

# Contraceptive methods and issues around the menopause: an evidence update

Shagaf H Bakour MD FRCOG,<sup>a,b,\*</sup> Archana Hatti MRCOG,<sup>c</sup> Susan Whalen DFSRH MRCOG<sup>d</sup>

<sup>a</sup>Senior Lecturer and Consultant Obstetrician and Gynaecologist, City Hospital, Dudley Road, Birmingham B18 7QH, UK

<sup>b</sup>Director of Medical Education, Aston Medical Research Institute (AMRI), Aston Medical School, Aston University, Birmingham B4 7ET, UK

<sup>c</sup>Specialist Trainee (ST4), Obstetrics and Gynaecology, City Hospital, Dudley Road, Birmingham B18 7QH, UK

<sup>d</sup>Consultant in Sexual Health, Sexual Health Department, Lyng Centre, Frank Fisher Way, West Bromwich B70 7AW, UK

\*Correspondence: Shagaf Bakour. Email: Shagaf.bakour@nhs.net

Accepted on 31 January 2017. Published Online 26 September 2017

## Key content

- There have been a number of recent advances and an increase in the number of contraceptive methods available to perimenopausal women.
- Other relevant issues, including transition to and diagnosis of menopause, the use of hormone replacement therapy with contraception, and when to stop contraception, are discussed.
- Some hormonal contraceptives have added benefits in the management of common perimenopausal gynaecological problems.
- Research and development into intrauterine contraception, microchip drug release technology, progesterone receptor modulators, male contraception and vaccines is currently underway.

## Learning objectives

- Understand that, although women's natural fertility declines after their mid-30s, effective contraception is required until menopause to prevent unintended pregnancies.

- Be aware that the risks of fetal chromosomal abnormalities, miscarriage, pregnancy complications and maternal morbidity and mortality increase for women aged 40 years and over.
- No contraceptive method is contraindicated on the basis of age alone.
- Clinicians must carefully consider comorbidities when prescribing women the most suitable contraception.

## Ethical issues

- Return of fertility can be delayed for up to 1 year after discontinuing progestogen-only injectable contraceptives; therefore, these contraceptives are not suitable for perimenopausal women considering future pregnancies.
- Contraceptive methods with a recognised post-fertilisation, pre-implantation effect may not be acceptable to some women.
- Women should be given information about all suitable contraceptive methods to make an informed choice.

**Keywords:** combined hormonal contraception / contraception / contraceptive device / menopause / progestogen-only contraception

Please cite this paper as: Bakour SH, Hatti A, Whalen S. Contraceptive methods and issues around the menopause: an evidence update. *The Obstetrician & Gynaecologist* 2017;19:289–97. DOI: 10.1111/tog.12416.

## Introduction

The World Health Organization (WHO) defines the menopause as permanent cessation of menstruation caused by the loss of ovarian follicular activity;<sup>1</sup> a retrospective diagnosis that is clinically confirmed after 12 months of amenorrhoea. Diagnosis is difficult when women use methods of contraception that interrupt the natural menstrual cycle. No accurate biological marker exists that truly defines the moment when fertility ceases. The period of time immediately before menopause is called perimenopause, and is when endocrinological, biological and clinical features of the approaching menopause commence. Perimenopause includes the first year after the last natural menstrual period.<sup>1</sup>

## Conception and demographics in older women

During the perimenopause, menstrual irregularities can occur with both prolonged or shorter anovulatory cycles and sometimes heavy menstrual bleeding (HMB). Hot flushes often begin at this time. Women's fecundity declines when they reach their mid-30s, with an associated increase in pregnancy loss secondary to oocyte ageing. However, a decrease in the ability to conceive does not occur until women are in their mid-40s.<sup>2</sup> The 2013 National Survey of Sexual Attitudes and Lifestyles (NATSAL) research project showed that 1 in 5 pregnancies conceived when the mother is aged 40 years or older are unplanned and 28% of these pregnancies end in termination.<sup>3</sup> In Western society,

relationship breakdown and re-partnering is increasing, and sexual intercourse occurs more frequently in new relationships.<sup>4</sup> Sexually transmitted infection (STI) rates are increasing most rapidly in women over the age of 40 years.<sup>5</sup> Only condoms protect against STI transmission, including HIV.

## Stopping contraception

During the perimenopause, follicle stimulating hormone (FSH) levels can fluctuate considerably.<sup>6</sup> Neither a single FSH measurement nor the presence or absence of menopausal symptoms can reliably predict loss of fertility. For women over the age of 50 years who do not use hormonal methods, contraception can be stopped after 1 year of amenorrhoea as fertility is unlikely to return. In women under 50 years of age, contraception should be continued for 2 years, as the return of fertile ovulation is more likely to occur.<sup>7</sup>

Hormonal contraception can affect bleeding patterns making it difficult for clinicians to advise when contraception can safely be stopped. For women over the age of 50 years using oral progestogen-only methods, subdermal implants and intrauterine systems, the Faculty of Sexual and Reproductive Healthcare (FSRH) recommends that contraception should be continued for 1 year after recording two FSH levels at >30 IU/l, taken at least 6 weeks apart.<sup>8</sup>

Combined hormonal contraception (CHC) affects FSH levels so should be stopped for at least 2 weeks prior to testing, although evidence is limited.<sup>9</sup> Return of ovulation is delayed when injectable methods such as medroxyprogesterone acetate (Depo Provera<sup>®</sup> [Pfizer Ltd., Sandwich, UK]) are stopped, so these should be stopped at least 1 year before taking FSH levels.<sup>10</sup>

Alternatively, women can consider stopping their method of contraception at the age of 55 years when most will have reached natural infertility.<sup>8</sup> Very few women continue to have fertile ovulation beyond this age. Despite this guidance, it is impossible to completely guarantee infertility after stopping contraception, so careful counselling is essential to balance the consequences of unplanned pregnancy with the potential health risks of continuing contraception.

