INTRODUCTION

As age increases, fertility of women declines, this is related to many factors but the most important is the quality and quantity of oocytes (1-6). The climacteric is the transition from normal ovulatory menstrual cycles to the cessation of ovulation and menstruation (7). The average age of onset of the perimenopause is 46 years and the average duration of the perimenopause is 5 years (8). During the perimenopause, intermittent ovulation and anovulation occur and therefore effective contraception is required for sexually active women to prevent unintended pregnancy. The balance between the risks and benefits of different contraceptive options changes with age and becomes increasingly relevant for women aged over 40 years.

The risks of congenital and chromosomal abnormalities, and spontaneous abortion increase for women over 40 years (9-12). 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 (13). 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) (14).

No contraceptive method is contraindicated by age alone. Contraceptive choice for women over the age of 40 years may be influenced by many factors e.g. natural decline in fertility, sexual function, menstrual dysfunction and associated medical conditions. Women over 40 years can be advised 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).

The World Health Organization Medical Eligibility Criteria for Contraceptive Use (WHOMEC) provides evidence-based recommendations to ensure that women can select the most appropriate method of contraception without unnecessary medical barriers. WHO Category 1: the use of the contraceptive method is unrestricted, WHO Category 2: the benefits of using the contraceptive method outweigh the risks, WHO Category 3: the risks associated with using the method outweigh the benefits, WHO Category 4: the use of the contraceptive method poses an unacceptable health risk (15).

Communicating the benefits and risks associated with contraceptive use involves an exchange of information to allow informed choices regarding contraceptive use (16, 17).
Combined hormonal contraception

Although two large cohort studies have shown that long-term combined hormonal contraception (COC) is safe for most women, the combined oral contraceptive pill (COC) is used by < 10% of women aged over 40 years (18-20).

Risks associated with combined hormonal contraceptive use include:

Cardiovascular and cerebrovascular disease

Morbidity and mortality from myocardial infarction (MI) is rare in women of reproductive age but increases with increasing age (21). Non-smokers without specific risk factors, such as hypertension, can be reassured that they have no increased risk of MI with COC use (22-24). The risks of using combined hormonal contraception outweigh the benefits for smokers aged 40 years or older.

Women aged 40 years or older with no other risk factors who have stopped smoking more than a year ago may consider using combined hormonal contraception. The excess risk of myocardial infarction (MI) associated with smoking falls significantly 1 year after stopping and is gone 3 to 4 years later, regardless of the amount smoked.

The risk of venous thromboembolism (VTE) increases with increasing age and there is a 3-5 fold increase in the relative risk of VTE with COC use (23-25). Nevertheless, the absolute risk of VTE for women using COC remains small (15-25 per 100 000 woman-years) (31).

There is a very small increase in the absolute risk of ischemic stroke but no increase in hemorrhagic stroke with COC use (27, 28).

Women aged over 40 years with cardiovascular disease, stroke, or migraine (even without aura) should be advised against the use of combined hormonal contraception (15, 27, 29-31).

Clinical Effectiveness Unit (CEU) of the Faculty of Family Planning and Reproductive Health Care (FFPRHC) suggests, however, that clinicians prescribing COC to women aged over 40 years should consider a monophasic pill with <30 microgram ethinylestradiol with a low dose of norethisterone or levonorgestrel as a suitable first-line option (32, 33).

Breast cancer

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 (34).

A meta-analysis of case-control studies showed an increased risk of breast cancer diagnosis for current COC users (35). 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 (36). 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 (35). Any excess risk does not appear to be influenced by family history, age at first use, dose or type of hormone (35, 36).

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

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 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

Conflicting evidence exists on bone loss in the perimenopause (38, 39). Nevertheless the majority of studies have not supported rapid bone loss in the perimenopause before the last menstrual period (40). Also conflicting evidence exists on the effect of COC on age-related loss in bone mineral density (BMD) (41, 42).
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
A systematic review (43) confirmed findings from other studies (44, 45) that the risk of ovarian cancer is reduced by at least 50% with COC use (<40 µg EE).

In addition, a systematic review64 supported previous case-control studies (47, 48) that the risk of endometrial cancer is reduced by 50% with 50 µg COCs. This protection was apparent after 3 years’ use and continued for 15 years after discontinuation (49).

Colorectal cancer
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 (50). It has not been established, however, if this protective effect occurs with low-dose COCs (51).

Benign breast disease
Observational studies suggested a reduced risk of benign breast disease with oral contraceptive use (52, 53). Nevertheless, these observational studies have failed to eliminate bias and confounding. Women can be advised that there may be a reduction in the incidence of benign breast disease with COC use.

Menstrual bleeding patterns
A Cochrane Review did not identify evidence that COCs reduce the incidence of primary dysmenorrhea (54). However, a small randomized, double-blind, placebo controlled trial subsequently published showed a significant reduction in menstrual cramps with COC use (55). 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 (56). A Cochrane Review concluded that there is insufficient evidence to confirm that COC reduces menstrual blood loss (57). The one small randomized trial included in this review showed a 43% reduction in measured menstrual blood loss with COC use over two cycles (58).

Vasomotor symptoms
A small, placebo-controlled, randomized, 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.

