Faculty of Family Planning and Reproductive Health Care
Clinical Effectiveness Unit

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FFPRHC Guidance (October 2003)
First Prescription of Combined Oral Contraception

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This Guidance provides information for clinicians on the steps to be taken before providing a woman with her first prescription for combined oral contraception. It updates and replaces previous Faculty Guidance.[1] A key to the grades of recommendations, based on levels of evidence, is given at the end of this document. Details of the methods used by the Clinical Effectiveness Unit (CEU) in developing this Guidance, and evidence tables summarising the research basis of the recommendations, are available on the Faculty website (www.ffprhc.org.uk). Abbreviations used include: blood pressure (BP), body mass index (BMI), bone mineral density (BMD), breakthrough bleeding (BTB), *British National Formulary* (BNF), combined oral contraception (COC), Committee on Safety of Medicines (CSM), confidence interval (CI), deep vein thrombosis (DVT), emergency contraception (EC), ethinyl oestradiol (EE), Faculty Aid to Continuing Professional Development Topics (FACT), Family Planning Association (fpa), follicle-stimulating hormone (FSH), general practitioner (GP), intermenstrual bleeding (IMB), luteinising hormone (LH), microgram (µg), myocardial infarction (MI), odds ratio (OR), oral contraception (OC), pulmonary embolism (PE), relative risk (RR), Scottish Intercollegiate Guideline Network (SIGN), sexually transmitted infection (STI), Summary of Product Characteristics (SPCs), venous thromboembolism (VTE), World Health Organization (WHO), WHO *Medical Eligibility Criteria* (WHOMEC), WHO *Selected Practice Recommendations* (WHOSPR).

What is combined oral contraception (COC)?

Combined oral contraception (COC) is the most commonly used contraceptive method by women aged 16 to 49 years.[2] This Guidance provides evidence-based recommendations and good practice points for clinicians advising women considering their *first prescription* of COC. A holistic approach to contraceptive provision involves considering the individual's overall sexual and reproductive health needs. By informing women of potential risks, benefits and uncertainties in language they can understand, clinicians can enable women to reach their own contraceptive choices. Access for women can be enhanced by service innovations such as nurse prescribing, Patient Group Directions and convenient clinic times.

In current practice, low-dose COCs, containing 20–35 micrograms (µg) ethinyl oestradiol (EE) in combination with a progestogen, have generally replaced older COCs containing 50 µg EE or more. In this Guidance, the term COC refers to low-dose (20–35 µg EE) monophasic preparations, unless otherwise stated. Progestogens include: norethisterone and levonorgestrel; desogestrel and gestodene; norgestimate; and the newest progestogen, drospirenone. The terms 'second' and 'third' generation can be confusing and unhelpful and so will not be used in this Guidance.

Recommendations

✓ **A holistic approach should be taken when advising women about contraceptive choices.**

✓ **Contraceptive services should be organised to optimise women's access and choices.**

What should a clinician assess before prescribing COC?

Clinical history taking and examination allow an assessment of medical eligibility for COC use. In this context, the clinical history should include medical, sexual [to assess risk of sexually transmitted infection (STI)], family and drug history, as well as details of reproductive health and previous contraceptive use. With this information, clinicians can advise women appropriately on their contraceptive options, taking account of both medical and social factors.

Who is medically eligible to use COC?

The World Health Organization *Medical Eligibility Criteria for Contraceptive Use*[3] (WHOMEC) provides evidence-based recommendations to ensure that women can select their most appropriate method of contraception without unnecessary medical barriers. Eligibility, rather than ineligibility (or contraindication), is described. Circumstances where benefits of COC use outweigh risks (WHO 1, 'unrestricted use' and WHO 2, 'benefits outweigh risks') are summarised in Table 1, as are circumstances where risks of COC use outweigh benefits (WHO 3, 'risks outweigh benefits' and WHO 4, 'unacceptable health risk'). Evidence to support important *ineligibility* criteria is discussed here. Where this Guidance suggests a more cautious approach compared to the WHOMEC, this is highlighted in the tables and text.

Age. Women may start COC any time after menarche (WHO 1) and continue until the menopause (WHO 2) unless there are co-existing disorders or risk factors.[3] Risk of cardiovascular disease increases with age and must be taken into account when counselling women aged over 40 years considering use of COC.

Smoking. Myocardial infarction (MI) and stroke are rare in women of reproductive age but smoking is an important independent risk factor. Heavy smokers (>15 cigarettes per day) have a three-fold increase in the risk of MI[4] and a two-fold increase in the risk of stroke compared to non-

Table 1 *WHO* Medical Eligibility Criteria for Contraceptive Use[3]

CATEGORY WHO 1 – Unrestricted use	CATEGORY WHO 2 – Benefits outweigh risks
Age – menarche to <40 years	**Age** – ≥40 years
Parity – nulliparous and parous	**Breastfeeding** – >6 months postpartum
Postpartum – >21 days if not breastfeeding	**Smoking** – aged <35 years
Post-abortion – immediately after first and second trimester	**Obesity** – BMI >30
Past ectopic pregnancy	**History of hypertension in pregnancy**
History of pelvic surgery	**VTE** – in a first-degree relative
Minor surgery without immobilisation	**Major surgery without immobilisation**
Varicose veins	**Superficial thrombophlebitis**
Non-migrainous headaches – mild or severe	**Known hyperlipidaemias**
Epilepsy – not using liver enzyme-inducers	**Valvular heart disease** – uncomplicated
Vaginal bleeding – unsuspicious irregular, heavy or prolonged	**Migraine headaches** – without focal symptoms in women aged <35 years
Endometriosis	**Vaginal bleeding** – suspicious for serious condition before evaluation
Benign ovarian tumour	**CIN and cervical cancer**
Severe dysmenorrhoea	**Breast disease** – undiagnosed breast lump
Trophoblastic disease[a] – benign and malignant	**Diabetes** – NIDDM and IDDM, non-vascular disease
Cervical ectropion	**Gallbladder disease** – asymptomatic or treated with a cholecystectomy
Breast disease – benign breast disease or a family history of breast cancer	**History of cholestasis** – pregnancy-related
Endometrial or ovarian cancer	**Sickle cell disease**
PID – current or within the last 3 months	
STI – current or within the last 3 months, vaginitis or increased risk of STI	
HIV/AIDS – current HIV/AIDS, risk of HIV/AIDS	
Schistosomiasis, pelvic and non-pelvic TB, malaria	
Anaemias – thalassaemia, iron deficiency	
Antibiotics – excluding rifampicin and griseofulvin	

