FACULTY OF FAMILY PLANNING & REPRODUCTIVE HEALTH CARE
ROYAL COLLEGE OF OBSTETRICIANS & GYNAECOLOGISTS

Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit

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FFPRHC Guidance (January 2005)
Contraception for women aged over 40 years

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This Guidance provides information for clinicians and for women aged over 40 years considering the use of contraception. 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 (in alphabetical order) used include: BMD, bone mineral density; CEU, Clinical Effectiveness Unit; CI, confidence interval; COC, combined oral contraception; DMPA, depot medroxyprogesterone acetate; EE, ethinylestradiol; HPV, human papilloma virus; IUD, copper-bearing intrauterine contraceptive device; LNG-IUS, levonorgestrel-releasing intrauterine system; MI, myocardial infarction; OR, odds ratio; POC, progestogen-only contraception; POP, progestogen-only pill; RR, relative risk; STI, sexually transmitted infection; VTE, venous thromboembolism; WHO, World Health Organization; WHOMEC, WHO *Medical Eligibility Criteria for Contraceptive Use*; WHOSPR, WHO *Selected Practice Recommendations for Contraceptive Use*.

Background

This guidance updates a previous Faculty Approved Continuing professional development Topic (FACT) on Perimenopausal Contraception.[1] The perimenopause (or climacteric) refers to the transition from normal ovulatory menstrual cycles to the cessation of ovulation and menstruation.[2] Neither the onset nor the completion of the perimenopause is well defined. The average age of onset of the perimenopause is 46 years (range, 39–51 years for 95% of women).[3] The average duration of the perimenopause is 5 years (range, 2–8 years for 95% of women).[3] During the perimenopause, intermittent ovulation and anovulation occur and therefore effective contraception is required for sexually active women to prevent unintended pregnancy. It is only when the postmenopause is confirmed (after 1 year of amenorrhoea) that contraception can be stopped. The balance between the risks and benefits of different contraceptive options changes with age and becomes increasingly relevant for women aged over 40 years. Contraceptive choice for women over the age of 40 years may be influenced by many factors: frequency of intercourse, natural decline in fertility, sexual function, the wish for non-contraceptive benefits, menstrual dysfunction and concurrent medical conditions. This Guidance provides evidence-based recommendations to guide clinicians, women and couples in making decisions about contraceptive choices for women aged over 40 years.

Do sexually active women aged over 40 years still require contraception?

1 Women should be informed that although a natural decline in fertility occurs from the age of 37 years, effective contraception is required to prevent unplanned pregnancy (Grade B).

2 Women should be informed that the risks of congenital and chromosomal abnormalities, spontaneous abortion, pregnancy complications, and of maternal morbidity and mortality increase for women over the age of 40 years (Grade B).

As age increases, fertility declines for women[4] and to a lesser degree for men.[4,5] This natural decline in fertility is related to many factors but the quality and quantity of oocytes is important. *In vitro* fertilisation studies show a decline in fertility from age 37 years and improved pregnancy outcomes when ova from younger women are used by women aged over 40 years instead of their own.[6] The number of oocytes rapidly declines from age 37 years.[7–9]

The annual conception rate for women aged 40 years and over in England and Wales is 10.2 per 1000.[10,11] Nevertheless, the birth rate is lower (9.8 births per 1000),[11] reflecting the increased rate of spontaneous and induced abortion in this age group.[12–16] The incidences of stillbirth and ectopic pregnancy increase with increasing maternal age.[12] Congenital abnormalities complicate 152 births in every 10 000 for women aged over 40 years.[17] The risk of Down syndrome, in particular, increases to 1 in 84 for women aged over 40 years.[12]

A retrospective review of maternities in St Mary's Hospital, London, UK showed a significant increase in pregnancy complications for women aged over 40 years (e.g. gestational diabetes, placenta praevia, preterm delivery, operative vaginal delivery, elective and emergency Caesarean section, postpartum haemorrhage, small for gestational age newborns, and stillbirth).[18] The *Confidential Enquiries into Maternal Deaths in the United Kingdom* highlights increased maternal age as a risk factor for maternal mortality. The maternal mortality rate for women aged over 40 years is 35.5 per 100 000 maternities (as compared with 20.7 per 100 000 aged 35–39 years).[19]

The Clinical Effectiveness Unit (CEU) advises that although fertility declines from the age of 37 years, contraception is required for sexually active women over the age of 40 years who do not wish to become pregnant.

How can a clinician assess medical eligibility for contraceptive use by a woman aged over 40 years?

3 A clinician should take a clinical history (including sexual history) to allow assessment of contraceptive options, taking account of cardiovascular and cerebrovascular disease and neoplasia, which increase with increasing age (Good Practice Point).

A clinical history (including sexual and reproductive history) allows assessment of medical eligibility for contraceptive use. A sexual history should allow assessment of the risk of sexually transmitted infection (STI), particularly for women with new partners, as well as sexual function. Clinicians can then advise women appropriately on contraceptive options, taking account of both medical and social factors and age-specific medical conditions (e.g. cardiovascular and cerebrovascular disease and neoplasia).[20] The World Health Organization *Medical Eligibility Criteria for Contraceptive Use*[21] (WHOMEC) provides evidence-based recommendations to ensure that women can select the most appropriate method of contraception without unnecessary medical barriers. Eligibility rather than ineligibility (or contraindication) is described. Categories include circumstances where generally the benefits of contraceptive use outweigh risks (WHO Category 1: the use of the contraceptive method is unrestricted and WHO Category 2: the benefits of using the contraceptive method outweigh the risks). Categories also include circumstances where the risks of contraceptive use generally outweigh benefits (WHO Category 3: the risks associated with using the method outweigh the benefits and WHO Category 4: the use of the contraceptive method poses an unacceptable health risk).

Which contraceptive methods can be used by a woman aged over 40 years?

4 Women aged over 40 years can be advised that no contraceptive method is contraindicated by age alone (Grade C).

5 Women aged over 40 years should be advised of the risks and non-contraceptive benefits of all contraceptive methods (Grade C).

No contraceptive method is contraindicated by age alone.[21] Communicating the benefits and risks associated with contraceptive use involves an exchange of information to allow informed choices regarding contraceptive use.[22,23]

Combined hormonal contraception

6 Women aged over 40 years can be advised that combined hormonal contraception can be used unless there are co-existing diseases or risk factors (Grade B).