## Hormone replacement therapy and contraception

Although very little data are available to inform practice in this area, sequential hormone replacement therapy (HRT), the type recommended in the perimenopause, is not contraceptive as it inhibits ovulation in only 40% of women.<sup>11</sup> Contraception must be used alongside HRT to avoid unplanned conception. Progestogen-only methods and intrauterine contraception (IUC) are suitable.

Combined progestogen and estrogen HRT must be used in women with an intact uterus as there is no evidence that the

progestogen in most hormonal contraception methods provides endometrial protection. The exception is the Mirena<sup>®</sup> (Bayer plc, Newbury, UK) levonorgestrel-releasing intrauterine system (IUS) (52 mg IUS), which is licensed for this indication for 4 years but evidence supports its use for 5 years.<sup>8</sup>

Women using combined methods of contraception can use regimens with shorter pill-free intervals to reduce the risk of menopausal symptoms.<sup>12</sup>

## Choice of methods of contraception

Women must be advised on all available methods of contraception, including long-acting reversible methods (LARC), so they can make an informed choice.<sup>13</sup> No method of contraception is contraindicated based on age alone, up to the age of 50 years.<sup>8</sup> Table 1 summarises the main advantages, risks and reliability of contraceptive methods for perimenopausal women.<sup>14,15</sup> Table 2 shows the contraceptive methods chosen by UK women in this age group.<sup>16</sup>

It is essential to acquire a personal, sexual and family history, and pregnancy should be excluded (see Box 1).<sup>17</sup> Body mass index and blood pressure should be checked and STI screening offered, particularly before an IUC device is inserted. Pelvic examination is only required prior to fitting an IUC. Cervical cytology should be offered in line with the National Cervical Screening Programme.

### Combined hormonal contraception

The use of CHC beyond the age of 50 years is not recommended, although a lack of safety evidence in this age group means it cannot be completely ruled out.<sup>18</sup> Combined methods can be given orally, transdermally (Evra<sup>®</sup> [Janssen-Cilag International NV, Beerse, Belgium]) and vaginally (NuvaRing<sup>®</sup> [Merck & Co., Inc. NJ, USA]), but less data are available on the patch and the vaginal ring. Combined monthly injections (Cyclofem<sup>®</sup> and Mesigyna<sup>®</sup>) are available in many countries, but not in the USA or Europe.

Most combined pills contain the synthetic estrogen ethinyl estradiol. Newer methods (Zoely<sup>®</sup> [Merck Sharp & Dohme Limited, Hoddesdon, UK] and Qlaira<sup>®</sup> [Bayer plc, Newbury, UK]) contain estradiol but there is no established difference in their safety profiles. Estradiol formulations have shorter hormone-free intervals, so may reduce the occurrence of hot flushes during the pill-free week in standard regimens. Combined pills cause shorter withdrawal bleeds and more amenorrhoea than standard pills, but more unscheduled bleeding; this may be unacceptable to perimenopausal women. With all ethinyl estradiol pills, if less frequent bleeds are desirable or hot flushes occur during the pill-free week, tailored regimens with prolonged pill-taking or shorter pill-free intervals are effective, reliable and safe.<sup>18</sup>

**Table 1.** Advantages, disadvantages and failure rates for all available contraceptive methods in perimenopausal women<sup>14,15</sup>

Method	Advantages	Disadvantages	Risk of failure in first year of typical nonperfect use <sup>57</sup> (%)
Combined hormonal contraception	Regular bleeding pattern Reduction in menstrual bleeding and flushes	Increased risk of thrombosis, and breast and cervical cancer Daily dosing required	9.0
Progesterone-only pills	Very few medical contraindications	Irregular bleeding Daily dosing required	9.0
Progesterone-only injectable	Long-acting method Often induces amenorrhoea	Masks menopause Bone mineral density concerns Unable to remove after injection	6.0
Progesterone-only implant	Very few contraindications Easily reversible	Irregular bleeding Requires trained operative	0.05
Copper intrauterine device	Hormone-free Does not mask menopause Long-acting method	Heavy menstrual bleeding and pelvic cramps Unsuitable if woman has a distorted uterine cavity	0.8
Levonorgestrel-releasing device	Long-acting method Treatment for heavy menstrual bleeding Endometrial protection with hormone replacement therapy	Irregular bleeding Unsuitable if woman has a distorted uterine cavity	0.2

**Table 2.** Contraceptive methods chosen by UK women aged 40–44 and 44–49 years (adapted from Lader D. *Opinions survey report No. 41: contraception and sexual health 2008/09*. Richmond: Office for National Statistics; 2009)<sup>16</sup>

Method	Age 40–44 (%)	Age 45–49 (%)
None	25	28
Pill	10	13
Male condom	21	11
Withdrawal	6	4
Intrauterine system	9	11
Injection	2	4
Implant	0	1
Patch	1	0
Natural method	4	5
Other	0	1
Female sterilisation	18	19
Vasectomy	28	30

CHC users have a small increased risk of developing breast cancer (odds ratio [OR] 1.5) compared with non-users,<sup>19</sup> but risks decrease after cessation. A first-degree relative with breast cancer does not preclude the use of combined hormonal methods. CHC use does not increase overall cancer risks and does not increase cancer mortality risk.<sup>20</sup>

