Journal of Gynecology Obstetrics and Human Reproduction 48 (2019) 297–307

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Review

Update on the contraceptive contraindications

D. Serfaty*

Hôpital St Louis, 75010, Paris, France

ARTICLE INFO

Article history:
Received 29 June 2018
Received in revised form 25 January 2019
Accepted 19 February 2019
Available online 20 February 2019

Keywords:
Contraception
Contraindications
Medical eligibility criteria

ABSTRACT

Background: The choice of contraceptive methods has considerably increased over recent years. However, all available methods are not appropriate for all women, especially those with medical conditions or individual characteristics in whom any pregnancy, particularly unintended pregnancy, is at higher risk. The safety of contraception is crucial for these women and evidence-based guidance to help healthcare providers choosing a suitable method has been published. The aim of our review is to make an update on the main contraceptive contraindications.
Methods: The World Health Organisation Medical Eligibility Criteria for Contraceptive Use (WHO-MEC) published in 2015 are referred to throughout this review. The rationale behind the recommendations for women with cardiovascular, rheumatic, neurologic, gynaecological or endocrine disorders was first analysed. The national adaptations of the WHO-MEC, especially the French, British, and American ones, were then scrutinized.
Main findings: Overall, the MECs considered tend to provide the same recommendations. However, there are some noticeable differences that may be useful to know. Hence, for a given condition, differences in categorisation have been noticed where limited or controversial scientific evidence relating to this condition exists, especially regarding hormonal contraceptives. Some medical conditions or characteristics, included in some MECs but not in others, have also been identified.
Conclusion: MECs represent valuable tools to help clinicians to prescribe the most acceptable and safe contraceptive method for each individual woman. Although it may be useful to consult different MECs for some complex conditions, prescribers should always bear in mind that these MECs are only guidelines and that their clinical judgment should always prevail.

Introduction

According to the United Nations, 63.6% of the women in the 15–49 age group worldwide, married or living with a partner are using some contraceptive methods [1]. It is obvious that not all these methods are appropriate for all women, and that there are medical contraindications to each contraceptive that one should be aware of.

In 1996, the World Health Organisation (WHO) established some “medical eligibility criteria for contraceptive use” (WHO-MEC) on the basis of “evidence-based medicine” in order to assist healthcare providers in their judgement regarding whether a particular contraceptive method is safe for a given woman. Regularly updated, these criteria form the basis for defining the contraindications to any contraceptive method, and should serve as references rather than directives [2].

This WHO guidance on the safety of contraceptives in the context of specific health conditions is intended for interpretation at country levels in a manner that reflects the diversity of situations and settings in which contraceptives are provided. Hence, it has been adapted in numerous countries with the input of national experts who take into consideration their own experience with the contraceptive methods available [3–8]. Although nationally-adapted guidelines are essentially identical across the major industrialised countries, some notable differences may exist. For instance, for the same condition, the risk level in the use of a given contraceptive can sometimes differ between national guidelines [9]. Furthermore, despite their non-negligible prevalence certain conditions are not included in some national guidelines [10].

Overall, before selecting an appropriate contraceptive method for a woman with a medical condition, the prescriber should carefully review her medical history, fully assess her current disease status and prognosis, as well as her particular risks in case of pregnancy. The prescriber is then required to consider not only the WHO-MEC, which are evolving, but also the national adaptation of these guidelines and even specialised books [10–12] to determine the

* Corresponding author at: 9 rue de Villersexel, 75007, Paris, France.
E-mail address: drserfatyfncgm@aol.com (D. Serfaty).

http://dx.doi.org/10.1016/j.jogoh.2019.02.006

possible contraindications to the contraceptive methods desired by the woman or couple and decide which one will be the most appropriate.

The aim of this review is to make an update on the contraceptive contraindications.

Contraindications according to the WHO-MEC for contraceptive use

For each medical condition, the WHO-MEC 2015 classified each contraceptive method into four categories as defined in Table 1 [2]. The medical conditions for which some contraceptive methods are not recommended or contraindicated (category 3 or 4) are described hereafter by class of diseases and summarised in Table 2. For all the other medical conditions detailed in the WHO-MEC 2015 but not addressed in this review, none of the contraceptive methods are contraindicated (category 1 or 2). Breastfeeding and postpartum have already been dealt with separately [13].

Cardiovascular risk factors or diseases

Hormonal contraceptives (irrespective of administration route) have long been associated with rare, but potentially serious thromboembolic complications [14–17].

The risk of venous thromboembolism (VTE) is about three times greater in users of combined hormonal contraceptives (CHCs) than in non-users, but much lower than during pregnancy or lactation [14]. The dose of oestrogen is the major cause for VTE. Hence, ethinylœstradiol doses in COCs $\geq$ 50 μg are associated with higher VTE risks than lower-dosed formulations [14]. The type of progestogen, either less androgenic or anti-androgenic, was also suggested as influencing the VTE risk [18], the highest elevations in VTE risks being observed with certain third and fourth-generation progestogens (e.g. desogestrel, gestodene, drospirenone) compared with levonorgestrel-containing COCs [14,18–20].

Arterial events among users of combined oral contraceptives (COCs) are rare [17], but associated with higher mortality and disability risks [21,22]. In a meta-analysis based on 11 studies conducted after 1990, i.e. in women taking the oestroprogestative pills most commonly in use today, the pooled risk of myocardial infarction among current users of hormonal contraceptives was multiplied by 1.7 [15,17]. This risk does not differ substantially between the various generations of COCs [15]. Similar results were obtained in other meta-analyses regarding the myocardial infarction risk and also the ischemic stroke risk [15].

The cardiovascular morbidity related to CHCs most likely results from the strong hepatic actions of oestrogens [18]. Ethinylœstradiol is known to modify several haemostatic factors resulting in a procoagulant state and a slight fibrinolytic imbalance, favouring thrombosis. Non- or antiandrogenic progestogens have only minimal counteracting effect on ethinylœstradiol [10,18]. Among the progestogen-only contraceptives (POC), only injectable DMPA may worsen underlying cardiovascular conditions by aggravating the lipid and glucose profiles of users [10,22–24].

Several cardiovascular risk factors were suggested as increasing the thrombogenic effects of CHCs: tobacco (> 15 cigarettes/daily), age (> 35 years), obesity, hypertension, some inherited thrombophilias, history of VTE/DVT, or other risk factors for thrombosis (e.g. prolonged immobilisation) [14].

Therefore, in women with multiple cardiovascular risk factors, CHCs are contraindicated (WHO-MEC: COC, P, CVR, CIC = 3/4), while POC may be recommended (WHO-MEC: POP, LNG/ETG, LNG-IUD = 2), with the exception of injectable DMPA and NET-EN (WHO-MEC = 3) (Table 2). The same reasoning is valid for hypertension with blood pressure $\geq$ 160/100 mm Hg and hypertension with vascular disease. Other situations in which CHCs are contraindicated include thromboembolism, complicated valvular heart disease, thrombogenic mutations, ischemic heart disease, history of stroke (WHO-MEC: COC, P, CVR, CIC = 4). According to the WHO-MEC, initiation of an oral or implantable POC is not contraindicated in women with history of ischemic heart disease or cerebrovascular accident. However, if a new arterial event occurs under this contraception, continuation is rather inadvisable (WHO-MEC = 3), risks exceeding potential benefits.