The combined oral contraceptive pill (COC) is used by 8% of women aged over 40 years.[24] Currently there are no data on the uptake of the combined contraceptive patch. The majority of data on risks associated with combined hormonal contraceptive use relate to studies of women using COC. Nevertheless, in the third edition of WHOMEC, combined contraceptive patches are included in the section under COC.[21] The combined vaginal ring is not currently available in the UK. Two large cohort studies[25,26] have shown that long-term COC is safe for most women.

Risks associated with combined hormonal contraceptive use

Cardiovascular and cerebrovascular disease

7 Non-smokers at any age with no specific risk factors can be advised that they have no increased risk of myocardial infarction (MI) with COC use (Grade B).

8 The risks of using combined hormonal contraception outweigh the benefits for smokers aged ≥35 years (Grade C).

9 Women aged ≥35 years with no other risk factors who have stopped smoking more than a year ago may consider using combined hormonal contraception. The excess risk of MI associated with smoking falls significantly 1 year after stopping and is gone 3–4 years later, regardless of the amount smoked (Grade B).

10 Women should be advised that although the relative risk of venous thromboembolism with COC use can increase up to five-fold, in absolute terms the risk is still very small (Grade B).

11 Women should be advised there is a very small increase in the absolute risk of ischaemic stroke but no increase in haemorrhagic stroke with COC use (Grade B).

12 Women aged over 40 years with cardiovascular disease, stroke or migraine (even without aura) should be advised against the use of combined hormonal contraception (Grade C).

13 Clinicians prescribing COC to women aged over 40 years should consider a monophasic pill with ≤30 μg ethinylestradiol with a low dose of norethisterone or levonorgestrel as a suitable first-line option (Good Practice Point).

Morbidity and mortality from myocardial infarction (MI) is rare in women of reproductive age but increases with increasing age.[20] Non-smokers without specific risk factors, such as hypertension, can be reassured that they have no increased risk of MI with COC use [relative risk (RR) 0.9, 95% confidence interval (CI) 0.3–2.7].[27–29]

The incidence of hypertension increases with increasing age and hypertension itself is associated with an increased risk of MI.[27] The risk of venous thromboembolism (VTE) increases with increasing age and there is a three- to five-fold increase in the relative risk of VTE with COC use.[28–30] Nevertheless, the absolute risk of VTE for women using COC remains small (15–25 per 100 000 woman-years).[31] The annual risk of death from cardiovascular disease in non-smokers at the age of 40–44 years that is attributable to COC is very small (22 per million users). Nevertheless, this is 10-fold greater than the attributable risk at age 20–24 years (2 per million users).

Smoking is an independent risk factor for cardiovascular disease.[27,32] Heavy smokers (>15 cigarettes per day) have a three-fold increase in the risk of MI compared to non-smokers (RR 3.3, 95% CI 1.6–6.7).[27] The excess risk of MI for heavy smokers is increased in current COC users (RR 20.8, 95% CI 5.2–83.1).[27] Moreover, for heavy smokers the rate ratio of death from all causes is doubled (rate ratio 2.14, 95% CI 1.81–2.53).[25] There appeared to be no increased risk of MI in previous light smokers (<15 cigarettes per day) (RR 1.3, 95% CI 0.6–2.8).[27] Two case-control studies[32,33] have identified a two-fold increase in the risk of VTE associated with smoking [odds ratio (OR) 2.0, 95% CI 1.3–3.3].[32]

A hospital-based, case-control study found that an increased risk of MI was still apparent within 2 years of stopping smoking (RR 1.2, 95% CI 1.8–3.8).[34] However, most of the risk was reduced 2 years after smoking cessation and gone by 3 years.[34] This did not appear to vary

with amount smoked, the duration of smoking, age or other risk factors. A population-based, case-control study confirmed a three-fold reduction in the risk of MI 1 year after stopping and any excess risk was gone 4–6 years after stopping.[35] Evidence suggests a rapid reduction in the excess risk of MI associated with smoking after stopping and therefore the CEU advises that previous smokers aged ≥35 years may consider the use of COC one or more years after stopping.

A meta-analysis of case-control and cohort studies showed the risk of MI decreased when the dose of ethinylestradiol (EE) decreased (20 μg COC: RR 0.92, 95% CI 0.21–4.08; 30 μg COC: RR 1.97, 95% CI 1.43–2.71).[36] Nevertheless, confidence intervals are wide and this reduction may not be simply due to a dose response. Previous Guidance from the CEU recommends that a monophasic COC containing 30–35 μg EE is a suitable first-line pill.[37] The CEU suggests, however, that when prescribing COC to women aged over 40 years a monophasic pill with ≤30 μg EE should be considered.

Morbidity and mortality from stroke is uncommon in women of reproductive age but increases with increasing age.[20,25,38] A case-control study showed normotensive non-smokers have a two-fold increase in the risk of ischaemic stroke with COC use.[38] No significant increase in risk of haemorrhagic stroke with COC use has been shown.[39] Hypertension increases the risk of stroke.[28,39,40] Hypertensive COC users have a 10-fold increased risk of haemorrhagic stroke[39] and a smaller increase in ischaemic stroke compared to normotensive COC users.[38]

Smoking increases the risk of stroke, and heavy smokers have a two-fold increase in the risk of stroke compared to non-smokers.[40,41] When heavy smokers use COC the risk of ischaemic stroke is increased (OR 7.2, 95% CI 3.23–16.1).[40]

Migraine increases the risk of ischaemic stroke three-fold.[38,41] The absolute risk of stroke in migraine sufferers, however, is low (17–19 per 100 000 woman-years).[42] Three case-control studies support an increased risk of stroke in COC users with migraine, compared to users without migraine.[38,41,43,44] WHOMEC recommends that the risks of combined contraceptive use by women aged ≥35 years with migraine even without aura, or for women of any age with cardiovascular or cerebrovascular disease, outweigh any benefits (WHO Category 3 or 4).[21]

Breast cancer

14 Women aged over 40 years should be advised that any increase in risk of breast cancer associated with COC use is likely to be small, is reduced to no excess risk 10 years after stopping, but is in addition to their own background risk which increases with age (Grade B).