Progestogen-only contraception
The POP is used by 7% of women aged over 40 years who are currently using a method of contraception. 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 levonorgestrel-releasing intrauterine system (LNG-IUS) (18). Limited data on the use of progestogen-only emergency contraception in this age group have been published (60).

The risks and benefits associated with progestogen-only contraception (POC) are less well studied than combined contraception.

Potential risks associated with POC

Cardiovascular and cerebrovascular disease
Few studies have been large enough to evaluate the risk of MI, VTE, or stroke associated with the use of POC (61). 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 (61).

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 (15).

Women with a history of ischemic heart disease or stroke should be advised that the risks of initiating a progestogen-only injectable outweigh the benefits; however, the benefits of initiating progestogen-only pills (POPs), implants, or the
levonorgestrel-releasing intrauterine system (LNG-IUS) outweigh the risks (15).

**Breast cancer**
Most evidence on breast cancer and POPs and injectables has been reassuring (62, 63). 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**
Although the relationship between bone densitometry and fracture risk in women aged over 40 years who are using injectable POC is unclear (64-69). The long-term use of progestogen-only injectable contraception is associated with a reduction in bone mineral density (BMD) but this returns to normal after cessation (64, 70, 71).

**Bleeding patterns**
Counseling regarding bleeding patterns is crucial when women are considering progestogen-only methods, as abnormal bleeding is a common side effect in women using POC (72, 73). Clinicians should carefully consider when the investigation of abnormal bleeding may be indicated in women aged over 40 years (74, 75).

**Non-contraceptive benefits of POC**

**Endometrial and ovarian cancers**
Progestogen-only methods may reduce the risk of endometrial and ovarian cancers (63, 76). 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 (48, 49).

**Tubal Sterilization**
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 (77). 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 (77).

Women should be informed that if tubal occlusion fails, the resulting pregnancy may be ectopic (121), they should be also 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 (77). Hysteroscopic methods of tubal occlusion are still under evaluation.

**Barrier contraception**
Women aged over 40 years commonly rely on male condoms (29%) (18). In this age group, female condoms and spermicides alone are unpopular (1%). Female barrier methods (diaphragms and cervical caps) are used by 3% (18). In a recent publication, the WHO recommends condoms without nonoxynol-9 spermicidal lubricant for prevention of pregnancy or STI (78). This is due to risks associated with mucosal irritation with frequent nonoxynol-9 use. Where possible women and men should be advised to use non-spermicidally lubricated condoms. Nevertheless, the use of spermicide with diaphragms or cervical caps is still recommended (79).

**Intrauterine contraceptive device**
The IUD is the method used by 9% of women aged >40 years (18). 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 (80, 81). Women should be advised to seek medical advice to exclude infection and gynecological pathology, if menstrual abnormalities occur after the first 6 months of use (82).

**Natural family planning methods**
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 (15). The withdrawal method is used by 2% of women aged >40 years (18). Nevertheless, the withdrawal method is associated with a high failure rate and is not advocated as a reliable contraceptive method.

**Follow-up for women over 40 years using contraception**

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. 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.

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

The menopause is usually diagnosed clinically and in retrospect after 1 year of amenorrhea (8). The average age at which the menopause occurs is 50.7 years (range, 44-56 years for 95% of women) (8, 83). Few women (10%) stop menstruating abruptly and only 1% have a premature menopause (<40 years) (84). Expert opinion has advised continued use of contraception until there have been 2 years of amenorrhea if the woman is aged <50 years as there may be a risk of ovulation, despite amenorrhea. The probability of menstruation (and possibly ovulation) after a year of amenorrhea for women aged >45 years has been estimated by the WHO to be 2–10% (85). Women can be advised to stop contraception at the age of 55 years as most (95.9%) will be menopausal by this age. Women using combined HRT cannot be advised to rely on this as contraception, and that a POP can be used with HRT to provide effective contraception. Women using estrogen replacement therapy may choose the LNG-IUS to provide endometrial protection.

**Stopping Non-hormonal Contraception**

Women using non-hormonal contraception can be advised to stop contraception after 1 year of amenorrhea (or 2 years if the last menstrual period occurred for a woman aged less than 50 years). Women who have an IUD with more than 300 mm² of copper inserted at age 40 years or older can be advised to retain the device until the menopause.

**Stopping Hormonal Contraception**

Women using exogenous hormones should be advised that amenorrhea is not a reliable indicator of ovarian failure.

**Stopping Combined Contraception**

Women using combined contraception should be advised to switch to another suitable contraceptive method at the age of 50 years. Follicle-stimulating hormone (FSH) is not a reliable indicator of ovarian failure in women using combined hormones, even if measured during the hormone-free or estrogen-free interval.

**Stopping POPs and Implants**

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 greater than 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 less than 50 years).

**Stopping Progestogen-Only Injectables**
Women should be counseled 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.

Removing the LNG-IUS

Women who have the LNG-IUS inserted at age 45 years or older for contraception or for the management of menorrhagia can be counseled about retaining the device for up to 7 years.

REFERENCES

60. Ineichen B, Logie J, Rowlands S, Lawrenson R. Patterns