Rheumatic diseases

An example of rheumatic diseases that mainly affect women is systemic lupus erythematosus (SLE), a chronic, multi-organ, remitting-relapsing disease [25–27]. The majority of SLE women can now have successful live births thanks to treatment and management improvements. However, adverse outcomes still exceed the rate of pregnancy complications in the general population, and patients with positive antiphospholipid antibodies (aPLs), representing 25–50% of SLE patients, are at increased risk of complications (preterm labour, pre-eclampsia, thrombosis, and flares depending on the disease activity level before conception) [26–31].

Contraception to avoid unplanned or unwanted pregnancies, especially during high disease activity periods, treatment with teratogenic immunosuppressants, or in case of positive aPLs, is therefore an important issue for SLE women [27,29,30].

According to WHO-MEC and specialised publications, CHCs are strictly prohibited for SLE patients with positive or unknown aPLs primarily due to fear of disease flare-ups and increased risk of thromboembolic events (Table 2) [2,25,32–34]. Regarding progestogen-only contraceptives (POP, DMPA, NET-EN, LNG/ETG, LNG-IUD), they are not recommended because the risk of thrombosis, although lower, is not absent [2,26,31], and due to a high rate of gynaecological side effects depending on the hypoestrogenic condition [26,31,34]. Also, long-term use of DMPA was observed to result in bone mineral density reduction, reversible after treatment discontinuation, but which has to be taken into account in these women that are *per se* predisposed to osteoporosis due to their active disease or steroids intake [26,31]. Cu-IUD and barrier methods can be used safely in any of these patients [2,31,33].

Table 1
Definitions and interpretation of the WHO-MEC categories.

	Definition of category	Interpretation of the category in practice
Category 1	A condition for which there is no restriction for the use of the contraceptive method	Use method in any circumstances
Category 2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks	Generally use the method
Category 3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method	Use of method is not usually recommended unless other more appropriate methods are not available or not acceptable
Category 4	A condition which represents an unacceptable health risk if the contraceptive method is used	Method not to be used

Neurologic conditions

Among neurological disorders posing a contraceptive challenge, special attention has been paid to migraine that affects about 13% of people with the highest prevalence seen among reproductive-aged women [35]. A consistent link has actually been established between migraine and various cardiovascular events, in particular ischemic stroke [35–37]. Additionally, especially in migraine with aura, available data suggest that CHCs may worsen migraine symptoms and even further increase the risk of stroke due to the prothrombotic effect of oestrogen [38–40].

On the basis of this clinical evidence, WHO has limited the use of hormonal contraception in migraine patients (Table 2) [2]. For women with migraine with aura, CHCs are strictly contraindicated at any age, while progestogen-only contraceptives (POP, DMPA, implants and LNG-IUD) are not recommended as continuation (WHO-MEC = 3). In migraine without aura, the continuation of CHCs is not recommended at less than 35 years (WHO-MEC = 3) and prohibited at 35 years of age and over (WHO-MEC = 4).

Breast cancer

Women who have or had gynaecological cancer need special guidance in choosing a contraceptive method. Breast cancer is the most common malignancy in reproductive-aged women [41,42]. Although woman's fertility can be affected by treatments,

Table 2
WHO-MEC for some common risk factors or diseases.

	COC P CVR	CIC	POP	DMPA NET-EN	LNG ETG	Cu-IUD	LNG-IUD	Barr		
								Co	S	D
CARDIOVASCULAR RISK FACTORS OR DISEASES										
SMOKING										
Age ≥ 35 years										
< 15 cigarettes/day	3	2	1	1	1	1	1	1	1	1
≥ 15 cigarettes/day	4	3	1	1	1	1	1	1	1	1
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE										
e.g. older age, smoking, diabetes, hypertension and known dyslipidaemias	3/4	3/4	2	3	2	1	2	1	1	1
HYPERTENSION										
History of hypertension, where blood pressure CANNOT be evaluated (incl. hypertension in pregnancy)	3	3	2	2	2	1	2	1	1	1
Adequately controlled hypertension, where blood pressure CAN be evaluated	3	3	1	2	1	1	1	1	1	1
Elevated blood pressure levels (properly taken measurements)										
SYS 140-159 or DIA 90-99 mm Hg	3	3	1	2	1	1	1	1	1	1
SYS ≥ 160 or DIA ≥ 100 mm Hg	4	4	2	3	2	1	2	1	1	1
Vascular disease	4	4	2	3	2	1	2	1	1	1
DEEP VEIN THROMBOSIS (DVT) / PULMONARY EMBOLISM (PE)										
History of DVT/PE	4	4	2	2	2	1	2	1	1	1
Acute DVT/PE	4	4	3	3	3	1	3	1	1	1
DVT/PE and established on anticoagulant therapy	4	4	2	2	2	1	2	1	1	1
Major surgery with prolonged immobilisation	4	4	2	2	2	1	2	1	1	1
KNOWN THROMBOGENIC MUTATIONS										
e.g. Factor V Leiden, prothrombin mutation, protein S, protein C, and antithrombin deficiencies	4	4	2	2	2	1	2	1	1	1
ISCHAEMIC HEART DISEASE										
Current and history	4	4	I: 2 / C: 3	3	I: 2 / C: 3	1	I: 2 / C: 3	1	1	1
STROKE										
History of cerebrovascular accident	4	4	I: 2 / C: 3	3	I: 2 / C: 3	1	2	1	1	1
VALVULAR HEART DISEASE										
Complicated valvular heart disease (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)	4	4	1	1	1	2	2	1	1	2
RHEUMATIC DISEASES										
SYSTEMIC LUPUS ERYTHEMATOSUS										
Positive or unknown antiphospholipid antibodies	4	4	3	I: 3 / C: 3	3	I: 1 / C: 1	3	1	1	1