The annual risk of breast cancer increases with increasing age regardless of hormone use. By the age of 35 years a woman has a 1 in 500 risk of developing breast cancer. This increases to a 1 in 100 risk by the age of 45 years.[45] A meta-analysis of case-control studies showed an increased risk of breast cancer diagnosis for current COC users (RR 1.24, 95% CI 1.15–1.33).[46] This suggests a 24% increase in the background risk and is relevant in particular to women aged over 40 years when the background risk normally increases. A more recent population-based, case-control study showed that current COC users have no increased risk of breast cancer (RR 1.0, 95% CI 0.8–1.3).[47] Any excess risk of breast cancer associated with COC use increases quickly after starting, does not increase with duration of use, and has gone 10 years after stopping.[46] Any excess risk does not appear to be influenced by family history, age at first use, dose or type of hormone.[46,47]

The CEU recommends that women aged >40 years who continue or start COC can be advised that any increase in risk of breast cancer is likely to be small, is reduced to no excess risk 10 years after stopping, but is in addition to the background risk which increases with age.

Cervical cancer

15 Women should be advised that COC use appears to increase the risk of cervical cancer and cervical intraepithelial neoplasia after 5 years' use (Grade B).

A systematic review of case-control and cohort studies showed an increased risk of cervical cancer (invasive and *in situ*) and cervical intraepithelial neoplasia (CIN III) with increasing duration of hormonal contraceptive use.[48] The data are insufficient to show if this risk falls after stopping hormonal contraception. This systematic review confirmed findings from a previous case-control study[49] that for women who are human papilloma virus (HPV)-positive, the risk of cervical cancer increases with increasing duration of hormonal contraceptive use. A small, increased risk is also seen with increasing duration of use for women who were HPV-negative.[50,51] With >10 years' use, the risk of cervical cancer increased two-fold (HPV-negative: RR 2.2, 95% CI 1.9–2.4; HPV-positive: RR 2.5, 95% CI 1.6–3.9).[52] Women should be advised that oral contraceptive use is associated with an increased risk of cervical cancer with increasing duration of use and may disappear after stopping oral contraception.

Non-contraceptive benefits associated with combined hormonal contraceptive use

Bone health

16 Women can be advised that COC use over the age of 40 years may be associated with an increase in bone mineral density (Grade B).

Conflicting evidence exists on bone loss in the perimenopause.[52,53] Nevertheless the majority of studies have not supported rapid bone loss in the perimenopause before the last menstrual period.[50,52]

Conflicting evidence exists on the effect of COC on age-related loss in bone mineral density (BMD).[51,54] A meta-analysis, which included 14 studies (a randomised trial, case-control studies and cross-sectional studies) provided evidence from nine studies that low-dose COC had a positive effect on BMD.[55] Four studies included in the meta-analysis did not show any associated increase in BMD but no study identified a reduction in BMD with COC use.[55] A randomised controlled trial found an increase in BMD at the lumbar spine, femoral neck, trochanter, intertrochanteric region, total hip and at Ward's triangle with COC use.[56]

The effect of COC on BMD may be selective and only seen in perimenopausal women with low endogenous oestrogen. Indeed, a case-control study has shown an increase in BMD in perimenopausal women with COC use but no increase in younger, normally menstruating women.[57]

The clinical impact of COC on increasing BMD has

been investigated. The two, large, British cohort studies to investigate oral contraceptive pill use and fracture did not show a protective effect of COC on fracture risk.[58,59] Moreover, both suggested a 20% increase in fracture risk for ever-users of oral contraception.[58] Neither study included many women over the age of 50 years and no protective effect of oral contraceptive use against fractures was shown in premenopausal women. A population-based, case-control study demonstrated that COC use may be associated with a 25% reduction in hip fracture in postmenopausal women who had used COC over the age of 40 years (OR 0.75, 95% CI 0.59–0.96).[60] However, it is unclear from these data if there is a similar decrease with COCs containing ≤30 μg EE.

The CEU advises that women can be informed that combined contraceptive use over the age of 40 years may be associated with an increase in BMD, does not appear to reduce overall risk of fractures before the menopause, but may reduce the risk of hip fracture in the postmenopause.

Ovarian and endometrial cancers

17 Women can be advised of at least a 50% reduction in risk of ovarian and endometrial cancer with COC use which continues for 15 years after stopping (Grade B).

A systematic review[61] confirmed findings from other studies[62,63] that the risk of ovarian cancer is reduced by at least 50% with COC use (<40 μg EE). Mortality from ovarian cancer is reduced with increasing duration of COC use[25] and the risk reduction lasts for at least 15 years after stopping.[61]

In addition, a systematic review[64] supported previous case-control studies[65,66] that the risk of endometrial cancer is reduced by 50% with 50 μg COCs. Mortality from endometrial cancer is decreased with COC use.[25] A large, Swedish population, case-control study identified a 70% reduction in risk of endometrial cancer for COCs with <40 μg EE (OR 0.3, 95% CI 0.1–0.9).[67] This protection was apparent after 3 years' use and continued for 15 years after discontinuation.[67]

Colorectal cancer

18 Women can be advised that there is a reduction in the risk of colorectal cancer with COC use (Grade B).

Studies on the risk of colorectal cancer with COC use are reassuring.[68–70] Evidence to support a reduction in the risk of colorectal cancer with oral contraceptive use was obtained from a meta-analysis, which identified an overall RR of 0.82 (95% CI 0.74–0.92).[70] It has not been established, however, if this protective effect occurs with low-dose COCs.[71]

Benign breast disease

19 Women can be advised that there may be a reduction in the incidence of benign breast disease with COC use (Grade B).

A review of epidemiological studies suggested a reduced risk of benign breast disease with oral contraceptive use.[72] A cohort study reported a reduction in proliferative benign breast disease associated with oral contraceptive use.[73] Nevertheless, these observational studies have failed to eliminate bias and confounding.

Menstrual bleeding patterns

20 Women can be advised that, in clinical practice, menstrual bleeding and pain may be reduced with COC use (Grade B).

A Cochrane Review did not identify evidence that COCs reduce the incidence of primary dysmenorrhoea.[74] However, a small randomised, double-blind, placebo-controlled trial subsequently published showed a significant reduction in menstrual cramps with COC use.[75] A Cochrane Review found that COC was less effective than gonadotrophin-releasing hormone agonists in the relief of menstrual pain, but was as effective at relieving dyspareunia and non-menstrual pain.[76] A Cochrane Review concluded that there is insufficient evidence to confirm that COC reduces menstrual blood loss.[77] The one small randomised trial included in this review showed a 43% reduction in measured menstrual blood loss with COC use over two cycles.[78] Moreover, in clinical practice, women describe less bleeding and pain with COC use.

