

# Contraception in 2021

## An update

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Several long- and shorter-acting contraceptive methods are available in Australia, including traditional hormonal and nonhormonal intrauterine devices (IUDs) and combined hormonal oral contraceptives. The low-dose hormonal IUD and a progestogen-only pill that reliably inhibits ovulation are newer options. GPs should be aware of the advantages and disadvantages of each method to support patients' informed contraceptive decision-making across their reproductive years.

Contraceptive choice is influenced by multiple factors, which can change over an individual's reproductive life course, from adolescence through to the perimenopause. These include medical eligibility, method effectiveness, risks and side effects, a desire for noncontraceptive benefits for conditions including heavy menstrual bleeding and acne, ease of use, access and costs, as well as personal preference. The role of the practitioner is to support shared and informed decision-making, which includes providing information about currently available methods.

This article provides an overview of long-acting reversible contraceptives (LARCs), combined hormonal methods, progestogen-only pills, depot injections and emergency contraceptive pills. It includes discussion about more recently available options,

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such as the new smaller-framed lower-dose 19.5 mg levonorgestrel (LNG) intrauterine device (IUD) introduced in 2020, and the drospirenone 4 mg progestogen-only pill available since mid-2021. Other methods, including barrier and permanent methods, are outside the scope of this article. However, it is important to note that the promotion of condom use should be considered in addition to another effective method of contraception for people of all ages who are at risk of sexually transmitted infections (STIs).

### The contraceptive consultation

A key component of the contraceptive consultation is ensuring the contraceptive method recommended is safe for the patient to use. In Australia, safety considerations regarding contraception options are guided by the UK Faculty of Sexual and Reproductive Health Medical Eligibility Criteria (UK MEC).<sup>1</sup> This system has four categories, outlined in Table 1, which support the practitioner in determining whether it is safe to provide a particular contraceptive method based on the patient's individual circumstances and medical history.

Although measurement of blood pressure and body mass index (BMI) are not required before initiating nonhormonal methods and most progestogen-only methods, a contraceptive consultation can be an opportune time to perform these routine health checks, as well as checking STI screening needs and whether the patient's cervical screening test is up to date.

After a method has been selected, practical considerations need to be discussed, including timing of initiation, how to manage method deviations, such as missed pills or late vaginal ring insertion, and practical advice about the management of troublesome side effects, including irregular bleeding patterns. The updated *Therapeutic Guidelines* provides practical guidance for practitioners on all aspects of contraception and selected patient information sheets.<sup>2</sup> The Family Planning Alliance Australia (FPAA) contraceptive efficacy chart and contraception fact sheets can be used to support informed choice and effective method use and are available from family planning organisation websites ([www.familyplanningallianceaustralia.org.au/resources/](http://www.familyplanningallianceaustralia.org.au/resources/)).

**TABLE 1. UK MEDICAL ELIGIBILITY CRITERIA (UK MEC) FOR CONTRACEPTIVE USE<sup>1</sup>**

| UKMEC | Definition of category   |
|-------|--|
| MEC 1 | A condition for which there is no restriction for the use of the method  |
| MEC 2 | A condition where the advantages of using the method generally outweigh the theoretical or proven risks  |
| MEC 3 | A condition where the theoretical or proven risks usually outweigh the advantages of using the method. The provision of a method requires expert clinical judgement and/or referral to a specialist contraceptive provider, since use of the method is not usually recommended unless other more appropriate methods are not available or not acceptable |
| MEC 4 | A condition which represents an unacceptable health risk if the method is used   |

### Long-acting reversible contraceptives

LARCs comprise hormonal and copper (nonhormonal) IUDs and the etonogestrel (ENG) contraceptive implant. Uptake of IUDs is increasing in Australia, particularly among those aged under 25 years.<sup>3</sup> Hormonal and copper IUDs have the highest continuation rates of all reversible methods, with 70% of users continuing to three years of use.<sup>4</sup> Pregnancy must be excluded before IUD insertion because of the potential for premature delivery and septic abortion if a pre-existing pregnancy continues and the IUD cannot be removed.<sup>5</sup> Screening for STIs in at-risk individuals, such as those aged under 30 years, is recommended before IUD insertion. If a copper IUD is being inserted for emergency contraception within five days of unprotected intercourse, an early pregnancy not yet diagnosable by a urine pregnancy test must also be excluded through the patient's history about recent contraception use.

Copper IUDs are immediately effective, regardless of which stage of the menstrual cycle they are inserted, but hormonal IUDs are immediately effective only if started between days 1 and 5 of the menstrual cycle and take seven days to become effective if inserted at any other time.

### Benefits

IUDs and implants are the most effective LARC methods.<sup>6</sup> There are no medication interactions to consider when

recommending an IUD.<sup>7</sup> They are safe to insert in nulliparous people and in those who have not had vaginal sex, although insertion may be technically more difficult in these circumstances. They have few contraindications, are safe to use during lactation and have high user satisfaction and continuation rates. Both IUDs and implants are rapidly reversible, with an expected quick return to fertility.<sup>8</sup> LARCs are also cost effective because of their long duration of use and are a first-line method for people of all reproductive ages.<sup>9</sup>

### Contraindications and complications

Contraindications to IUDs include a current pelvic infection and significant distortion of the uterine cavity. IUDs can be inserted at the time of a surgical abortion and in the postpartum period. Postpartum insertion, including after caesarean section, is UK MEC 1 if performed within 48 hours after delivery, or from four weeks postpartum onwards; however, the insertion of an IUD within 48 hours after delivery is associated with higher expulsion rates than insertion at four to six weeks postpartum. Insertion between 48 hours and four weeks postpartum is UK MEC 3.<sup>1</sup> Because of the increased risk of uterine perforation in the early postpartum period, IUD insertion in the primary care setting is usually delayed until six to eight weeks after a delivery.<sup>10</sup> Hormonal IUDs have additional contraindications to

consider, which are similar to those of other progestogen-only methods (Table 2). Copper IUDs should not be used in those with Wilson's disease.