In non-hormonal contraception users, the risk of venous thromboembolism (VTE) is 2 per 10 000 women per year. Use of CHC increases that risk up to six-fold, depending on the progestogen chosen, with pills containing levonorgestrel, norethisterone and norgestimate having the lowest risk.<sup>21</sup> VTE risk increases with age, rising exponentially over the age of 50 years. Risk is highest in

**Box 1.** Criteria for excluding pregnancy (adapted from Faculty of Sexual and Reproductive Healthcare [FSRH])<sup>15</sup>

Health professionals can be 'reasonably certain' that a woman is not currently pregnant if:

- there are no symptoms or signs of pregnancy
- there has been no intercourse since last normal menses
- a reliable contraception method has been correctly and consistently used
- miscarriage or termination occurs within the first 7 days of the onset of normal menstruation

A negative pregnancy test adds weight only if  $\geq 3$  weeks has passed since the last unprotected sexual intercourse.

the first few months after commencing CHC; incidence then decreases over the first year of use. VTE risk rises again when restarting CHC after a break as short as 1 month, and therefore continuing CHC rather than stopping and starting is the safer option.<sup>18</sup>

Well-researched published exclusions to the use of CHC are detailed in the UK Medical Eligibility Criteria (UKMEC), including smoking over the age of 35 years.<sup>15</sup>

### Progestogen-only pills

Many women find oral contraception most acceptable. Progesterone-only pills (POPs) are an effective alternative to CHC in women with comorbidities: the low progestogen dose has very few contraindications and POPs can be continued safely until natural fertility is lost.

POPs do not cause blood pressure to increase,<sup>22</sup> their effect on lipid profiles and diabetes is minimal and VTE risk is not

increased.<sup>23</sup> They are safe for use in women suffering from migraine with aura.<sup>24</sup> The limited evidence available does not support a causal link between POP use and breast cancer. However, there is a small increased risk of breast cancer in women who take POPs, but this risk is reduced when the user stops taking these pills.<sup>25</sup> Another advantage of POPs is they can be used in smokers over the age of 35 years.<sup>24</sup>

Traditional POPs contain norethisterone or levonorgestrel, and newer POPs contain desogestrel. Both can be used until the age at which natural loss of fertility is assumed.<sup>26</sup> POPs help to reduce HMB and dysmenorrhea<sup>27</sup> and there is no delay in return of fertility when POPs are stopped.

Disadvantages of POPs include an irregular bleeding pattern and narrow window of safety for missed pills. A missed pill is one that is taken more than 3 hours late, or with desogestrel pills, more than 12 hours late. Although some older studies suggest that they may be of use, POPs do not improve menopausal hot flushes<sup>8</sup> like the combined contraceptive pill.

### Implants

The only contraceptive implant available in the UK and the USA is the etonorgestrel-containing Nexplanon<sup>®</sup> (Merck Sharp & Dohme Limited, Hoddesdon, UK), a 4 cm x 2 mm rod that is implanted in the inner aspect of the upper arm, usually on the non-dominant side. It has similar indications and a similar side effect profile to the desogestrel-containing POPs. This implant should be fitted and removed by an operator trained to Faculty of Sexual and Reproductive Healthcare (FSRH) safety standards.<sup>28</sup>

Nexplanon<sup>®</sup> is the most effective reversible method of contraception and can be used for up to 3 years with immediate return of fertility on removal. There is no user failure rate, but additional contraceptive protection is advised if not fitted within the first 5 days of menstruation. It can be used safely by nearly all women throughout their reproductive years to menopause, even in women with comorbidities. Unlike injectable contraceptive methods, this implant has no effect on bone mineral density. There is no evidence to suggest an increased failure rate in women weighing up to 149 kg,<sup>28</sup> and no limit to the number of times the implant can be replaced at 3-yearly intervals.

About 20% of women with this implant have amenorrhoea; a desirable side effect for some women, for example, those with irregular perimenopausal bleeding after exclusion of pathology. However, 1 in 5 women have the device removed within the first year because of persistent or irregular bleeding.<sup>29</sup> This can mask other causes of irregular bleeding such as endometrial cancer, although this diagnosis remains rare in perimenopausal women using hormonal contraception.<sup>30</sup>

### Injectable contraception

Three injectable contraceptives are available: Depo Provera<sup>®</sup> (medroxyprogesterone acetate 150 mg, given intramuscularly

at 12-week intervals), Noristerat<sup>®</sup> (Bayer plc, Newbury, UK) (norethisterone enantate 200 mg, given intramuscularly at 8-week intervals) and the recently licensed Sayana Press<sup>®</sup> (Pfizer Limited, Sandwich, UK) (medroxyprogesterone acetate 104 mg, given subcutaneously at 13-week intervals). All are reliable long-acting methods of contraception, with very low user failure rates. Although Depo Provera<sup>®</sup> is licensed for 12 weeks, there is evidence that pregnancy rates remain low for up to 14 weeks after administration.<sup>31</sup>

Depo Provera<sup>®</sup> is the most commonly used injectable method of contraception. Sayana Press<sup>®</sup> has equivalent efficacy and an almost identical side effect profile, and is licensed for self-administration in the UK.<sup>32</sup> More than 50% of women become amenorrhoeic after 1 year of use and nearly 70% after 2 years of use.<sup>33</sup> This is very desirable for some women and can be a way to manage irregular bleeding in the perimenopause.