CATEGORY WHO 3 – Risks outweigh benefits	CATEGORY WHO 4 – Unacceptable health risk (i.e. should not be used)
Breastfeeding – between 6 weeks and 6 months postpartum and primarily breastfeeding	**Breastfeeding** – <6 weeks postpartum
Postpartum – <21 days	**Smoking** – aged >35 years and smoking >15 cigarettes/day
Smoking – aged >35 years and smoking <15 cigarettes/day	**Cardiovascular disease** – multiple risk factors for arterial cardiovascular disease
Hypertension[c] – a history of hypertension when BP cannot be measured, adequately controlled BP where it can be measured, elevated BP 140–159 mmHg systolic and 90–99 mmHg diastolic	**Hypertension**[c] – BP >160 mmHg systolic, >100 mmHg diastolic
Migraine – without focal symptoms in women aged ≥35 years	**VTE** – current or past history
Breast disease – past history of breast cancer and no evidence of recurrence for 5 years	**Major surgery with prolonged immobilisation**
Gallbladder disease – symptomatic medically treated or current	**Current ischaemic heart disease**
Cirrhosis – mild compensated	**Stroke**
Commonly used drugs which affect liver enzymes[b] – antibiotics (rifampicin and griseofulvin) and certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone)	**Valvular heart disease** – complicated by pulmonary hypertension, atrial fibrillation, history of subacute bacterial endocarditis
	Migraine headaches – with focal neurological symptoms at any age
	Breast disease – current breast cancer
	Diabetes – nephropathy, retinopathy, neuropathy or other vascular disease, or diabetes of >20 years duration
	Cirrhosis[d] – severe decompensated
	Liver tumours – benign and malignant

[a]RCOG Guidelines suggest avoiding hormonal contraception until serum human chorionic gonadotrophin (hCG) is normal.
[b]If, after counselling, women using liver enzyme-inducers wish to use COC, a high-dose COC with additional barrier contraception is advised and for 28 days after liver enzyme-inducers are discontinued.
[c]CEU advised consistently measured BP over 140 mmHg systolic and 90 mmHg diastolic
[d]WHOMEC previously recommended active viral hepatitis were advised against use of COC (WHO 4); for carriers COC use was unrestricted (WHO 1).
AIDS, acquired immune deficiency syndrome; BP, blood pressure; CEU, Clinical Effectiveness Unit; CIN, cervical intraepithelial neoplasia; COC, combined oral contraception; HIV, human immunodeficiency virus; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; PID, pelvic inflammatory disease; RCOG, Royal College of Obstetricians and Gynaecologists; STI, sexually transmitted infection; TB, tuberculosis; VTE, venous thromboembolism; WHO, World Health Organization.

smokers.[5,6] In heavy smokers, the risk of MI is further increased with COC use [relative risk (RR), 20.8; 95% CI 5.2–83.1], as is the risk of ischaemic stroke [odds ratio (OR) 7.2; 95% CI 3.23-16.1].[5] Two recent case-control studies[7,8] have also identified a two-fold increase in the risk of venous thromboembolism (VTE) associated with smoking (OR 2.0; 95% CI 1.3–3.3).[7] A recently reported large study compared mortality in relation to contraceptive use and smoking[9] and confirmed that the risks associated with COC use are confined to smokers. For women who smoke >15 cigarettes per day the rate ratio of death from all causes is doubled (rate ratio 2.14; 95% CI 1.81–2.53). The risks of stroke, MI and VTE increase with age, therefore smokers over the age of 35 years are advised against the use of COC (WHO 3).[3] Smokers under the age of 35 years can use COC but should be given information regarding health risks associated with smoking and given support to stop.

Obesity. Body mass index (BMI) >40 kg/m^2 constitutes morbid obesity[10] and is an independent risk factor for cardiovascular disease and VTE. Despite this, WHOMEC recommends that the benefits of COC use by women with a BMI ≥30 kg/m^2 outweigh the risks (WHO 2).[3] No upper limit of BMI is given, but additional risk factors should be considered. The *British National Formulary* (BNF), however, recommends that women with a BMI >39 kg/m^2

should not use COC.[11] Evidence from recent case-control studies suggests that VTE risk increases with increasing BMI.[8,7,12] The VTE risk increased two-fold for women with a BMI >30 (OR 1.9; 95% CI 1.1–3.1) and increased almost four-fold with a BMI >35 (OR 3.8; 95% CI 1.8–8.0).[8] Further evidence to support an increased risk with increasing BMI was obtained from two further studies.[7,12] After counselling, women may still choose to use COC but consideration should be given to the use of alternative contraceptive methods.

Hypertension is associated with an increased risk of MI[4] and stroke.[5,13,14] Hypertensive COC users have a 10-fold increased risk of ischaemic stroke[5] and of haemorrhagic stroke[13] compared to normotensive non-users. Pooled data from four large phase III clinical trials suggest that COC has a negligible effect on blood pressure (BP) itself.[15] Women with BP consistently greater than 140 mmHg systolic or 90 mmHg diastolic should be advised against use of COC.[3]

Venous thromboembolism (VTE). WHOMEC recommend women with a personal history or current VTE [deep vein thrombosis (DVT) and pulmonary embolism (PE)] should be advised against the use of COC (WHO 4). WHOMEC, however, suggests that the benefits of COC use outweigh the risks for women with a family history (first-degree relative) of VTE (WHO 2).[3] A recent cohort study suggested that having a positive or negative family history of VTE did not allow women who were carriers of thrombophilia mutations to be identified with any degree of sensitivity.[16] A family history of VTE, however, may alert clinicians to those women who may have an increased risk of VTE.[17] Venous thrombosis is a disease for which there is evidence of synergism between genetic causes (factor V Leiden mutation, prothrombin 20210A, protein C and protein S deficiency, antithrombin III deficiency, antiphospholipid syndrome) and acquired risk factors (pregnancy, puerperium, hormonal contraceptive use, surgery, trauma, immobilisation, malignancy).[18] Even when a genetic thrombophilia is identified, not every woman will develop venous thrombosis. Exposure to acquired risk factors, such as COC, may increase the risk but only for some women. The CEU recommends that women with a family history of VTE in a first-degree relative, under the age of 45 years, should be advised that the risks of COC use might outweigh the benefits. Alternative contraceptive options should be considered but if alternatives are unacceptable a thrombophilia screen may help decision-making (refer to section on examinations and tests).

Migraine. The International Headache Society classifies migraine with focal symptoms as indicating ischaemia. Focal symptoms include: homonymous visual disturbances; unilateral paraestheia and/or numbness; unilateral weakness; and aphasia or unclassifiable speech disorder.[19] Visual symptoms progress from 'fortification spectra' (a star-shaped figure near the point of fixation with scintillating edges) to scotoma (a bright shape which gradually increases in size). Flashing lights are not identified as focal symptoms.[20] Migraines increase the risk of ischaemic stroke three-fold, but it is unclear if migraine without focal symptoms is associated with any increased risk.[5,6] The absolute risk of stroke in migraine sufferers however, is low (17–19 per 100 000 woman-years).[21] Three case-control studies support an increased risk of stroke in COC users with migraine, compared to users without migraine.[5,6,21,22] WHOMEC recommends that women of any age with focal migraine should be advised against the use of COC (WHO 4).[3] Similar advice should be given to women aged over 35 years with non-focal migraine (WHO 3). Women with a history of one or two episodes of focal migraine some years ago may choose a trial of COC.

