can use without restriction the following contraceptive methods: POPs, progestogen-only injectables (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1).

≥ 6 months postpartum

- Breastfeeding women who are ≥ 6 months postpartum can use without restriction the following contraceptive methods: POPs, progestogen-only injectables (DMPA and NET-EN), and LNG and ETG implants (MEC Category 1).

6b. Recommendations for use of levonorgestrel-releasing intrauterine devices (LNG-IUDs)

< 48 hours postpartum

- Breastfeeding women who are < 48 hours postpartum can generally use LNG-IUDs (MEC Category 2).

≥ 48 hours to < 4 weeks postpartum

- Breastfeeding (and non-breastfeeding) women generally should not have an LNG-IUD inserted from 48 hours to < 4 weeks postpartum (MEC Category 3).

≥ 4 weeks postpartum

- Breastfeeding (and non-breastfeeding) women can use an LNG-IUD without restriction at ≥ 4 weeks postpartum (MEC Category 1).

Puerperal sepsis

- Breastfeeding (and non-breastfeeding) women with puerperal sepsis should not have an LNG-IUD inserted (MEC Category 4).

Remarks

- Animal data suggest an effect of progesterone on the developing brain; whether similar effects occur following progestogen exposure in humans is unclear *(1–3)*. Available data from clinical and observational trials do not suggest an increased risk for either breastfeeding performance or infant health outcomes with use of progestogen-only injectables compared to outcomes in studies using other progestogen-only methods *(4–8)*. However, the Guideline Development Group felt that, as infants in the first 6 weeks of life may be exposed to higher hormone levels with use of progestogen-only injectables, as compared to the exposure using other methods of progestogen-only contraceptives (POCs), the theoretical risks of progestogen-only injectables may outweigh the benefits, particularly in settings with access to a wide variety of contraceptive methods.
- Due to heterogeneity of study designs, contraceptive methods/formulations and outcome measures, a meta-analysis was not performed.
- 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Forty-seven articles reporting on 45 different studies were identified in the systematic review that investigated the use of POCs in breastfeeding women and reported clinically relevant outcomes of infant growth, health or breastfeeding performance. Direct evidence demonstrates no effect of POCs on breastfeeding performance *(4–51)*, and generally demonstrates no harmful effects on infant growth, health or development *(6, 7, 28, 42)*. However, these studies have been inadequately designed to determine whether a risk of long-term effects exists.

One randomized trial found that immediate insertion of the LNG-IUD was associated with decreased breastfeeding duration compared with delayed insertion *(5)*. Two other randomized controlled trials assessing early versus delayed initiation of POCs failed to show a difference in breastfeeding outcomes *(4, 16)*. In other studies, initiation of LNG-IUD after 4 weeks postpartum demonstrated no detrimental effect on breastfeeding outcomes *(11, 13, 45)*.

Quality of the evidence
< 6 weeks postpartum:

Breastfeeding outcomes

Progestogen-only pills (POPs):

Breastfeeding continuation, breastfeeding duration:	low
Use of supplementation:	very low

Progestogen-only injectables (DMPA/NET-EN):

Breastfeeding duration and use of supplementation:	low
Breastfeeding continuation:	very low

Progestogen-containing implants:

Breastfeeding continuation, breastfeeding episodes, breastfeeding duration, and use of supplementation:	very low

LNG-IUD:

Breastfeeding continuation anxd breastfeeding duration:	very low

Infant outcomes

POPs:

Infant growth:	very low

Progestogen-only injectables (DMPA/NET-EN):

Infant growth:	low

Progestogen-containing implants:

Infant growth:	low

LNG-IUD:

Infant growth:	very low

Progestogen-only injectables (DMPA/NET-EN):

Infant growth:	low

Progestogen-containing implants:

Infant growth:	low

LNG-IUD:

Infant growth:	very low

≥ 6 weeks postpartum:

Breastfeeding outcomes

POPs:

Breastfeeding duration:	low
Breastfeeding continuation and use of supplementation:	very low

Progestogen-only injectables (DMPA/NET-EN):

Breastfeeding duration:	low
Breastfeeding continuation and use of supplementation:	very low

Progestogen-containing implants:

Breastfeeding duration and use of supplementation:	low
Breastfeeding continuation:	very low

LNG-IUD:

Breastfeeding duration and use of supplementation:	very low

Infant outcomes

POPs:

Infant growth:	low

GRADE table 1 (Question 1): Among breastfeeding women (and their infants), does the use of progestogen-only contraceptives (POCs) and levonorgestrel-releasing intrauterine devices (IUDs) have an impact on breastfeeding or infant health outcomes compared with those not using POCs? (Direct evidence)

Question 2: Among breastfeeding women (and their infants), does the use of progestogen-only contraceptives (POCs) and levonorgestrel-releasing intrauterine devices (LNG-IUDs) initiated up to 6 weeks postpartum have an impact on breastfeeding or infant health outcomes compared with initiation after 6 weeks postpartum? (Direct evidence)

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Progestogen-only pill (POP) vs combined oral contraceptive (COC) initiated at < 6 weeks postpartum								
Breastfeeding continuation	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Low	Norethindrone vs ethinyl estradiol (EE) COC (1 RCT): 64% vs 64%, RR 0.99 (95% CI 0.76–1.3) at 8 weeks; 41% vs 44%, RR 0.94 (95% CI 0.63–1.4) at 6 months
Use of supplementation	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Low	Norethindrone vs EE COC (1 RCT): no difference at 8 weeks (data not provided)
Infant growth	1 RCT (n=127)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Low	Norethindrone vs EE COC (1 RCT): no difference in percent change in weight ($P = 0.56$), length ($P = 0.41$), or head circumference ($P = 0.79$) from weeks 2–8
LNG-IUD initiated at < 6 weeks postpartum vs non-hormonal contraception								
Breastfeeding continuation	1 RCT (n=110)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Very low	LNG-UD (30 mcg/d or 10 mcg/d) vs Cu-IUD (1 RCT): 58% vs 79% at 8 months, RR 0.74 (95% CI 0.57–0.95)
Breastfeeding duration	1 RCT (n=110)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Very low	LNG-IUD 30 mcg/d vs LNG IUD 10 mcg/d vs Cu-IUD (1 RCT): 197 vs 182 vs 208 days ($P > 0.05$)
Infant growth	1 RCT (n=110)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	NA	Very low	LNG-IUD (30 mcg/d or 10 mcg/d) vs Cu-IUD (1 RCT): no differences through 12 months

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Progestogen-only injectable initiated at < 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	3 cohort studies (n=617)	Very serious limitations (1 fair, 2 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	No clear differences in 2 studies; in a 3rd study weaning occurred later with DMPA or NET-EN
Use of supplementation	5 cohort studies (n=1370)	Very serious limitations (1 fair, 4 poor)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	All 5 studies found DMPA or NET-EN associated with similar or lower likelihood of exclusive breastfeeding
Duration of breastfeeding	5 cohort studies (n=1732)	Very serious limitations (1 fair, 4 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	All 5 studies found DMPA associated with no difference or increased duration of breastfeeding vs non-hormonal methods
Infant growth	6 cohort studies (n=4403)	Very serious limitations (5 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	None of 5 studies found DMPA or NET-EN associated with decreased infant growth; 1 study found progestogen-only injectable associated with increased weight gain through 3 months
POPs initiated at < 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	1 non-randomized trial (n=273); 3 cohort studies (n=756)	Serious limitations (1 fair-quality cohort study, 3 poor-quality studies)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	None of 4 studies found various POPs associated with lower likelihood of breastfeeding continuation; 2 studies found POPs associated with higher likelihood of breastfeeding continuation
Breastfeeding initiation	1 RCT (n=20) and 1 non-randomized trial (n=20)	Very serious limitations (2 poor)	No serious inconsistency	Very serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	1 RCT found no difference between norethisterone at ≤ 14 hours postpartum (PP) vs placebo in breastfeeding initiation; 1 non-randomized trial found lynestrenol at 2 days PP associated with initiation of breastfeeding at 3 vs 5 days PP with placebo

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Duration of breastfeeding	2 cohort studies (n=572)	Very serious limitations (2 poor)	No serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	2 studies found POPs associated with somewhat longer duration of breastfeeding vs non-hormonal comparators
Use of supplementation	2 cohort studies (n=1000)	Very serious limitations (1 fair, 1 poor)	Serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	1 fair-quality study found norgestrel associated with more frequent supplementary feeding but no difference in proportion of women supplementing; 1 poor-quality study found LNG associated with somewhat later initiation of supplementation (5.4 vs 4.6 months PP)
Infant growth	1 RCT (n=20), 1 non-randomized trial (n=20); 3 cohort studies (n=1083)	Serious limitations (2 fair-quality cohort studies, 3 poor-quality studies)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	4 studies found no difference on measures of infant growth; 1 small, poor-quality, non-randomized study found greater increase with lynestrenol than placebo
Progestogen-containing implants initiated at < 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	3 cohort studies (n=520)	Very serious limitations (1 fair, 2 poor)	Serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	3 studies reported conflicting findings regarding effects of progestogen-containing implants on measures of breastfeeding continuation; the 1 fair-quality study found no difference between nomegestrol implant in 2nd month PP vs Cu-IUD
Breastfeeding episodes	2 cohort studies (n=392)	Very serious limitations (1 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	2 studies found no differences in breastfeeding frequency
Duration of breastfeeding	1 cohort study (n=80)	Serious limitations (1 fair)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	1 fair-quality cohort study found no difference between etonogestrel (ETG) implant at 28–56 days PP vs Cu-IUD in duration of breastfeeding

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Use of supplementation	3 cohort studies (n=430)	Very serious limitations (1 fair, 2 poor)	Serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	2 studies found no difference in use of supplementation; 1 study found norethindrone associated with increased likelihood of supplementation at 3 months
Infant growth	6 cohort studies (n=870)	Serious limitations (2 fair, 4 poor)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and assessment of outcomes[a]	Low	2 fair-quality and 2 poor-quality studies found no difference in measures of infant growth; 1 poor-quality study found LNG associated with more weight gain than Cu-IUD; 1 poor-quality study found LNG associated with slower weight gain than Cu-IUD or barrier/no method
Multiple progestogen-only methods initiated at < 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	1 cohort study (n=319)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	1 study found no difference between LNG implant or POP prior to discharge vs non-hormonal contraception in breastfeeding continuation at 2–6 weeks PP
Use of supplementation	1 cohort study (n=319)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	1 study found no difference between LNG implant or POP prior to discharge vs non-hormonal contraception in use of supplementation at 2–6 weeks PP
Non-orally available progesterone initiated at < 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	2 cohort studies (n=1092)	Very serious limitations (1 fair, 1 poor)	Serious inconsistency	Serious imprecision	No indirectness	None	Very low	1 fair-quality study found progesterone pellets at 30–35 days PP associated with decreased likelihood of breastfeeding at 6 months (51% vs 58%) and 12 months (11% vs 18%); 1 poor-quality study found no difference between progesterone pellets at 30 or 60 days vs Cu-IUD or placebo injection in breastfeeding rates
Use of supplementation	2 cohort studies (n=1092)	Very serious limitations (1 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	None	Very low	2 studies found no differences in use of supplementation