Anovulatory cycles are common in women aged over 40 years.[79,80] The luteal phase (after ovulation) is around 14 (range, 13.3–15) days' duration, but shortens in women over the age of 40 years (range, 11–12.9 days).[79] Subsequently cycles become increasing long, and longitudinal studies have confirmed that an increase in cycle length is common in women 2–8 years before the menopause.[81] COCs can provide cycle regularity, which can be a particular advantage to women aged over 40 years.

Vasomotor symptoms

21 Women can be advised that, in clinical practice, COC may reduce hot flushes (Grade C).

A small, placebo-controlled, randomised, double-blind trial showed that low-dose COC (20 μg EE and 1 mg norethisterone acetate) reduced the incidence of vasomotor symptoms (hot flushes) by 50% with 6 months of use. The study was small and the results were not statistically significant but clinically symptomatic improvement was apparent.[82]

Other benign conditions

Case-control and cohort studies suggest a reduction in the incidence of functional ovarian cysts[83,84] and benign ovarian tumours[85] for women using COC. A meta-analysis identified a 30% reduction in the incidence of rheumatoid arthritis with COC use.[86] Small randomised trials have shown significant reductions in acne lesions with COCs.[87,88] A Cochrane Review found no causal association between COC and additional weight gain.[89]

Progestogen-only contraception

The risks and benefits associated with progestogen-only contraception (POC) [pills, injectables, implants and the levonorgestrel-releasing intrauterine system (LNG-IUS)] are less well studied than combined contraception. Information about benefits and risks, highlighting specific concerns, are summarised here. Studies investigating women using progestogen-only methods are liable to a degree of prescriber bias, as women who use these methods are likely to have underlying disease, which may have precluded COC use. Most data relate to the use of progestogen-only pills (POPs) and injectables; however, it is likely that the risks associated with progestogen-only implants and the LNG-IUS are no greater than for other progestogen-only methods.

The POP is used by 7% of women aged over 40 years who are currently using a method of contraception.[24] Progestogen-only injectables and implants are used by 2% of women aged over 40 years. Only 2% of women aged over 40 years appear to use the LNG-IUS.[24] Limited data on the use of progestogen-only emergency contraception in this age group have been published.[90,91]

Potential risks associated with POC

Cardiovascular and cerebrovascular disease

22 Women should be advised that although data are limited there is no apparent increase in risk of cardiovascular disease (MI, VTE) or stroke with POC (Grade B).

23 Women with current VTE should be advised that the risks of using progestogen-only methods outweigh the benefits. Women with previous VTE, however, can be advised that the benefits of using progestogen-only methods outweigh the risks (Grade C).

24 Women with a history of ischaemic heart disease or stroke should be advised that the risks of initiating a progestogen-only injectable outweigh the benefits, however, the benefits of initiating POPs, implants or the LNG-IUS outweigh the risks (Grade C).

Few studies have been large enough to evaluate the risk of cardiovascular disease (MI, VTE) or stroke associated with the use of POC.[92] This is in part because there is a low incidence of cardiovascular and cerebrovascular morbidity in women of reproductive age and also because of the relatively limited use of POC worldwide. The WHO collaborative, hospital-based, case-control study did not identify an increase in cardiovascular disease (MI, VTE) or stroke with the use of oral or injectable POC in normotensive women.[92] The risk of stroke was increased 10-fold in hypertensive POP users; however, the risk of MI or VTE did not increase (with POP or injectable progestogen use).[92] No increase in the risk of stroke was identified for normotensive women using POC.[40] No data were identified on the use of other progestogen-only methods.

WHOMEC provides recommendations on the use of POC for women with cardiovascular and cerebrovascular disease. WHOMEC differentiates between continuing progestogen-only methods in women who are diagnosed with VTE, ischaemic heart disease or stroke, and women with pre-existing disease who wish to initiate POC.[21]

Breast cancer

25 Women can be advised that the limited evidence currently available does not suggest a significant increase in the risk of breast cancer with POPs and injectables. The use of implants and the LNG-IUS are unlikely to pose an increased risk (Grade C).

A meta-analysis included few women using POPs and injectables.[46] Data show that the risk of breast cancer with POPs and injectables was broadly similar to that for COCs, with some evidence of an increased risk with use in the previous 5 years.[46] A recent prospective cohort study also showed that the risk of breast cancer with POPs (RR 1.6, 95% CI 1.0–2.4) appears to be similar to the risk associated with COCs (RR 1.5, 95% CI 1.0–2.0).[93] There is no risk 10 or more years after stopping.[46]

A pooled analysis of two case-control studies showed that women using the progestogen-only injectable (depot medroxyprogesterone acetate, DMPA) had no increase in the risk of breast cancer compared to never-users (RR 1.1, 95% CI 0.97–1.4).[94] Nevertheless, current or recent DMPA users had a higher relative risk of breast cancer (RR 2.0, 95% CI 1.5–2.8). Those women who had used DMPA >5 years before, had no increase in risk of breast cancer and this risk was not influenced by duration of use.[94] A smaller, case-control study indicated no increase in the risk of breast cancer with use of progestogen-only injectables, mostly DMPA (RR 0.9, 95% CI 0.7–1.2).[95] There were no consistent associations with age when used or duration of use. Overall, most evidence on breast cancer and POPs and injectables has been reassuring.[96]

The CEU advises that current evidence does not suggest a significant increase in the risk of breast cancer with POPs and injectables. The use of implants and the LNG-IUS are unlikely to pose an increased risk.

Bone health

26 Women can be advised that long-term use of progestogen-only injectable contraception is associated with a reduction in BMD but this returns to normal after cessation (Grade B).

27 The relationship between bone densitometry and fracture risk in women aged over 40 years who are using injectable POC is unclear (Grade C).