Complications associated with IUDs include a risk of perforation, particularly in the postpartum period, and infection in the first 20 days after insertion, with each of these complications occurring in around 0.2% of insertions. The risk of expulsion is around 5%.<sup>11</sup> A pregnancy that occurs with an IUD in place has a greater chance of being ectopic, although the overall risk of an ectopic pregnancy is lower than for those not using contraception. Ectopic pregnancies occurring with a hormonal or copper IUD in place account for around 50% and 20% of pregnancies, respectively.<sup>12</sup>

### Hormonal IUDs

The 19.5 mg and 52 mg LNG IUDs are subsidised on the PBS. Their efficacy is 99.7 to 99.9%.<sup>12,13</sup> Both are indicated for contraception and the 52 mg LNG IUD is also indicated for the treatment of heavy menstrual bleeding and as part of menopausal hormone therapy to protect the endometrium. Although preliminary studies indicate the 52 mg LNG IUD might be effective as emergency contraception, its use is not currently recommended for this indication.<sup>14,15</sup>

Both LNG IUDs are licensed for five years' use, and the 52 mg LNG IUD can be left in place until menopause is determined or until the age of 55 years if inserted in a person aged 45 years or older (off label).<sup>11</sup> The 19.5 mg LNG IUD is smaller than the 52 mg LNG IUD, appears to be easier to insert and is associated with less pain on insertion. In a community study, around two-thirds of nulliparous users reported their insertion pain as none or mild.<sup>16</sup>

### Benefits

Although both LNG IUD types have been shown to decrease bleeding days and dysmenorrhoea, only the 52 mg LNG IUD has been extensively studied for these benefits.<sup>17</sup> It has been shown to be effective in reducing endometriosis and

adenomyosis-associated dysmenorrhoea and is very effective at reducing heavy menstrual bleeding.<sup>18-22</sup>

### Side effects

Irregular bleeding or spotting in the first few months of use is common with both devices.<sup>17</sup> The 19.5 mg LNG IUD appears to be associated with a higher mean number of bleeding or spotting days and lower rates of amenorrhoea than the 52 mg LNG IUD.<sup>23</sup> However, the significance of these differences to users may be small as discontinuation of either IUD because of bleeding problems is uncommon.<sup>24,25</sup>

Although the 19.5 mg LNG IUD is associated with around a 50% lower systemic exposure to LNG than the 52 mg device, initial data do not show any significant differences in acne, breast discomfort, pelvic pain or weight gain between devices.<sup>17</sup> Both devices increase the risk of benign, asymptomatic ovarian cysts, with the 52 mg LNG IUD having a higher risk. Cysts are likely to resolve spontaneously.<sup>17</sup>

### Copper IUDs

Copper IUDs are around 99.5% effective, have the advantage of being hormone-free and provide extremely effective emergency contraception.<sup>12,26</sup> Two copper IUDs are available in Australia, lasting five or 10 years, depending on the type. Both can be left in place until menopause if inserted at the age of 40 years or over.<sup>11</sup> They are not subsidised on the PBS and cost around \$75.

Use of copper IUDs is associated with heavier and slightly more prolonged menstrual bleeding and has no benefit in relation to dysmenorrhoea.<sup>19,27</sup> These factors are an important consideration in choice of IUD type (copper or hormonal) for those with heavy menstrual bleeding, iron deficiency anaemia and endometriosis. Irregular bleeding is common in the first few months of use but usually settles.

### Etonogestrel implant

The ENG implant is PBS subsidised. It lasts for three years, regardless of the user's BMI, and is 99.95% effective.<sup>28,29</sup> The ENG

**TABLE 2. MEDICAL ELIGIBILITY CRITERIA (MEC) 3 AND 4 CONDITIONS FOR PROGESTOGEN-ONLY METHODS**

| Condition or risk factor  | LNG IUD | ENG implant | DMPA | POP |
|---|---------|-------------|------|-----|
| Multiple risk factors for cardiovascular disease (e.g. older age, smoking, diabetes, hypertension and obesity)                | 2       | 2           | 3    | 2   |
| Hypertension, with vascular disease   | 2       | 2           | 3    | 2   |
| Past history of ischaemic heart disease, stroke or transient ischaemic attack (TIA)   | 2       | 2           | 3    | 2   |
| Development of ischaemic heart disease, stroke or TIA during use  | 3       | 3           | 3    | 3   |
| Initiation with unexplained vaginal bleeding (suspicious for a serious condition) before evaluation                           | 4       | 3           | 3    | 2   |
| Continuation of the method if unexplained vaginal bleeding suspicious for a serious condition develops while using the method | 2       | 3           | 3    | 2   |
| Current breast cancer   | 4       | 4           | 4    | 4   |
| Past breast cancer  | 3       | 3           | 3    | 3   |
| Severe (decompensated) cirrhosis  | 3       | 3           | 3    | 3   |
| Hepatocellular adenoma or malignant liver tumour  | 3       | 3           | 3    | 3   |

Abbreviations: DMPA = depot medroxyprogesterone acetate; ENG = etonogestrel; IUD = intrauterine device; LNG = levonorgestrel; POP = progestogen-only pill. Adapted from: UK Medical Eligibility Criteria for Contraceptive Use (UKMEC): Faculty of Sexual and Reproductive Healthcare.<sup>1</sup>

implant can be started any time post-partum, including in those who are breastfeeding, and can continue to be safely changed three-yearly until menopause is determined or until the age of 55 years. Unlike IUDs, its efficacy can be affected by the concurrent use of liver enzyme-inducing medications and switching to an alternative unaffected method is recommended for long-term use (Table 3).<sup>7</sup> Major contraindications are as for other progestogen-only methods (Table 2).<sup>1</sup>

### Starting an ENG implant

The ENG implant can be inserted any-time in the menstrual cycle. It is immediately effective if started between days 1 to 5 of the cycle; otherwise, it takes seven days to become effective. When started at a time that an early undetectable pregnancy cannot be excluded (referred to as 'Quick Start'), a urine pregnancy

test is recommended in four weeks' time, with a follow-up system in place to ensure a possible pregnancy diagnosis is not delayed.<sup>30</sup> An ENG implant can be inserted straight after a delivery or surgical abortion, or within the first five days of a medical abortion, including at the time of prescribing mifepristone (the first tablet of a two-step process).<sup>31</sup> It cannot be used to protect the endometrium as part of menopausal hormone therapy.