	COC P CVR	CIC	POP	DMPA NET-EN	LNG ETG	Cu-IUD	LNG-IUD	Barr Co	Barr S	Barr D
Severe thrombocytopenia	2	2	2	3 2	2	3 2	2	1	1	1
NEUROLOGIC CONDITIONS										
MIGRAINE WITHOUT AURA										
Age < 35 years	I C 2 3	I C 2 3	I C 1 2	2	2	1	2	1	1	1
Age ≥ 35 years	3 4	3 4	1 2	2	2	1	2	1	1	1
MIGRAINE WITH AURA										
Any age	4	4	I C 2 3	I C 2 3	I C 2 3	1	I C 2 3	1	1	1
BREAST CANCER										
Current	4	4	4	4	4	1	4	1	1	1
Past and no evidence of current disease for 5 years	3	3	3	3	3	1	3	1	1	1
OTHER REPRODUCTIVE TRACT INFECTIONS OR DISORDERS										
Unexplained vaginal bleeding (suspicion for serious condition) – before evaluation	2	2	2	3	3	I C I C 4 2 4 2		1	1	1
Immediate post-septic abortion	1	1	1	1	1	4	4	1	1	1
Gestational trophoblastic disease										
Decreasing or undetectable β-hCG levels	1	1	1	1	1	3	3	1	1	1
Persistently elevated β-hCG levels or malignant disease	1	1	1	1	1	4	4	1	1	1
Cervical cancer (awaiting treatment)	2	2	1	2	2	I C I C 4 2 4 2		1	2	1
Endometrial cancer	1	1	1	1	1	I C I C 4 2 4 2		1	1	1
Ovarian cancer	1	1	1	1	1	I C I C 3 2 3 2		1	1	1
Uterine fibroids with distortion of the uterine cavity	1	1	1	1	1	4	4	1	1	1
Anatomical abnormalities – Distorted uterine cavity incompatible with IUD insertion	-	-	-	-	-	4	4	1	1	NA
Current pelvic inflammatory disease	1	1	1	1	1	I C I C 4 2 4 2		1	1	1
HIV/AIDS and OTHER INFECTIONS										
High risk of HIV	1	1	1	1	1	2	2	1	4	4
Asymptomatic or mild HIV clinical disease (WHO stage 1 or 2)	1	1	1	1	1	2	2	1	3	3
Severe or advanced HIV clinical disease (WHO stage 3 or 4)	1	1	1	1	1	I C I C 3 2 3 2		1	3	3
History of toxic shock syndrome	-	-	-	-	-	- - - -		1	1	3
Pelvic tuberculosis	1	1	1	1	1	I C I C 4 3 4 3		1	1	1
Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1	1	1	I C I C 4 2 4 2		1	1	1
ENDOCRINE CONDITIONS										
DIABETES										
With nephropathy/retinopathy/neuropathy	3/4	3/4	2	3	2	1	2	1	1	1
Other vascular disease or diabetes of > 20 years' duration	3/4	3/4	2	3	2	1	2	1	1	1
GASTROINTESTINAL CONDITIONS										
SYMPTOMATIC GALL BLADDER DISEASE										
Medically treated	3	2	2	2	2	1	2	1	1	1
Current	3	2	2	2	2	1	2	1	1	1

	COC P CVR		CIC		POP	DMPA NET-EN	LNG ETG	Cu-IUD	LNG-IUD	Barr		
										Co	S	D
HISTORY OF CHOLESTASIS												
Past-COC related	3		2		2	2	2	1	2	1	1	1
VIRAL HEPATITIS												
Acute or flare	I	C	I	C	1	1	1	1	1	1	1	1
	3/4	2	3	2								
CIRRHOSIS												
Severe (decompensated)	4		3		3	3	3	1	3	1	1	1
LIVER TUMOURS												
Benign hepatocellular adenoma	4		3		3	3	3	1	3	1	1	1
Malignant (hepatoma)	4		3/4		3	3	3	1	3	1	1	1

Barr: barrier methods; C: continuation; CIC: combined injectable contraceptive; Co: condom; COC: combined oral contraceptive; Cu-IUD: copper-bearing intrauterine device; CVR: combined contraceptive vaginal ring; D: diaphragm (with spermicide), cervical cap; DIA: diastolic; DMPA: depot medroxyprogesterone acetate (injectable); DVT: deep venous thrombosis; I: initiation; LNG/ETG: levonorgestrel and etonorgestrel (implants); LNG-IUD: levonorgestrel-releasing intrauterine device; NA: not applicable; NET-EN: noresthisterone enanthate injectable contraceptive; P: combined contraceptive patch; PE: pulmonary embolism; POC: progestogen-only contraceptive; POP: progestogen-only pill; S: spermicide; SYS: systolic.

contraception is a crucial aspect during and beyond breast cancer. Indeed, pregnancy is strongly discouraged in case treatments are known to potentially increase the risk of congenital malformations [43,44].

The contraceptive needs of breast cancer women who have not completed their childbearing obviously depend on their fertility, aspirations and compliance ability, but their choice should be limited to reversible non-hormonal methods [42,45,46], since current evidence on whether hormonal contraceptives affect survival after oestrogen or non-oestrogen dependent breast cancer is inconclusive. A recent large-scale observational study argues in favour of their contraindication in breast cancer women, as the relative risk of breast cancer was found to be higher among women currently or recently using such contraceptives than among those who never used them [47].

Consistently, according to WHO-MEC, hormonal-containing contraceptives are unacceptable in women with current breast cancer (Table 2) [2]. These methods are not recommended for women over 5 years' post-diagnosis. Cu-IUDs and barrier methods are considered as safe first-line options (regardless of their efficacy) in any case.

Other gynaecological cancers and some disorders contraindicate the use of IUD contraceptive methods (Table 2).

Endocrine conditions

Among endocrine disorders, diabetes is increasingly prevalent worldwide. Pregnant women with poorly-controlled diabetes face increased risk of adverse consequences (spontaneous abortion, hypertension, pre-eclampsia, worsening of pre-existing retinopathy or nephropathy) as well as foetal/neonatal complications [48]. Contraception for young diabetics is therefore of great importance to delay conception until optimal glycaemic control and/or stabilisation of microvascular complications [48].

The diabetes' type, its duration, and the diabetic complications or cardiovascular risk factors should be considered for the choice of a contraceptive. Hormonal methods are recognised as safe for women with uncomplicated diabetes of less than 20 years duration. In diabetic patients with uncontrolled microvascular complications such as severe retinopathy, active macular oedema, or nephropathy with persistent proteinuria, more robust data regarding the safety of CHCs are required, since their deleterious effects on microvessels cannot be excluded [48]. According to WHO-MEC, these methods should not be proposed, or with extreme caution, to these patients (Table 2) [2]. In type 1 or 2 diabetic women with cardiovascular complications and/or vascular risk factors (dyslipidaemia, hypertension, tobacco consumption, diabetes duration > 20 years, obesity, etc.), great caution should also be exercised before the introduction of any combined contraceptive [48,49]. Progestogen-only contraceptives (except DMPA/NET-EN classified as category 3 due to possible glycaemic control worsening and increased thromboembolic risk) as well as non-hormonal methods are the alternative options [48,50,51]. Importantly, the general poor tolerance of progestogen-only pills, particularly due to frequent uterine bleeding, must be taken into account [48].

Gastrointestinal conditions

Oestrogens and progestogens are cleared through hepatic metabolism, and oestrogens act directly on the liver independently of administration route [10,52]. Hormonal contraceptives' use was also suggested as increasing the risk of hepatobiliary damages [53,54]. These considerations must be taken into account in women with hepatic disorders seeking an appropriate contraceptive.

As COC-induced cholestasis is highly recurrent and thought to result from a genetic predisposition [53,55], patients with a history of COC-related cholestatic jaundice should thereafter avoid CHCs (WHO-MEC = 3) [2,56].

Long-term use of COCs may be related with the development of hepatocellular carcinomas and adenomas [53,57]. Women with current or previous benign or malignant hepatic tumours should therefore stop taking or not take CHCs (Table 2) [2,53,56]. On the basis of available data, these methods should also not be used in women with severe decompensated cirrhosis (WHO-MEC = 4). Regarding progestogen-only contraceptives including LNG-IUD, they are not recommended for both women with liver tumours or cirrhosis (WHO-MEC = 3) [2,57,58].

For women with acute or flare viral hepatitis, the risks of initiating CHCs generally outweigh their benefits and, depending on disease severity, should not be used in some cases; while the benefits of CHCs continuation generally outweigh the risks [2,58].

Finally, oestrogens can possibly alter biliary function and increase the cholesterol saturation, which require special caution (Category 3) when CHCs are used in patients with gall bladder disease [2,59].