Conflicting evidence exists on the degree of bone loss around the menopause.[53] Nevertheless, most evidence suggests there is no significant decrease in BMD until at least 3 years after the menopause.[97] Most concerns about BMD and progestogen-only methods are specific to injectable progestogens and, in particular, DMPA. Studies show that BMD at the femoral neck and lumbar spine is reduced with DMPA use compared to non-users.[98,99] Any loss in BMD recovers when DMPA is stopped.[100] Cross-sectional studies have shown that serum oestradiol in DMPA users is within the normal early follicular phase range (15–318 pmol/l).[101,102] After up to 5 years of DMPA use, most women have serum oestradiol levels above those of postmenopausal women and most are not oestrogen-deficient. Two studies have failed to show a correlation between serum oestradiol levels and BMD.[102,103] The CEU suggests that women aged over 40 years who are continuing or considering initiation of DMPA should be advised that studies have found an association between long-term use and loss of BMD. Women with additional risk factors for low BMD (i.e. smokers, those on long-term, high-dose corticosteroid therapy, those with thyroid disease or with a family history) should be discouraged from using DMPA. A meta-analysis found that bone densitometry can predict the risk of fracture but not those individuals who will subsequently have a fracture.[104] The role of bone densitometry in the management of women aged over 40 years and using DMPA is unclear.[100,103,105–108] WHOMEC recommends that the benefits of using DMPA in women aged over 45 years outweigh any risks.[21]

Bleeding patterns

28 Women should be advised that irregular bleeding is a common side effect with POC. Clinicians should carefully consider when the investigation of abnormal bleeding may be indicated in women aged >40 years (Grade C).

Abnormal bleeding is common in women using POC.[109,110] The WHO *Selected Practice Recommendations for Contraceptive Use* (WHOSPR)[111] and the UK version[112] provide guidance on the management of abnormal bleeding for women using POC. Nevertheless some progestogen-only methods may be useful in the management of menorrhagia and irregular bleeding because of associated amenorrhoea. Amenorrhoea was reported by 46% of women using DMPA at 3 months and by almost 60% of women at 12 months.[113]

The LNG-IUS is licensed for use in the management of idiopathic menorrhagia.[114,115] Large epidemiological studies have shown that premature removal of the LNG-IUS was less common if women were amenorrhoeic.[110] Amenorrhoea can be expected in up to 25% of women 6 months after insertion and continuation rates were highest in women aged 39–48 years. Moreover, prospective non-randomised studies have identified a higher rate of amenorrhoea (44% after 6 months and 50% after 12 months).[116] A study in perimenopausal women using the LNG-IUS showed a reduction in blood loss, with 38% amenorrhoeic at 12 months and 62% amenorrhoeic at 24 months.[117] The LNG-IUS may be a very useful treatment option for menorrhagia, which is particularly common in women aged >40 years.

Counselling regarding bleeding patterns is crucial when women are considering progestogen-only methods. Guidance on the investigation of women aged over 40 years with abnormal bleeding is outside the remit of this Guidance and readers are referred to Guidance from the Royal College of Obstetricians and Gynaecologists (RCOG).[118,119]

Non-contraceptive benefits of POC

Endometrial and ovarian cancers

Progestogen-only methods may reduce the risk of endometrial and ovarian cancers.[96,120] However, most studies have included too few women to have adequate power to identify if there is an increase or decrease in risk of endometrial or ovarian cancer with POC.[66,67] The Cancer and Steroid Hormone Study[66] included very few women using a POP; however, the risk of endometrial cancer was not increased (OR 0.6, 95% CI 0.1–5.0). A large, Swedish population-based, case-control study found similar results for POPs (OR 0.5, 95% CI 0.2–1.1).[67]

Sterilisation

29 Counselling and advice on sterilisation procedures should be provided to women and men within the context of a service providing a full range of information and access to other long-term reversible methods of contraception. This should include information on the advantages and disadvantages and relative failures (Grade C).[121]

30 Women should be informed that vasectomy carries a lower failure rate and that there is less risk related to the procedure (Grade B).[121]

Sterilisation is the most commonly used method of contraception by women aged >40 years. Similar numbers of couples use either female sterilisation (42%) or vasectomy (45%).[24] Evidence-based guidelines from the RCOG provide recommendations on sterilisation and the relevant recommendations are reproduced here.[121]

Tubal occlusion

31 Women, particularly those at increased risk from conditions such as previous abdominal surgery or obesity, should be informed of the risks of laparoscopy and the chances of laparotomy being necessary if there are problems with the laparoscopy procedure (Grade B).[121]

32 Women should be informed that tubal occlusion is associated with a failure rate and that pregnancy can occur several years after the procedure. The lifetime risk of failure, in general, is estimated to be 1 in 200. The longest period of follow-up data available for the most common method used in the UK, the Filshie clip, suggests a failure rate after 10 years of 2 or 3 per 1000 procedures (Grade B).[121]

33 Women should be informed that if tubal occlusion fails, the resulting pregnancy may be ectopic (Grade B).[121]

34 Although women requesting sterilisation should understand that the procedure is intended to be permanent, they should be given information about the success rates associated with reversal, should this procedure be necessary (Grade B).[121]

35 Women should be reassured that tubal occlusion is not associated with an increased risk of heavier or longer periods when performed after 30 years of age. There is an association with subsequent increased hysterectomy rate, although there is no evidence that tubal occlusion leads to problems that require hysterectomy (Grade B).[121]

36 Hysteroscopic methods of tubal occlusion are still under evaluation and should only be used within the present guidance system for new surgical interventions (Grade C).[121]

Vasectomy

37 Men should be informed that vasectomy has an associated failure rate and that pregnancies can occur several years after vasectomy. The rate should be quoted as approximately 1 in 2000 after clearance has been given (Grade B).[121]

38 Although men requesting vasectomy should understand that the procedure is intended to be permanent, they should be given information on the success rates associated with reversal should this procedure be necessary (Grade B).[121]

39 Men should be advised to use effective contraception until azoospermia has been confirmed. The way in which azoospermia is confirmed will depend on local protocols (Grade C).[121]

40 Men requesting vasectomy can be reassured that there is no increase in testicular cancer or heart disease associated with vasectomy. The association in some reports of an increased risk of being diagnosed with prostate cancer is at present considered to be non-causative (Grade B).[121]

41 Men should be informed about the possibility of chronic testicular pain after vasectomy (Grade B).[121]

Barrier contraception

42 Women should be advised to use condoms with non-spermicidal lubricant where possible (Grade C).

Women aged over 40 years commonly rely on male condoms (29%).[24] In this age group, female condoms and spermicides alone are unpopular (1%). Female barrier methods (diaphragms and cervical caps) are used by 3%.[24] In a recent publication, the WHO recommends condoms without nonoxynol-9 spermicidal lubricant for prevention of pregnancy or STI.[122] This is due to risks associated with mucosal irritation with frequent nonoxynol-9 use.[122] Where possible women and men should be advised to use non-spermicidally lubricated condoms.[122] Nevertheless, the use of spermicide with diaphragms or cervical caps is still recommended.[123]

Copper intrauterine contraception

43 Asymptomatic women aged ≥40 years who are having an IUD inserted and have been identified as being at higher risk for STI should have an endocervical swab for *Chlamydia trachomatis* as a minimum, together with an endocervical swab for *Neisseria gonorrhoea* depending on local prevalence. There is no indication to test for other lower genital tract organisms (Grade C).