### Complications and side effects

Insertion and removal of the ENG implant may cause scarring and a local reaction and carries a small risk of infection. Deep insertion may sometimes occur, and specialist intervention is required for removal of all impalpable devices. It is now recommended that the device be inserted over the triceps, to avoid the rare complication of intravascular insertion.<sup>32,33</sup>

**TABLE 3. CONTRACEPTIVE EFFICACY WITH CONCURRENT USE (OR USE IN THE PAST 28 DAYS) OF LIVER ENZYME-INDUCING MEDICATIONS<sup>7</sup>**

| Contraceptive method                     | Efficacy potentially affected? | Recommendation   |
|--|--------------------------------|--|
| Copper and hormonal intrauterine devices | No                             | Recommended  |
| Depot medroxyprogesterone acetate        | No                             | Recommended  |
| Etonogestrel contraceptive implant       | Yes                            | Not recommended  |
| Combined oral contraceptive              | Yes                            | Use alternative methods if possible. If chosen, increase dose and alter regimen <sup>7</sup> |
| Vaginal ring                             | Yes                            | Not recommended  |
| Progestogen-only pill                    | Yes                            | Not recommended  |
| Levonorgestrel emergency contraception   | Yes                            | Use copper intrauterine device if possible. If used, a double dose is recommended*           |
| Ulipristal emergency contraception       | Yes                            | Not recommended  |

\* Use of a double dose of levonorgestrel is off label and not approved by the Australian TGA.

Troublesome bleeding is the most common side effect of the ENG implant. It is important to inform users upfront that their bleeding pattern will change but that it is not possible to predict on an individual basis how it will change. Amenorrhoea occurs in around 20% of users and frequent bleeding (more than five episodes per 90 days) or prolonged bleeding (an episode that lasts more than 14 days) in 25%. Around 55% have no or light and infrequent bleeding. Generally, the initial bleeding pattern predicts ongoing bleeding, although there is some settling during the first three to six months after insertion.<sup>34</sup> Users should also be provided at the time of insertion with information about the availability of strategies for managing troublesome bleeding should it occur (Box).

Users may also experience headaches, mood changes or emotional lability, acne, breast tenderness and loss of libido.<sup>35</sup> Pre-existing acne improves in some users.<sup>36</sup> Weight gain is a frequently reported side effect, although causal evidence is lacking.<sup>35-38</sup>

### Combined hormonal contraception

Combined hormonal contraceptives (CHCs) include combined oral contraceptives (COCs) and the vaginal ring. COCs are the most common method of contraception used in Australia with a large number of choices available, containing ethinylestradiol, estradiol or its pro-drug estradiol valerate in combination with one of nine progestogens.<sup>39</sup> The vaginal ring is a slow-release combination of ethinylestradiol and ENG and is treated in the same way as COCs with regard to drug interactions, side effects and contraindications. It is not PBS listed. CHCs are safe to use in those without contraindications until the age of 50 years, after which switching to another method is recommended. They are generally considered safe to use from six weeks postpartum onwards, including in those who are breastfeeding. CHCs are 99.5% effective when used perfectly, but only 93% effective during the first year of use in typical use, usually because of missed pills or delayed vaginal ring insertion.<sup>40</sup>

### STRATEGIES FOR MANAGING TROUBLESOME BLEEDING IN PEOPLE USING LONG-ACTING REVERSIBLE CONTRACEPTION

1. Exclude other causes (e.g. pregnancy, sexually transmitted infections, liver enzyme-inducing medications, and vaginal, cervical or uterine pathology)
2. Reassure that bleeding can be expected and is not harmful (if no suspicion of another cause)
3. Consider medication management (if no contraindications – see [www.fpns.org.au](http://www.fpns.org.au) for a list of contraindications)
  - First-line options include:
    - a combined hormonal contraceptive, taken continuously or cyclically for three months
    - a five-day course of an NSAID (e.g. mefenamic acid 500mg up to three times daily)
    - a five-day course of tranexamic acid 500mg twice daily, especially if the bleeding is heavy
  - Second-line options include (with low-level, anecdotal or conflicting evidence):
    - a five-day course of tranexamic acid 500mg twice daily, for lighter bleeding
    - a 21-day course of norethisterone 5 mg three times daily
    - a 20-day course of a levonorgestrel progestogen-only pill 30mcg twice daily
    - early removal and replacement of the implant or hormonal IUD, or shortening the interval between injections from 12 to 10 weeks
4. Consider removal or cessation of the contraception option

Adapted from: Family Planning Alliance Australia (FPAA). Guidance for management of troublesome vaginal bleeding with progestogen-only long-acting reversible contraception (LARC) (available online at: [www.fpns.org.au/health-information/contraception/guidance-management-troublesome-vaginal-bleeding-progestogen-only](http://www.fpns.org.au/health-information/contraception/guidance-management-troublesome-vaginal-bleeding-progestogen-only)) and Therapeutic guidelines. Intrauterine contraceptive devices: damaging adverse effects of intrauterine devices (available online at: [https://tgldcdp.tg.org.au/viewTopic?topicfile=IUDs#toc\\_d1e821](https://tgldcdp.tg.org.au/viewTopic?topicfile=IUDs#toc_d1e821)).

### Benefits

CHCs are associated with a decrease in acne, menstrual pain and bleeding. Users can manipulate their menstrual cycles.<sup>41</sup> CHCs also decrease the risk of ovarian, endometrial

and bowel cancer, and can have benefit in managing premenstrual dysphoric disorder and perimenopausal symptoms.<sup>42-44</sup>

### Contraindications

Contraindications for CHCs are mostly related to risk factors for, or a personal history of, arterial and venous disease. MEC 3 and 4 contraindications include a history of migraine with aura, smoking in those aged over 35 years, hypertension, BMI above 35 kg/m<sup>2</sup>, a first-degree relative aged 45 years or younger with a venous thromboembolism (VTE), or a personal history of breast cancer. Table 4 summarises the important MEC 3 and 4 conditions for CHC use. CHCs are not generally recommended for those concurrently using a liver enzyme-inducing medication (Table 3).<sup>7</sup>

### Starting a CHC

CHCs can be started at any time of the cycle and will be immediately effective if active hormones are started on days 1 to 5 of a normal menstrual cycle. Otherwise, they take seven days to become effective.