Are the contraindications defined by the WHO-MEC sufficient?

Differences between national MECs

Although the WHO-MEC offer valuable guidelines, they are not updated often enough, as scientific evidence evolves. Hence, according to more recent MEC produced by other countries/health

authorities [3–8], several other health conditions or medically-relevant characteristics may also make the use of certain contraceptive methods unsafe [9].

Furthermore, for the same medical condition considered by these guidelines, the category in which a specific contraceptive is classified may be different from the category proposed by the WHO [3–8]. These categorisation differences may be useful to know and are summarised in Table 3. Note that medical conditions were not listed in Table 3 if there was no difference in categories between WHO-MEC and UK, US or French-MEC.

Cardiovascular risk factors or diseases

Several divergent viewpoints exist for some major contraceptive methods that can be offered to women with cardiovascular risk factors or diseases (Table 3):

Less stringent positions than those of the WHO-MEC have been taken towards DMPA and NET-EN by the UK-MEC in case of hypertension (Category 2 *vs* 3), and towards progestogen-only contraceptives by the US-MEC in case of acute DVT/PE (Category 2 *vs* 3). This categorisation is surprising, especially in the case of DMPA, the VTE risk relative to the current use of this contraceptive being significantly increased versus non-users [14]. More stringent positions are held by the French-MEC: DMPA and NET-EN being considered as methods that cannot be usually recommended in patients with history of DVT/PE (Category 3 *vs* 2). In patients with a history of stroke, the UK-MEC and the French-MEC do not recommend the continuation of LNG-IUD (Category 3), while the WHO-MEC state it can be used (Category 2).

Rheumatic diseases

The positions of the UK and French-MEC are less stringent than those of the WHO-MEC regarding the use of POP, DMPA, NET-EN, LNG/ETG, and LNG-IUD by SLE women with unknown or positive aPLs. The formers consider that these methods should generally be used in this clinical situation (Category 2), while the WHO-MEC do not usually recommend them (Category 3).

Neurologic conditions

Positions held by the UK and US-MEC applied for all women with migraine without aura irrespective of their age, while the WHO-MEC make a distinction between women aged less than 35 years and those aged 35 and over. According to the US-MEC, there are no restrictions on the continuation of COC, P, CVR in women with migraine without aura (Category 2), while according to the WHO-MEC, continuation of these contraceptives cannot be usually recommended in patients aged < 35 years (Category 3) and should be absolutely contraindicated in those aged ≥ 35 years (Category 4). Interestingly, in women with migraine with aura, irrespective of age, the UK-MEC and the US-MEC consider there is no restriction in the continuation of POP, DMPA, NET-EN, LNG/ETG, LNG-IUD (Category 2 and Category 1, respectively), while the WHO-MEC recommend their discontinuation (Category 3).

Breast cancer

Women who carry deleterious mutations in breast cancer susceptibility genes, such as BRCA1 and BRCA2, have a significantly higher risk of breast cancer. The UK-MEC do not recommend the use of COC, P and CVR in these patients (Category 3). According to the WHO-MEC, current evidence however, does not suggest that the increased risk of breast cancer among BRCA mutation carriers is modified by the use of combined oral contraceptives (WHO-MEC: COC, P, CVR = 1).

Endocrine conditions

In diabetic women with nephropathy, retinopathy, neuropathy and in those with another vascular disease or a > 20-year history of diabetes, the UK-MEC rather surprisingly consider that DMPA and NET-EN can generally be used (Category 2) unlike the WHO-MEC (Category 3).

In obese women with body mass index ≥ 35 kg/m^2, the use of COC, P, CVR is not recommended by the UK-MEC (Category 3), while the WHO-MEC estimate these contraceptive methods can generally be used (Category 2).

Gastrointestinal conditions

No noticeable differences were observed between the WHO-MEC and the UK, US, and French-MEC (see Table 3).

Medical conditions not included in MEC and debatable situations

Several health conditions that are obviously contraindications for the use of some contraceptive methods are not included in any of these guidelines. For example, neither the WHO, UK, US nor French-MEC included in their last updated version contraceptive recommendations for adult women with polycystic ovary syndrome, prolactinemia, hereditary angioedema, renal insufficiency, or pancreatitis or history of pancreatitis associated with severe hypertriglyceridemia.

Furthermore, some of the conditions considered by the WHO-MEC as non-contraindicated situations are questionable.

One example of this is sickle cell disease, an inherited haemoglobinopathy characterised by intermittent vaso-occlusive events and chronic haemolytic anaemia. Effective contraception is strongly recommended in women suffering this condition due to the risk of obstetrical complications and the teratogenic potential of treatments [10,60]. The WHO-MEC state that the benefits of combined hormonal contraceptives outweigh the risks related to pregnancy (Category 2). This position is surprising given that the sickling process increases the risk of clotting and thrombosis, and that the potential for an additive effect on the VTE risk related to oestrogen-containing hormonal contraceptives is still a matter of debate [10,61]. Moreover, the use of Cu-IUD is questionable as it may worsen anaemia. As long as scientific evidence about these safety concerns remains inconclusive, prescribers should exercise caution when choosing a contraceptive for women with sickle cell disease.

The absence of contraindication for etonorgestrel implant in the WHO-MEC, while progestogen-only pills, and of course CHCs, are not allowed in women requiring long-term treatment with enzymatic inducers, is also debatable. Indeed, oestrogen and progestogen being partially metabolised by cytochrome P450 3A4 (CYP3A4), CYP3A4 inducers may affect their metabolism, whatever their administration route, decrease their plasma concentrations, with a possible reduced contraceptive efficacy [10]. Well-known CYP3A4 inducers include anticonvulsants (e.g. barbiturates, carbamazepine, phenytoin, topiramate, oxcarbazepine) and antibiotics (e.g. rifampicin, rifabutin). Since exposure to some of these medicines during pregnancy may be associated with birth defects, prescribers should be cautious when choosing a regular contraceptive method for women requiring these drugs, notably by taking into account the likely duration of concurrent use of both medications and by suggesting alternative or additional methods for combined and progestogen-only contraceptives, including implants [10].

Comorbidities

Finally, as a general rule, when prescribing contraception, clinicians should not only consider the medical condition the woman may have, but also any potentially-related comorbidities. Given the current MEC do not provide specific recommendations for each condition with their comorbid disorders, one potential

Table 3
Major differences between WHO-MEC and UK, US and French-MEC for some common risk factors or diseases.