44 Women should be informed that menstrual abnormalities (including spotting, light bleeding, heavy or longer menstrual periods) are common in the first 3–6 months of IUD use. Women should be advised to seek medical advice to exclude infection and gynaecological pathology, if menstrual abnormalities occur after the first 6 months of use (Grade C).

Guidance on the copper intrauterine device (IUD) as long-term contraception has been published by the CEU.[124] Recommendations particularly relevant to women aged >40 years are highlighted here. The IUD is the method used by 9% of women aged >40 years.[24]

Testing for STI prior to IUD insertion should be based on a relevant sexual history taking account of risk factors (a new sexual partner or a change in sexual partner in the last year) and not based on age alone. If a woman is higher risk (>25 years with a new sexual partner or two or more partners in the last 12 months) then an endocervical swab for *Chlamydia trachomatis* is advised, and an endocervical swab for *Neisseria gonorrhoea* depending on local prevalence. There is no indication to test for other lower genital tract organisms in asymptomatic women.[124]

Menstrual bleeding problems are common in women aged over 40 years and also common in IUD users.[112] Menstrual abnormalities, including spotting and light bleeding or heavy or longer periods, are common in the first 3–6 months of IUD use[111,112] and persist in a minority of women. These bleeding patterns are not harmful and usually decrease over time. However, women should be advised to seek medical advice, to exclude gynaecological pathology and infection, if bleeding problems persist or occur as a new event.[111]

Natural family planning methods

The withdrawal method is used by 2% of women aged >40 years.[24] Nevertheless, the withdrawal method is associated with a high failure rate and is not advocated as a reliable contraceptive method.

The numbers of women over the age of 40 years who rely on fertility awareness methods are unknown. Such methods can be more difficult to learn by women with irregular cycles.[21]

When can a woman over the age of 40 years be advised to stop contraception?

45 In general, women can be advised to stop contraception at the age of 55 years as most (95.9%) will be menopausal by this age (Grade C).

46 Measuring follicle-stimulating hormone on at least two occasions 1 or 2 months apart may predict ovarian failure and be helpful in some situations when advising women when to stop contraception (Grade C).

A systematic review of 16 cross-sectional and longitudinal studies assessed the accuracy of symptoms, signs and blood tests in the diagnosis of the perimenopause.[125] No single parameter allows an accurate diagnosis of the perimenopause. A woman's age and menstrual cycle may be most clinically useful in determining the likelihood of the approaching menopause. However, it is only when the menopause can be confirmed that a woman can be advised to discontinue contraception.

The menopause is usually diagnosed clinically and in retrospect after 1 year of amenorrhoea.[3] The average age at which the menopause occurs is 50.7 years (range, 44–56 years for 95% of women).[3,126,127] Few women (10%) stop menstruating abruptly and only 1% have a premature menopause (<40 years).[128] Expert opinion has advised continued use of contraception until there have been 2 years of amenorrhoea if the woman is aged <50 years as there may be a risk of ovulation, despite amenorrhoea. The probability of menstruation (and possibly ovulation) after a year of amenorrhoea for women aged >45 years has been estimated by the WHO to be 2–10%.[129]

A population study found that 52.4% of women are menopausal by the age of 50 years.[3] However, one-third of women will need contraception for at least 1 year after the age of 50 years and a woman may therefore wish to continue with her usual method.[3] By age 55 years, most women (95.9%) are menopausal and by age 59 years virtually all are menopausal. Vasomotor symptoms occur sporadically in 85% of perimenopausal women and are not a reliable indicator of ovarian failure. In general, the CEU advises that contraception may be stopped at the age of 55 years at which time most women will be postmenopausal and natural loss of fertility can be assumed. Nevertheless, this will need to be tailored to an individual woman (for example, any woman not using exogenous hormones but who continues to experience regular menstruation at the age of 55 years should continue with contraception).

Serum levels of follicle-stimulating hormone (FSH) and sex steroids (oestrogen and progesterone) fluctuate around the menopause.[2,97,130,131] The level of luteinising hormone (LH) remains within the normal range at this time.[2] An increase in FSH stimulates ovarian folliculogenesis, which occurs at an accelerated rate up until the menopause when all follicles are depleted.[8,9,53] Increased folliculogenesis results in increased oestrogen production, which may contribute to irregular bleeding.

A single elevated FSH (in the early phase of the menstrual cycle) in a perimenopausal woman suggests altered folliculogenesis and impaired fertility[53] but cannot reliably predict ovarian failure. FSH increases 10–20-fold in the first 3 years of the menopause and persistent high

concentration predicts ovarian failure.[130] It has been common practice to consider ovarian failure highly likely when two measurements of FSH >30 IU/l are obtained at least 1 or 2 months apart.[1] Oestradiol decreases and LH increases after the menopause[97] but neither are helpful in its diagnosis.

Stopping non-hormonal contraception

47 Women using non-hormonal contraception can be advised to stop contraception after 1 year of amenorrhoea (or 2 years if the last menstrual period occurred for a woman aged <50 years) (Grade C).

48 After counselling about declining fertility, risks associated with IUD insertion and contraceptive efficacy, women who have an IUD with >300 mm^2 of copper inserted at age ≥40 years can be advised to retain the device until the menopause (Grade C).

It is generally accepted that non-hormonal contraception can be stopped 1 year after the last menstrual period (LMP) in a woman aged ≥50 years. If the LMP occurred in a woman aged <50 years, however, contraception should be continued until 2 years of amenorrhoea.[1,126]

It is accepted practice that a copper IUD with ≥300 mm^2 copper that is inserted at or after the age of 40 years can be retained until the postmenopause.[124,132] This use falls outside the manufacturers' recommended duration of use. Women should be counselled about declining fertility with age, the risks associated with insertion (infection, perforation, expulsion) and potential loss of contraceptive efficacy if used beyond the recommended life of the device. An IUD should be removed after the menopause, but if it cannot be removed easily in an outpatient setting then consideration should be given to the benefits and risks of surgery versus retention of the IUD.[124]

Stopping hormonal contraception

49 Women using exogenous hormones should be advised that amenorrhoea is not a reliable indicator of ovarian failure (Good Practice Point).