When starting a COC, some pills are packaged to start with a nonhormonal sugar pill and will take longer to be effective. If an early undiagnosable pregnancy cannot be excluded, a pregnancy test is recommended in four weeks' time, even if scheduled bleeding occurs.<sup>45</sup>

Active hormone pills can be taken continuously for extended periods to minimise bleeding by running pill packets or vaginal rings together without a hormone-free break. A hormone-free break of four days can be initiated if unscheduled bleeding occurs, as long as at least 21 active pills have been taken consecutively before the break.<sup>46,47</sup> There is one extended use COC available, with a 30 mcg ethinylestradiol and 150 mcg LNG combination pill packaged for the user to take 84 consecutive hormone pills, followed by seven 10 mcg ethinylestradiol pills. It is designed for bleeding to occur once every three months, as opposed to once per month as with other COCs.<sup>48</sup>

Blood pressure and BMI should be documented at initiation and annually.

No routine investigations are necessary.<sup>45</sup> In those who have no contraindications, prescribing 12 months of CHCs is important to maximise continuation rates.<sup>49,50</sup>

### Choosing a CHC

A low-dose pill containing ethinylestradiol 20 or 30 mcg and LNG is the recommended first-choice CHC.<sup>45</sup> These pills have been extensively studied and have similar discontinuation rates to other CHCs when compared in head-to-head trials.<sup>51,52</sup> Some brands of these pills are subsidised on the PBS. A list of COCs available in Australia appears on the Family Planning Victoria website ([www.fpv.org.au/assets/resources/Combined\\_hormonal\\_contraceptive\\_pill\\_chart\\_UPDATED\\_11.21-005.pdf](http://www.fpv.org.au/assets/resources/Combined_hormonal_contraceptive_pill_chart_UPDATED_11.21-005.pdf)). Any other CHC can be used first line, but there appears to be a small increased risk of VTE with ethinylestradiol pills containing cyproterone acetate, desogestrel, dienogest, drospirenone or gestodene and the vaginal ring compared with pills containing ethinylestradiol 20 to 30 mcg and LNG or norethisterone.<sup>53</sup>

### Risks

#### Serious risks

Some serious risks are associated with CHC use; however, the absolute risk for most individuals of reproductive age is low. All CHCs increase the risk of VTE to around threefold above baseline, with the highest risk occurring in the first year of use.<sup>54,55</sup> There appears to be a small increase in ischaemic heart disease and stroke.<sup>56</sup> There may also be a small but reversible increased risk of breast cancer.<sup>57</sup> Although the use of CHCs is associated with a small increase in the risk of cervical cancer, the attributable risk is likely to be low in Australia because of the human papillomavirus vaccination and national cervical screening programs.<sup>42</sup>

#### Other risks

Use of CHCs is associated with a small increase in blood pressure, with the exception of drospirenone-containing pills and pills with estradiol or estradiol valerate in place of ethinylestradiol.<sup>58-60</sup> There is a

small increase in the risk of inflammatory bowel disease.<sup>61</sup> Although evidence is insufficient to determine whether there is an increased risk of gallbladder disease, there are some restrictions in the use of CHCs in those with the condition.<sup>62</sup>

Several side effects have been reported by users of CHCs; however, it is difficult to prove cause and effect. Weight gain is a common complaint but has not been demonstrated for pills containing 35 mcg or less ethinylestradiol.<sup>63</sup> Unscheduled bleeding is common, particularly with the lowest ethinylestradiol dose pills, but usually settles over a few months.<sup>64</sup> General side effects of CHCs often settle with time and include:<sup>65</sup>

- headache
- nausea
- breast tenderness
- unscheduled bleeding
- amenorrhoea
- acne (usually improves)
- bloating
- mood changes
- reduced libido
- weight gain
- melasma (also known as chloasma).

In addition, vaginal ring users may report:

- increased vaginal discharge
- device discomfort for the user or partner
- expulsion of the ring.

### Missed CHC pills

A COC pill is not considered missed until it is more than 24 hours late. The rules for missed COC pills can also be applied to the vaginal ring and are outlined in the Flowchart.

### Progestogen-only pills

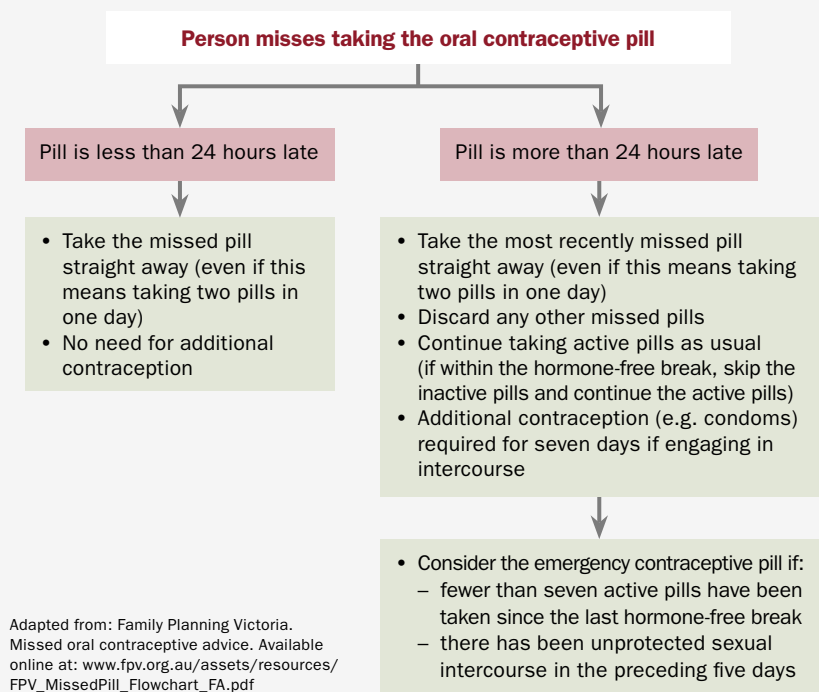
Two types of progestogen-only pills (POPs) are available in Australia, which differ in their mechanism of action. The 'traditional' low-dose pills containing LNG 30 mcg or norethisterone 350 mcg have been available for many years and are PBS-listed. They act primarily by thickening the cervical mucus and have a narrow three-hour window of pill taking to maintain efficacy.<sup>66</sup> Recently, a new POP type