Which drug interactions are relevant to prescribing COC?
A drug history should include enquiry into non-prescription (over-the-counter) agents as well as prescription medication. Some drugs may have their bioavailability increased by interaction with COC with potentially toxic effects. These include theophylline and cyclosporin.[11]

Liver enzyme-inducing drugs increase the metabolism of oestradiol and progestogens[23] and the efficacy of COC may be reduced. WHOMEC recommends that the risks of COC use by women taking liver enzyme-inducing drugs outweigh potential benefits (WHO 3).[3] However, if a woman using a liver enzyme-inducing drug still chooses to use COC, established UK practice is to use a regimen containing at least 50 µg EE daily.[24–26] In the light of lack of evidence, and the potentially serious sequelae of unintended pregnancy (particularly in women with epilepsy using enzyme-inducing anticonvulsants), women may be advised to use a barrier method in addition to a high-dose COC.[27] Additional contraception is also required for 28 days after a liver enzyme-inducer is stopped.[25] The most commonly used COC containing 50 µg EE (Ovran®, Wyeth Laboratories) was discontinued in 2002. An alternative preparation containing 50 µg mestranol (Norinyl-1®, Pharmacia) is available. Two studies have provided conflicting evidence of the bioequivalence of 50 µg EE and mestranol.[28,29] On balance, it appears that although interindividual variation may occur, 50 µg EE and mestranol are comparable.[29] An alternative regimen involves use of two low-dose COCs (providing a total daily dose of 50–60 µg EE) but no trials have compared bioavailability to that of a single dose.

Women using the liver enzyme-inducing antibiotic, rifampicin, long-term should be advised as for other enzyme-inducing drugs.[30] Advice regarding short-term antibiotics including rifampicin when used as prophylaxis is provided later in this Guidance (Recommendation 33).

Women who are established users of non-enzyme-inducing antibiotics (more than 3 weeks) should be advised that, unless their antibiotic is changed, barrier contraception is not required in addition to COC.

The Committee on the Safety of Medicines (CSM) advises[31] stopping St John's Wort if using COC. Some antiretroviral medications are also potent liver enzyme-inducers.

Which examinations and tests are needed prior to prescribing COC?
The WHO *Selected Practice Recommendations for Contraceptive Use*[32] (WHOSPR) recommends examinations and tests that should be performed before providing different methods of contraception. Breast examination, pelvic and genital examination, cervical cytology screening and routine laboratory tests including haemoglobin measurement do not contribute substantially to COC safety and are therefore not recommended routinely (Class C).

Blood pressure measurement. A consensus meeting of UK experts recommended that correctly measured BP was essential and mandatory in all women prior to COC use.

Thrombophilia screen. Routine thrombophilia screening prior to COC use is not recommended.[33] WHOMEC does not specifically refer to women with thrombophilias. Approximately 1 in 3000 people have reduced levels of

naturally occurring anticoagulants (antithrombin III, protein C or protein S). This predisposes them to DVT and PE.[34] As many as 1 in 20 people, however, may be heterozygous for factor V Leiden or prothrombin gene mutation (G20210A) which increase their risk of DVT and PE, but to a lesser degree.[33,34]

Women with the most common thrombophilia, factor V Leiden mutation, have up to a 35-fold increased risk of VTE with COC use.[35,36] However, many such women will never develop venous thrombosis. The low incidence of VTE in women of reproductive age also means that even such an increase in relative risk results in a low absolute risk (around three additional cases of VTE per year per 1000 pill users with factor V Leiden).[36] Women with a family history of VTE in a first-degree relative under the age of 45 years may be at increased risk of VTE. However, not all women with a family history and an identified thrombophilia will develop venous thrombosis.[33] Using family history alone may deny COC to many women. A thrombophilia screen in this instance may be informative, together with family history, when women still wish to use COC. The interpretation of a thrombophilia screen which is positive or negative is often difficult and should be performed in consultation with a haematologist or other expert.[33]

Antiphospholipid syndrome is uncommon but identified more often in women with a history of recurrent miscarriage than in the general population. Thrombophilia screening in this instance is warranted.[37]

Screening for STI. A sensitively taken clinical history supports the assessment of a woman's risk of STI. The WHOSPR suggests that testing for STI, such as *Chlamydia trachomatis*, is not essential for the safe and effective use of COC. However, the Scottish Intercollegiate Guideline Network (SIGN) recommends opportunistic testing for *C. trachomatis* in all sexually active women under the age of 25 years, and for women over 25 years who in the last year had a change of sexual partner, or two or more sexual partners.[38]

Recommendations – Clinical history taking

1 Women can be advised that they may use COC from menarche to the menopause unless there are medical or other contraindications (Grade C).

2 Women aged >35 years who smoke should be advised that the risks of COC use outweigh the benefits (Grade B).

3 Women with a BMI >30 should be counselled regarding an increased risk of VTE and consider alternative contraceptive methods (Grade B).

4 Women of any age with focal migraine should be advised that the risks of COC use outweigh the benefits (Grade B).

5 Women using liver enzyme-inducing drugs should be counselled regarding the risks of reduced efficacy (Grade C).

6 Women using liver enzyme-inducing drugs who, having considered other methods, still choose to use COC should be prescribed a regimen containing 50 µg EE or mestranol. Additional barrier contraception should be advised until 4 weeks after cessation of the liver enzyme-inducer (Grade C).

7 Women who are established users of non-enzyme-inducing antibiotics (over 3 weeks) do not require additional contraceptive protection when starting COC (Grade C).

✓ Clinicians should take a clinical history, including details of sexual and reproductive health, non-prescription medications and lifestyle, to be able to advise on eligibility for safe COC use.

✓ Women should be advised of the health risks associated with smoking.

Recommendations – Examination and tests

8 Women with a BP measurement consistently over 140 mmHg systolic and/or 90 mmHg diastolic should be advised against use of COC (Grade C).

9 A thrombophilia screen is not recommended routinely before prescribing COC (Grade C).

10 For women with a family history of VTE in a first-degree relative under the age of 45 years who, having considered other contraceptive methods, still wish to use COC, a thrombophilia screen should be performed (Grade C).

11 Ideally the risk of STI should be assessed and opportunistic *Chlamydia* testing offered when appropriate but this is not essential for safe use (Grade C).

✓ The interpretation of a thrombophilia screen should be undertaken in consultation with a haematologist or other expert and in tandem with a detailed family history

What do women need to know when considering COC?

How can women interpret the risks and benefits of COC?

Three large cohort studies[9,39,40] have shown that long-term oral contraceptive (OC) use is safe for the vast majority of women and not associated with an increase in mortality. Communicating risk involves an exchange of information and opinion between women and clinicians leading to better understanding and informed decisions regarding contraceptive use.[41,42] COC use is associated with both serious health risks and 'nuisance' side effects, and different women may rate their importance differently. Observational studies have shown that even among well-educated women, understanding of relative and absolute risks is poor.[43] Risk tables have been developed to help explain degrees of risk to women.[44] A 1 in 100 000 risk of being affected by a disease is judged to be a negligible risk. This would equate to one person in a large UK town being affected. The perceived risk, however, can depend on how the information is given, the seriousness and incidence of the disease. For example, in absolute terms, the risk of VTE increases from 5 to 15 per 100 000 women-years with COC use. In relative terms, however, the risk increases three-fold.[45] Using appropriate language and written materials, and providing a comparison of risks and benefits, may help a woman judge the level of risk that is acceptable to her (Table 2). Currently, studies that attempt to quantify the net risk/benefit profile of COC are limited.

What are the non-contraceptive benefits of COC?