Some women require advice about stopping hormonal contraception around the menopause. Menstrual bleeding patterns are unhelpful when a woman is using exogenous hormones. Amenorrhoea may be due to contraceptive hormones (POPs, injectables, implants or the LNG-IUS). Regular bleeding may be due to contraceptive hormones (COC). Assessments of FSH levels are unreliable when women are using combined contraception even if measured in the pill-free interval. However, FSH levels can be measured while using progestogen-only contraception (POPs, injectables, implants and the LNG-IUS).[133]

Stopping combined contraception

50 Women using combined contraception should be advised to switch to another suitable contraceptive method at the age of 50 years (Good Practice Point).

51 FSH is not a reliable indicator of ovarian failure in women using combined hormones, even if measured during the hormone-free or oestrogen-free interval (Good Practice Point).

The CEU does not recommend the use of combined contraception beyond the age of 50 years. Women aged 50 years should be counselled about the benefits and risks of combined contraception and about suitable alternative methods such barrier methods or the POP. After stopping combined contraception, barrier methods can be used until the menopause is confirmed (1 year of amenorrhoea or 2 years if aged <50 years). Alternatively, a POP may be a suitable option for women who wish to continue with an oral regimen. Advice on stopping the POP is given in Figure 1.

The menopause cannot be reliably diagnosed when using combined contraception or combined hormone replacement therapy (HRT). FSH may be assessed 6 or more weeks after discontinuing combined hormones and if found to be >30 IU/l on two or more occasions at least 1 or 2 months apart with accompanying amenorrhoea then this is highly suggestive of ovarian failure. However, in clinical practice FSH may only be helpful if a woman switches to another hormonal method and cannot rely on an assessment of bleeding (in particular amenorrhoea) to diagnose the menopause.

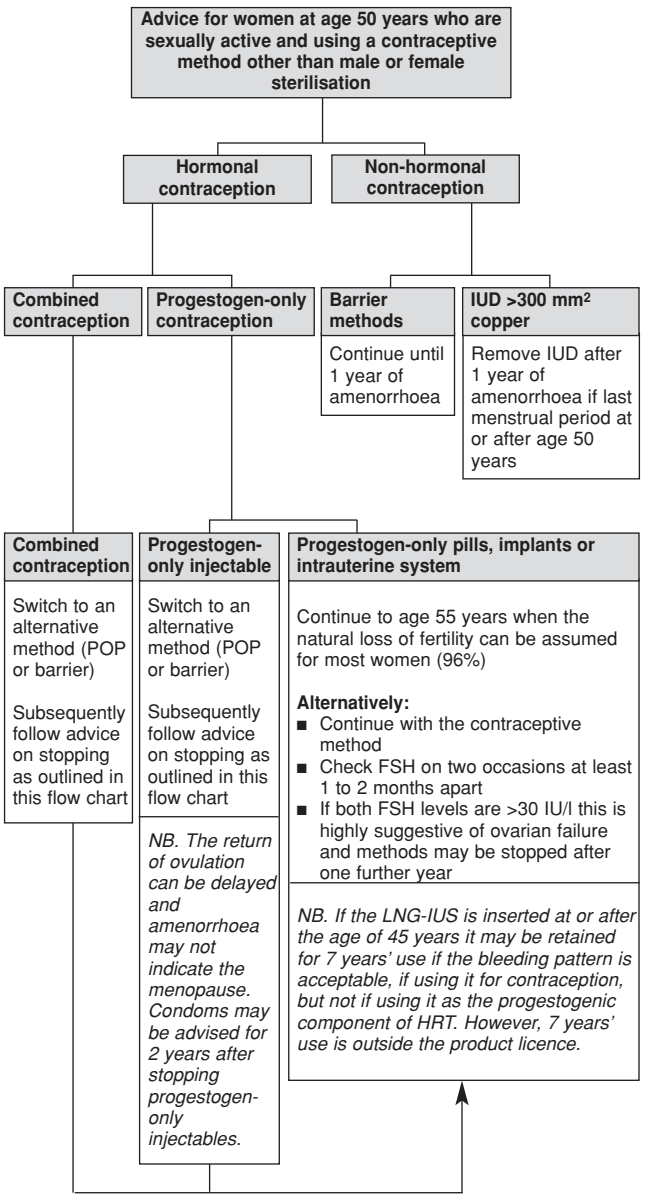

Figure 1 *Advice for women at age 50 years on stopping contraception. FSH, follicle-stimulating hormone; HRT, hormone replacement therapy; IUD, intrauterine device; LNG-IUS, levonorgestrel-releasing intrauterine system; POP, progestogen-only pill.*

Stopping POPs and implants

52 Women can be advised that a POP or implant can be continued until the age of 55 years when natural loss of fertility can be assumed. Alternatively, the woman can continue with the POP or implant and have FSH levels checked on two occasions 1 or 2 months apart, and if both levels are >30 IU/l this is suggestive of ovarian failure. In this case the woman may continue with the POP, implant or barrier contraception for another year (or 2 years if aged <50 years) (Good Practice Point).

Stopping progestogen-only injectables

53 Women should be counselled about the risks and benefits of continuing with the progestogen-only injectable at the age of 50 years and be advised to switch to a suitable alternative (Good Practice Point).

WHOMEC recommends that that the benefits of using injectable progestogen-only methods over the age of 45 years outweigh the risks (WHO Category 2).[21] Previous advice was to discontinue injectable progestogens at the age of 45 years when any loss of BMD could recover before the natural decline at the menopause.[1] Evidence for rapid bone loss in the perimenopause is outweighed by evidence of no loss of BMD until into the menopause. The CEU advises that the effect of DMPA on BMD should be discussed with women around the age of 45 years. If there are no risk factors for osteoporosis and the woman is unwilling to consider an alternative option, DMPA can be continued to age 50 years and then stopped and a suitable alternative contraceptive used (Figure 1). Ovulation can be delayed after stopping DMPA and thus amenorrhoea cannot be relied upon. It may be advisable for women to use condoms for 2 years after stopping DMPA.