**TABLE 4. MEDICAL ELIGIBILITY CRITERIA (MEC) 3 AND 4 CONDITIONS FOR COMBINED HORMONAL METHODS**

| Condition or risk factor  |  | MEC |
|---|--|-----|
| Postpartum: breastfeeding; <6 weeks   |  | 4   |
| Postpartum:<br>non-breastfeeding  | <3 weeks, without other risk factors for venous thromboembolism (VTE)                            | 3   |
|   | <3 weeks, with other risk factors for VTE  | 4   |
|   | 3 to <6 weeks, with other risk factors for VTE   | 3   |
| Smoking or vaping and age<br>≥35 years  | <15 cigarettes/day   | 3   |
|   | ≥15 cigarettes/day or vaping any amount  | 4   |
|   | Stopped smoking or vaping <1 year ago  | 3   |
| Obesity; body mass index ≥35 kg/m <sup>2</sup>  |  | 3   |
| Multiple risk factors for cardiovascular disease (e.g. smoking/vaping, diabetes, hypertension, obesity and dyslipidaemias)  |  | 3   |
| Hypertension  | Adequately controlled  | 3   |
|   | Consistently elevated systolic blood pressure (BP) 140 to 159 mmHg or diastolic BP 90 to 99 mmHg | 3   |
|   | Consistently elevated systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg                            | 4   |
|   | Vascular disease   | 4   |
| Ischaemic heart disease, stroke or transient ischaemic attack   |  | 4   |
| Complicated valvular and congenital heart disease (e.g. pulmonary hypertension, history of subacute bacterial endocarditis) |  | 4   |
| History of VTE  |  | 4   |
| Current VTE (on anticoagulant)  |  | 4   |
| VTE in first-degree relative at age <45 years   |  | 3   |
| Major surgery with prolonged immobilisation   |  | 4   |
| Immobility, unrelated to surgery  |  | 3   |
| Known thrombogenic mutation   |  | 4   |
| Continuation of use in the setting of new onset migraine without aura   |  | 3   |
| Migraine with aura  |  | 4   |
| Past history of migraine with aura, none for five years   |  | 3   |
| Initiation: undiagnosed breast mass   |  | 3   |
| Carriers of known gene mutations associated with breast cancer  |  | 3   |
| Current breast cancer   |  | 4   |
| Previous breast cancer  |  | 3   |
| Diabetes with nephropathy, retinopathy, neuropathy or other vascular disease  |  | 3   |
| Gallbladder disease: medically treated or current   |  | 3   |
| History of cholestasis: related to past combined hormonal contraception   |  | 3   |
| Initiation: during acute episode or flare viral hepatitis   |  | 3   |
| Severe (decompensated) cirrhosis  |  | 4   |
| Hepatocellular adenoma or malignant liver tumour  |  | 4   |
| Systemic lupus erythematosus with positive antiphospholipid antibodies  |  | 4   |
| Positive antiphospholipid antibodies  |  | 4   |

Adapted from: UK Medical Eligibility Criteria for Contraceptive Use (UKMEC): Faculty of Sexual and Reproductive Healthcare.<sup>1</sup>

## THE RULES FOR MISSED COMBINED HORMONAL AND DROSPIRENONE-ONLY CONTRACEPTIVE PILLS



containing 24 tablets of drospirenone 4 mg and four inactive sugar tablets has become available that primarily acts to suppress ovulation and has a 24-hour window for tablet taking.<sup>67</sup> The drospirenone 4 mg POP is not available on the PBS.

The efficacy of both types of POPs is considered the same as that of CHCs: 99.5% in perfect use and 93% in typical use.<sup>40</sup> However, traditional LNG- and norethisterone-containing POPs are considered to have a more vulnerable efficacy, and failure rates are higher in those aged under 40 years than in older users.<sup>68</sup> Both types of POPs can be used until menopause is determined or until 55 years of age and are safe to use at any time postpartum, including in those who are breastfeeding.

### Benefits, contraindications and medication interactions

A small study in adolescents using the drospirenone 4 mg POP showed a reduction in dysmenorrhoea and use of pain

medication to control it.<sup>69</sup> POPs provide a safe alternative in those with contraindications to CHC, such as migraine with aura, and are an appealing alternative to LARCs in those who do not wish to undergo a procedure.

Major contraindications are as for other progestogen-only methods (Table 2).<sup>1</sup> Efficacy can be affected by the concurrent use of liver enzyme-inducing medications, and the POP is not recommended in long-term users of these medications (Table 3).<sup>7</sup>

### Starting a progestogen-only pill

POPs can be started at any time in the cycle and will be immediately effective if started on days 1 to 5 of the menstrual cycle. Otherwise, the traditional POPs take 48 hours (three pills) and the drospirenone POP takes seven days to become effective. If an early undiagnosable pregnancy cannot be excluded, a urine pregnancy test is recommended in four weeks' time, even if scheduled bleeding occurs.<sup>45</sup>

### Side effects and serious risks

To date, no serious risks have been established for the POP. The most common side effect is irregular bleeding, which occurs in around 40% of those taking traditional POPs; around 20% experience amenorrhoea, and 40% have regular cycles.<sup>70-72</sup> The drospirenone 4 mg POP has been developed to induce a monthly scheduled withdrawal bleed during the hormone-free break. Although unscheduled bleeding is initially common, both scheduled and unscheduled bleeding and spotting decline over time. Amenorrhoea increases from 10% in the first cycle to 45% in cycle 9.<sup>73</sup> Overall bleeding patterns are generally acceptable to users.<sup>74,75</sup> Other side effects can include acne, mood changes, weight gain and loss of libido.

### Missed POPs

A traditional POP is considered to be a missed pill when it is taken three or more hours late. Condoms should be used during intercourse until three consecutive pills have been taken, and emergency contraception should be considered if unprotected sex occurs during this time. The missed pill rules for the drospirenone 4 mg POP are the same as those for CHCs (Flowchart).