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Infant growth	2 cohort studies (n=1092)	Very serious limitations (1 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	None	Very low	2 studies found no differences in infant growth
LNG-IUD initiated at > 6 weeks postpartum vs non-hormonal								
Duration of breastfeeding	1 RCT (n=320)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	LNG-IUD at 6–8 weeks PP vs Cu-IUD (1 RCT): 149 vs 160 days
Use of supplementation	1 RCT (n=320)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	LNG-IUD at 6–8 weeks PP vs Cu-IUD (1 RCT): no difference in exclusive breastfeeding
Infant growth	1 RCT (n=320)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	LNG-IUD at 6–8 weeks PP vs Cu-IUD (1 RCT): no difference in infant growth
Progestogen-only injectable initiated at > 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	1 RCT (n=170)	Very serious limitations (1 poor)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	DMPA at 6 weeks PP vs non-hormonal (1 RCT): no difference in rates of discontinuation
Duration of breastfeeding	1 cohort study (n=1538)	Serious limitations (1 fair)	Cannot determine (1 study)	No serious imprecision	No indirectness	None	Low	DMPA or NET-EN at 6–8 weeks PP vs non-hormonal contraception (1 cohort study): no difference in duration of breastfeeding
Use of supplementation	1 RCT (n=170); 1 cohort study (n=212)	Very serious limitations (2 poor)	No serious inconsistency	Serious imprecision	No indirectness	None	Very low	2 studies found no differences in use of supplementation
Infant growth	1 RCT (n=170); 2 cohort studies (n=1750)	Very serious limitations (1 fair-quality cohort study, 2 poor-quality studies)	No serious inconsistency	No serious imprecision	No indirectness	Variability in outcomes[a]	Low	None of 3 studies found decreased infant growth with DMPA or NET-EN; 2 studies reported some findings suggesting greater weight gain

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
POP initiated at > 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	1 RCT (n=144)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	Norgestrel at 6 weeks PP vs non-hormonal contraception (1 RCT): no difference in discontinuation of breastfeeding
Duration of breastfeeding	2 cohort studies (n=1709)	Serious limitations (2 fair)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions[a]	Low	2 studies found no difference in breastfeeding duration
Use of supplementation	1 RCT (n=144); 1 non-randomized trial (n=120)	Very serious limitations (2 poor)	Serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	1 RCT found no difference in use of supplementation and 1 non-randomized trial found lower mean age at supplementation with lynestrenol vs IUD + placebo (11 vs 15 weeks, *P* not reported)
Infant growth	1 RCT (n=144); 3 non-randomized studies (n=1829)	Serious limitations (2 fair-quality cohort studies, 2 poor-quality studies)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	4 studies found no difference in measures of infant growth
Progestogen-only implant or progestogen-containing IUD initiated at > 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	2 cohort studies (n=57)	Very serious limitations (2 poor)	No serious inconsistency	Very serious imprecision	No indirectness	None	Very low	2 studies found no difference in breastfeeding rates
Breastfeeding duration	4 cohort studies (n=2329)	Serious limitations (4 fair)	No serious inconsistency	No serious imprecision	No indirectness	Variability in outcomes[a]	Low	4 studies found no difference in breastfeeding duration

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Use of supplementation	3 cohort studies (n=549)	Serious limitations (2 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	3 studies found no difference in use of supplementation
Infant growth	6 cohort studies (n=2386)	Serious limitations (4 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	6 studies found no difference in measures of infant growth
Multiple progestogen-only methods initiated at > 6 weeks postpartum vs non-hormonal								
Breastfeeding duration	1 cohort study (n=34)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	DMPA, POP or LNG-IUD vs non-hormonal contraception (1 cohort study): 183 vs 183 days (P =0.38)
Infant growth	1 cohort study (n=140)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	DMPA at 6 weeks PP vs non-hormonal contraception (1 cohort study): no difference in weight through 26 weeks PP
Non-orally available progesterone initiated at > 6 weeks postpartum vs non-hormonal								
Breastfeeding continuation	2 cohort studies (n=788)	Very serious limitations (1 fair, 1 poor)	No serious inconsistency	No serious imprecision	No indirectness	Variability in interventions[a]	Very low	1 fair-quality study found elcometrine implant associated with higher breastfeeding rate at 3 and 5 months (but not at 9 and 12 months); 1 poor-quality study found no difference between progesterone pellets vs Cu-IUD or placebo at 6 or 13 months PP
Breastfeeding duration	1 cohort study (n=200)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	Nesterone implant at 55–60 days PP vs Cu-IUD (1 cohort study): 273 vs 263 days (NS)
Infant growth	3 cohort studies (n=988)	Serious limitations (2 fair, 1 poor)	No serious inconsistency	No serious imprecision	No indirectness	Variabilty in interventions and outcomes[a]	Low	3 studies found no differences in measures of infant growth

Factor	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Earlier vs later initiation of progestogen-only methods								
Breastfeeding continuation	2 RCTs (n=165) and 1 cohort study (n=35)	Serious limitations (2 fair-quality RCTs, 1 poor-quality cohort study)	No serious inconsistency	Serious imprecision	No indirectness	Variabilty in interventions and outcomes[a]	Low	1 RCT found immediate LNG-IUD associated with lower breastfeeding rate at 6 months vs initiation at 6–8 weeks PP (6% vs 24%, $P = 0.02$); 1 cohort study found norethindrone implant at 6 days PP associated with lower rate at 8 months (57% vs 67%); 1 RCT found no difference in rate of lactation failure
Breastfeeding duration	1 RCT (n=96)	Serious limitations (1 fair)	Not applicable 1 study)	Very serious imprecision	No indirectness	None	Very low	Immediate LNG-IUD vs 6–8 weeks PP (1 RCT): 5 vs 8.5 weeks (P=0.06)
Use of supplementation	3 RCTs (n=205) and 4 cohort studies (n=660)	Serious limitations (3 fair-quality RCTs, 1 fair- and 3 poor-quality cohort studies)	Serious inconsistency	No serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Very low	Inconsistent effects on use of supplementation among 7 studies
Infant growth	1 RCT (n=40) and 3 cohort studies (n=543)	Very serious limitations (1 fair-quality RCT, 3 poor-quality cohort studies)	No serious inconsistency	Serious imprecision	No indirectness	Variability in interventions and outcomes[a]	Low	4 studies found no differences in measures of infant growth

CI: confidence interval; COC: combined oral contraceptive; Cu-IUD: copper-bearing intrauterine device; EE: ethinyl estradiol; LNG-IUD: levonorgestrel intrauterine device; NA: not applicable; NS: not significant; POP: progestogen-only pill; PP: postpartum; RCT: randomized controlled trial; RR: relative risk.

[a] Refers to variability in the progestogen evaluated, timing of initiation of POC, outcome measures assessed, and/or timing of outcome assessment.

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7. Recommendations for safety of depot medroxyprogesterone acetate delivered subcutaneously

Question 1: What is the safety of depot medroxyprogesterone acetate (104 mg/0.65 mL) delivered subcutaneously (DMPA-SC) for women with medical conditions or other specific characteristics established within the World Health Organization's eligibility criteria for contraceptive use? (Direct evidence)

A. Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women of reproductive age with medical conditions or other specific characteristics
Intervention	Use of DMPA-SC
Comparator	Users of DMPA-intramuscular (DMPA-IM); for endometriosis included non-comparative prospective data
Outcome	Serious adverse events (i.e. ectopic pregnancy or method discontinuation due to a medical condition) or outcomes related to medical conditions (i.e. changes in weight, contraceptive efficacy, changes in bone mineral density)
Databases searched	PubMed and Cochrane Library

B. Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women of reproductive age using DMPA-SC
Intervention	Presence of medical condition or specific characteristics
Comparator	No medical condition or specific characteristic
Outcome	Serious adverse events (i.e. changes in weight, contraceptive efficacy, changes in bone mineral density)
Databases searched	PubMed and Cochrane Library

Question 2: Among healthy women or among a general population of women of reproductive age, do those who use depot medroxyprogesterone acetate (104 mg/0.65 mL) delivered subcutaneously (DMPA-SC) have an increased risk for serious adverse events or other relevant outcomes compared with those who use DMPA delivered intramuscularly (DMPA-IM)? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Healthy women or general population of reproductive-age women
Intervention	Use of DMPA-SC
Comparator	Users of DMPA-IM
Outcome	Serious adverse events or outcomes relevant to medical conditions (i.e. changes in weight, blood pressure, vaginal bleeding)
Databases searched	PubMed and Cochrane Library

Recommendations

Age:

- Young women (menarche to < 18 years) can generally use DMPA (MEC Category 2).
- Women between the ages of 18 and 45 years can use DMPA without restriction (MEC Category 1)
- Women > 45 years old can generally use DMPA (MEC Category 2).

Endometriosis:

- Women with endometriosis can use DMPA without restriction (MEC Category 1).

HIV:

- Women living with HIV who have asymptomatic or mild clinical disease (WHO stage 1 or 2) can use DMPA without restriction (MEC Category 1).
- Women living with HIV who have severe or advanced HIV clinical disease (WHO stage 3 or 4) can use DMPA without restriction (MEC Category 1).

Obesity:

- Women with a body mass index (BMI) ≥ 30 kg/m^2 can use DMPA without restriction (MEC Category 1).

- Young women (menarche to < 18 years) with a BMI ≥ 30 kg/m^2 can generally use DMPA (MEC Category 2).
- There is evidence for differential weight gain among normal-weight and obese adolescents who use DMPA, but not those using norethisterone enanthate (NET-EN). However, NET-EN is MEC Category 2 due to evidence regarding potential effects of NET-EN on bone mineral density among adolescents.

Remarks

- The Guideline Development Group determined that no change to the existing recommendations for DMPA was warranted with inclusion of DMPA-SC as a new method.
- The body of evidence evaluating use of DMPA-SC and DMPA-IM among healthy women of reproductive age suggests a similar safety profile. Due to heterogeneity of study designs and outcome measures, a meta-analysis was not performed.
- DMPA-SC 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

A randomized trial evaluating changes in bone mineral density (BMD) among adult DMPA-SC and IM users demonstrated no differences at two years of follow-up *(1)*. Limited evidence from three Phase 3 contraceptive trials reported no consistent differences in weight change or bleeding patterns according to age; adolescents aged < 18 years were not included in any studies *(1–3)*. Two prospective, non-comparative studies demonstrated that women with endometriosis treated with DMPA-SC for six months experienced minimal weight gain and decreases in BMD; serious adverse events were rare and DMPA-SC improved pain symptoms associated with the condition *(4, 5)*. A randomized cross-over study reported that women living with HIV tolerated injection of DMPA-SC and that experiences of serious adverse events were rare and occurred at similar rates as in users of DMPA-IM *(6)*. Evidence from three Phase 3 contraceptive trials and four reports from a small prospective cohort study reported similar contraceptive efficacy, weight change, bleeding patterns and other adverse effects, including variations in a number of biomarkers, among obese and non-obese DMPA-SC users *(1, 3, 7–12)*.