Removing the LNG-IUS

54 Women who have the LNG-IUS inserted at age ≥45 years for contraception or for the management of menorrhagia can be counselled about retaining the device for up to 7 years (Good Practice Point).

There are data from randomised trials of contraceptive efficacy for up to 7 years continuous LNG-IUS use.[134,135] However, the LNG-IUS has a licence for only 5 years' use.[115] After 5 years' use, women should be advised to return for review to discuss the need for removal and replacement. Women using the LNG-IUS for menorrhagia and whose symptoms are well controlled may continue with the LNG-IUS beyond its licensed duration. However, women using the LNG-IUS to deliver local progestogens to protect against endometrial neoplasia when using oestrogen HRT should have the device replaced every 5 years regardless of age at insertion. The CEU advises that women having the LNG-IUS inserted at age ≥45 years for contraception or for the management of menorrhagia can be advised to retain the device for 7 years' use. This use is outside product licence.[136]

For women using HRT is contraception also required?

55 Women using combined HRT cannot be advised to rely on this as contraception (Grade B).

56 Women can be advised that a POP can be used with HRT to provide effective contraception (Good Practice Point).

57 Women using oestrogen replacement therapy may choose the LNG-IUS to provide endometrial protection (Grade A).

Providing contraceptive advice for sexually active women using HRT, and not relying on sterilisation, can be difficult. A clinical assessment of the menopause is problematic in a woman using HRT. Most women in this age group will be using combined sequential HRT. Combined continuous HRT regimens are not appropriate in this age group due to bleeding. Measurement of FSH is unreliable. If a woman will not discontinue HRT to allow an assessment of bleeding patterns or FSH, barrier methods or an IUD can be continued to age 55 years. The need for contraception by women using HRT is unclear. A small study identified that oral combined HRT did not reliably inhibit ovulation in women aged 42–52 years.[137] Prior to starting HRT, regular menstrual cycles were strongly associated with ovulation.[137] Starting HRT inhibited ovulation in only 40% of women with regular cycles. Half of the women with anovulation and irregular cycles resumed ovulation when starting HRT.

POPs contain less progestogen than some HRT regimens.[138] Nevertheless, despite this higher dose of progestogen, the Summary of Product Characteristics does not advise use as contraception.[139] No studies were identified which investigated the effects of HRT or topical vaginal oestrogen in women using POC and subsequent contraceptive efficacy.[140,141] No studies have investigated failure rates of POP when using oral or vaginal oestrogen.

Randomised trials show that the LNG-IUS is effective in providing endometrial protection from the stimulatory effects of oestrogen.[142–147] Endometrial protection is provided for both postmenopausal and perimenopausal women.[142–145] Women using the LNG-IUS who develop vasomotor symptoms and who wish to use oestrogen replacement may be advised that they can rely on their LNG-IUS for endometrial protection. Currently, the UK product licence for use of the LNG-IUS in this way is awaited (expected January 2005).

What follow-up is required for women over 40 years using contraception?

58 Women aged over 40 years should be advised to return for follow-up if they develop any problems with contraception or develop any new medical history that may influence contraceptive choice or when they reach the age of 50 years (Grade C).

The UK version of WHOSPR recommends that at the initial visit up to 12 months' supply of contraceptive pills may be offered, depending on the woman's desires and anticipated use.[112] Restricting supplies could result in discontinuation of effective methods and increase the risk of pregnancy. Flexibility in pill supply, to allow women to obtain supplies readily without the need for repeated visits, should be balanced with easy access if problems arise. The minimum frequency of follow-up recommended for safe and effective use of each method refers to general situations and may vary between users. Women with more specific medical problems may require more frequent follow-up.

A yearly follow-up visit is recommended for women using COC or POP. Women should be advised to return if they experience problems. Women should be advised to return when the 3 years' use of a progestogen-only implant is complete. Women using an IUD should be advised to return if problems arise and should return when it is time to have the device removed.

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This Guidance is also available online at www.ffprhc.uk. Evidence tables are available on the FFPRHC website. These summarise relevant published evidence on contraception for women aged over 40 years, which was identified and appraised in the development of this Guidance. The clinical recommendations within this Guidance (i.e. the text appearing within the blue and red boxes) 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

Electronic searches were performed in general between 1990 and 2004 for: MEDLINE (CD Ovid version); EMBASE (1990–2004); PubMed; The Cochrane Library (to September 2004) 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 contraception for women aged over 40 years. 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.

Questions for Contraception for Women Aged Over 40 Years

The following questions and answers have been developed by the FFPRHC Education Committee.

Indicate your answer by ticking the appropriate box for each question	*True*	*False*
1 The perimenopause refers to the phase spanning the transition from normal ovulatory cycles to the cessation of ovulation and menstruation.	☐	☐
2 Women aged over 40 years have a low conception rate, but are much more likely to undergo induced abortion when faced with an unplanned pregnancy than women in their 20s.	☐	☐
3 In healthy, non-smoking, women aged 40–44 years, the risks of mortality from cardiovascular disease attributable to the combined pill outweigh potential benefits.	☐	☐
4 WHOMEC recommends that the risks of combined contraception in women over the age of 35 years who have migraine with or without aura outweigh any benefits.	☐	☐
5 The risk of endometrial and ovarian carcinomas increases over the age of 40 years. Women in this age group should be informed of at least a 50% reduction in the risk of these cancers with use of combined oral contraception.	☐	☐
6 A woman who develops a venous thrombosis or has a myocardial infarction or a cerebrovascular accident whilst taking the progestogen-only pill (POP), may be advised that continuing to use this method of contraception represents an acceptable risk.	☐	☐
7 There is evidence that tubal occlusion may precipitate menorrhagia.	☐	☐
8 Some 95.9% of women will have undergone the menopause by the age of 55 years.	☐	☐
9 A woman having the levonorgestrel-releasing intrauterine system inserted at age ≥45 years can be advised that the device can be retained for up to 7 years, providing it is not being used in combination with oestrogen hormone replacement therapy (HRT).	☐	☐
10 A POP does not provide effective contraception when used at the same time as HRT.	☐	☐

Answers

1 True, 2 True, 3 False, 4 True, 5 True, 6 False, 7 False, 8 True, 9 True, 10 False