### Depot medroxyprogesterone injection

Depot medroxyprogesterone acetate (DMPA) is PBS subsidised and is given by deep intramuscular injection 12 weekly ( $\pm 2$  weeks). It is 99.8% effective in perfect use and 96% in typical use.<sup>40</sup> Its efficacy is unaffected by liver enzyme-inducing medications and it is generally considered safe to use at any time postpartum or post-abortion. Because of theoretical concerns about effects on lipids and bone density, a switch to another method is recommended at the age of 50 years.<sup>76</sup>

### Starting DMPA

DMPA can be given any time in the menstrual cycle. However, if an early

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undetected pregnancy cannot be excluded, a pregnancy test is recommended in 4 weeks' time, with a follow-up recall system in place. It can be given straight after a delivery or a surgical abortion, or within the first five days of a medical abortion, including at the time of prescribing mifepristone (first tablet of a two-step process). A concern is that administration around the time of mifepristone may be associated with a small increase in the risk of a failed abortion.<sup>31</sup>

A blood pressure check is required at initiation of DMPA and on annual assessment. Measurement of lipid levels is recommended for those with cardiovascular risk factors who are considering this method. Baseline BMI can be useful to

measure as DMPA use has been associated with weight gain.<sup>77</sup>

### **Contraindications, side effects and serious risks**

Major contraindications are similar to other progestogen-only methods, with additional precautions related to cardiovascular disease risk (Table 2).<sup>1</sup>

Troublesome bleeding is the most common side effect of DMPA, although at least 50% of users become amenorrhoeic. Users should be informed that their bleeding pattern will change but that it is not possible to predict how it will change on an individual basis. Users should also be provided with information at the time of insertion about the

availability of strategies for managing troublesome bleeding should it occur (see Box).

Unlike other methods of contraception, DMPA is associated with weight gain. Around 20% of users gain 10% of their body weight in the first year of use.<sup>77</sup> Use of DMPA is associated with loss of bone density that is considered reversible.<sup>78-81</sup> Data on the effects on fracture risk are inconclusive.<sup>82,83</sup> Detailed assessment of risk factors for osteoporosis should take place for new users, particularly those aged under 18 years, and every two years for continuing users.<sup>45</sup> Users also may complain of headaches, mood changes including emotional lability, acne, breast tenderness and loss of libido.



**TABLE 5. COMPARISON OF EMERGENCY CONTRACEPTION PILL (ECP) OPTIONS<sup>1,2,85-91</sup>**

| Characteristic  | Ulipristal   | Levonorgestrel  |
|---|--|---|
| Time it can be taken after unprotected intercourse        | Up to five days (120 hours)  | Up to four days (96 hours)*   |
| Efficacy  | Most effective ECP (but not as effective as the copper IUD)  | Less effective than the ulipristal ECP and copper IUD   |
| UKMEC 3 or 4 criteria                                     | Nil  | Nil   |
| Use if obesity  | Possible reduced effectiveness if BMI more than 30 kg/m <sup>2</sup> or weight more than 85 kg (consider a copper IUD instead)   | Possible reduced effectiveness if BMI over 26 kg/m <sup>2</sup> or weight over 70 kg (consider a double dose, <sup>†</sup> or a copper IUD) |
| Use if breastfeeding                                      | Low risk to infant (consider expressing and discarding breast milk for 24 hours after taking)  | Safe  |
| Drug interactions   | <ul style="list-style-type: none"> <li>Liver enzyme-inducing medications (alternative method recommended)</li> <li>Oral corticosteroids (alternative method recommended)</li> <li>Hormonal contraception use in the preceding seven days or following five days (may be less effective)</li> </ul> | Liver enzyme-inducing medications (double dose recommended) <sup>†</sup>  |
| Timing for initiating or restarting ongoing contraception | Wait five days before restarting or initiating a hormonal contraception method   | Can immediately restart or initiate a hormonal contraception method (excluding LNG IUDs) using 'Quick Start'                                |

Abbreviations: BMI = body mass index; IUD = intrauterine contraceptive device; LNG = levonorgestrel; UK MEC = United Kingdom Medical Eligibility Criteria for Contraceptive Use.

\* Levonorgestrel is effective if taken within 96 hours of unprotected sexual intercourse; however, it is only approved by the Australian TGA for use within 72 hours.

<sup>†</sup> Use of a double dose of levonorgestrel is off label and not approved by the Australian TGA.

## Emergency contraception

The most effective emergency contraception is a copper IUD inserted within five days of unprotected intercourse.<sup>26</sup> It also provides ongoing long-term contraception, although finding a provider who can insert an IUD within the required timeframe can be challenging.<sup>84</sup>

Two types of emergency contraceptive pills (ECPs) are available over the counter at pharmacies; the ulipristal 30 mg ECP and the LNG 1.5 mg ECP. Both act by preventing or delaying ovulation and prevent around 85% of expected pregnancies.<sup>85</sup> Both are safe to use, with no known contraindications except allergy to the constituents and a known pregnancy. Should they be inadvertently taken in early pregnancy, there is no evidence of a teratogenic effect on the fetus. Ulipristal is licensed for use up to five days (120 hours) after unprotected

intercourse and, although its efficacy is maintained across this period, users are advised to take it as early as possible for an optimal effect. LNG ECPs are licensed up to three days (72 hours) but have some effectiveness up to 96 hours after unprotected intercourse.<sup>86</sup> Emergency contraception is not subsidised on the PBS. See Table 5 for a comparison between ECP types.<sup>1,2,85-91</sup>

## Conclusion

Raising awareness about all contraceptive options is important for facilitating informed choice. The method that suits an individual during adolescence may be very different to the method that meets their needs during the mid-reproductive years and later at the perimenopause. Efficacy, contraindications, adverse effects and potential benefits of each contraceptive option

should be discussed to help find a suitable method for the individual patient. MT

## References

A list of references is included in the online version of this article ([www.medicinetoday.com.au](http://www.medicinetoday.com.au)).