The main concern with injectable methods is bone health: approximately 5% of bone is lost within the first 2 years of use.<sup>34</sup> Longer-term use causes no further loss of bone, but research suggests that bones take longer to recover when this method is stopped.<sup>35</sup> It is unknown whether or not bones make a full recovery. In a small study, there was no difference in bone mineral density after 3 years between women who became postmenopausal while using Depo Provera<sup>®</sup> and those who never used this method.<sup>36</sup> Another trial found that Depo Provera<sup>®</sup> users have a higher fracture risk than non-users prior to starting, but Depo Provera<sup>®</sup> does not increase the subsequent risk of fractures.<sup>37</sup> Bone loss after 2 years of Depo Provera<sup>®</sup> use is equivalent to bone lost during pregnancy and breastfeeding for 6 months. The FSRH recommends that women consider stopping injectable contraceptives at the age of 50 years, but add that continuing beyond this age is unlikely to result in unacceptable adverse outcomes.

Another disadvantage of Depo Provera<sup>®</sup> is that the injection cannot be removed if side effects or health concerns arise. The FSRH's position is that the risks of the method outweigh the benefits in women with multiple risk factors for cardiovascular disease.<sup>8</sup>

### Intrauterine device

The intrauterine device (IUD) is an effective and safe form of long-term contraception in women over 40 years of age. IUDs should contain at least 300 mm of copper<sup>8</sup> wound onto a plastic frame, with bands of copper on the horizontal arms as well as the stem (Figure 1). The TT380 slimline<sup>®</sup> (Durbin PLC, South Harrow, UK) and Cu T 380 A<sup>®</sup> (Pregna International Ltd, Mumbai, India) are examples of gold-standard 10-year IUDs. Also available is Gynefix<sup>®</sup> (Control Europe NV, Gent, Belgium), a frameless device with copper bands mounted onto a monofilament thread (Figure 2). The expected reduction in IUD-associated dysmenorrhoea with a



**Figure 1.** Example of a banded intrauterine device.



**Figure 2.** Example of a frameless intrauterine device.

frameless device has not been shown in practice, but it might be useful for women with distorted cavities; for example women with small fibroids where a framed device may be harder to fit.

IUDs can be used both as emergency and continuing contraception for a period of 5–10 years. They prevent fertilisation when inserted precoitally, and when inserted postcoitally, they prevent implantation after fertilisation.<sup>38</sup> When inserted in women older than 40 years they can be used until menopause,<sup>8</sup> although this use is outside of the manufacturer's license. IUDs must be removed after menopause or when no longer required.

IUDs have minimal systemic effects so can be safely used in women with comorbidities that are more common in perimenopausal women,<sup>39</sup> such as diabetes, hypertension, cardiovascular, cerebrovascular and thrombotic diseases.

IUDs are associated with intermenstrual bleeding, spotting and prolonged bleeding, especially within the first 3–6 months.<sup>8</sup> These bleeding patterns are usually harmless and self-limiting, but counselling is necessary to prevent early discontinuation in perimenopausal women. If they persist, it is essential to exclude STIs and gynaecological pathologies.

STIs are not increased with IUDs, but fitting in the presence of STIs can increase the risk of pelvic inflammatory disease (PID) within the first 3 weeks of use.

### Intrauterine system

An IUS is a reliable, cost-effective contraceptive option for women, which releases very low systemic levels of levonorgestrel locally into the endometrium. Approximately 4% of UK perimenopausal women<sup>40</sup> use an IUS for contraception.

Two IUS devices are currently available; Mirena<sup>®</sup> or Levosert<sup>®</sup> (Gedeon Richter Plc., Budapest, Hungary), both of which contain 52 mg of levonorgestrel (52 mg IUS), and Jaydess<sup>®</sup> (Bayer plc, Newbury, UK) which contains 13.5 mg of levonorgestrel (13.5 mg IUS). Mirena<sup>®</sup> is licensed for contraceptive use for 5 years; Levosert<sup>®</sup> and Jaydess<sup>®</sup> for 3 years. However, the FSRH evidence-based guidance supports the use of Mirena<sup>®</sup> in women older than 45 years of age for up to 7 years, or to menopause if the woman remains amenorrhoeic.<sup>39</sup>

Mirena<sup>®</sup> is licensed for the treatment of HMB, and to give endometrial protection when used with estrogen-only HRT.<sup>41</sup> Neither Jaydess<sup>®</sup> or Levosert<sup>®</sup> are licensed for these indications. The newer and lower dose-containing Jaydess<sup>®</sup> has an insertion diameter smaller than the 52 mg IUS, so can be used in smaller uteri, nulliparous women and older women in the later years of reproduction.<sup>42</sup>

For women of perimenopausal age, the most important health benefit of the 52 mg IUS is its effect on menstrual bleeding. Within 3 months of insertion this IUS reduced blood loss by over 80% in women with HMB. A Cochrane review<sup>42</sup> showed that using an IUS is more effective than norethisterone for the management of HMB. IUS devices are equal to ablation and hysterectomy for improving women's quality of life. IUSs are also effective for reducing fibroid-associated bleeding, and improve endometriosis-associated pain. Guidelines published by the National Institute for Health and Care Excellence (NICE) should be followed if the IUS is fitted to manage HMB. A 52-mg IUS can also be used for endometrial protection during tamoxifen treatment.<sup>43</sup>

There is no evidence to support a link between breast cancer and IUS use. IUSs have minimal systemic side effects,

no risk of venous thromboembolism or other systemic diseases, and no evidence of weight gain, hence they are a safe option for perimenopausal women, especially those with HMB.