	WHO-MEC	Fr, UK, or US-MEC
CARDIOVASCULAR RISK FACTORS OR DISEASES		
MULTIPLE RISK FACTORS FOR ARTERIAL CARDIOVASCULAR DISEASE (e.g. older age, smoking, diabetes, hypertension and known dyslipidaemias)		
COC, P, CVR	3/4	3 (UK)
HYPERTENSION (Elevated blood pressure levels (properly taken measurements) - systolic ≥ 160 mm Hg or diastolic ≥ 100 mm Hg)		
POP, LNG/ETG, LNG-IUD	2	1 (UK)
DMPA, NET-EN	3	2 (UK)
HISTORY OF DVT/PE		
COC, P, CVR	4	3* (US)
DMPA, NET-EN	2	3 (FR)
ACUTE DVT/PE		
POP, LNG/ETG, DMPA, NET-EN, LNG-IUD	3	2 (US)
Cu-IUD	1	2 (US)
DVT/PE AND ESTABLISHED ON ANTICOAGULANT THERAPY		
COC, P, CVR	4	3* (US)
Cu-IUD	1	2 (US)
STROKE (history of cerebrovascular accident)		
LNG-IUD	2	I: 2; C: 3 (UK) 3 (FR)
COMPLICATED VALVULAR HEART DISEASE (pulmonary hypertension, risk of atrial fibrillation, history of acute bacterial endocarditis)		
Cu-IUD, LNG-IUD	2	1 (US)
RHEUMATIC DISEASES		
SYSTEMIC LUPUS ERYTHEMATOSUS with positive or unknown antiphospholipid antibodies		
POP, DMPA, NET-EN, LNG/ETG, LNG-IUD	3	2 (UK, Fr)
NEUROLOGIC CONDITIONS		
MIGRAINE WITHOUT AURA – Age < 35 years		
COC, P, CVR	I: 2; C: 3	2 (US)
POP	I: 1; C: 2	1 (US)
DMPA, NET-EN, LNG/ETG, LNG-IUD	2	1 (US)
MIGRAINE WITHOUT AURA – Age ≥ 35 years		
COC, P, CVR	I: 3; C: 4	I: 2; C: 3 (UK) 2 (US)
POP	I: 1; C: 2	1 (US)
DMPA, NET-EN, LNG/ETG, LNG-IUD	2	1 (US)
MIGRAINE WITH AURA – Any age		
POP, DMPA, NET-EN, LNG/ETG, LNG-IUD	I: 2; C: 3	2 (UK) 1 (US)
BREAST CANCER		
CARRIERS OF KNOWN GENE MUTATIONS ASSOCIATED WITH BREAST CANCER (e.g. BRCA1/BRCA2)		
COC, P, CVR	1	3 (UK)
OTHER REPRODUCTIVE TRACT INFECTIONS OR DISORDERS		
GESTATIONAL TROPHOBLASTIC DISEASE		
Undetectable β-hCG levels		
Cu-IUD, LNG-IUD	3	1 (US) 1 (UK)
Decreasing β-hCG levels		
Cu-IUD, LNG-IUD	3	I: 2; C: 1 (US)
Persistently elevated β-hCG levels or malignant disease		
Cu-IUD, LNG-IUD	4	I: 2; C: 1 (US)[§] I: 4; C: 2 (US)[#]
OVARIAN CANCER		
	WHO-MEC	**Fr, UK, or US-MEC**
Cu-IUD, LNG-IUD	I: 3; C: 2	I: 1; C: 1 (US, UK)
ENDOCRINE CONDITIONS		
DIABETES WITH NEPHROPATHY/RETINOPATHY/NEUROPATHY		
DMPA, NET-EN	3	2 (UK)
DIABETES WITH OTHER VASCULAR DISEASE OR DIABETES OF > 20 YEARS' DURATION		
DMPA, NET-EN	3	2 (UK)
OBESITY with BMI ≥ 35 kg/m²		
COC, P, CVR	2	3 (UK)
GASTROINTESTINAL CONDITIONS		
VIRAL HEPATITIS – Acute or flare		
COC, P, CVR	I: 3/4, C: 2	I: 3, C: 2 (UK)

Barr: barrier methods; BMI: body mass index; BRCA: breast cancer susceptibility genes; C: continuation; CIC: combined injectable contraceptive; Co: condom; COC: combined oral contraceptive; Cu-IUD: copper-bearing intrauterine device; CVR: combined contraceptive vaginal ring; D: diaphragm (with spermicide), cervical cap; DMPA: depot medroxyprogesterone acetate (injectable); DVT: deep venous thrombosis; Fr: French; I: initiation; LNG/ETG: levonorgestrel and etonorgestrel (implants); LNG-IUD: levonorgestrel-releasing intrauterine device; NET-EN: noresthisterone enanthate injectable contraceptive; P: combined contraceptive patch; PE: pulmonary embolism; POC: progestogen-only contraceptive; POP: progestogen-only pill; S: spermicide.
[a]Lower risk for recurrent DVT/PE.
[b]With no evidence or suspicion of intrauterine disease.
[c]With evidence or suspicion of intrauterine disease.

Table 4
WHO-MEC for obesity and its related comorbidities *(adapted from Shaw KA and Edelman AB, 2013)* [64].

	COC	P CVR	POP	DMPA	LNG ETG	Cu-IUD	LNG-IUD
Obesity	2	2	1	1	1	1	1
Age > 40	2	2	1	2	1	1	1
Hypertension[a]	3	3	1	2	1	1	1
Diabetes mellitus[b]	2	2	2	2	2	1	2
Hyperlipidaemia	2/3	2/3	2	2	2	1	2
Cardiovascular disease (CVD)	4	4	2	3	2	1	2
Multiple CVD risk factor[c]	3/4	3/4	2	3	2	1	2
Bariatric surgery malabsorptive[d]	3	1	3	1	1	1	1
Bariatric surgery restrictive[d]	1	1	1	1	1	1	1

COC: combined oral contraceptive; Cu-IUD: copper-bearing intrauterine device; CVR: combined contraceptive vaginal ring; DMPA: depot medroxyprogesterone acetate (injectable); LNG/ETG: levonorgestrel and etonorgestrel (implants); LNG-IUD: levonorgestrel-releasing intrauterine device; P: combined contraceptive patch; POP: progestogen-only pill.
[a] If blood pressure < 160/100 mm Hg and can be assessed.
[b] Without evidence of peripheral or vascular disease.
[c] Such as older age, smoking, diabetes, hypertension.
[d] US-MEC recommendations.

option is weighing the condition-specific recommendation by the comorbidity that elicits the highest eligibility category. In the example of obesity, particular attention should be paid to concomitant cardiovascular disease and/or risk factors (Table 4).

In such a situation, a multidisciplinary approach is generally required to determine the most appropriate contraceptive method. Consulting some specialised books on contraception may also be helpful [10–12,62,63].

Focus on barrier contraceptive methods

There are few restrictions on the use of barrier methods (e.g. condoms, diaphragms, cervical caps and spermicides) (Table 5). Furthermore, most of these hormone-free methods can be obtained without prescription and do not require consultation with a healthcare provider before use. Condoms can be used as a primary or as an additional contraceptive method, but also to reduce the risk of sexually-transmitted infections, including acquired immunodeficiency syndrome. Spermicides alone or in combination with diaphragm or cervical cap can be used safely without restrictions, except by high-risk HIV women (WHO-MEC = Category 4) or by those living with HIV and/or receiving antiretrovirals (WHO-MEC = Category 3). Actually, the repeated and high doses of the widely used spermicide nonoxynol-9 have been associated with genital lesions and thus a potential increased risk of HIV acquisition. As a matter of prudence, the same precaution of use applies to benzalkonium chloride-containing spermicides, although no such destructive effects on vaginal or cervical mucosa have been reported with these products.