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# Contraception in 2021

## An update

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### References

- Faculty of Sexual and Reproductive Healthcare (FSRH). UK medical eligibility criteria for contraceptive use. London: FSRH; 2016 (updated September 2019). Available online at: <https://www.fsrh.org/standards-and-guidance/documents/ukmec-2016/fsrh-ukmec-full-book-2019.pdf> (accessed November 2021).
- Sexual and Reproductive Health Experts Group. Contraception. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; 2020. Available online at: <https://www.tg.org.au> (accessed November 2021). [Login required]
- Services Australia. Medicare item reports. Canberra: Australian Government; 2021. Available online at: [http://medicarestatistics.humanservices.gov.au/statistics/mbs\\_item.jsp](http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp) (accessed November 2021).
- Diedrich JT, Zhao Q, Madden T, Secura GM, Peipert JF. Three-year continuation of reversible contraception. *Am J Obstet Gynecol* 2015; 213: 662 e1-e8.
- Brahmi D, Steenland MW, Renner RM, Gaffield ME, Curtis KM. Pregnancy outcomes with an IUD in situ: a systematic review. *Contraception* 2012; 85: 131-139.
- Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. *New Engl J Med* 2012; 366: 1998-2007.
- Faculty of Sexual and Reproductive Healthcare (FSRH). CEU Guidance: drug interactions with hormonal contraception. London: FSRH; 2017 (updated 2019). Available online at: <https://www.fsrh.org/standards-and-guidance/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/> (accessed November 2021).
- Girum T, Wasie A. Return of fertility after discontinuation of contraception: a systematic review and meta-analysis. *Contracept Reprod Med* 2018; 3: 9.
- Concepcion K, Lacey S, McGeechan K, Estoesta J, Bateson D, Botfield J. Cost-benefit analysis of enhancing the uptake of long-acting reversible contraception in Australia. *Aust Health Rev* 2020; 44: 385-391.
- Heinemann K, Reed S, Moehner S, Do Minh T. Risk of uterine perforation with levonorgestrel-releasing and copper intrauterine devices in the European Active Surveillance Study on Intrauterine Devices. *Contraception* 2015; 91: 274-279.
- Faculty of Sexual and Reproductive Healthcare (FSRH). Intrauterine Contraception. London: FSRH; 2015 (updated September 2019). Available online at: <https://www.fsrh.org/standards-and-guidance/documents/ceuguidanceintrauterinecontraception/> (accessed November 2021).
- Heinemann K, Reed S, Moehner S, Minh TD. Comparative contraceptive effectiveness of levonorgestrel-releasing and copper intrauterine devices: the European Active Surveillance Study for Intrauterine Devices. *Contraception* 2015; 91: 280-283.
- Gemzell-Danielsson K, Apter D, Dermout S, et al. Evaluation of a new, low-dose levonorgestrel intrauterine contraceptive system over 5 years of use. *Eur J Obstet Gynecol Reprod Biol* 2017; 210: 22-28.
- Turok DK, Gero A, Simmons RG, et al. Levonorgestrel vs. copper intrauterine devices for emergency contraception. *N Engl J Med* 2021; 384: 335-344.
- Faculty of Sexual and Reproductive Healthcare (FSRH). FSRH CEU Statement: Response to recent publication Turok et al. (2021) 'Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception'. London: FSRH; 2021. Available online at: <https://www.fsrh.org/standards-and-guidance/documents/fsrh-ceu-statement-response-to-recent-publication-turok-et-al/fsrh-ceu-statement-ing-ius-vs-cu-iud-for-ec-feb-2021.pdf> (accessed November 2021).
- Beckert V, Aqua K, Bechtel C, et al. Insertion experience of women and health care professionals in the Kyleena Satisfaction Study. *Eur J Contracept Reprod Health Care* 2020; 25: 182-189.
- Gemzell-Danielsson K, Schellschmidt I, Apter D. A randomized, phase II study describing the efficacy, bleeding profile, and safety of two low-dose levonorgestrel-releasing intrauterine contraceptive systems and Mirena. *Fertil Steril* 2012; 97: 616-622.
- Xiao B, Wu SC, Chong J, Zeng T, Han LH, Luukkainen T. Therapeutic effects of the levonorgestrel-releasing intrauterine system in the treatment of idiopathic menorrhagia. *Fertil Steril* 2003; 79: 963-969.
- Lindh I, Milsom I. The influence of intrauterine contraception on the prevalence and severity of dysmenorrhea: a longitudinal population study. *Hum Reprod* 2013; 28: 1953-1960.
- Brown J, Farquhar C. Endometriosis: an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2014; (3): CD009590.
- Pontis A, D'Alterio MN, Pirarba S, de Angelis C, Tinelli R, Angioni S. Adenomyosis: a systematic review of medical treatment. *Gynecol Endocrinol* 2016; 32: 696-700.
- Imai A, Matsunami K, Takagi H, Ichigo S. Levonorgestrel-releasing intrauterine device used for dysmenorrhea: five-year literature review. *Clin Exp Obstet Gynecol* 2014; 41: 495-498.
- Goldthwaite LM, Creinin MD. Comparing bleeding patterns for the levonorgestrel 52 mg, 19.5 mg, and 13.5 mg intrauterine systems. *Contraception* 2019; 100: 128-131.
- Nelson AL. LNG-IUS 12: a 19.5 levonorgestrel-releasing intrauterine system for prevention of pregnancy for up to five years. *Expert Opin Drug Deliv* 2017; 14: 1131-1140.
- Nelson A, Apter D, Hauck B, et al. Two low-dose levonorgestrel intrauterine contraceptive systems: a randomized controlled trial. *Obstet Gynecol* 2013; 122: 1205-1213.
- Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. *Hum Reprod* 2012; 27: 1994-2000.
- Milsom I, Andersson K, Jonasson K, Lindstedt G, Rybo G. The influence of the Gyne-T 380S IUD on menstrual blood loss and iron status. *Contraception* 1995; 52: 175-179.
- Family Planning Alliance Australia (FPAA). Obesity and Etonogestrel implant use. Albany: FPAA; 2020. Available online at: <https://www.fpv.org.au/assets/img/content/Obesity-and-Etonogestrel-implant-use-Dec20.pdf> (accessed November 2021).
- Polis CB, Bradley SE, Bankole A, Onda T, Croft T, Singh S. Typical-use contraceptive failure rates in 43 countries with demographic and health survey data: summary of a detailed report. *Contraception* 2016; 94: 11-17.
- Faculty of Sexual and Reproductive Healthcare (FSRH). FSRH Guideline. Quick starting contraception. London: FSRH; 2017. Available online at: <https://www.fsrh.org/standards-and-guidance/documents/quick-starting-contraception/>