DMPA-IM and DMPA-SC appear to be therapeutically equivalent; the two formulations demonstrate similar pharmacokinetics, effects on serum estradiol levels and high contraceptive efficacy *(1)*. In addition, similar effects on weight change, bleeding patterns and experience of other adverse effects have been reported among healthy reproductive age users *(1, 3, 13)*.

Quality of the evidence

DMPA-SC and age:	very low
DMPA-SC and endometriosis:	very low
DMPA-SC and HIV:	very low
DMPA-SC and obesity:	very low
DMPA-SC versus DMPA; contraceptive efficacy (indirect):	very low
DMPA-SC versus DMPA; weight gain (indirect):	very low
DMPA-SC versus DMPA; changes in bleeding pattern (indirect):	very low.

GRADE table 1 (Question 1): What is the safety of depot medroxyprogesterone acetate (104 mg/0.65 mL) delivered subcutaneously (DMPA-SC) for women with medical conditions or other specific characteristics established within the World Health Organization's eligibility criteria for contraceptive use? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
DMPA-SC use in women in different BMI categories								
Contraceptive efficacy	1 RCT and 1 cohort from an RCT (n=2321)	Serious limitations (2 fair)	No serious inconsistency	No serious imprecision	No indirectness	None	Very low	No pregnancies in women in all BMI categories
Weight gain	2 non-randomized studies (n=2336)	Serious limitations (1 fair-quality and 1 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Very low	No differences in weight gain across BMI categories
Changes in bleeding patterns	1 study with pooled data from 3 studies (n=2321)	Serious limitations (1 fair)	Cannot determine (1 study)	No serious imprecision	No indirectness	None	Very low	No differences in bleeding patterns across BMI categories
Change in bone mineral density	1 cohort study (n=15)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	No indirectness	None	Very low	No differences in BMD changes across BMI categories
DMPA-SC use in women in different age groups								
Weight gain	1 study with pooled data from 3 studies (n=2321)	Serious limitations (1 fair)	Cannot determine (1 study)	No serious imprecision	No indirectness	None	Very low	No differences in weight gain across age categories
Changes in bleeding patterns	1 study with pooled data from 3 studies (n=2321)	Serious limitations (1 fair)	Cannot determine (1 study)	No serious imprecision	No indirectness	None	Very low	No differences in bleeding patterns across age categories

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Changes in bone mineral density	1 RCT (n=534)	No serious limitations (1 good)	Cannot determine (1 study)	Serious imprecision	No indirectness	BMD changes not reported by age category, enrolled women aged 18–35 years	Very low	Smaller decrease in median BMD with DMPA-SC vs DMPA-IM
DMPA-SC in women with endometriosis								
Weight gain	2 uncontrolled studies (n=289)	Very serious limitations (1 fair)	No serious inconsistency	Serious imprecision	No indirectness	No comparison group of women without endometriosis	Very low	Weight gain 0.70–0.95 kg at 6 months and 0.90–1.35 kg at 18 months
Change in bleeding pattern	2 uncontrolled studies (n=289)	Very serious limitations (1 fair)	No serious inconsistency	Serious imprecision	No indirectness	No comparison group of women without endometriosis	Very low	Increase in amenorrhoea 20% at 3 months and 24% at 6 months in 1 study; 1 study reported 35 bleeding or spotting days in 1st 90 days and 24 in 2nd 90 days
DMPA-SC vs DMPA-IM in women with HIV								
Contraceptive efficacy	1 RCT (n=357)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	Pregnancy rate 1.1% with both DMPA-SC and DMPA-IM
Change in bleeding pattern	1 RCT (n=357)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	No differences in menstrual irregularity, heavier bleeding

BMD: bone mass density; BMI: body mass index; DMPA: depot medroxyprogesterone acetate; IM: intramuscular; RCT: randomized controlled trial; SC: subcutaneous.

GRADE table 2 (Question 2): Among healthy women or among a general population of women of reproductive age, do those who use depot medroxyprogesterone acetate (104 mg/0.65 mL) delivered subcutaneously (DMPA-SC) have an increased risk for serious adverse events or other relevant outcomes compared with those who use DMPA delivered intramuscularly (DMPA-IM)? (Indirect evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
DMPA-SC vs DMPA-IM use in healthy women								
Contraceptive efficacy	1 RCT (n=534)	No serious limitations (1 good)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	Low rates of pregnancy with DMPA-SC and DMPA-IM
Weight gain	1 study with pooled data from 3 studies (n=2321)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	Median weight gain 4.5 kg with DMPA-SC vs 5.8 kg with DMPA-IM at 36 months
Change in bleeding pattern	1 RCT (n=534)	No serious limitations (1 good)	Cannot determine (1 study)	Serious imprecision	No indirectness	None	Very low	No differences in rates of intermenstrual bleeding or amenorrhoea between DMPA-SC vs DMPA-IM

DMPA: depot medroxyprogesterone acetate; IM: intramuscular; RCT: randomized controlled trial; SC: subcutaneous.

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8. Recommendations for safety of Sino-implant (II)

Question 1: What is the safety of the contraceptive implant Sino-implant (II) for women with medical conditions established within the World Health Organization's eligibility criteria for contraceptive use? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women with medical conditions or other specific characteristics
Intervention	Use of Sino-implant (II)
Comparator	Non-use of a hormonal contraceptive (i.e. either use of no contraceptive method or use of a non-hormonal method such as barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/vasectomy, etc.) or users of other implants (Norplant, Jadelle, Implanon/Nexplanon)
Outcome	Serious adverse events (i.e. ectopic pregnancy or method discontinuation due to a medical condition) or outcomes related to medical conditions (i.e. changes in weight, blood pressure, vaginal bleeding)
Databases searched	PubMed and Cochrane Library

Question 2: Among healthy women or among a general population of women of reproductive age, do those who use Sino-implant (II) have an increased risk for serious adverse events or other relevant outcomes compared with those who do not use Sino-implant (II)? (Indirect evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Healthy women or general population of reproductive-age women
Intervention	Use of Sino-implant (II)
Comparator	Users of non-hormonal contraceptive methods (i.e. either use of no contraceptive method or use of a non-hormonal method such as barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/ vasectomy, etc.) or users of other implants (Norplant, Jadelle, Implanon/Nexplanon)
Outcome	Serious adverse events (i.e. ectopic pregnancy or method discontinuation due to a medical condition) or outcomes related to medical conditions (i.e. changes in weight, blood pressure, vaginal bleeding)
Databases searched	PubMed and Cochrane Library

Recommendations

- Recommendations for Sino-implant (II) will be the same recommendations as for other levonorgestrel implants (see p. 143–158).

Remarks

- Although there was no direct evidence regarding Sino-implant (II) among women with medical conditions, studies were identified that looked at safety of the implant among healthy women compared to those who do not use the SI (II). In addition, the safety data from studies of other levonorgestrel (LNG) implants among women with medical conditions is used due to the similarity of SI (II) and other LNG implants in hormone formulation, quality profile and daily release rates. Given this, the panel decided to make the same recommendations for SI (II) as the other LNG implants. Due to heterogeneity of study designs and outcome measures, a meta-analysis was not performed.
- The Sino-implant (II) 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.

- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

No studies were identified that provided direct evidence on the use of the Sino-implant (II) among women with medical conditions in the MEC that included a comparison group. When looking at the studies on healthy women, evidence from four studies comparing SI (II) users with users of other LNG-containing implants demonstrates that SI (II) has a similar safety profile with no significant differences in serious adverse events such as ectopic pregnancy or discontinuation due to medical problems *(1–3)*.

When investigating serious adverse events in healthy women using SI (II), three articles were identified *(1–3)*. These three articles reported on four randomized controlled trials (RCTs) and found no difference between users of SI (II) and users of SI (I) or Norplant with respect to incidence of serious adverse events. Similar effects on selected markers of disease in healthy women were seen for healthy women using SI (II) compared to women using SI (I) or Norplant. These markers of disease were liver function *(3)*, weight *(1, 4–6)*, blood pressure *(1, 6)*, bone mineral density *(7)*, ovarian cysts and benign myomas *(6)*. Two studies provided limited evidence regarding menorrhagia *(1, 8)*. The studies suggest that SI (II) is not harmful and may be beneficial for women with menorrhagia. One RCT found an increased pregnancy rate among women weighing 70 kg or over using SI (II) *(9)*, while another RCT failed to find this association and also reported no association between duration of use, weight and pregnancy *(3)*.

Quality of the evidence

Women with medical conditions or other specific characteristics:
(intervention versus comparator; outcome)

Sino-implant (II) versus non-use of Sino-implant (II); serious adverse events (direct):	no evidence

Healthy women or general population of reproductive age women:
(intervention versus comparator; outcome)

Sino-impant (II) versus non-use of Sino-implant (II); various outcomes (indirect):	
Ectopic pregnancy:	low
Weight gain:	moderate
Blood loss:	low
Bone mineral density:	very low
Blood pressure:	low
Other adverse events:	very low
Pregnancy:	very low

GRADE table 1 (Question 2): Among healthy women or among a general population of women of reproductive age, do those who use Sino-implant (II) have an increased risk for serious adverse events or other relevant outcomes compared with those who do not use Sino-implant (II)? (Indirect evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Sino-implant (II) vs Sino-implant (I) or Norplant in healthy women								
Ectopic pregnancy	4 RCTs (24 972)	Serious limitations (4 fair)	No serious inconsistency	Serious imprecision	No indirectness	None	Low	Very few ectopic pregnancies and no clear difference in risk in 4 RCTs of SI (II) vs SI (I) or Norplant
Weight gain	3 RCTs (n=4443); 1 cohort study (n=617)	Serious limitations (2 fair- and 1 poor-quality RCT, 1 very poor-quality cohort study)	No serious inconsistency	No serious imprecision	No indirectness	None	Moderate	No difference between SI (II) and SI (I) or Norplant in weight gain in 3 studies; less weight gain with SI (II) than control (no method or non-hormonal) in 1 study
Blood loss, change in haemoglobin	2 RCTs (n=389)	Serious limitations (1 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	None	Low	No clear difference in blood loss or haemoglobin levels with SI (II) vs SI (I) or Norplant
Bone mineral density (BMD)	1 cross-sectional study (n=166)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	Serious indirectness (intermediate outcome)	None	Very low	No difference between SI (II), SI (I) and Norplant in BMD after ≥ 3 years
Blood pressure (BP)	1 RCT (n=2297); 1 cohort study (n=617)	Very serious limitations (1 fair-quality RCT, 1 very poor-quality cohort study)	No serious inconsistency	No serious imprecision	No indirectness	Variability in measures of blood pressure effects	Low	1 RCT found very few cases of increased BP with SI (II), SI (I), or Norplant; 1 cohort study found higher BP with control (no method or non-hormonal) than SI (II)
Other adverse events	2 RCTs (n=22 672)	Serious limitations (2 fair)	No serious inconsistency	No serious imprecision	No indirectness	Variability in outcomes measured	Very low	No difference between SI (II) and SI (I) or Norplant in various adverse events or reasons for removal

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Effects of weight on contraceptive efficacy in women using Sino-implant (II)								
Pregnancy	2 RCTs (n=10 940)	Serious limitations (2 fair)	Serious inconsistency	Serious imprecision	No indirectness	None	Very low	1 RCT found higher pregnancy rate in women ≥ 70 kg than women < 60 kg (*P* not reported); 1 RCT found no association between weight and risk of pregnancy

BMD: bone mineral density; BP: blood pressure; RCT: randomized controlled trial; SI (I): Sino-implant (I); SI (II): Sino-implant (II).