Dysmenorrhoea. A Cochrane Review found insufficient evidence to determine if COCs reduce primary

Table 2 *Risk–benefit profiles for COC to consider before first COC prescription*[a]

Disease	Rates per 100 000 women	Relative risk with COC use
Risks		
Coronary artery disease[1]	1500	No increase
Stroke[1]	100	Two-fold increase in ischaemic stroke No increase in haemorrhagic stroke
VTE	5	Three-fold increase with levonorgestrel and norethisterone COCs Five-fold increase with desogestrel and gestodene COCs
Breast cancer[2]	(1 in 9 women will develop breast cancer at some time in their lives. The estimated risk of developing breast cancer up to age 30 years is 1 in 1900, up to 40 years is 1 in 200 and up to age 50 years is 1 in 50)	Any increased risk likely to be small and will vary with age; no increased risk 10 years after stopping
Cervical cancer	11	Small increase after 5 years and a two-fold increase after 10 years
Benefits		
Ovarian cancer	22	Halving of risk lasting for 10 or more years
Endometrial cancer	15	Halving of risk lasting for 10 or more years

[a]Statistics from National Statistics: www.statistics.gov.uk.[63] Prevalence of treated coronary heart disease and stroke recorded in general practice in England and Wales for women aged up to 54 years.[1] NHS Screening Programme:[2] www.cancerscreening.nhs.uk.
COC, combined oral contraception; VTE, venous thromboembolism.

dysmenorrhoea.[46] A subsequent small, randomised, double blind, placebo-controlled trial, however, showed a significant reduction in menstrual cramps with COC use.[47]

Menorrhagia. A Cochrane Review concluded that there is insufficient evidence to confirm that COC reduces menstrual blood loss.[48] The one small, randomised trial included in this review showed a 43% reduction in measured menstrual blood loss with COC use over two cycles.[49] Clinically, women describe less bleeding with COC use.

Endometriosis. A Cochrane Review identified one randomised trial which suggested COC was less effective than gonadotrophin-releasing hormone agonists in the relief of menstrual pain, but it was as good at relieving dyspareunia and non-menstrual pain.[50]

Ovarian cancer. A systematic review of four cohort and 21 case-control studies identified a 40–50% reduction in the risk of developing ovarian epithelial cancer in women who had used COCs containing >35 µg EE.[51] Evidence supporting this protective effect, even with COCs containing <35 µg EE, was obtained from a recent retrospective, case-control study (OR 0.5; 95% CI 0.3–0.6).[52] Mortality from ovarian cancer is reduced with increasing duration of COC use,[9] and reduction in ovarian cancer risk lasts for up to 15 years after stopping COC.[51]

Ovarian cysts. Case control and cohort studies suggest a reduction in the incidence of functional ovarian cysts[53,54] and benign ovarian tumours[55] for women using COC.

Endometrial cancer. Case-control studies have demonstrated a reduction in risk of endometrial cancer by 50% with COC use.[56] This was supported by a systematic review of three cohort and 16 case-control studies.[57] Mortality from endometrial cancer is also reduced with COC use.[9] This effect was apparent after 5 years' use and continued for up to 10 years after discontinuation. No direct evidence was identified to confirm that these protective effects are similar for contemporary low-dose COCs.

Colonic cancer. The Nurses Health Study identified a reduction in risk of colonic cancer associated with COC use. Further evidence to support a reduction in risk of colonic cancer with OC use was obtained from a meta-analysis, which identified an overall RR of 0.82 (95% CI 0.74–0.92).[58] It has not been established, however, if this protective effect occurs with low-dose COCs.[59]

Osteoporosis. COCs may have a protective effect on age-related loss of bone mineral density (BMD).[60] Further evidence to support this has been provided by a recent small, prospective, cross-sectional study in low-dose COC users.[61] However, other recent cross-sectional studies have failed to identify any changes in BMD with COC use.[62] A population-based, case-control study demonstrated that OC use over the age of 40 years was associated with a significant reduction in the incidence of hip fracture after the menopause. Ever-use of COC was associated with a 25% reduction in hip fracture in women using COC over the age of 40 years.[63]

Acne vulgaris. Small randomised trials have shown significant reductions in acne lesions with COCs containing either desogestrel or levonorgestrel.[64,65]

Other benign conditions. A meta-analysis identified a 30% reduction in the incidence of rheumatoid arthritis with COC use.[66] A review of epidemiological studies identified a reduced risk of benign breast disease.[67] Hospital-based, case-control studies from the late 1970s do not provide sufficient evidence of a protective effect of COC against pelvic inflammatory disease.[68] There is a lack of evidence of COC being effective in the management of premenstrual syndrome and other mood disorders.[69]

What are the risks associated with COC?
Venous thromboembolism (VTE). There is a three- to five-fold increase in the risk of VTE with COC use, which does not appear to be related to the dose of EE.[14] COCs containing gestodene or desogestrel are associated with almost a two-fold increase in the risk of VTE compared to COCs containing norethisterone or levonorgestrel. Apparent relationships between progestogen type and risk of VTE[70] may be due to the confounding or bias, which

may occur in observational studies[71] but this increased risk has biological plausibility.[72] Presenting risk in relative terms may sound more alarming than presenting risk in absolute terms. The absolute VTE risk for COC non-users is low (5 per 100 000 woman-years). The risk of VTE increases to 15 per 100 000 woman-years with use of COCs containing levonorgestrel and norethisterone and to 25 per 100 000 woman-years for COCs containing desogestrel and gestodene.[73] VTE is uncommon in women of reproductive age and, although the risk of VTE increases up to five-fold with COC use, the absolute risk remains small. For comparison, the risk of VTE in pregnancy is 60 per 100 000 woman-years.

The increased risk of VTE with COC is apparent within 4 months of starting[70] and returns to that of non-users within 3 months of discontinuation.[70] Case-control studies have shown a reduction in VTE risk with increasing duration of use.[7,12,74] This may be due to thrombophilias being 'unmasked' with COC use. In the first year of use, for women with thrombophilia the incidence of VTE was more than 10 times higher than in later years.[75]

Studies investigating the VTE risk associated with COC have included very few women using COCs containing norgestimate [Cilest® (Janssen-Cilag) and Yasmin® (Schering Health)].[12,76] Norgestimate is metabolised to levonorgestrel, and may have a VTE risk comparable to levonorgestrel- and norethisterone-containing COCs. There is insufficient evidence, however, to support or refute this.[77,78] Little evidence was identified regarding the VTE risk with drospirenone-containing COC.[79]

Dianette® (Schering Health) contains 35 µg EE and 2 mg cyproterone acetate as an alternative to progestogen but is not licensed as a COC. A case-control study, which used extracted data from the General Practice Research Database, has shown a four-fold increase in the risk of VTE with Dianette compared to COC containing levonorgestrel.[80] Duration of use did not affect this risk. In the UK the CSM advises: Dianette is not indicated solely as a contraceptive; it is a treatment option for women with severe acne, which has not responded to oral antibiotics, or for moderately severe hirsutism; it should be withdrawn 3–4 months after the treated condition has resolved[81] or if there is no improvement in symptoms.