Barrier methods may thus represent an alternative or an additional contraceptive option for women with decreased fertility such as breast-feeding and perimenopausal women [13,64], and women in whom other methods are contraindicated or not tolerated, after having been properly informed about the lower efficacy of these methods. Actually, it is important to keep in mind that barrier methods have relatively higher typical-use failure rates than hormonal or intrauterine methods and must be used correctly to maximise their effects. The overall risk to benefit balance should therefore be carefully weighed on an individual basis taking particularly into account the potential risk of an eventual pregnancy.

Role of the prescribers and providers of a contraceptive method

The choice of a contraceptive method should be first the choice of the woman/couple who requests birth control. The prescriber is involved in this choice at various levels:

- by screening the potential contraindications associated with the patient's desired method.
- by informing the patient, without flooding her with an excess of information, on the mode of action, the main risks and potential benefits related to the method.
- by ensuring that the selected contraceptive best corresponds to the user's personality, while respecting as best as possible her health, her desire for future pregnancy and allowing her to have a full sexual life.

During patient's follow-up visits, the prescriber or the practitioner has to ascertain the correct use of the chosen method, its general and psychological tolerability. The appropriateness of the contraceptive method should be regularly reassessed by taking into account (i) the background conditions, sexuality, age, parity, smoking and other naturally variable parameters, (ii) the desire of the woman/couple, that is sometimes changing, and finally (iii) the continuous progress made in the fields of human reproduction and birth control.

Conclusion

Nowadays, no one can be unaware of the contraindications to the various contraceptives, which are now well classified.

The WHO-MEC for Contraceptive Use offer guidance to prescribers regarding the safe use of contraceptive methods and are periodically revised. Although WHO-MEC are generally sufficient for the medical conditions gynaecologists and other providers generally face, it is important to know that other MEC for contraceptive use exist and may provide additional information.

As a general remark, among all contraceptive methods, hormonal contraceptives, and particularly combined hormonal contraceptives, are contraindicated for use in the largest number of pathological conditions, while there are very few, if any, medical conditions that contraindicate progestogen-only contraceptives (except injectable DMPA), long-acting reversible contraceptives (LARC: e.g. IUD, progestogen-only implant), and local contraceptive agents or devices (condoms, diaphragms, cervical caps, spermicides).

However, it should be remembered that WHO-MEC as well as US, UK and French-MEC only address the question of the safety of contraceptives and not their effectiveness. Hence, the individual health risk that pregnancy may pose (maternal and perinatal morbidity and mortality), especially unintended pregnancy, should always be taken into account.

The compliance ability of women is also an important issue that the prescribers have to consider. The non-contraceptive benefits of

Table 5
WHO-MEC regarding the use of barrier methods in selected medical conditions.

	Barr		
	Co	S	D
CARDIOVASCULAR RISK FACTORS OR DISEASES			
Smoking - Age < 35 years	1	1	1
Smoking - Age ≥ 35 years, whatever the number of cigarettes/day	1	1	1
Multiple risk factors for arterial cerebrovascular disease, e.g. older age, smoking, diabetes, hypertension and known dyslipidemias	1	1	1
Hypertension	1	1	1
History of DVT/PE	1	1	1
Acute DVT/PE	1	1	1
DVT/PE and established on anticoagulant therapy	1	1	1
Major surgery with prolonged immobilisation	1	1	1
Known thrombogenic mutations (e.g. Factor V Leiden, prothrombin mutation, protein S, protein C, and antithrombin deficiencies)	1	1	1
Current and history of ischemic heart disease	1	1	1
Stroke (history of cerebrovascular accident)	1	1	1
Complicated valvular heart disease (pulmonary hypertension, risk of atrial fibrillation, history of acute bacterial endocarditis)	1	1	2
RHEUMATIC DISEASES			
Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies	1	1	1
Severe thrombocytopenia	1	1	1
NEUROLOGIC CONDITIONS			
Migraine without aura, at any age	1	1	1
Migraine with aura, at any age	1	1	1
GYNAECOLOGICAL DISORDERS OR INFECTIONS			
Current breast cancer	1	1	1
Past breast cancer and no evidence of current disease for 5 years	1	1	1
Unexplained vaginal bleeding (suspicion for serious condition) – before evaluation	1	1	1
Immediate post-septic abortion	1	1	1
Gestational C trophoblastic disease	1	1	1
Cervical cancer (awaiting treatment)	1	2	1
Endometrial cancer	1	1	1
Ovarian cancer	1	1	1
Uterine fibroids with distortion of the uterine cavity	1	1	1
Anatomical abnormalities – distorted uterine cavity incompatible with IUD insertion	1	1	NA
Current pelvic inflammatory disease	1	1	1
HIV/AIDS and OTHER INFECTIONS			
Asymptomatic or mild HIV clinical disease	1	3	3
Severe or advanced HIV clinical disease (WHO stage 3 or 4)	1	3	3
High risk of HIV	1	4	4
Pelvic tuberculosis	1	1	1
Current purulent cervicitis or chlamydial infection or gonorrhoea	1	1	1
ENDOCRINE DISORDERS			
Diabetes – With nephropathy/retinopathy/neuropathy	1	1	1
Diabetes – Other vascular disease or diabetes of > 20 years' duration	1	1	1
HEPATOBILIARY DISORDERS			
Medically-treated gall bladder disease	1	1	1
Current gall bladder disease	1	1	1
Past-COC related cholestasis	1	1	1
Acute or flare of viral hepatitis	1	1	1
Severe (decompensated) cirrhosis	1	1	1
Benign hepatocellular adenoma	1	1	1
Malignant hepatoma	1	1	1

Barr: barrier methods; Co: condom; COC: combined oral contraceptive; D: diaphragm (with spermicide) and cervical cap; DVT: deep venous thrombosis; NA: not applicable; PE: pulmonary embolism; S: spermicide.

different contraceptive methods may favour it. If the compliance is of negligible importance with LARC methods, its role becomes essential to ensure optimal efficacy of other methods such as oral contraceptives. This is also particularly relevant for barrier methods, such as spermicides, often regarded as less effective but that can provide a suitable efficacy when given to women at low risk of pregnancy such as lactating [13] or perimenopausal women [65], and when used in compliance with the instructions for use of these methods.

In any case, two principles should be respected: the utmost must be done to find an acceptable contraceptive solution, even in the most complex cases; and the proposed contraceptive solution should never be harmful for the patient: ***primum non nocere***.

Declaration of interest statement

Dr D. Serfaty is a scientific consultant to Laboratoire Innotech International.

References

[1] United Nations, Department of Economic and Social Affairs, Population Division. Trends in contraceptive use worldwide 2015 (ST/ESA/SER.A/349). 2015.
[2] WHO. Medical eligibility criteria for contraceptive use. 5th edition 2015.
[3] Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U. S. medical eligibility criteria for contraceptive use. MMWR Recomm Rep 2016;65(3)1–103, doi:http://dx.doi.org/10.15585/mmwr.rr6503a1 2016.
[4] FSRH. UK medical eligibility criteria for contraceptive use. 2016. . [Accessed 14 June 2018] https://www.fsrh.org/ukmec/.