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9. Recommendations for use of emergency contraceptive pills, including adding the condition of obesity and the new method, ulipristal acetate

Question 1: Among women with certain characteristics or medical conditions, are those who use levonorgestrel (LNG), ulipristal acetate (UPA) or combined oral contraceptive (COC) regimens for emergency contraceptive pills (ECPs) at increased risk for adverse events compared with those who do not use these forms of emergency contraception? (Direct evidence)

Selection criteria for the systematic review

Study design	Primary research articles in all languages, including pharmacokinetic studies
Population	Women with characteristics or medical conditions outlined in the *Medical eligibility criteria* (MEC) update (pregnancy, breastfeeding, past ectopic pregnancy, history of severe cardiovascular complications, angina pectoris, migraine, severe liver disease, CYP3A4 inducers, repeated [ECP] use and rape).
Intervention	Use of hormonal ECPs (COCs, LNG or UPA)
Comparator	Non-use of hormonal ECPs
Outcome	Any adverse events (did not include side-effects)
Databases searched	PubMed and Cochrane Library

Question 2: Among women who use levonorgestrel (LNG), ulipristal acetate (UPA) or combined oral contraceptive (COC) regimens for emergency contraceptive pills (ECPs), are those with obesity at increased risk for adverse events or pregnancy compared with those who do not have obesity? (Direct evidence)

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women using hormonal ECPs (COCs, LNG or UPA)
Intervention	Obesity
Comparator	Non-obesity
Outcome	Any adverse events or pregnancy
Databases searched	PubMed and Cochrane Library

Recommendations

- For pregnant women, emergency contraceptive pill (ECP) use is not applicable. 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.
- Women who are breastfeeding can use COCs or LNG regimens for ECPs without restriction (MEC Category 1). Women who are breastfeeding can generally use UPA (MEC Category 2). Breastfeeding is not recommended for one week after taking UPA since it is excreted in breast-milk. Breast-milk should be expressed and discarded during that time *(1).*
- Women who have experienced past ectopic pregnancies can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1).
- Women with history of severe cardiovascular disease, including ischaemic heart disease, cerebrovascular attack, or other thromboembolic conditions, can generally use COCs, LNG or UPA for ECPs (MEC Category 2).
- Women with migraines can generally use COCs, LNG or UPA for ECPs (MEC Category 2).
- Women with severe liver disease, including jaundice, can generally use COCs, LNG or UPA for ECPs (MEC Category 2).
- Women using CYP3A4 inducers (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, efavirenz, fosphenytoine, nevirapine, oxcarbazepine, primidone, rifabutin, St John's wort/*Hypericum perforatum*) can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1). Strong CYP3A4 inducers may reduce the effectiveness of ECPs.
- There are no restrictions on repeated ECP use for COCs, LNG or UPA (MEC Category 1). Recurrent 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 use of combined hormonal contraceptives (CHCs) or progestogen-only contraceptives (POCs).
- There are no restrictions for use of COCs, LNG or UPA for ECPs in cases of rape (MEC Category 1).
- Women who are obese can use COCs, LNG or UPA for ECPs without restriction (MEC Category 1). ECPs may be less effective among women with BMI $\geq$ 30 kg/m^2 than among women with BMI $<$ 25 kg/m^2. Despite this, there are no safety concerns.

Remarks

- Ulipristal acetate (UPA) was added as a new method to the MEC.
- The duration of use of ECPs is less than the duration of regular use of COCs or POPs and thus would be expected to have less clinical impact for women with history of severe cardiovascular complications, migraine or severe liver disease (including jaundice). There are no restrictions for the use of ECPs in cases of rape.
- The Guideline Development Group (GDG) decided to remove the condition "angina pectoris" from the MEC recommendations for ECPs. This condition does not appear elsewhere in the MEC and there was no evidence suggesting safety concerns for ECP use among women with angina pectoris.
- The GDG decided to change the term "history of severe cardiovascular complications" to "history of severe cardiovascular disease" to be more consistent with terminology used elsewhere in the MEC.
- According to labelling information, rifampicin markedly decreases UPA levels by 90% or more, which may decrease its efficacy *(1)*. Theoretical concerns, therefore, extend to use of other CYP3A4 inducers as well as LNG and COCs, which have similar metabolic pathways to UPA.
- Due to heterogeneity of study designs and outcome measures, a meta-analysis was not performed.
- 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Four direct studies examined LNG-ECP use among pregnant or breastfeeding women *(2–5)*. No studies were identified that examined UPA- or COC-ECP use among women with medical conditions or characteristics. One cohort study and one randomized controlled trial analysed outcomes among breastfeeding women *(3–4),* and two cohort studies analysed outcomes among breastfeeding women *(2, 5)*. Poor pregnancy outcomes appear rare among pregnant women who used ECPs during conception cycle or early in pregnancy. Breastfeeding outcomes do not seem to differ between women exposed to LNG and those unexposed. One pharmacokinetic study demonstrates that LNG does pass to breast-milk but is found in minimal quantities *(6).*

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 *(7)*.

There is limited evidence from one study that suggests obese women with BMI $\geq$ 30 kg/m^2 experience an increased risk of pregnancy after use of LNG compared with women with BMI $<$ 25 kg/m^2 *(8)*. Evidence from two studies suggests that 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 one of the studies *(8, 9)*.

Quality of the evidence

Women with certain characteristics or medical conditions:
(intervention versus comparator; outcome)

Breastfeeding women

LNG-ECP use versus non-use of LNG-ECP; breastfeeding outcomes:	very low
LNG-ECP use versus non-use of LNG-ECP; infant growth/behaviour:	very low

Currently pregnant women

LNG-ECP use versus non-use of LNG-ECP; adverse pregnancy outcomes:	very low

GRADE methodology was not used to assess quality of evidence for studies that did not report clinical outcomes, including pharmacokinetic studies.

Women using LNG-, UPA- or COC-ECPs:
(intervention versus comparator: outome)

Obesity versus non-obesity; risk of pregnancy:	moderate

GRADE tables 1 (Question 1): Among women with certain characteristics or medical conditions, are those who use levonorgestrel (LNG), ulipristal acetate (UPA) or combined oral contraceptive (COC) regimens for emergency contraceptive pills (ECPs) at increased risk for adverse events compared with those who do not use these forms of emergency contraception? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Quality	Estimate of effect
LNG-ECP during breastfeeding vs no LNG-ECP							
Breastfeeding outcomes	1 cohort study (n=143); 1 RCT (n=1158)	Serious limitations (1 poor-quality cohort, 1 fair-quality RCT); some outcomes based on subjective self-report	No inconsistency	No serious imprecision	No indirectness	Very low	No differences in breast-milk volume in 2 studies; no difference in duration of lactation, resumption of menstruation or pattern of breastfeeding in 1 study
Infant growth and behaviour	1 cohort study (n=143); 1 RCT (n=1158)	Very serious limitations (1 poor-quality cohort, 1 fair-quality RCT); outcomes poorly defined	No inconsistency	No serious imprecision	No indirectness	Very low	No differences in infant growth or behaviour
LNG-ECP during pregnancy vs no LNG-ECP							
Pregnancy outcomes	2 cohort studies (n=780)	Very serious limitations (1 poor, 1 fair)	No inconsistency	Serious imprecision	No indirectness	Very low	No differences in risk of spontaneous abortion or still birth, ectopic pregnancy, or other pregnancy complications
Neonatal or fetal outcomes	2 cohort studies (n=780)	Very serious limitations (1 poor, 1 fair)	No inconsistency	Serious imprecision	No indirectness	Very low	No differences in rates of birth defects or fetal growth

GRADE table 2 (Question 2): Among women who use levonorgestrel (LNG), ulipristal acetate (UPA) or combined oral contraceptive (COC) regimens for emergency contraceptive pills (ECPs), are those with obesity at increased risk for adverse events or pregnancy compared with those who do not have obesity? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Obese (BMI ≥ 30 kg/m^2) vs overweight (25–30 kg/m^2) vs normal or underweight (< 25 kg/m^2)								
Pregnancy	3 cohorts from clinical trials (n=4690) (analysed in 2 meta-analyses that included 2 studies each; 1 study included in both analyses)	Serious limitations (2 studies with secondary analyses from clinical trials with methodological limitations)	No serious inconsistency	No serious imprecision	No indirectness	Dose-effect observed in 1 meta-analysis (not evaluated in the other)	Moderate	Obese vs normal or underweight (n=2701, 2 studies): OR 3.6 (95% CI 2.0–6.5) for any ECP; OR 4.4 (95% CI 2.0–9.4) for LNG-ECP and OR 2.6 (95% CI 0.89–7.0) for UPA-ECPa Overweight vs normal or underweight (n=2976, 2 studies): OR 1.5 (95% CI 0.75–3.0) for any ECP; 2.1 (95% CI 0.86–4.9) for LNG-ECP and 0.97 (95% CI 0.27–2.8) for UPA-ECPa; (n=2173, 2 studies): OR 2.1 (95% CI 1.0–4.3) for UPA-ECPb

BMI: body mass index; CI: confidence interval; OR: odds ratio.

a Estimates adjusted for conception probability, further intercourse, age, time from unprotected intercourse to treatment, and pregnancy history.

b Estimate adjusted for further acts of unprotected intercourse, age, race, ever being pregnant, smoking, and hours since unprotected intercourse (up to 120 hours) not statistically significant in univariate analyses.

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10. Recommendations for intrauterine devices among women with increased risk for sexually transmitted infections

Question 1: Among women with an increased risk of sexually transmitted infections (STIs), does intrauterine device (IUD) insertion increase risk for pelvic inflammatory disease (PID) compared with women with an increased risk of STIs that do not undergo IUD insertion?

Selection criteria for the systematic review

Study design	Randomized controlled trials, cohort studies and case-control studies
Population	Women at increased risk of STIs
Intervention	Initiation of copper-bearing IUD (Cu-IUD) or levonorgestrel-releasing IUD (LNG-IUD)
Comparator	Non-initiation of Cu-IUD or LNG-IUD
Outcome	PID
Databases searched	PubMed and Cochrane Library

Recommendations

- Many women with increased risk of sexually transmitted infections (STIs) can generally undergo either Cu-IUD or LNG-IUD initiation (MEC Category 2). Some women at increased risk (very high individual likelihood) of STIs generally should not have an IUD inserted until appropriate testing and treatment occur (MEC Category 3). 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.
- Women at increased risk of STIs can generally continue use of either Cu-IUD or LNG-IUD (MEC Category 2).