IUSs should be removed after menopause. Actinomyces-like organisms (ALOs) can be found in IUD and IUS users. In the absence of pain, pyrexia or unscheduled bleeding the device can be left in situ as the risk of actinomyces-related PID is very low.<sup>44</sup>

### Barrier contraception

Both men and women have barrier methods of contraception available to them. Condoms account for 10% of contraceptive use in the perimenopausal age group<sup>40</sup>. Use of diaphragms and caps with spermicides are used by <1% of UK women. Barrier contraception is safe to use until menopause is confirmed.

Condoms are 98% effective and women's barrier methods are up to 95% effective; however, effectiveness of both methods is user-dependent.<sup>45</sup> Erectile dysfunction can prevent condom use for some men. Diaphragms and caps must be used with spermicide, correctly inserted, and remain in place for 6 hours after intercourse.<sup>45</sup> Condoms have the advantage of protecting against STIs, rates of which are known to be increasing in perimenopausal women.

Oil-based lubricants and estrogen-containing vaginal creams and pessaries should not be used with condoms or latex diaphragms.<sup>45</sup> They can weaken latex and most non-latex condoms, thereby increasing the risk of failure caused by breakage. They do not affect silicone diaphragms and female condoms. Non-oil-based lubricants should be used and these can also improve sexual difficulties secondary to vaginal dryness. Non-latex diaphragms and condoms should be offered to those with latex allergy.

### Natural family planning methods

Fertility awareness methods, also called 'natural methods', are used by 4% of older women in the UK.<sup>40</sup> These methods include monitoring body temperature, cervical mucus and the length of the menstrual cycle, and plotting the values on a chart to predict the fertile time. Devices such as Persona<sup>®</sup> (Swiss Precision Diagnostics, Bedford, UK) are also available to buy, which monitor urine hormone levels.<sup>46</sup> Natural family planning (NFP) methods become less reliable in the perimenopause because ovulation becomes more difficult to predict as cycles become less regular and ovulation markers are difficult to interpret. Both the woman and her partner must be motivated to use this method consistently and correctly.

### Withdrawal method

Withdrawal is natural form of contraception used by approximately 5% of UK perimenopausal couples.<sup>40</sup> It prevents approximately 50% of pregnancies that would have

happened without using the method.<sup>41</sup> With lower fertility rates in the perimenopause, withdrawal can be used as an adjunct to other methods, like NFP.

### Sterilisation

Female sterilisation is a permanent and highly successful form of contraception used by about 18% of UK women over the age of 40 years.<sup>40</sup> All women considering sterilisation must be counselled regarding LARC methods, as these are as reliable as sterilisation. A woman who is approaching menopause and will shortly reach natural sterility should consider LARC rather than pursue a surgical method of time-limited value.

Sterilisation involves occluding the fallopian tubes and can be done laparoscopically, via mini-laparotomy, during caesarean section, or hysteroscopically. Hysteroscopic techniques can be done under local anaesthetic; however, another form of contraception must be used until tubal occlusion is confirmed after 3 months.

Vasectomy has a lower failure rate after proven azoospermia (1 in 2000)<sup>47</sup> and lower complication rates, although chronic postvasectomy pain occurs in up to 14% of men.<sup>47</sup> Female sterilisation has a failure rate of 1:200.<sup>47</sup> Other than preventing pregnancy, sterilisation confers none of the other benefits of hormonal contraceptives, and is associated with surgical risks.

### Emergency contraception

There are three methods of emergency contraception (EC) available in the UK: levonorgestrel (LNG; Levonelle<sup>®</sup> [Bayer plc, Newbury, UK]), an oral progestogen; ulipristalacetate (UPA; ellaOne<sup>®</sup> [Laboratoire HRA Pharma, Paris, France]), an oral selective progestogen receptor modulator; and the copper IUD. All are safe for use during the perimenopause. LNG and UPA inhibit or delay ovulation for up to 7 days, which is beyond the natural span of sperm within the genital tract, and can both be used more than once in the same menstrual cycle.<sup>15</sup>

Levonorgestrel can be used up to 72 hours after unprotected sexual intercourse (UPSI) but becomes less effective as time passes.<sup>49</sup> UPA remains effective for up to 120 hours after UPSI.<sup>49</sup> Although levonorgestrel works only up until the start of the pre-ovulatory LH surge,<sup>50</sup> UPA works up to just before the LH peak.<sup>51</sup>

Copper IUDs are the most effective form of EC and should always be offered when EC is requested. IUDs effectively prevent implantation after fertilisation as soon as they are fitted. This mechanism of action should be explained because methods that act after fertilisation are not acceptable to some women. IUS devices are not licenced for use as EC and should therefore not be used.

Following EC with levonorgestrel, reliable continuing contraception should be started as soon as possible –

ideally straight away – along with an additional barrier method until the hormonal method becomes effective. Commencing progestogen hormonal contraception immediately after UPA increases the risk of breakthrough ovulation so should not be commenced for at least 5 days after UPA is given.<sup>52</sup> Abstinence or a barrier method of contraception should be used instead.

There is no evidence that failed EC results in increased fetal abnormality rates,<sup>48</sup> so a request for EC should rarely be refused, even where menstrual cycles have become irregular.

## Future developments

### Intrauterine contraception

Like the frameless IUD, Gynefix<sup>®</sup>, a frameless levonorgestrel-releasing IUS, has also been developed but is not yet licensed.<sup>53</sup> However, the intrauterine ball (IUB) (Figure 3) has recently been licensed in Austria and will likely be marketed elsewhere in Europe and North America. It is a frameless IUD consisting of a shaped memory alloy (Nitinol<sup>®</sup>) thread that holds 20 tiny copper spheres. The device becomes spherical once delivered into the uterus and might have greater potential for use in non-uniform endometrial cavities.<sup>54</sup> As a hormone-free method, there will be no contraindications to its use in perimenopausal women.