[5] HAS. Contraception chez la femme à risque cardiovasculaire. July. Fiche Mémo; 2013. . [Accessed 14 June 2018] https://www.has-sante.fr/portail/jcms/c_1638478/fr/contraception-chez-la-femme-a-risque-cardiovasculaire.
[6] HAS. Guide – Affection de longue durée. September. Cirrhoses; 2008. . [Accessed 14 June 2018] https://www.has-sante.fr/portail/jcms/c_718958/fr/ald-n-6-cirrhoses.
[7] HAS. Contraception chez la femme adulte en âge de procréer (hors post-partum et post-IVG). October. Fiche mémo; 2017. . [Accessed 14 June 2018] https://www.has-sante.fr/portail/jcms/c_1752542/fr/contraception-chez-la-femme-adulte-en-age-de-procreer-hors-post-partum-et-post-ivg.
[8] HAS. Méthodes contraceptives: focus sur les méthodes les plus efficaces disponibles. Document de synthèse. March. 2013. . [Accessed 14 June 2018] https://www.has-sante.fr/portail/jcms/c_1369314/fr/methodes-contraceptives-focus-sur-les-methodes-les-plus-efficaces-disponibles.
[9] Millar S, Trussell J. Medical eligibility criteria on both sides of the Atlantic Ocean. Contraception 2017;96:307–9, doi:http://dx.doi.org/10.1016/j.contraception.2017.07.164.
[10] Serfaty D. La Contraception Edition. Paris: ESKA; 2016.
[11] Hatcher, et al. Contraceptive technology. 20th revised edition New York: Ardent Media; 2011 from RA.
[12] Guillebeaud J. Contraception today. 8th edition CRC Press; 2016.
[13] Serfaty D. Contraception in breastfeeding women: place for spermicides. J Gynecol Obstet Biol Reprod (Paris) 2015;44(1):18–27.
[14] Practice Committee of the American Society for Reproductive Medicine. Combined hormonal contraception and the risk of venous thromboembolism: a guideline. Fertil Steril 2017;107(1):43–51, doi:http://dx.doi.org/10.1016/j.fertnstert.2016.09.027.
[15] Plu Bureau G, Sabbagh E, Hugon-Rodin J. Hormonal contraception and vascular risk: CNGOF Contraception Guidelines. Gynecol Obstet Fertil Senol 2018;46(12):823–33, doi:http://dx.doi.org/10.1016/j.gofs.2018.10.007.
[16] Plu Bureau G, Maitrot Mantelet L, Hugon Rodin J, Canonico M. Hormonal contraceptives and venous thromboembolism: an epidemiological update. Best practice and research. Clinical Endocrinology and Metabolism. 2013;27(1):25–34, doi:http://dx.doi.org/10.1016/j.beem.2012.11.002.
[17] Plu Bureau G, Hugon Rodin J, Maitrot Mantelet L, Canonico M. Hormonal contraceptives and arterial disease: an epidemiological update. Best practice and research. Clin Endocrinol Metabol 2013;27(1):35–45, doi:http://dx.doi.org/10.1016/j.beem.2012.11.003.
[18] Sitruk-Ware R. Hormonal contraception and thrombosis. Fertil Steril 2016;106(6):1289–94, doi:http://dx.doi.org/10.1016/j.fertnstert.2016.08.039.
[19] Dragoman MV, Tepper NK, Fu R, Curtis KM, Chou R, Gaffield ME. A systematic review and meta-analysis of venous thrombosis risk among users of combined oral contraception. Int J Gynecol Obstet 2018;141(3):287–94, doi:http://dx.doi.org/10.1002/ijgo.12455.
[20] Oedingen C, Scholz S, Razum O. Systematic review and meta-analysis of the association of combined oral contraceptives on the risk of venous thromboembolism: the role of the progestogen type and estrogen dose. Thromb Res 2018;165:68–78, doi:http://dx.doi.org/10.1016/j.thromres.2018.03.005.
[21] Lalude OO. Risk of cardiovascular events with hormonal contraception: insights from the Danish cohort study. Curr Cardiol Rep 2013;15(7):374, doi:http://dx.doi.org/10.1007/s11886-013-0374-2.
[22] Lidegaard O. Hormonal contraception, thrombosis and age. Expert Opin Drug Saf 2014;13(10):1353–60, doi:http://dx.doi.org/10.1517/14740338.2014.950654.
[23] Tepper NK, Whiteman MK, Marchbanks PA, James AH, Curtis KM. Progestin-only contraception and thromboembolism: a systematic review. Contraception 2016;94(6):678–700, doi:http://dx.doi.org/10.1016/j.contraception.2016.04.014.
[24] Bonassi Machado R, Gandolpho AC, Santana N, Bocardo RC, Palandri N, Morassutti Machado R. Contraception for women with heart disease: an update. Minerva Ginecol 2017;69(3):259–68, doi:http://dx.doi.org/10.23736/S0026-4784.17.04041-2.
[25] Culwell KR, Curtis KM, del Carmen Cravioto M. Safety of contraceptive method use among women with systemic lupus erythematosus: a systematic review. Obstet Gynecol 2009;114(2 Pt 1):341–53, doi:http://dx.doi.org/10.1097/AOG.0b013e3181ae9c64.
[26] Lazzaroni MG, Dall'Ara F, Fredi M, Nalli C, Reggia R, Lojacono A, et al. A comprehensive review of the clinical approach to pregnancy and systemic lupus erythematosus. J Autoimmun 2016;74:106–17, doi:http://dx.doi.org/10.1016/j.jaut.2016.06.016.
[27] Lateef A, Petri M. Systemic lupus erythematosus and pregnancy. Rheum Dis Clin N Am 2017;43:215–26, doi:http://dx.doi.org/10.1016/j.rdc.2016.12.009.
[28] Ostensen M, Clowse M. Pathogenesis of pregnancy complications in systemic lupus erythematosus. Curr Opin Rheumatol 2013;25(5):591–6, doi:http://dx.doi.org/10.1097/BOR.0b013e328363ebf7.
[29] Clowse ME. Lupus activity in pregnancy. Rheum Dis Clin North Am 2007;33(2):237–52.
[30] de Jesus GR, Mendoza-Pinto C, de Jesus NR, Dos Santos FC, Klumb EM, Carrasco MG, et al. Understanding and managing pregnancy in patients with lupus. Autoimmune Dis 2015;2015:943490, doi:http://dx.doi.org/10.1155/2015/943490.
[31] Lourenço B, Kozu KT, Leal GN, Silva MF, Fernandes EG, França CM, et al. Contraception for adolescents with chronic rheumatic diseases. Rev Bras Reumatol Engl Ed 2017;57(1):73–81, doi:http://dx.doi.org/10.1016/j.rbre.2016.07.016.
[32] Rojas-Villarraga A, Torres-Gonzalez JV, Ruiz-Sternberg ÁM. Safety of hormonal replacement therapy and oral contraceptives in systemic lupus erythematosus: a systematic review and meta-analysis. PLoS One 2014;9(8)e104303, doi:http://dx.doi.org/10.1371/journal.pone.0104303 eCollection 2014.
[33] Andreoli L, Bertsias GK, Agmon-Levin N, Brown S, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis 2017;76(3):476–85, doi:http://dx.doi.org/10.1136/annrheumdis-2016-209770.
[34] Gensous N, Doassans-Comby L, Lazaro E, Duffau P. Lupus érythémateux systémique et contraception : revue systématique de la littérature. Rev Med Interne 2017;38:358–67.
[35] Gryglas A, Smigiel R. Migraine and stroke: What's the link? What to do?. Curr Neurol Neurosci Rep 2017;17:22, doi:http://dx.doi.org/10.1007/s11910-017-0729-y.
[36] Cappy H, Lucas C, Catteau-Jonard S, Robin G. Migraine and contraception. Gynecol Obstet Fertil 2015;43(3):234–41, doi:http://dx.doi.org/10.1016/j.gyobfe.2015.01.006.
[37] Kurth T, Winter AC, Eliassen AH, Dushkes R, Mukamal KJ, Rimm EB, et al. Migraine and risk of cardiovascular disease in women: prospective cohort study. BMJ 2016;353:i2610, doi:http://dx.doi.org/10.1136/bmj.i2610.
[38] Champaloux SW, Tepper NK, Monsour M, Curtis KM, Whiteman MK, Marchbanks PA, et al. Use of combined hormonal contraceptives among women with migraines and risk of ischemic stroke. Am J Obstet Gynecol 2017;216(5)489, doi:http://dx.doi.org/10.1016/j.ajog.2016.12.019 e1-489.e7.
[39] Sacco S, Merki-Feld GS, Ægidius KL, Bitzer J, Canonico M, Kurth T, et al. European Headache Federation (EHF) and the European Society of Contraception and Reproductive Health (ESC). Hormonal contraceptives and risk of ischemic stroke in women with migraine: a consensus statement from the European Headache Federation (EHF) and the European Society of Contraception and Reproductive Health (ESC). J Headache Pain 2017;18(1):108, doi:http://dx.doi.org/10.1186/s10194-017-0815-1.
[40] Allais G, Chiarle G, Bergandi F, Benedetto C. The use of progestogen-only pill in migraine patients. Expert Rev Neurother 2016;16(1):71–82, doi:http://dx.doi.org/10.1586/14737175.2016.1127161.
[41] Gonçalves V, Sehivic I, Quinn G. Childbearing attitudes and decisions of young breast cancer survivors: a systematic review. Hum Reprod Update 2013;1–14, doi:http://dx.doi.org/10.1093/humupd/dmt039.
[42] Casey PM, Faubion SS, MacLaughlin KL, Long ME, Pruthi S. Caring for the breast cancer survivor's health and well-being. World J Clin Oncol 2014;5(4):693–704, doi:http://dx.doi.org/10.5306/wjco.v5.i4.693.
[43] Hamy AS, Abuellellah H, Hocini H, Coussy F, Gorins A, Serfaty D, et al. Contraception after breast cancer: a retrospective review of the practice among French gynecologists in the 2000's. Eur J Gynaecol Oncol 2014;35(2):149–53.
[44] Güth U, Huang DJ, Bitzer J, Moffat R. Unintended pregnancy during the first year after breast cancer diagnosis. Eur J Contracept Reprod Health Care 2016;21(4):290–4, doi:http://dx.doi.org/10.1080/13625187.2016.1180678.
[45] Bakkum-Gamez JN, Laughlin SK, Jensen JR, Akogyeram CO, Pruthi S. Challenges in the gynecologic care of premenopausal women with breast cancer. Mayo Clin Proc 2011;86(3):229–40, doi:http://dx.doi.org/10.4065/mcp.2010.0794.
[46] Serfaty D. In: Abrégés, editor. Contraception. 4e édition Paris: Elsevier Masson SAS; 2011.
[47] MØrch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard O. Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med 2017;377:2228–39, doi:http://dx.doi.org/10.1056/NEJMoa1700732.
[48] Gourdy P. Diabetes and oral contraception. Best Pract Res Clin Endocrinol Metab 2013;27(1):67–76, doi:http://dx.doi.org/10.1016/j.beem.2012.11.001.
[49] Gourdy P, Bachelot A, Catteau-Jonard S, Chabbert-Buffet N, Christin-Maître S, Conard J, et al. Hormonal contraception in women at risk of vascular and metabolic disorders: guidelines of the French Society of Endocrinology. Ann Endocrinol (Paris) 2012;73(5):469–87, doi:http://dx.doi.org/10.1016/j.ando.2012.09.001.
[50] Afsana F. Contraception and diabetes. J Pak Med Assoc 2016;66(Suppl. 1)S96–8 11.
[51] O'Brien SH, Koch T, Vesely SK, Schwarz EB. Hormonal contraception and risk of thromboembolism in women with diabetes. Diabetes Care 2017;40:233–8, doi:http://dx.doi.org/10.2337/dc16-1534.
[52] Kapp N. WHO provider brief on hormonal contraception and liver disease. Contraception 2009;80(4):325–6, doi:http://dx.doi.org/10.1016/j.contraception.2009.01.020.
[53] Mallat A. Foie et contraception orale. Post'U. 2010;239–44.
[54] Björnsson ES. Drug-induced cholestasis. In: Carey EJ, Lindor KD, editors. Cholestatic liver disease, clinical gastroenterology. . p. 13, doi:http://dx.doi.org/10.1007/978-1-4939-1013-7_2.
[55] Meier Y, Zodan T, Lang C, Zimmermann R, Kullak-Ublick GA, Meier PJ, et al. Increased susceptibility for intrahepatic cholestasis of pregnancy and contraceptive-induced cholestasis in carriers of the 1331T&C polymorphism in the bile salt export pump. World J Gastroenterol 2008;14(1):38–45.
[56] Lindberg MC. Hepatobiliary complications of oral contraceptives. J Gen Intern Med 1992;7(2):199–209.
[57] Ledda C, Loreto C, Zammit C, Marconi A, Fago L, Matera S, et al. Non-infective occupational risk factors for hepatocellular carcinoma: a review (Review). Mol Med Rep 2017;15(2):511–33, doi:http://dx.doi.org/10.3892/mmr.2016.6046.
[58] Kapp N, Tilley IB, Curtis KM. The effects of hormonal contraceptive use among women with viral hepatitis or cirrhosis of the liver: a systematic review. Contraception 2009;80(4):381–6, doi:http://dx.doi.org/10.1016/j.contraception.2009.04.007.