Remarks

- The Guideline Review Committee advised that this recommendation be revised to clarify the Category 2/3 recommendation in the MEC fourth edition. However, as no new evidence was identified to update this recommendation, there was no evidence to take through the GRADE process. This was addressed by the Guideline Development Group (GDG), who decided that the best course of action was to revise the clarification. The GDG highlighted the universal recommendation for dual protection with condoms, especially for women at increased risk of STIs.
- IUDs do not protect against 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Using an algorithm to classify STI risk status among IUD users, one study reported that 11% of women at high risk of STI experienced IUD-related complications compared with 5% of those not classified as high risk *(1)*. In another small study, the incidence of PID after IUD insertion was low (2.2%) in a cohort of women considered to be at high risk based on high background rates of STIs in the general population *(2)*.

Quality of the evidence

For STI and IUD:	No new evidence

References

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11. Recommendations for use of progesterone-releasing vaginal ring

Question 1: Among breastfeeding women and their infants, does the use of the progesterone-releasing contraceptive vaginal ring (PVR), compared with non-use of progestogen-only contraceptive (POC) methods, affect maternal health, breastfeeding performance, infant growth or infant health? (Direct evidence)

Selection criteria for the systematic review

Study Design	Randomized controlled trials, cohort studies and case-control studies
Population	Breastfeeding women
Intervention	PVR
Comparator	Non-use of a POC method (i.e. either use of no contraceptive method or use of a non-hormonal method such as condoms or other barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/vasectomy, etc.)
Outcome	Maternal adverse events, breastfeeding performance (e.g. duration of lactation, continuation, supplementation), infant health (growth, development, or adverse health events), pregnancy
Databases searched	PubMed and Cochrane Library

Recommendations

- Women who breastfeed and are ≥ 4 weeks postpartum, can use without restrictions the progesterone-releasing vaginal ring (PVR) (MEC Category 1). A woman who uses the PVR must be actively breastfeeding (e.g. at least four breastfeeding episodes per day) to maintain the efficacy of the method.

Remarks

- If the progesterone-releasing vaginal ring (PVR) is accidentally used during pregnancy, there is no known harm to the woman, the course of her pregnancy, or the fetus.
- Due to heterogeneity of study designs and outcome measures, a meta-analysis was not performed.
- The PVR 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.
- Voluntary use of contraception by women is critical for upholding their reproductive rights. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence

Seven prospective cohort studies examined the effect of using the progesterone-releasing vaginal ring (PVR) on maternal health, breastfeeding performance, infant health and infant growth, compared with other hormonal and non-hormonal contraceptive methods, during the first year postpartum or longer *(1–7)*.

Of the six studies that evaluated various measures of breastfeeding performance, neither duration of lactation *(1, 4, 7)*, the proportion of women fully breastfeeding *(2)*, the number of breastfeeding episodes *(2, 5)*, nor the timing of supplementary food introduction *(6)* significantly differed among PVR users compared with users of non-hormonal or progestogen-only contraceptives (POCs) during 12 months of observation.

No statistically significant differences in infant weight gain were observed among PVR users compared with women using non-hormonal or POCs *(3, 4, 6)* and similar patterns of infant weight gain were observed in another study that compared PVR and IUD users *(5)*. One study reported no significant difference in infant health *(5)*.

Quality of the evidence

Among breastfeeding women, use of PVR versus non-PVR contraceptive; various outcomes:

Pregnancy:	low
Breastfeeding outcomes:	low
Infant weight:	low

GRADE table 1 (Question 1): Among breastfeeding women and their infants, does the use of the progesterone-releasing contraceptive vaginal ring (PVR), compared with non-use of progestogen-only contraceptive (POC) methods, affect maternal health, breastfeeding performance, infant growth and infant health? (Direct evidence)

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Progesterone-releasing vaginal ring (PVR) vs intrauterine device (IUD), Norplant or progesterone-only pill (POP)								
Pregnancy	7 cohort studies (n=3397)	Serious limitations (5 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	Few pregnancies and similar pregnancy rates in breastfeeding women using PVR vs IUD (6 studies), Norplant (2 studies), or POP (1 study)
Use of supplementation	4 cohort studies (n=1129)	Serious limitations (3 fair, 1 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	No difference between PVR and IUD (3 studies), Norplant (2 studies), or POP (1 study) in proportion fully breastfeeding; 1 study found ring associated with fewer supplementation episodes and days than IUD at all follow-up periods ($P < 0.001$)
Breastfeeding duration	4 cohort studies (n=1117)	Serious limitations (2 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	No difference between PVR and IUD (4 studies), Norplant (2 studies), or POP (1 study)
Breastfeeding episodes	2 cohort studies (n=2083)	Serious limitations (2 fair)	No serious inconsistency	No serious imprecision	No directness	None	Low	No differences between PVR and IUD (2 studies)
Continuation of use	5 cohort studies (n=2722)	Serious limitations (3 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	4 studies found PVR associated with lower continuation/higher discontinuation vs IUD; 1 study found PVR associated with higher continuation/lower discontinuation
Bleeding episodes	3 cohort studies (n=2279)	Very serious limitations (1 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	No clear differences between PVR vs IUD (3 studies), Norplant (1 study), or POP (1 study)
Infant weight gain	7 cohort studies (n=3397)	Serious limitations (5 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	None	Low	No difference between ring vs IUD (7 studies), Norplant (2 studies), or POP (1 study)

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12. Recommendations for use of hormonal contraception among women at high risk of HIV, women living with HIV, and women living with HIV using antiretroviral therapy

Background

Owing to the public health importance of recommendations on hormonal contraceptive use for women at risk of HIV and women living with HIV, the following recommendations were issued ahead of this fifth edition of the MEC in the document entitled *Hormonal contraceptive methods for women at high risk of HIV and living with HIV: 2014 guidance statement,* which was approved by the WHO Guidelines Review Committee (GRC) on 7 July 2014 *(1).*

Question 1: Does the use of a particular method of hormonal contraception directly increase the risk of HIV acquisition in women?

Selection criteria for the systematic review

Study design	Randomized controlled trials and observational cohort studies
Population	Women of reproductive age at risk of HIV infection
Intervention	Use of a hormonal contraceptive method (injectables, oral contraceptives, implants, patches, rings or LNG-IUDs)
Comparator	Non-use of a hormonal contraceptive method (i.e. either use of no contraceptive method or use of a non-hormonal method such as condoms or other barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/vasectomy, etc.)
Outcome	Incident, laboratory-confirmed HIV infection in women

Question 2: Does the use of various hormonal contraceptive methods accelerate HIV disease progression in women living with HIV?

Selection criteria for the systematic review

Study design	Randomized trials and cohort studies
Population	Women of reproductive age living with HIV
Intervention	Use of a hormonal contraceptive method (injectables, oral contraceptives, implants, patches, rings or LNG-IUDs)
Comparator	Non-use of hormonal contraceptive methods (i.e. either use of no method or use of a non-hormonal method such as condoms or other barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/vasectomy, etc.)
Outcomes	Risk of HIV disease progression (as indicated by HIV viral load, CD4 count, progression to AIDS, ART initiation, death, or a composite outcome of progression to AIDS, ART initiation or death).

Question 3: Does the use of various hormonal contraceptive methods increase the risk of female-to-male HIV sexual transmission?

Selection criteria for the systematic review

Study designs	(a) Randomized trials and cohort studies (reporting direct evidence, with incident HIV infection rates in male sexual partners as an outcome variable); (b) randomized controlled trials, cohort studies, cross-sectional studies (reporting indirect evidence, assessing proxy measures for infectivity in women)
Population	Women of reproductive age living with HIV
Intervention	Use of a hormonal contraceptive method (injectables, oral contraceptives, implants, patches, rings or LNG-IUDs)
Comparator	Non-use of hormonal contraceptive methods (i.e. either use of no method or use of a non-hormonal method such as condoms or other barrier methods, withdrawal, copper-bearing IUDs, tubal ligation/vasectomy, etc.)
Outcomes	Risk of HIV transmission to male partners (measured either directly by HIV seroconversion among previously HIV-negative male partners, or indirectly by measurement of genital HIV shedding or plasma viral load in women as a proxy for infectivity).

Question 4: Are there any possible interactions between hormonal contraceptive methods and antiretroviral (ARV) medications?

Selection criteria for the systematic review

Study design	Clinical trials, observational studies, case series and pharmacokinetic studies
Population	Women of reproductive age
Intervention	Hormonal contraception and antiretroviral therapy (ART)
Comparator	Hormonal contraception and no ART; non-comparative studies examining changes in outcomes over time
Outcome	Contraceptive hormone pharmacokinetics, contraceptive effectiveness (pregnancy, ovulation, ovarian activity, breakthrough bleeding), ARV pharmacokinetics, ARV effectiveness (HIV disease progression, viral load, CD4 count), and adverse effects of either the hormonal contraceptive or the ARV medication.

12a. Recommendations among women at high risk of HIV infection:

- Women at high risk of acquiring HIV can use the following hormonal contraceptive methods without restriction: combined oral contraceptive pills (COCs), combined injectable contraceptives (CICs), contraceptive patches and rings, progestogen-only pills (POPs), progestogen-only injectables (DMPA and NET-EN), and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 1).
- 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.
- Women at high risk of acquiring HIV can generally use LNG-releasing IUDs (LNG-IUDs) (MEC Category 2).

Remarks

- It is critically important that women and couples at risk of HIV infection be informed about and have access to male and female condoms, and other measures to prevent and reduce their risk of HIV infection and sexually transmitted infections (STIs), regardless of which form of contraception they choose.
- Hormonal contraceptives, including COCs, CICs, POPs, POIs, progestogen-only implants, and LNG-IUDs do not protect against STIs/HIV.

Summary of the evidence (Question 1: HIV acquisition)

Twenty-two prospective observational studies have assessed the risk of HIV acquisition among women using a method of hormonal contraception versus the risk of HIV acquisition in women using a non-hormonal contraceptive method (i.e. condoms, Cu-IUD, withdrawal) or no contraceptive method *(2–27)*.

Combined hormonal contraceptives

Eight studies assessed the use of COCs and were considered to be "informative but with important limitations" *(28)*. Seven of these studies found no statistically significant association between use of COCs and HIV acquisition *(3, 5-11)*, although one study among sex workers in Kenya did *(12)*.

Progestogen-only contraceptives

Five studies assessed the use of NET-EN injectables and were considered to be "informative but with important limitations" *(28)*. Four of them reported no statistically significant association with HIV acquisition *(3, 8, 9, 13)*, while one did *(11)*.

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" *(28)*. The results were mixed: three of the studies showed a significant increase in risk *(5, 11, 12)*, one showed a significant increase in risk using one statistical model but this association was not statistically significant using another statistical model *(6, 7)*, and five showed no significant increase in risk *(3, 8–10, 13)*.