Ischaemic and haemorrhagic stroke. Previous Faculty Guidance on hormonal contraception and stroke summarised available evidence.[14] The annual incidence of ischaemic stroke in women aged under 35 years is low (3 per 100 000), but increases with age.[5] A case-control study showed that COC use by healthy non-smokers increases the risk of ischaemic stroke two-fold.[5] There was no significant increase in risk of haemorrhagic stroke.[13] Mortality from haemorrhagic and ischaemic stroke is not increased with COC use.[9]

Ischaemic heart disease. Non-smokers can be reassured they are at no increased risk of MI with COC use (RR 0.9; 95% CI 0.3–2.7).[4,14]

Breast cancer. A meta-analysis of case-control studies showed an increased risk of breast cancer diagnosis whilst using COC (RR 1.24; 95% CI 1.15–1.33).[82] This suggests a 24% increase in breast cancer risk, above the background risk. Women had no increased risk 10 years after stopping COC. A more recent population-based, case-control study provided new evidence on low-dose COC and breast cancer risk.[83] Current COC users appear to have no increased risk (RR 1.0; 95% CI 0.8–1.3) compared to never-users but the upper limit of the confidence interval was the same as in the Collaborative Group Study. Any increased risk does not appear to be influenced by family history, duration of COC use, age at first use, or dose or type of hormone – and may be explained by increased health surveillance and increased detection in COC users. Mortality from breast cancer was not increased with any duration of COC use.[9] Women should be advised that any increase in risk of breast cancer associated with COC use is likely to be small.

An observational study identified that ever-users of high-dose COCs who had a first-degree relative with breast cancer had a three-fold increase in the risk of breast cancer compared to never-users (RR 3.3; 95% CI 1.67–6.7).[84] The risk was less if second-degree relatives had disease (RR 1.2; 95% CI 0.8–2.0). The risk of breast cancer in women with a genetic mutation is greater than in the general population, but the majority of breast cancers are not due to mutations. A case-control study investigated the risk of developing breast cancer in women with BRCA mutations when exposed to OCs.[85] Carriers of BRCA2 had no additional increased risk, above their background risk, with OC use (OR 0.94; 95% CI 0.72–1.24). Carriers of BRCA1, however, had a small increase in their risk (OR 1.2; 95% CI 1.02–1.4). Women with a family history of breast cancer can be advised that any increased risk with COC use is small.

Cervical cancer. The crude rate of cervical cancer per 100 000 women in the UK is 11.[86] A recent systematic review of case-control and cohort studies including women with both invasive cervical cancer and cervical intraepithelial neoplasia (II or III)[87] provided evidence that suggests increasing duration of OC use increases the risk of invasive and in situ cervical disease. No significant risk of invasive cervical cancer was shown with OC use less then 5 years (RR 1.29; 95% CI 0.88–1.91).[88] With more than 5 years' use the risk of invasive cervical cancer increases four-fold (RR 4.01; 95% CI 2.01–8.02).[88] When invasive carcinoma and cervical intraepithelial neoplasia were investigated together OC use for less than 5 years increased the risk by 10% (RR 1.1; 95% CI 1.1–1.2).[87] With 10 or more years of use, the risk is doubled (RR 2.2; 95% CI 1.9–2.4). Results did not differ when confounding factors such as human papilloma virus infection, sexual partners, barrier contraception and cervical screening were taken into account. Women should be advised that OC use for less than 5 years is associated with a negligible increased risk of cervical cancer, but the risk increases with duration of use. The National Health Service (NHS) cervical cytology screening programme has reduced mortality from cervical cancer and women should be encouraged to take part in routine cervical screening.[89]

Other cancers. A FACT on COC and cancer has reviewed recent literature.[90] Primary liver cancer is rare but COC use increases the risk depending on duration of use. No evidence has been identified to support an association between COC and melanoma. In the UK, women with gestational trophoblastic disease are advised against the use of hormonal contraception until serum human chorionic gonadotrophin levels are normal.[91]

'Breakthrough' and intermenstrual bleeding. A randomised trial provided information on the bioavailability of oestrogen and progestogen and associated bleeding patterns.[92] Intermenstrual bleeding (IMB) appeared more common with COCs containing 30 µg EE than with those containing 50 µg, but the difference was not statistically significant and studies were small. No relationship was identified between serum steroid levels and bleeding.

Further randomised trials[93] showed that breakthrough bleeding (BTB) was significantly more frequent in women using a 20 µg rather than a 30 µg COC. BTB occurred in up to two thirds of cycles throughout the 12 months' treatment. No link between BTB and loss of contraceptive efficacy has been established.[94,95]

Weight gain. A Cochrane Review did not support a causal association between COC and weight gain.[96]

Recommendations – Non-contraceptive benefits

12 Women may be advised that menstrual pain and blood loss may be reduced with COC use (Grade C).

13 Women may be advised of a reduction in risk of ovarian cancer and ovarian cysts with COC use (Grade B).

14 Women may be advised of a reduction in risk of endometrial cancer with COC use (Grade C).

Recommendations – Risks

15 Women should be advised that although the relative risk of VTE with COC use can increase up to five-fold, in absolute terms the risk is still very low and still considerably lower than the risk of VTE in pregnancy (Grade B).

16 Dianette should be used only for severe acne when oral antibiotics have failed, or for moderately severe hirsutism. It should be discontinued 3–4 months after the condition treated has resolved (Grade C).

17 Women should be advised of a very small increase in the absolute risk of ischaemic stroke with COC use (Grade B).

18 Healthy non-smokers can be advised that they have no increased risk of MI with COC use (Grade B).

19 Women with and without a family history of breast cancer may be advised that any increased risk of breast cancer with COC use is likely to be small (Grade B).

20 Women should be advised that OC use for less than 5 years does not increase the risk of cervical cancer but the risk increases with more than 5 years' use (Grade B).

21 Women can be advised that there is no evidence of weight gain with COC use (Grade A).

22 Women should be advised that BTB can occur with COC use but, in the absence of missed or late pills, vomiting or drug interactions, has not been shown to be a measure of efficacy (Grade B).

✓ Women should be provided with information on warning signs of VTE, which should prompt immediate medical consultation.

✓ Women should be encouraged to participate in the NHS cervical screening programme to reduce their risk of cervical cancer.

✓ Women should be advised of possible causes of unscheduled bleeding, such as missed and late pills, STI, vomiting and drug interactions, and when to seek medical advice.

What information do women need to use COC appropriately?

A randomised trial showed improvement in cycle control after the initial 3 months of COC use.[92] Women should be encouraged to continue with their first COC for at least 3 months before considering an alternative and should also be advised on the use of condoms to protect against STI when using COC.

How do COCs work?

COCs act on the hypothalamo-pituitary-ovarian axis. Luteinising hormone (LH) and follicle-stimulating hormone (FSH) are reduced, and follicle growth and ovulation are inhibited.[97] Seven consecutive pills are needed to inhibit ovulation and continued pill-taking maintains ovarian quiescence.[32] COC also has effects on cervical mucus and the endometrium, which contribute to its contraceptive effect. The usual 7-day pill-free interval allows endometrial shedding and most women will have a withdrawal bleed. If the withdrawal bleed is absent or very light, women should be advised to attend for review – especially if associated with missed or late pills, vomiting, severe diarrhoea or potential drug interactions.

How effective are COCs?