[59] Bourlière M, Castellani P. Foie et traitements hormonaux. Hépato-gastro & Oncologie digestive 2003;10(4).
[60] Binette A, Howatt K, Waddington A, Reid RL. Ten challenges in contraception. J Womens Health 2017;26(1):44–9, doi:http://dx.doi.org/10.1089/jwh.2016.5854.
[61] Smith-Whitley K. Reproductive issues in sickle cell disease. Blood 2014;124(24):418–24, doi:http://dx.doi.org/10.1182/blood-2014-07-577619.
[62] Raccah-Tebeka B, Plu-Bureau G. La contraception en pratique. Elsevier Masson; 2013.
[63] World Health Organization Department of Reproductive Health and Research (WHO/RHR) and Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (CCP). Knowledge for health project. Family planning: a global handbook for providers (2011 update). Baltimore and Geneva: CCP and WHO; 2011.
[64] Shaw KA, Edelman AB. Obesity and oral contraceptives: a clinician's guide. Best Pract Res Clin Endocrinol Metab 2013;27(1):55–65, doi:http://dx.doi.org/10.1016/j.beem.2012.09.001.
[65] Serfaty D. Contraception during perimenopause: The spermicides option. J Gynecol Obstet Hum Reprod 2017;46(3):211–8, doi:http://dx.doi.org/10.1016/j.jogoh.2016.10.007.