Two studies assessed implants, one of which was classified as "unlikely to inform the primary question" *(4, 28)*. Neither of these studies reported a statistically significant increased risk of HIV acquisition, but confidence intervals were wide *(4, 21)*.

Quality of the evidence (Question 1: HIV acquisition)

For progestogen-only injectables (DMPA and NET-EN) and COCs:	low
For implants:	very low

12b. Recommendations among women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2):

- Women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) can use the following hormonal contraceptive methods without restriction: combined oral contraceptive pills (COCs), combined injectable contraceptives (CICs), contraceptive patches and rings, progestogen-only pills (POPs), progestogen-only injectables (DMPA and NET-EN), and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 1).
- Women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2) can generally use the LNG-IUD (MEC Category 2).
- Because there may be interactions between certain methods of hormonal contraception and certain antiretroviral medications (ARVs), refer to the recommendations on ART medication interactions (see p. 72).

Remarks

- Hormonal contraceptives do not protect against sexually transmitted infections (STIs), including HIV. Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission to non-infected sexual partners, and for protection against other STIs. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.
- Voluntary use of contraception by women living with HIV who wish to prevent pregnancy is critical for upholding their reproductive rights and continues to be an important strategy for reducing vertical HIV transmission. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence (Question 2: disease progression; Question 3: female-to-male transmission)

Two systematic reviews investigating Questions 2 and 3 informed the contraceptive eligibility recommendations for women living with asymptomatic or mild HIV clinical disease (WHO stage 1 or 2).

Combined hormonal contraceptives (CHCs)

Out of eight available studies, seven suggested no association between use of COCs and progression of HIV, as measured by CD4 count < 200 cells/mm^3, initiation of ART, or mortality *(29–35)*. 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 (Cu-IUDs) *(36, 37)*.

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 *(5)*. The other study also did not find a statistically significant association for COCs *(4)*.

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 *(38–53)*.

Progestogen-only contraceptives (POCs)

Out of six available studies, five suggested no association between use of progestogen-only injectable (POI) contraceptives and progression of HIV, as measured by CD4 count < 200 cells/mm^3, initiation of ART, or mortality *(31–35)*. One randomized trial found an increased risk of a composite outcome of declining CD4 count or death among oral contraceptive (OC) users (COCs and POPs) when compared with users of Cu-IUDs; this study, however, had significant loss to follow-up and method-switching among groups, limiting its interpretation *(36, 37)*. One study found no difference in ART

initiation or CD4 count between users and non-users of the LNG-IUD *(54)*.

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 study reported a statistically significant association between POI contraception and female-to-male transmission of HIV *(5)*, while another study did not find a statistically significant association between use of DMPA and female-to-male HIV transmission *(4)*. The findings of 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 been mixed. The majority of indirect studies measuring whether various hormonal contraceptive methods affect plasma HIV viral load have found no effect *(38–53)*.

Quality of the evidence

Disease progression – progestogen-only injectables (DMPA and NET-EN) and OCs (COCs and POPs):	low
Disease progression – LNG-IUD:	very low
Disease transmission (direct evidence) – progestogen-only injectables (DMPA and NET-EN) and OCs (COCs and POPs):	very low

Note: As there remains considerable uncertainty regarding the best way to measure genital HIV shedding (with respect to collection method, RNA versus DNA, and cell-associated versus cell/free measures of DNA and RNA), studies providing indirect evidence assessing proxy measures of transmission did not undergo a GRADE assessment.

12c. Recommendations among women living with severe or advanced HIV clinical disease (WHO stage 3 or 4)

- Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) can use the following hormonal contraceptive methods without restriction: combined oral contraceptive pills (COCs), combined injectable contraceptives (CICs), contraceptive patches and rings, preogestogen-only pills (POPs), progestogen-only injectables (DMPA and NET-EN), and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 1).
- Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) should generally not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease (WHO stage 1 or 2). However, women who already have an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation). LNG-IUD users with severe or advanced HIV clinical disease should be closely monitored for pelvic infection.
- Because there may be interactions between certain methods of hormonal contraception and certain antiretroviral medications (ARVs), refer to the recommendations on ART medication interactions (see p. 72).

Remarks

- Hormonal contraceptives do not protect against sexually transmitted infections (STIs), including HIV. Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission to non-infected sexual partners, and for protection against other STIs. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.
- Voluntary use of contraception by women living with HIV who wish to prevent pregnancy is critical for upholding their reproductive rights and continues to be an important strategy for reducing vertical HIV transmission. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.

Summary of the evidence (Question 2: disease progression; Question 3: female-to-male transmission)

Two systematic reviews investigating Questions 2 and 3 informed the contraceptive eligibility recommendations for women living with severe or advanced HIV clinical disease (WHO stage 3 or 4).

All of the identified studies excluded women with severe or advanced HIV clinical disease (WHO stage 3 or 4) from enrolment, although some participants experienced progression to severe or advanced disease during the trials.

Combined hormonal contraceptives (CHCs)

Out of eight available studies, seven suggest no association between use of COCs and progression of HIV, as measured by CD4 count < 200 cells/mm^3, initiation of ART, or mortality *(29–35)*. One randomized 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 (Cu-IUDs) *(36, 37)*.

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 oral contraceptives (OCs) *(5)*. The other study also did not find a statistically significant association for OCs *(4)*.

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 *(38–53)*.

Progestogen-only contraceptives (POCs), including LNG-IUD

Out of six available studies, five suggested no association between use of progestogen-only injectable contraceptives and progression of HIV, as measured by CD4 count < 200 cells/mm^3, initiation of ART, or mortality *(31–35).* One randomized trial found an increased risk of a composite outcome of declining CD4 count or death among OC (COC and POP) users when compared with Cu-IUD users; this study, however, had significant loss to follow-up and method-switching among groups, limiting its interpretation *(36, 37)*. One study found no difference in ART initiation or CD4 count between users and non-users of the LNG-IUD *(54)*.

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 with known hormonal contraceptive use status. One of these studies reported a statistically significant association between injectable contraception and female-to-male transmission of HIV *(5)*, while the other study did not find a statistically significant association between use of DMPA and female-to-male HIV transmission *(4)*.

The findings of 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 been mixed. The majority of indirect studies measuring whether various hormonal contraceptive methods affect plasma HIV viral load have found no effect *(38–53)*.

Quality of the evidence

Disease progression – progestogen-only injectables (DMPA and NET-EN) and OCs (COCs and POPs):	low
Disease progression – LNG-IUD:	very low
Disease transmission (direct evidence) – progestogen-only injectables (DMPA and NET-EN) and OCs (COCs and POPs):	very low

Note: As there remains considerable uncertainty regarding the best way to measure genital HIV shedding (with respect to collection method, RNA versus DNA, and cell-associated versus cell/free measures of DNA and RNA), studies providing indirect evidence assessing proxy measures of transmission did not undergo a GRADE assessment.

12d. Recommendations among women living with HIV using antiretroviral therapy (ART)

- Women taking any nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) can use all hormonal contraceptive methods without restriction: combined oral contraceptive pills (COCs), contraceptive patches and rings, combined injectable contraceptives (CICs), progestogen-only pills (POPs), progestogen-only injectables (DMPA and NET-EN), and levonorgestrel (LNG) and etonogestrel (ETG) implants (MEC Category 1).
- Women using ART containing either efavirenz or nevirapine can generally use COCs, patches, rings, CICs, POPs, NET-EN and implants (MEC Category 2). However, women using efavirenz or nevirapine can use DMPA without restriction (MEC Category 1).
- Women using the newer non-nucleoside/nucleotide reverse transcriptase inhibitors (NNRTIs), etravirine and rilpivirine, can use all hormonal contraceptive methods without restriction (MEC Category 1).
- Women using protease inhibitors (e.g. ritonavir and ARVs boosted with ritonavir) can generally use COCs, contraceptive patches and rings, CICs, POPs, NET-EN, and LNG and ETG implants (MEC Category 2), and can use DMPA without restriction (MEC Category 1).

- Women using the integrase inhibitor raltegravir can use all hormonal contraceptive methods without restriction (MEC Category 1).
- Women using ARV medication can generally use LNG-IUDs (MEC Category 2), provided that their HIV clinical disease is asymptomatic or mild (WHO stage 1 or 2). Women living with severe or advanced HIV clinical disease (WHO stage 3 or 4) generally should not initiate use of the LNG-IUD (MEC Category 3 for initiation) until their illness has improved to asymptomatic or mild HIV clinical disease. However, women who already have an LNG-IUD inserted and who develop severe or advanced HIV clinical disease need not have their IUD removed (MEC Category 2 for continuation). LNG-IUD users with severe or advanced HIV clinical disease should be closely monitored for pelvic infection.

Remarks

- Hormonal contraceptives do not protect against sexually transmitted infections (STIs), including HIV. Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission to non-infected sexual partners, and for protection against other STIs. Female condoms are effective and safe, but are not used as widely by national programmes as male condoms.
- Voluntary use of contraception by women living with HIV who wish to prevent pregnancy is critical for upholding their reproductive rights and continues to be an important strategy for reducing vertical HIV transmission. All women have the right to evidence-based, comprehensive contraceptive information, education and counselling to ensure informed choice. Women's contraceptive choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Decision-making for contraceptive methods usually requires the need to make trade-offs among the different methods, with advantages and disadvantages of specific contraceptive methods varying according to individual circumstances, perceptions and interpretations.
- Women living with HIV and using ARVs should discuss the potential impact of certain ARVs on contraceptive efficacy with their health-care provider.

Summary of the evidence (Question 4: hormonal contraception–ART interactions)

Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)

NRTIs do not appear to have significant risk of interactions with hormonal contraceptive methods *(55, 56)*.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

Three clinical studies, including one large study, found use of nevirapine-containing ART did not increase ovulation or pregnancy rates in women using COCs *(57–60)*. For efavirenz-containing ART, a pharmacokinetic study showed consistent significant decreases in contraceptive hormone levels in women using COCs, and a small clinical study showed higher ovulation rates in women taking efavirenz-containing ART and COCs *(57, 61, 62)*. Etravirine and rilpivirine do not interact with COCs *(63, 64)*. One retrospective chart review of women using efavirenz-containing ART showed increased contraceptive failure rates for women using LNG implants *(65)*. Based primarily on pharmacokinetic data, the effectiveness of DMPA is likely not affected by NNRTIs, and vice versa *(66, 67)*.

Protease inhibitors (PIs)

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 *(68)*. One study found higher progestin levels with concurrent PI use in users of POPs *(69)*. Based primarily on pharmacokinetic data, the effectiveness of DMPA is likely not affected by PIs, and vice versa *(66, 67)*.

Integrase inhibitors

The integrase inhibitor raltegravir does not appear to interact with COCs *(55, 56, 70, 71)*.

Quality of the evidence

Hormonal contraception + ART versus hormonal contraception alone:	very low
Efavirenz-containing ART versus other ART in women using hormonal contraception:	very low
ART + hormonal contraception versus ART alone:	low

GRADE table 1 (Question 1): Does the use of a particular method of hormonal contraception directly increase the risk of HIV acquisition in women?