Efficacy data for COCs are usually presented in terms of 'perfect' and 'typical' use. The 'perfect use' failure rate for COC is quoted as 0.1%, and the 'typical use' rate as 5%.[98] Even in well-designed trials, the true efficacy of a hormonal method is difficult to assess.[99,100] The Pearl index represents the number of failures (unintended pregnancies) per 100 woman-years of exposure. The Pearl index for COC has been estimated at 0.3–4.0 per 100 woman-years.

When to start COC?

Starting COC for women with menstrual cycles. Ideally COC should be started on the first day of menstruation and in line with Summary Product Characteristics (SPCs). The WHOSPR[32] recommends that COC can be started up to, and including, Day 5 of the menstrual cycle without the need for additional contraception (Table 3). A woman may also commence COC at any other time in the menstrual cycle if it is reasonably certain she is not pregnant. In this situation, additional contraception is required until seven consecutive pills have been taken. Advice regarding starting COC in other circumstances, and when switching from another method of contraception, is summarised in Table 3. WHOSPR starting regimens are at odds with established UK clinical practice and with SPCs. However, evidence reviewed by WHO indicates that the risk of ovulation is low in the first 5 days of menstruation and women starting COC up to and including Day 5 may choose not to use additional barrier contraception.

Animal studies have shown that COC effectively inhibits ovulation when started up to, and including, Day 6.[101] A randomised, single-blind study investigated ovarian follicle development and subsequent ovulation in women starting COC on Days 1, 4 or 7 of the menstrual cycle.[102] This trial supported findings from an earlier cohort study[97] that ovulation did not occur with a Day 5 start. Vaginal ultrasonography and serum progesterone were used to

Table 3 *When to start COC in different circumstances*[25]

Circumstances for COC start	When to start COC	Additional contraceptive protection required
Women having menstrual cycles	Start COC up to and including Day 5	None
	At any other time if it is reasonably certain that woman is not pregnant	For 7 days
Amenorrhoeic	COC can be started at any time, if it is reasonably certain that she is not pregnant	For 7 days
Breastfeeding	If >6 months postpartum and amenorrhoeic COC can be given as for other amenorrhoeic women	For 7 days
	If she >6 months postpartum and her menstrual cycles have returned she can start COC as for other women having menstrual cycles	As for other women having menstrual cycles
Switching from other hormonal methods *(other than the IUS)*	COC can be started immediately if she has been using her hormonal method consistently and correctly, or if it is reasonably certain she is not pregnant. There is no need to wait for her next menstrual period	None
	If her previous method was an injectable, she should start COC when the repeat injection would have been given	None
Switching from a non-hormonal method *(other than the IUD)*	Start COC up to and including Day 5	None
	At any other time if it is reasonable certain that she is not pregnant	For 7 days
Switching from an IUD or IUS	COC can be started up to and including Day 5 after the start of menstrual bleeding. IUD/IUS can be removed at that time	None
	COC can be started at any other time, if it is reasonably certain she is not pregnant:	
	If she *has been* sexually active in this menstrual cycle	The IUD/IUS will provide contraceptive protection and should be removed with the next bleed
	If she *has not* been sexually active in this menstrual cycle	For 7 days or alternatively if the additional contraceptive protection is to be provided by the IUD/IUS it should be removed at the time of her next bleed
	If she is amenorrhoeic or has irregular bleeding, COC can be started as advised for other amenorrhoeic women	As for other amenorrhoeic women

COC, combined oral contraception; IUD, intrauterine device; IU, intrauterine system.

assess follicular activity and ovulation in 85 women. Ovarian follicular development occurred despite consistent COC use.[103] The ovaries were quiescent by Day 21, even when starting COC on Day 7. Follicular growth was more likely in women starting on Day 7 but ovulation did not occur.

Concerns regarding the risk of ovulation with these COC starting regimens in women with short menstrual cycles may be unfounded. Fewer than 5% of women aged between 15 and 44 years, and fewer than 2% of those aged 20 to 39 years, have a menstrual interval less than 20 days.[104] Fewer than 1% of women aged 14 to 42 years have a cycle length less than 15 days and those who do appear to be relatively young or old and relatively infertile.[105] After counselling regarding variations in cycle length and ovulation, some women may choose to use barrier methods when starting COC on any day other than Day 1.

Starting COC following pregnancy. Following a delivery over 24 weeks' gestation, COC should be started no earlier than 21 days postpartum.[3] Following termination of pregnancy (TOP), in line with previous recommendations from the Royal College of Obstetricians and Gynaecologists, contraception should, ideally, be started on the day of termination.[106] COC is not advised if less than 6 months postpartum and breastfeeding (WHO 3).[3]

What advice should be given regarding missed pills?
Women should be advised to try to take their COC at the same time every day, and certainly no later than 12 hours after their scheduled time.[32] No evidence was identified to suggest there is an optimal time to take COC, but women should choose the time when they are most likely to remember. If a pill is taken more than 12 hours late, then 'missed pill' rules should be applied (Table 4).

Observational and group comparative studies investigated the effects of COC omission on LH, FSH, oestradiol and progesterone.[7,97,107,108] There was no evidence of ovulation within 7 days of stopping COC, even if only seven consecutive pills had been taken.[109] During the hormone-free interval, there was evidence of follicular activity but no ovulation.[97,107,108] Women can be reassured that contraceptive efficacy is maintained during the routine hormone-free week. Open-labelled, randomised, comparative group trials have investigated the effects on ovulation of omitting the first three pills.[110] Although follicular activity was identified, ovulation did not occur. Studies have deliberately extended the hormone-free interval to 16 days,[111] or until the follicle reached 16 mm.[107] Again, although follicular activity was identified, ovulation was not. Contraceptive efficacy may be reduced if the hormone-free interval is extended to more than 9 days and this is reflected in the advice for women regarding missed pills.[109] Routinely, up to seven pills are 'missed' each month without the risk of

Table 4 *Missed pill instructions from WHO* Selected Practice Recommendations for Contraceptive Use[32]

'Missed pill' circumstances	Instruction for COC use	Indications for EC
One active pill missed (Days 1–21)	Take missed pill as soon as possible and the next pill at the usual time. Continue taking the pill as usual. No additional barrier contraception required	No EC required
Started a pill pack two or more days late	Start the new pack that day and continue to take pills as usual. Abstain from sex or use additional barrier contraception for the next 7 days	EC is indicated if the woman has had unprotected sex either in the pill-free week or in the first 7 days of the pack
Missed any two to four of the first seven active pills of the pack (Days 1–7)	Take the missed pill as soon as possible and the next pill at the usual time. Continue taking pills as usual. Abstain from sex or use additional barrier contraception for the next 7 days	EC is indicated if the woman has had unprotected sex either in the pill-free week or in the first 7 days of the pack
Missed any two to four of the middle seven active pills (Days 8–14)	Take the missed pill as soon as possible and take the next pill at the usual time. Continue taking the pill as usual. Additional barrier contraception not required	No EC required
Missed any two to four of the last seven active pills (Days 15–21)	Take the missed pill as soon as possible and take the next pill at the usual time. Continue taking the pill as usual and go straight on to the new packet. Additional barrier contraception not required	No EC required
Missed five or more pills in a row in any week (Days 1–21)	Take the missed pill as soon as possible and the next pill at the usual time. Continue taking the pills as usual and go straight onto the next packet. Abstain from sex or use additional barrier contraception for 7 days	EC is indicated if unprotected sex has occurred in the 7 days since missing the fourth pill
Missed one or more inactive pills in everyday packaging	Discard the missed inactive pills. Continue taking pill as usual. Start a new packet as usual. Additional contraceptive cover not required.	EC is not required

COC, combined oral contraception; EC, emergency contraception; WHO, World Health Organization.

pregnancy. WHOSPR advice for on 'missed pills' is summarised in Table 4.