### Microchip drug-release technology

Microchip drug-release technology, currently in development, will allow a progestogen-releasing microchip (Figure 4) to be implanted for up to 16 years of use, which can be switched on and off with a remote control.<sup>55</sup> This would allow planned pregnancy followed by immediate reactivation. Although this may be the future of LARC, there is potential for malicious control of the device.

### Male contraception

Contraception for men has been widely studied but so far the only available licensed methods are condoms and sterilisation. The drop in testosterone levels associated with azoospermia, and the time taken to achieve azoospermia, has



Figure 3. Example of an intrauterine ball.

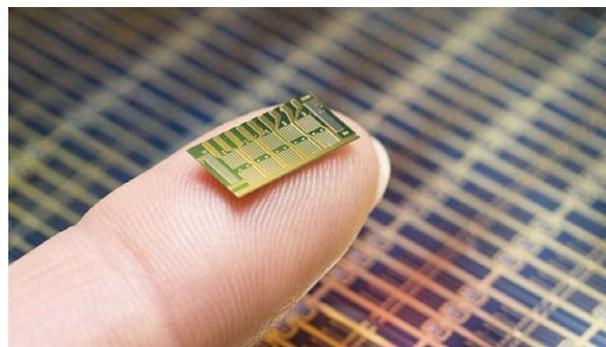


Figure 4. Magnified view of a progestogen-releasing microchip.

made the development of an acceptable method difficult. The ethics of contraception for men should be considered as it prevents pregnancy in women but might be associated with risks or side effects for the man. Contraceptives for men might be suitable for some couples in the perimenopause, especially if there are medical problems precluding the use of other methods, but it is unlikely that these will be marketed in the near future.

### Progesterone receptor modulators

Work continues to develop a vaginal ring releasing UPA, a selective progesterone receptor modulator (PRM) currently licensed as an EC, which will provide effective estrogen-free contraception.<sup>56</sup> Benign endometrial thickening and glandular cystic dilation can occur with this method, as well as unscheduled heavy bleeding.<sup>56</sup> Research is currently exploring the safety of this method of contraception, especially given that endometrial changes in perimenopausal women could be misdiagnosed if bleeding irregularities require investigation.

Research into the contraceptive effects of mifepristone, a selective PRM that effectively causes endometrial atrophy, is unlikely to continue because of its use in early medical abortion, and resulting licensing restrictions and methodical concerns.

### Vaccines

Vaccines against gametes have been a promising avenue of research in the past, but unpredictable response to vaccination and then early loss of immunity have meant their promise has not been fulfilled.<sup>57</sup>

## Conclusion

In the absence of accurate evidence-based advice on fertility, contraception and HRT, perimenopausal women remain at risk of an unplanned pregnancy. There is no method of contraception that is contraindicated for women under the age of 50 years on the basis of age alone. HRT does not provide

adequate contraception. After taking a comprehensive medical history, all women should be given information on all suitable methods of contraception so that they can make an informed choice. When giving contraceptive advice to perimenopausal women with multiple comorbidities, clinicians should carefully consider the associated risks. New research and product developments will widen the contraceptive choice for women in this age group.

## Disclosure of interests

SB is a TOG Editorial Board member, a member of the MRCOG Membership Exam Part III Committee, an MRCOG Membership Exam Part II Standard Setter, a reviewer for *StratOG* and *BJOG* and a former member of the Royal College of Obstetricians and Gynaecologists' Education Quality Assurance Committee.

SW is a member of the British Menopause Society, Chair of the West Midlands Association for Contraception and Sexual Health, and a Faculty of Sexual and Reproductive Health-registered trainer for the diploma and letters of competence in contraceptive techniques.

## Contribution to authorship

This paper was the sole work of SB, AH and SW. All authors approved the final version.

## Acknowledgements

Thanks to Claire Bailey, Specialist Trainee, for her comments on the manuscript.

## Supporting Information

Additional supporting information may be found in the online version of this article at <http://wileyonlinelibrary.com/journal/tog>