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Overall quality	Estimate of effect
Injectable contraceptive use vs non-use							
HIV acquisition	9 cohort studies[a] (n=28 219)	Serious limitations[a]	Serious inconsistency	No serious imprecision	No indirectness	Low	Injectables overall: hazard ratio (HR) or incidence rate ratio (IRR) range 0.94–2.0 in 9 studies: 6 studies increased risk (HR range 1.1–2.0), with statistically significant effects in 4 studies; 1 study no effect (HR 0.94, 95% CI 0.46–1.92); 2 studies no clear effect (NET-EN and DMPA reported separately with no clear association and opposite effects for each type of hormonal contraceptive) DMPA: HR range 0.46–2.0 in 6 studies: 4 studies increased risk (HR range 1.3–2.0), with statistically significant effects in 1 study; 2 studies trend towards decreased effect (HRs 0.46 and 0.75) NET-EN: HR range 0.87–2.5 in 5 studies: 4 studies increased risk (HR range 1.3–2.5), with statistically significant effects in 1 study; 1 study no effect (HR 0.87, 95% CI 0.60–1.2)
Oral contraceptive use vs non-use							
HIV acquisition	8 cohort studies[a] (n=27 585)	Serious limitations[a]	Serious inconsistency	No serious imprecision	No indirectness	Low to moderate	HR or IRR range 0.66–1.8 in 8 studies: 1 study increased risk (HR 1.5, 95% CI 1.0–2.1); 1 study trend towards increased risk (HR 1.8, 95% CI 0.55–5.8); 1 study trend towards decreased risk (IRR 0.66, 95% CI 0.09–4.78); 5 studies no effect (HR range 0.86–0.99)[b]
Implant use vs non-use							
HIV acquisition	1 cohort study (n=1272)	Serious limitations	Cannot determine (1 study)	Serious imprecision		Very low	HR 1.6 (95% CI 0.5–5.7)

CI: confidence interval; DMPA: depot medroxyprogesterone acetate; HR: hazard ratio; IRR: incidence rate ratio; NET-EN: norethisterone enanthate.

Note: For all the studies summarized for this question, effects are based on adjusted risk estimates; Cox model analysis results were used when different statistical methods were presented.

[a] Restricted to studies classified as "considered informative with important limitations"; while all of these studies had important limitations or risk of bias, no study had all three major flaws – i.e.: (i) no adjustment for any measure of condom use; (ii) unclear measurement of exposure to hormonal contraception; (iii) inter-survey interval (time between study visits) < 6 months – and therefore were given an overall quality rating of "low" rather than "very low". An explanation of the quality assessment for each study included in this table is described in the systematic review by Polis et al., 2014 *(28)*.

[b] One study (McCoy et al., 2013) stratified estimates for COC (HR 0.78, 95% CI 0.53–1.12) and POP (HR 0.91, 95% CI 0.49–1.50) *(3)*.

GRADE table 2 (Question 2): Does the use of various hormonal contraceptive methods accelerate HIV disease progression in women living with HIV?

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Quality	Estimate of effect
Hormonal contraception (oral or injectable) vs copper-bearing intrauterine device (Cu-IUD)							
Mortality	1 RCT (n=599)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Low	HR 1.4 (95% CI 0.7–3.0); absolute risk increase 0.88/100 woman-years; HR 1.1 (95% CI 0.38–3.0) for OC and 1.4 (95% CI 0.63–3.1) for DMPA
Progression to CD4 count < 200 cells/mm^3	1 RCT (n=599)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Low	HR 1.6 (95% CI 1.0 to 2.3); absolute risk increase 3.7/100 woman-years; HR 1.5 (95% CI 0.98–2.4) for OC and 1.8 (95% CI 1.3–2.6) for DMPA for CD4 count progression or initiation of ART
Mortality or progression to CD4 count < 200 cells/mm^3	1 RCT (n=599)	Serious limitations (1 fair)	Cannot determine (1 study)	Serious imprecision	No indirectness	Low	HR 1.6 (95% CI 1.1–2.3); absolute risk increase 4.6/100 woman-years; HR 1.5 (95% CI 1.0–2.3) for OC and 1.8 (95% CI 1.3–2.5) for DMPA for mortality, CD4 count progression or initiation of ART
Injectable contraceptive use vs non-use							
Mortality	5 cohort studies (n=7136)	Serious limitations (1 good, 3 fair, 1 poor)	Serious inconsistency	No serious imprecision	No indirectness	Low	HR range 0.41–1.4 in 5 studies (no estimate showed statistically significant effect)
Progression to AIDS or initiation of antiretroviral therapy (ART)	4 cohort studies (n=6308)	Serious limitations (1 good, 2 fair, 1 poor)	No serious inconsistency	No serious imprecision	No indirectness	Low-moderate	HR range 0.7–1.0 in 3 studies (no estimate showed statistically significant effect); 1 study reported HR 0.91 (95% CI 0.61–1.36) for ART initiation and HR 0.82 (95% CI 0.57–1.17) for progression to CD4 count < 200 cells/mm^3
Mortality, progression to AIDS or initiation of ART	4 cohort studies (n=6851)	Serious limitations (2 good, 2 fair)	No serious inconsistency	No serious imprecision	No indirectness	Low-moderate	HR range 0.72–1 in 4 studies; 1 study reported HR of 0.72 (95% CI 0.53–0.98); estimate not statistically significant in other studies

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Quality	Estimate of effect
Oral contraceptive use vs non-use							
Mortality	6 cohort studies (n=6864)	Serious limitations (1 good, 3 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	Low-moderate	HR range 0.28–1.1 in 4 studies (no estimate showed statistically significant difference)[a]; 2< 200 cells/mm^{3}studies reported no events
Progression to AIDS or initiation of ART	5 cohort studies (n=6078)	Serious limitations (1 good, 2 fair, 2 poor)	No serious inconsistency	No serious imprecision	No indirectness	Low	HR range 0.84–1.3 in 4 studies (no estimate showed statistically significant effect)[a]; 1 study reported HR 0.61 (95% CI 0.25–1.45) for ART initiation and HR 0.96 (95% CI 0.52–1.79) for progression to CD4 count < 200 cells/mm^3
Mortality, progression to AIDS or initiation of ART	4 cohort studies (n=6059)	Serious limitations (2 good, 2 fair)	No serious inconsistency	No serious imprecision	No indirectness	Low-moderate	HR range 0.65–1.0 in 4 studies (no estimate showed statistically significant effect)[a]
Levonorgestrel IUD vs no hormonal contraception							
Initiation of ART	1 study (n=40)	Very serious limitations (1 poor)	Cannot determine (1 study)	Very serious imprecision	No indirectness	Very low	43% vs 45%, $P = 0.91$

ART: antiretroviral therapy; CI: confidence interval; DMPA: depot medroxyprogesterone acetate; HR: hazard ratio; OC: oral contraceptives; RCT: randomized controlled trial.

[a] Includes data from Heffron et al. (2013) on risk with DMPA and OC separately *(29)*.

GRADE table 3 (Question 3): Does the use of various hormonal contraceptive methods increase the risk of female-to-male HIV sexual transmission?

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Quality	Estimate of effect[a]
Injectable hormonal contraceptive use vs non-use							
HIV transmission	2 cohort studies (n=2635)	Serious limitations (2 fair)[b]	Serious inconsistency	Very serious imprecision	No indirectness	Very low	HR 2.0 (95% CI 1.1–3.6) and 0.57 (95% CI 0.19–1.70)[c]
Oral hormonal contraceptive use vs non-use							
HIV transmission	2 cohort studies (n=2635)	Serious limitations (2 fair)[b]	No serious inconsistency	Very serious imprecision	No indirectness	Very low	HR 2.1 (95% CI 0.75–5.8) and 2.5 (95% CI 0.49–13)[c]

CI: confidence interval; HR: hazard ratio.

a Combined estimate from Heffron et al. (2012) for injectable or oral hormonal contraceptive use vs non-use: HR 2.0 (95% CI 1.1–3.4); absolute increase about 1 transmission/100 person-years *(5)*.

b Lutalo et al. (2013) rated fair-quality *(4)*, Heffron et al. (2012) not rated but limitations noted in assessment of condom use and potential for residual confounding *(5)*.

c HR 1.40 (95% CI 0.30–6.49) for injectable and 2.11 (95% CI 0.18–2.5) when adjusted for viral load.

GRADE table 4 (Question 4): Are there any possible interactions between hormonal contraceptive methods and ARV medications?

Outcome	Type and number of studies (number of participants)	Limitations	Inconsistency	Imprecision	Indirectness	Other factors	Quality	Estimate of effect
Hormonal contraception + antiretroviral therapy (ART) vs hormonal contraception alone								
Pregnancy	1 non-randomized trial (n=336); 1 cohort study (n=4531)	Serious limitations (1 good-quality non-randomized trial, 1 poor-quality cohort study)	No serious inconsistency	No serious imprecision	No indirectness	Variability in hormonal contraception	Very low	1 non-randomized trial found no difference in pregnancy rate with nevirapine-based ART + COC vs no ART; 1 cohort study found lower pregnancy rate prior to initiation of ART vs after initiation in women on various hormonal contraceptives, but estimates were imprecise (IRR 3.11 [95% CI 1.55–6.21] vs 5.38 [95% CI 2.89–10.00] for COC and 1.10 [95% CI 0.63–1.94] vs 1.97 [95% CI 1.28–3.01] for injectables)
Efavirenz (EFV) vs other ART in women using hormonal contraception								
Pregnancy	2 cohort studies (n=1197)	Serious limitations (2 fair)	Unclear	Serious imprecision	No indirectness	Denominators not provided in 1 study	Very low	1 study found 12.4% pregnancy rate with EFV vs 0% with nevirapine (NVP) or loopinavir (LPV)/ritonavir (RTV) in women using LNG implant; 1 study reported 1 failure with EFV vs 7 with NVP in women using various hormonal contraceptives, but denominators were unclear
ART + hormonal contraception vs ART alone								
ART effectiveness	3 cohort studies (n=679)	Serious limitations (2 fair, 1 poor)	No serious inconsistency	Serious imprecision	No indirectness	Variability in hormonal contraception, ART regimens, and measures of ART effectiveness	Low	No effect of hormonal contraception on measures of ART treatment failure in 3 studies (1 study of DMPA, 1 study of COCs, and 1 study of both)

CI: confidence interval; COC: combined oral contraceptive; DMPA: depot medroxyprogesterone acetate; IRR: incidence rate ratio.

Note: Table includes evidence from comparative studies reporting clinical outcomes.

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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	

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				
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.

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	COC	P	CVR	CIC	
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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	

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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)*.

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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	

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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	

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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.

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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	

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				
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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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				
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)*.

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.

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	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				
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.

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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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	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)			
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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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)			
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.

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)			
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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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.

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	POP	DMPA/ NET-EN	LNG/ETG	
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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.