How can compliance and efficacy be optimised?

Everyday pill packaging. A retrospective survey showed that women were most likely to miss pills in the week following the pill-free interval.[112] Everyday (ED) pills, which contain seven inactive tablets, are taken everyday without a break but no evidence was identified to determine if compliance is improved with this regimen. Women should be encouraged to read package inserts because some ED brands have inactive pills at the end of the pack, whilst others with inactive pills at the start of the pack need to be started with additional barrier contraception.

Advice regarding 'tricycling'. A recent prospective survey of women worldwide suggested that a majority of women dislike menstrual periods.[113] Women may be given the option of 'tricycling' COC (i.e. taking three packs consecutively without a hormone-free week) to avoid withdrawal bleeds. Two randomised trials have investigated bleeding patterns associated with tricycling COC.[103,114] Women taking COC continuously reported fewer bleeding days requiring sanitary protection, more amenorrhoea, less menstrual pain and less bloating than women using the standard 21-day regimen.[114] The rate of spotting was the same in the two groups and both groups reported high satisfaction with the bleeding patterns experienced.[103,114] Use of COC in this way is outside the product licence.

Advice regarding avoiding weekend bleeds. No evidence was identified regarding compliance and satisfaction of COC users when advised how to avoid weekend bleeds. Women may prefer not to bleed on certain days of the week and clinicians may discuss how to take COC to avoid withdrawal bleeds on these days. The COC can be restarted early in the pill-free interval to adjust the days of bleeding.

Advice regarding use of antibiotics. A recent non-systematic review of interactions between broad-spectrum (non-enzyme-inducing) antibiotics and COC highlights the lack of evidence.[115] EE undergoes extensive metabolism in its first pass through the gastrointestinal tract and liver. Inactive metabolites are excreted into the bile and, during a second pass through the gut, breakdown of these metabolites by bacteria releases more EE, which is reabsorbed. There is marked individual variation in the bioavailability of EE following oral administration and the impact of this enterohepatic circulation on serum hormone levels and efficacy is unclear.[25] Short-term (<3 weeks) broad-spectrum antibiotics may alter gut flora and pregnancies have been documented following their use in women using COCs.[115] Randomised controlled trials[116,117] and observational studies[118,119] investigated the effects of quinolone antibiotics on contraceptive steroid levels and ovulation in women using COCs and found no effect. Despite this lack of evidence on the clinical significance of the effects of antibiotics on gut flora, this Guidance advises additional contraception when starting a new broad-spectrum, non-enzyme-inducing antibiotic and for 7 days after discontinuation. Women who are established on a non-enzyme-inducing antibiotic long term do not require additional contraception unless they change to a different antibiotic.

Women who are given rifampicin short term (as meningococcal prophylaxis) should be advised to use a barrier method in addition to their COC and for 28 days after stopping rifampicin.[30] The usual hormone-free week should be omitted in the cycle of use.

Advice regarding severe diarrhoea and vomiting. WHOSPR recommends that women who vomit within 2 hours of taking COC should repeat the dose as soon as possible.[32] The general advice for women using OC who have vomiting or severe diarrhoea for more than 24 hours is to follow instructions for missed pills.

Recommendations

23 Women should be advised that COC works by inhibition of ovulation and also has effects on cervical mucus and endometrium (Grade B).

24 Women should be advised that COC can be over 99% effective at preventing pregnancy, if used consistently and correctly (Grade B).

25 Ideally COC should be started on Day 1 of the menstrual cycle but women may be advised that COC can be started up to and including Day 5 of the cycle without the need for additional contraception (Grade C).

26 Women should be advised that COC can be started at any other time in the cycle if there has been no risk of pregnancy, but additional contraception is required for the first 7 days (Grade C).

27 Women who are not breastfeeding should be advised to start COC after Day 21 postpartum (Grade C).

28 Women should be advised that, ideally, COC should be started on the day of a first- or second-trimester TOP, but can be started within 7 days to provide immediate contraceptive protection (Grade C).

29 Women should be advised that, routinely, COCs should be taken within 12 hours of the same time every day for 21 consecutive days (Grade C).

30 Women should be advised that contraception is still provided during the routine seven hormone-free days (Grade B).

31 Women should be advised to return for a pregnancy test if, following missed or late pills, vomiting or severe diarrhoea or use of any new drug, there is a very light or no withdrawal bleed (Grade C).

32 Women using non-enzyme-inducing, broad-spectrum antibiotics for short courses (<3 weeks) should be advised to use additional contraception during the course and for 7 days afterwards (Grade C).

33 Women using short courses of rifampicin for prophylaxis should be advised to use additional contraception during the course and for 4 weeks afterwards (Grade C).

✓ Women should be provided with appropriate written and verbal instruction regarding rules for missed or late pills, vomiting or severe diarrhoea, and the use of new medications.

✓ Women should be advised to use condoms in addition to COC if at risk of STI.

✓ Women may be given advice regarding 'tricycling' packs of COC to avoid withdrawal bleeds.

✓ Women may be advised how to adjust the pill-free interval to avoid weekend withdrawal bleeds.

✓ Women should be advised when COC is being recommended outside the product license, (for example, tricycling).

How can clinicians help women choose their first COC?

General advice

Women using COC for the first time should be advised to choose a safe, effective pill (Table 5). There are few direct, comparative data available to identify the best, first-line COC. A monophasic COC with 30–35 µg EE and a low dose of either norethisterone or levonorgestrel should be the first-line option.[120] The rationale for this advice is outlined below.

VTE risk

VTE risk associated with COCs containing norethisterone or levonorgestrel is less than that for COCs containing desogestrel and gestodene.[70] Provided women are fully advised regarding different VTE risks, there are no COCs that are not suitable to be used first-line and the choice of the woman should be take into consideration.

Contraceptive efficacy

Efficacy of 20 and 30 µg EE COCs has been compared in randomised trials and is not significantly different.[93]

Breakthrough bleeding

BTB may be more common with 20 µg than with 30 µg COCs.[93]

Metabolic effects

Effects of COCs containing different progestogens were not significantly different in randomised, crossover trials.[121] Although observational studies did identify differences, their clinical significance is unknown.

Triphasic and biphasic preparations

These have been shown in a systematic review to have a similar risk-benefit profile.[122] A Cochrane Review found a lack of evidence supporting biphasic and triphasic COCs, and suggested that the choice of progestogen may be more important than the phasic regimen.[123,124]

Price comparisons

Price may be important in choosing contraception.[120] There are insufficient data to allow cost effectiveness to be assessed and comparisons take account only of net price (Table 5).

Recommendations

34 A monophasic COC containing 30–35 µg EE with a low dose of either norethisterone or levonorgestrel is a suitable first-line option (Grade C).