**Infographic S1:** Contraceptive methods and issues around the menopause.

## References

- World Health Organization. *Research on the menopause in the 1990s: report of a WHO Scientific Group*. Geneva: World Health Organization; 1996. p. 12–4.
- O'Connor KA, Holman DJ, Wood JW. Declining fecundity and ovarian ageing in natural fertility populations. *Maturitas* 1998;**30**:127–36.
- Wellings K, Jones KG, Mercer CH, Tanton C, Clifton S, Datta J, et al. The prevalence of unplanned pregnancy and associated factors in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). *Lancet* 2013;**382**:1807–16.
- Rao K, Demaris A. Coital frequency among married and cohabiting couples in the United States. *J Biosoc Sci* 1995;**27**:135–50.
- Public Health England. *National STI surveillance data tables 2015 – Table 8*. London: Public Health England; 2015 [[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/534564/2015\\_Table\\_8\\_Attributes\\_by\\_gender\\_sexual\\_risk\\_age\\_group\\_2011-2015.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/534564/2015_Table_8_Attributes_by_gender_sexual_risk_age_group_2011-2015.pdf)].
- Burger HG. Diagnostic role of follicle-stimulating hormone (FSH) measurements during the menopausal transition – an analysis of FSH, oestradiol and inhibin. *Eur J Endocrinol* 1994;**130**:38–42.
- World Health Organization. *Progress in Reproductive Health. Contraception and the Late Perimenopause*. **40**(2). 1996.
- Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. *FSRH clinical guidance: contraception for women over 40*. London: FSRH; 2010 [<http://www.fsrh.org/pdfs/ContraceptionOver40July10.pdf>].
- Castracane VD, Gimpel T, Goldzieher JW. When is it safe to switch from oral contraceptives to hormonal replacement therapy? *Contraception* 1995;**52**:371–6.
- Jain J, Dutton C, Nicosia A, Wajszczuk C, Bode FR, Mishell DR Jr. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. *Contraception* 2004;**70**:11–8.
- Gebbie AE, Glasier A, Sweeting V. Incidence of ovulation in perimenopausal women before and during hormone replacement therapy. *Contraception* 1995;**52**:221–2.
- Casper RF, Dodin S, Reid RL. The effect of 20 µg ethinyl estradiol/1 mg norethindrone acetate (Minestrin™), a low-dose oral contraceptive, on vaginal bleeding patterns, hot flashes and quality of life in symptomatic perimenopausal women. *Menopause* 1997;**4**:139–47.
- National Collaborating Centre for Women's and Children's Health, National Institute for Health and Care Excellence. *Long-acting reversible contraception: the effective and appropriate use of long-acting reversible contraception (CG30)*. London: RCOG Press; 2013 [<http://www.nice.org.uk/guidance/cg30/evidence/full-guideline-194840605>].
- Association of Reproductive Health Professionals. *Choosing a birth control method. Contraceptive failure rates: table*. Washington, DC: ARHP; 2014 [<https://www.arhp.org/Publications-and-Resources/Quick-Reference-Guide-for-Clinicians/choosing/failure-rates-table>].
- Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *UK medical eligibility criteria for contraceptive use*. London: FSRH; 2016 [<https://www.fsrh.org/standards-and-guidance/external/ukmec-2016-digital-version/>].
- Lader D. *Opinions survey report No. 41: contraception and sexual health 2008/09*. Richmond: Office for National Statistics; 2009.
- Faculty of Family Planning and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *UK Selected practice Recommendations for Contraceptive Use*. London: Faculty of Sexual Family Planning and Reproductive Healthcare; 2002.
- Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *FSRH clinical guidance: combined hormonal contraception – August 2012*. London: FSRH; 2012 [<http://www.fsrh.org/pdfs/CEUGuidanceCombinedHormonalContraception.pdf>].
- Beaber E, Buist DS, Barlow WE, Malone KE, Reed SD, Li CL. Recent oral contraceptive use by formulation and breast cancer risk among women 20 to 49 years of age. *Cancer Res* 2014;**74**:4078–89.
- Hannaford PC, Selvaraj S, Elliot AM, Angus V, Iversen L, Lee AJ. Cancer risk among users of oral contraceptive: cohort data from the Royal College of General Practitioner's oral contraceptive study. *BMJ* 2007; **335**:651.
- Stegeman B, de Bastos M, Rosendaal FR, van Hylckama Vileg A, Helmerhorst FM, Stijnen T, et al. Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. *BMJ* 2013;**347**:f5298.
- Duijkers IJ, Heger-Mahn D, Drouin D, Skouby S. A randomised study comparing the effect on ovarian activity of a progestogen-only pill (POP) containing desogestrel and a new POP containing drospirenone in a 24/4 regimen. *Eur J Contracept Reprod Health Care* 2015;**16**:1–9.
- Mantha S, Karp R, Raghavan V, Terrin N, Bauer KA, Zwicker JJ. Assessing the risk of venous thromboembolic events in women taking progestin-only contraception: a meta-analysis. *BMJ* 2012;**345**:e4944.
- Nappi RE, Merki-Feld GS, Terreno E, Pellegrinelli A, Viana MJ. Hormonal contraception in women with migraine: is progestogen-only contraception a better choice? *J Headache Pain* 2013;**14**:66.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;**347**:1713–27.