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)					
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		

PROGESTOGEN-ONLY CONTRACEPTIVES (POCs)

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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)						
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)*.

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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.

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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

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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.
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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)

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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	

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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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† 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)		
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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	Cu-IUD	LNG-IUD	
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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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	Cu-IUD	LNG-IUD		
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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)*.

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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	

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)				
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	

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)				
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.

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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.

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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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	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.				
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	

BARRIER METHODS (BARR)				
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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.				
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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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.				
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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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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.				
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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.				
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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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.				
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	

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.				
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	

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.				
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	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.				
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	

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.				
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	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.				
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	

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.				
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	

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.				
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		
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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

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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

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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		
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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		
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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

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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

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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.

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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.

Annexes

Annex 1: Declarations of interest

Of the 58 experts who participated in this work, 14 declared an interest related to contraception. The WHO Secretariat and the Guidelines Development Group reviewed all declarations and found that two participants (Anna Glasier and Regine Sitruk-Ware) had disclosed an academic conflict of interest sufficient to preclude them from participating in the deliberations or development of recommendations relevant to ulipristal acetate (AG) and the progesterone-releasing vaginal ring (RSW).

Eliana Amaral received US$ 100 000 from WHO to conduct research on the peri-coital use of a levonorgestrel-containing emergency contraceptive pill.

Jean-Jacques Amy received €2500 in 2013 from Merck Sharpe & Dohme (MSD) to present a paper at a scientific symposium, and receives an annual stipend of €5000 from the European Society of Contraception and Reproductive Health to serve as the editor-in-chief for the Society's journal.

Sharon Cameron works at a research unit that received funding from Pfizer Ltd (United Kingdom) to undertake a feasibility study of self-administration of an injectable method of contraception and to conduct another study that will be used to apply to the Medicines and Healthcare Products Regulatory Authority (MHRA, United Kingdom) for a license for self-administration of an injectable contraceptive. HRA Pharma (France) provided funding to Cameron's research unit to conduct a trial on the effectiveness of ulipristal acetate (UPA). Cameron is a paid consultant on the European Advisory Board of Exelgyn.

Alison Edelman is a co-investigator of research studies funded by the United States National Institutes of Health (NIH), the Bill & Melinda Gates Foundation and the Society of Family Planning (USA). The research unit that Edelman works with receives funding from MSD and Bayer HealthCare on an ongoing basis to undertake acceptability, efficacy and safety studies on contraceptive pills, transdermal patches and hormone-releasing intrauterine devices.

Anna Glasier is as an expert consultant to HRA Pharma (France). Her husband also currently consults for HRA Pharma on an occasional basis (approximately once every two years), as a member of a scientific advisory board, and less frequently participates as a speaker or chairperson at international conferences on behalf of the company. Specifically, Glasier works with HRA Pharma on the development of new methods of emergency contraception (EC). She was the principal investigator of a large randomized controlled trial that resulted in the marketing of UPA for EC. Glasier was not personally remunerated; the clinic where she works and conducted the research received these funds. Since the publication of the study results in 2010, Glasier has been actively involved and has been paid a regular consultancy fee to advise HRA Pharma in their attempts to obtain approval for over-the-counter use of UPA, and on the work the company has undertaken relating to EC effectiveness according to the body weight of the user. She is also paid as a member of the company's Scientific Advisory Board and participates as a speaker or chairperson at international conferences on behalf of the company (approximately twice a year). Glasier has provided expert opinion on UPA to regulatory authorities and has represented HRA Pharma at these meetings. In the light of this relationship with a company that manufactures EC, including UPA, Glasier did not chair or take part in the discussions on EC and weight at the March 2014 meeting and absented herself from the meeting room when inclusion of UPA in the Medical eligibility criteria for contraceptive use (MEC) and Selected practice recommendations for contraceptive use (SPR) guidelines was discussed. Glasier has an independent research grant from Pfizer Ltd (United Kingdom) to conduct a study of the feasibility of pharmacists dispensing and injecting a subcutaneously administered injectable contraceptive. In addition, Glasier has an independent research grant from HRA Pharma to pay a clinical research fellow for up to three years to undertake research in contraception.

Andy Gray works at CAPRISA, a research unit that receives donations of antiretroviral medications from the NIH Clinical Research Products Management Center (including products manufactured by Abbott, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, GlaxoSmithKline, MSD, and Roche) for use in the clinical trials conducted through the AIDS Clinical Trials Group and International Maternal, Paediatric, Adolescent AIDS Clinical Trial network. The unit also received donated microbicide products from Gilead Sciences for a Phase IIb clinical trial.

Philip Hannaford works for an academic department that received fees from several manufacturers of oral contraceptives in the past for lectures on matters related to contraception, especial oral contraception.

Francesca Martinez received honoraria of €600 from Jansen (2013), Teva (in 2012), Bayer (in 2012), and S.M.B. (2012) to give lectures on contraception during scientific meetings that these pharmaceutical companies supported.

Olav Meirik received US$ 5000 from WHO in 2013 to conduct a survey to estimate the patterns of combined oral contraceptive

use among formulations containing "3rd and 4th generation" progestogens, and he serves as an unpaid senior research associate with the Instituto Chileno de Medicina Reproductiva (ICMER).

Chelsea Polis collaborated on a trial investigating the acceptability of a subcutaneous injectable contraceptive; data collection for this study ceased in 2013. Pfizer, Inc. donated the injectable units, which were not yet commercially available, to her research unit for the conduct of the trial, but did not provide any monetary support.

Regine Sitruk-Ware received €1500 twice in a four-year period from Bayer to provide lectures on the future targets for a non-hormonal contraceptive in the female reproductive tract, and €4500 in 2014 from MSD to advise the company on the development of a progestin, nomegestrol acetate. As a result of her research related to the development of the progesterone-releasing vaginal ring, Dr Sitruk-Ware did not participate in the deliberations that lead to the inclusion of this method in the guideline nor the formulation of recommendations for use of this contraceptive method.

Lisa Soule is employed by the United States Food and Drug Administration (FDA), which is a regulatory body for hormonal contraceptives in the USA. In her role at the meeting, she represented the interests of the FDA, which serves the public health and not any commercial interests.

Carolyn Westhoff receives an honorarium from Agile Therapeutics to serve on its Scientific Advisory Board (approximately US$ 2500 per quarter). She receives honoraria as a member of the Data Safety and Monitoring Boards of both MSD and Bayer HealthCare to monitor contraceptive safety studies conducted by these companies (about US$ 3500 per year and €2700 per year, respectively). Westhoff's research unit receives funding to conduct studies on intrauterine devices (Bayer Healthcare and Medicine 360), a trial of the efficacy of self-administration of an injectable method of contraception (Pfizer, Inc.) and a trial on the safety and effectiveness of oral contraceptive pills (MSD).

Julie Williams is employed by the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MRHA). She was the lead rapporteur for the European Medicines Agency (EMA) Article 31 referral for combined hormonal contraceptives (CHCs), which considered risk of venous thromboembolism across the different products and how this influenced the balance of benefits and risks of these products. The review was considered by the EMA's Pharmacovigilence Risk Assessment Committee (PRAC) and the output of this review included the agreed PRAC recommendation and the Committee on Medicinal Products for Human Use (CHMP) Opinion. Both the PRAC recommendation and the CHMP Opinion have been made publically available on the EMA website and have resulted in changes to the product information for CHCs included in this Article 31 referral.

Annex 2: Systematic reviews

The following systematic reviews of the epidemiological, clinical, and pharmacological evidence were conducted as part of the development of the Medical eligibility criteria for contraceptive use, Fifth edition. Reviews published in peer-reviewed journals are available through open-access; the annex will be periodically updated as reviews are published. Access to unpublished reviews can be requested through the following address: hrx-info@who.int

1. Combined hormonal contraceptive and age (bone health). Curtis Kathryn M, Jatlaoui Tara C. Working document for WHO Technical Consultation, unpublished.

2. Tepper Naomi K, Phillips Sharon J, Kapp Nathalie, Gaffield Mary E, Curtis Kathryn M., Combined hormonal contraceptive use among breastfeeding women: an updated systematic review, Contraception (2015) doi:10.1016/j.contraception.2015.05.006

3. Jackson Emily, Curtis Kathryn M, Gaffield Mary E., Risk of Venous Thromboembolism during the Postpartum Period: A Systematic Review, Obstet Gynecol (2011), doi: 10.1097/AOG.0b013e31820ce2db

4. Tepper Naomi K, Marchbanks Polly A, Curtis Kathryn M., Superficial venous disease and combined hormonal contraceptives: a systematic review, Contraception (2015), doi:10.10.1016/j.contraception.2015.03.010

5. Dragoman Monica V, Curtis Kathryn M, Gaffield Mary E., Combined hormonal contraceptive use among women with known dyslipidaemias: a systematic review of critical safety outcomes, Contraception (submitted).

6. Phillips Sharon J, Tepper Naomi K, Kapp Nathalie, Nanda Kavita, Temmerman Marleen, Curtis Kathryn M, Progestogen-only contraceptive use among breastfeeding women: A systematic review, Contraception (submitted).

7. Dragoman Monica V, Gaffield Mary E, Safety of depot medroxyprogestogen acetate delivered subcutaneously (DMPA – SC): A systematic review, Contraception (submitted).

8. Phillips Sharon J, Steyn Petrus S, Zhang Wen, Curtis Kathryn M. The safety of Sino-implant (II) for women with medical conditions or other characteristics: A systematic review (unpublished, plan for submission).

9. Jatlaoui Tara C, Riley Halley, Curtis Kathryn M., Safety data for levonorgestrel, ulipristal acetate and Yuzpe regimens for emergency contraception (unpublished, plan for submission).

10. Jatlaoui Tara C, Curtis Kathryn M, Safety and Effectiveness Data for Emergency Contraceptive Pills among Women with Obesity (unpublished).

11. Mollhajee Anshu P, Curtis Kathryn M, Peterson Herbert B, 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 Feb;73(2):145-53.

12. Carr Shannon L, Gaffield Mary E, Dragoman Monica V, Phillips Sharon J., Safety of the the progesterone-releasing vaginal ring (PVR) among lactating women: a systematic review, Contraception (2015), doi: 10.1016/j.contraception.2015.04.001

13. Polis Chelsea B, Phillips Sharon J, Curtis Kathryn M, Westreich Daniel J, Steyn Petrus S, Raymond Elizabeth, Hannaford Philip, Turner Abigail Norris, Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence, Contraception (2014), doi: 10.10.1016/j.contraception.2014.07.009

14. Phillips Sharon J, Curtis Kathryn M, Polis Chelsea B. Effect of hormonal contraceptive methods on HIV disease progression: a systematic review. AIDS 2013, 27:787-794.

15. Polis Chelsea B, Phillips Sharon J, Curtis Kathryn M. Hormonal contraceptive use and female-to-male HIV transmission: a systematic review of the epidemiologic evidence. AIDS 2013, 27:493-505.

16. Nanda Kavita, Hormonal contraceptive use in women treated with antiretroviral drugs (unpublished, update underway).

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