✓ There are no COCs that cannot be used first-line after counselling and the preference of the woman should be taken into consideration when prescribing COC.

Women aged less than 16 years

Consent. The Fraser Guidelines (England and Wales, 1985) established that a clinician can provide contraceptive advice or treatment to a patient aged under 16 years provided he or she is satisfied that the patient is competent to consent to the advice or treatment. The Age of Legal Capacity in Scotland (1991) assigns various legal rights to individuals over the age of 12 years.[125]

Table 5 *Quick reference guide to COC prescribing with approximate net prices per month of usea*

Type of progestogen in the COC	Oestrogen dose	Brand name (manufacturer)	Net price per month
Monophasic preparations			
Norethisterone or levonorgestrel	30–35 µg EE	Ovysmen® (Janssen-Cilag)	£0.55
		Brevinor® (Pharmacia)	£0.65
		Norimin® (Pharmacia)	£0.75
		Eugynon 30® (Schering Health)	£0.80
		Microgynon 30® (Schering Health)	£0.85
		Ovranette® (Wyeth)	£0.80
		Loestrin 30® (Parke-Davis)	£1.25
	20 µg EE	Loestrin 20® (Parke-Davis)	£0.85
Desogestrel or gestodene	30 µg EE	Marvelon® (Organon)	£2.25
		Femodene® (Schering Health)	£2.30
		Minulet® (Wyeth)	£2.30
	20 µg EE	Femodette® (Schering Health)	£2.75
		Mercilon® (Organon)	£2.85
Norgestimate	35 µg EE	Cilest® (Janssen-Cilag)	£2.15
Drospirenone	35 µg EE	Yasmin® (Schering Health)	£4.90
Everyday (ED) packaging with a variety of progestogen types and seven placebo pills	30 µg EE	Microgynon 30 ED® (Schering Health)	£0.85
		Logynon ED® (Schering Health)	£1.30
		Femodene ED® (Schering Health)	£2.30
Biphasic pills with varied progestogens	30–40 µg EE	BiNovum® (Janssen-Cilag)	£0.75
Triphasic pills with varied progestogens	30–40 µg EE	TriNovum® (Janssen-Cilag)	£1.05
		Synphase® (Pharmacia)	£1.15
		Logynon® (Schering Health)	£1.30
		Trinordiol® (Wyeth)	£1.45
		Tri-Minulet® (Wyeth)	£3.20
		Triadene® (Schering Health)	£3.20
Higher-dose pills	50 µg mestranol	Norinyl-1® (Pharmacia)	£0.75

British National Formulary, Vol. 45.[9]
COC, combined oral contraception.

Competency is a young person's ability to understand choices and their consequences, including the nature, purpose and possible risk of any treatment.[125]

Confidentiality. The duty of confidentiality owed to a patient aged under 16 years is deemed to be as great as that owed to any other patient.[125,126] Disclosure of information is a complex issue and health professionals working with young people should be aware of issues surrounding responsibilities and disclosure.[126]

Recommendations

35 COC can be prescribed, without parental consent, to a young woman aged less than 16 years if she is assessed to be competent to make an informed choice (Grade C).

36 Health professionals dealing with young people should be aware of local procedures for dealing with issues relating to child protection, confidentiality and disclosure (Grade C).

What follow-up arrangements are appropriate following first prescription of COC?

The WHOSPR[32] promotes flexibility of contraceptive supply with ease of access should problems arise. It recommends that women may be offered up to 12 months' supply of COC at the initial visit. A yearly routine follow-up visit, plus advice to return at any time if there are problems, is recommended. It may be appropriate to see some women for a follow-up appointment and re-instruction sooner than 12 months, and this can be arranged on an individual basis.

Patient information leaflets

A trial performed in primary care[127] randomised 523 women to one of six groups: (1) a control group representing routine practice where women are not retaught all the 'pill rules'; (2) a summary leaflet; (3) Family Planning Association (fpa) leaflet; (4) interactive questions; (5) questions and summary leaflet; or (6) questions and fpa leaflet. Women were excluded if aged less than 17 years or had psychiatric illnesses or learning difficulties. An 82% response rate was achieved. All single interventions produced a modest improvement in pill knowledge. The widely available fpa leaflet was associated with a three-fold increase in good pill knowledge at follow up.

Patient helplines

The National Sexual Health Strategy (England and Wales) highlights, as an action point, the improvement of the quality of helplines.[128] Women should be aware of appropriate local and national helplines providing advice on contraception and sexual health.

Recommendations

37 In the absence of special problems, women can be given up to 12 months' supply of COC at the first visit and encouraged to return at any time if problems arise (Grade C).

38 Appropriate written information should be provided to all women prescribed COC (Grade B).

✓ A follow-up visit 3 months after the initial COC consultation allows further instruction and assessment of any problems.

✓ Women should be provided with telephone numbers of appropriate local and national helplines providing advice on contraception and sexual health (Grade C).

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This Guidance was developed by the Clinical Effectiveness Unit (CEU) of the Faculty of Family Planning and Reproductive Health Care (FFPRHC): Gillian Penney (Director), Susan Brechin (Senior Lecturer/Unit Co-ordinator) and Alison de Souza (Research Assistant) in consultation with the Clinical Effectiveness Committee, which includes service user representation and an Expert Group of Health Care Professionals involved in Family Planning and Reproductive Health Care. The Expert Group comprised: Toni Belfield (Director of Information, fpa, London); Suzanne Burgess (SCMO Reproductive Healthcare, Croydon Primary Care Trust/Faculty of Family Planning Education Committee Member); Lynda Hayes (Senior Lecturer Women's Health, University of Central England, Birmingham); Mary Scott (General Practitioner, Dunfermline); Connie Smith (Co-director Westside Contraceptive Services, London); Sarah Wallage (Locum Consultant Gynaecology, Sexual and Reproductive Healthcare, Aberdeen).

This guidance is also available online at www.ffprhc.uk Evidence tables are available on the FFPRHC website. These summarise relevant published evidence on first pill prescription, which was identified and appraised in the development of this Guidance. The clinical recommendations within this Guidance are based on evidence whenever possible.

	Grades of Recommendations
A	Evidence based on randomised-controlled trials (RCTs)
B	Evidence based on other robust experimental or observational studies
C	Evidence is limited but the advice relies on expert opinion and has the endorsement of respected authorities
✓	Good Practice Point where no evidence exists but where best practice is based on the clinical experience of the Expert Group

Electronic searches were performed for: MEDLINE (CD Ovid version) (1996–2003); EMBASE (1996–2003); PubMed (1996–2003); the Cochrane Library (to 2003) and the US National Guideline Clearing House. The searches were performed using relevant medical subject headings (MeSH), terms and text words. The Cochrane Library was searched for systematic reviews, meta-analyses and controlled trials relevant to combined oral contraception. Previously existing guidelines from the FFPRHC, the Royal College of Obstetricians and Gynaecologists (RCOG), the World Health Organization (WHO) and reference lists of identified publications were also searched. Similar search strategies have been used in the development of other national guidelines. Selected key publications were appraised according to standard methodological checklists before conclusions were considered as evidence. Evidence was graded as above, using a scheme similar to that adopted by the RCOG and other guideline development organisations.