- 26 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *Progestogen-only pills*. London: FSRH; 2015 [https://www.fsrh.org/standards-and-guidance/documents/cec-ceu-guidance-pop-mar-2015/]
- 27 Ahrendt HJ, Karckt U, Pichi T, Mueller T, Ernst U. The effects of an oestrogen-free, desogestrel-containing oral contraceptive in women with cyclical symptoms: results from two studies on oestrogen-related symptoms and dysmenorrhoea. *Eur J Contracept Reprod Health Care* 2007;**12**: 354–61.
- 28 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *FSRH clinical guidance: progestogen-only implants – February 2014*. London: FSRH; 2014 [http://www.fsrh.org/pdfs/CEUGuidanceProgestogenOnlyImplants.pdf].
- 29 Lakha F, Glasier AF. Continuation rates of implanon in the UK: data from an observational study in a clinical setting. *Contraception* 2006;**74**: 287–9.
- 30 Cancer Research UK. *Uterine cancer (C54–C55), average number of new cases per year and age-specific incidence rates per 100 000 population, females, UK 2012–2014*. London: Cancer Research UK; 2016 [http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/uterine-cancer/incidence#heading-One].
- 31 Paulen M, Curtis K. When can a woman have repeat progestogen-only injectables depot medroxyprogesterone acetate or norethisterone enantate? *Contraception* 2009;**80**:391–408.
- 32 Pfizer Ltd. *Sayana Press 104 mg/0.65 ml suspension for injection*. Leatherhead: Electronic Medicines Compendium, Datapharm; 2017 [https://www.medicines.org.uk/emc/medicine/27798/SPC/SAYANA+PRESS+104+mg+0.65+ml+suspension+for+injection/].
- 33 Pfizer Ltd. *Depo-Provera 150 mg/ml injection*. Leatherhead: Electronic Medicines Compendium, Datapharm; 2016 [https://www.medicines.org.uk/emc/medicine/11121].
- 34 Clark M, Sowers M, Levy B, Nichols S. Bone mineral density loss and recovery during 48 months in first-time users of depo medroxyprogesterone acetate. *Fertil Steril* 2006;**86**:1466–74.
- 35 Kaunitz AM, Miller PD, Rice VM, Ross D, McClung MR. Bone mineral density in women aged 25–35 years receiving depot medroxyprogesterone acetate: recovery following discontinuation. *Contraception* 2006;**74**:90–9.
- 36 Cundy T, Cornish J, Roberts H, Reid IR. Menopausal bone loss in long-term users of depot medroxyprogesterone acetate contraception. *Am J Obstet Gynecol* 2002;**186**:978–83.
- 37 Lanza L, McQuay LJ, Rothman KJ, Bone HG, Kaunitz AM, Harel Z, et al. Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture. *Obstet Gynecol* 2013;**121**:593–600.
- 38 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *FSRH clinical guidance: intrauterine contraception – April 2015*. London: FSRH; 2015 [http://www.fsrh.org/pdfs/CEUGuidanceIntrauterineContraception-1.pdf].
- 39 Newton J, Tacchi D. Long-term use of copper intrauterine devices. A statement from the Medical Advisory Committee of the Family Planning Association and the National Association of Family Planning Doctors. *Lancet* 1990;**335**:1322–3.
- 40 Office for National Statistics. *Statistical Bulletin: Conceptions in England and Wales*. London: ONS; 2012 [http://webarchive.nationalarchives.gov.uk/20160109214216/http://www.ons.gov.uk/ons/rel/vsob1/conception-statistics-england-and-wales/2010/2010-conceptions-statistical-bulletin.html?format=print].
- 41 Hardman S, Gebbie AS. The contraception needs of perimenopausal women. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**:903–15.
- 42 Lethaby AE, Cooke I, Rees M. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. *Cochrane Database Syst Rev* 2005;(4):CD002126.
- 43 Dominick S, Hickey M, Chin J, Su HI. Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen. *Cochrane Database Syst Rev* 2015;(12):CD007245.
- 44 Westhoff C. IUDs and colonization or infection with Actinomyces. *Contraception* 2007;**75**:S48–50.
- 45 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *FSRH clinical guidance: barrier methods for contraception and STI prevention – August 2012*. London: FSRH; 2012 [https://www.fsrh.org/standards-and-guidance/documents/ceuguidancebarriermethodscontraceptionsdi/].
- 46 Bouchard T, Genius S. Personal fertility monitors for contraception. *CMAJ* 2004;**183**:73–6.
- 47 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *FSRH clinical guidance: male and female sterilisation – September 2014*. London: FSRH; 2014 [http://www.fsrh.org/pdfs/MaleFemaleSterilisation.pdf].
- 48 Faculty of Sexual and Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists. *CEU clinical guidance: emergency contraception – March 2017*. London: FSRH; 2017 [https://www.fsrh.org/standards-and-guidance/current-clinical-guidance/emergency-contraception/].
- 49 Glasier A, Cameron ST, Fine PM, Logan SJ, Casale W, Van Horn J, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet* 2010;**375**:555–62.
- 50 Croxatto HB, Brache V, Pavez M, Cochon L, Forcelledo ML, Alvarez F, et al. Pituitary-ovarian function following the standard levonorgestrel emergency contraceptive dose or a single 0.75-mg dose given on the days preceding ovulation. *Contraception* 2004;**70**:442–50.
- 51 Brache V, Cochon L, Jesam C, Maldonado R, Salvatierra AM, Levy DP, et al. Immediate pre-ovulatory administration of 30 mg ulipristal acetate significantly delays follicular rupture. *Hum Reprod* 2010;**25**:2256–63.
- 52 Brache V, Cochon L, Duijkers IJ, Levy DP, Kapp N, Monteil C, et al. A prospective, randomized, pharmacodynamic study of quick-starting a desogestrel progestin-only pill following ulipristal acetate for emergency contraception. *Hum Reprod* 2015;**30**:2785–93.
- 53 Wildemeersch D, Jandi S, Pett A, Nolte K, Hasskamp T, Vrijens M. Use of frameless intrauterine devices and systems in young nulliparous and adolescent women: results of a multicentre study. *Int J Womens Health* 2014;**6**:727–34.
- 54 OCON Medical Ltd. *Safe and hormone free birth control: IUBTM copper pearls*. Modiin: OCON Medical Ltd [http://www.oconmed.com/en/support/brochures/].
- 55 Microchips Biotech, Inc. *Microchips announces clinical results for first successful human trial of implantable, wireless microchip drug delivery device*. Lexington, MA: Microchips Biotech, Inc; 2012 [http://microchipsbiotech.com/news-pr-item.php?news=4].
- 56 Huang Y, Jensen JT, Brache V, Cochon L, Williams A, Miranda MJ, et al. A randomized study on pharmacodynamic effects of vaginal rings delivering the progesterone receptor modulator ulipristal acetate: research for a novel estrogen-free, method of contraception. *Contraception* 2014;**90**:565–74.
- 57 Naz RK, Gupta SK, Gupta JC, Vyas HK, Talwar AG. Recent advances in contraceptive vaccines development: a mini-review. *Hum Reprod* 2005;**12**:3271–83.