- [www.fsrh.org/standards-and-guidance/documents/fsrh-clinical-guidance-quick-starting-contraception-april-2017/](http://www.fsrh.org/standards-and-guidance/documents/fsrh-clinical-guidance-quick-starting-contraception-april-2017/) (accessed November 2021).
31. National Institute for Health and Care Excellence. Abortion care; 2019. Available online at: <https://www.nice.org.uk/guidance/ng140/resources/abortion-care-pdf-66141773098693> (accessed November 2021).
  32. Australian product information Implanon NXT (etonogestrel) subdermal implant. Sydney: Organon Pharma; 2021. Available online at: <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-02693-3> (accessed November 2021).
  33. Pearson S, Stewart M, Bateson D. Implanon NXT: expert tips for best-practice insertion and removal. *Aust Fam Physician* 2017; 46: 104-108.
  34. Mansour D, Korver T, Marintcheva-Petrova M, Fraser IS. The effects of Implanon on menstrual bleeding patterns. *Eur J Contracept Reprod Health Care* 2008; 13 Suppl 1: 13-28.
  35. Urbancsek J. An integrated analysis of nonmenstrual adverse events with Implanon. *Contraception* 1998; 58(6 Suppl): 109S-115S.
  36. Croxatto HB. Clinical profile of Implanon: a single-rod etonogestrel contraceptive implant. *Eur J Contracept Reprod Health Care* 2000; 5 Suppl 2: 21-28.
  37. Bahamondes L, Brache V, Ali M, Habib N; WHO Study Group on Contraceptive Implants for Women. A multicenter randomized clinical trial of etonogestrel and levonorgestrel contraceptive implants with nonrandomized copper intrauterine device controls: effect on weight variations up to 3 years after placement. *Contraception* 2018; 98: 181-187.
  38. Vickery Z, Madden T, Zhao Q, Secura GM, Allsworth JE, Peipert JF. Weight change at 12 months in users of three progestin-only contraceptive methods. *Contraception* 2013; 88: 503-508.
  39. Richters J, Fitzadam S, Yeung A, et al. Contraceptive practices among women: the second Australian study of health and relationships. *Contraception* 2016; 94: 548-555.
  40. Sundaram A, Vaughan B, Kost K, et al. Contraceptive failure in the United States: estimates from the 2006-2010 National Survey of Family Growth. *Perspect Sex Reprod Health* 2017; 49: 7-16.
  41. ACOG Practice Bulletin No. 110: noncontraceptive uses of hormonal contraceptives. *Obstet Gynecol* 2010; 115: 206-218.
  42. Iversen L, Sivasubramaniam S, Lee AJ, Fielding S, Hannaford PC. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' oral contraception study. *Am J Obstet Gynecol* 2017; 216: 580.e1-580.e9.
  43. 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: 139-147.
  44. Lopez LM, Kaptein AA, Helmerhorst FM. Oral contraceptives containing drospirenone for premenstrual syndrome. *Cochrane Database Syst Rev* 2012; (2): CD006586.
  45. Contraception: An Australian Clinical Practice Handbook. 4th ed. Ashfield, NSW: Family Planning New South Wales, Family Planning Victoria and True Relationships and Reproductive Health; 2016.
  46. Nash Z, Thwaites A, Davies M. Tailored regimens for combined hormonal contraceptives. *BMJ* 2020; 368: m200.
  47. Family Planning Alliance Australia (FPAA). 4 day pill free break. Albury: FPAA; 2020. Available online at: <https://www.fpv.org.au/assets/img/content/4-Day-pill-break-Dec20.pdf> (accessed November 2021).
  48. Australian product information Seasonique® (levonorgestrel and ethinylestradiol) film coated tablet. Theramex Australia Pty Ltd. Updated 10 March 2021. Available online at: <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-PI-01279-1&d=20211124172310101> (accessed November 2021).
  49. Steenland MW, Rodríguez M-I, Marchbanks PA, Curtis KM. How does the number of oral contraceptive pill packs dispensed or prescribed affect continuation and other measures of consistent and correct use? A systematic review. *Contraception* 2013; 87: 605-610.
  50. Faculty of Sexual and Reproductive Healthcare (FSRH). FSRH Guideline. Combined Hormonal Contraception. London: FSRH; 2019 (updated 2020). Available online at: <https://www.fsrh.org/standards-and-guidance/documents/combined-hormonal-contraception/> (accessed November 2021).
  51. Macias G, Merki-Feld GS, Parke S, Mellinger U, Serrani M. Effects of a combined oral contraceptive containing oestradiol valerate/dienogest on hormone withdrawal-associated symptoms: results from the multicentre, randomised, double-blind, active-controlled HARMONY II study. *J Obstet Gynaecol* 2013; 33: 591-596.
  52. Oddsson K, Leifels-Fischer B, Wiel-Masson D, et al. Superior cycle control with a contraceptive vaginal ring compared with an oral contraceptive containing 30 microg ethinylestradiol and 150 microg levonorgestrel: a randomized trial. *Hum Reprod* 2005; 20: 557-562.
  53. Therapeutic Goods Australia (TGA). Update - dienogest and risk of venous thromboembolism. Canberra: TGA; 2021. Available online at: <https://www.tga.gov.au/publication-issue/update-dienogest-and-risk-venous-thromboembolism> (accessed November 2021).
  54. van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. *BMJ* 2009; 339: b2921.
  55. Lidegaard O, Lokkegaard E, Svendsen AL, Agger C. Hormonal contraception and risk of venous thromboembolism: national follow-up study. *BMJ* 2009; 339: b2890.
  56. Roach RE, Helmerhorst FM, Lijfering WM, Stijnen T, Algra A, Dekkers OM. Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke. *Cochrane Database Syst Rev* 2015; (8): CD011054.
  57. Morch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard O. Contemporary hormonal contraception and the risk of breast cancer. *N Engl J Med* 2017; 377: 2228-2239.
  58. Shufelt CL, Bairey Merz CN. Contraceptive hormone use and cardiovascular disease. *J Am Coll Cardiol* 2009; 53: 221-231.
  59. Cagnacci A, Zanin R, Napolitano A, Arangino S, Volpe A. Modification of 24-h ambulatory blood pressure and heart rate during contraception with the vaginal ring: a prospective study. *Contraception* 2013; 88: 539-543.
  60. Grandi G, Napolitano A, Cagnacci A. Metabolic impact of combined hormonal contraceptives containing estradiol. *Expert Opin Drug Metab Toxicol* 2016; 12: 779-787.
  61. Khalili H, Higuchi LM, Ananthakrishnan AN, et al. Oral contraceptives, reproductive factors and risk of inflammatory bowel disease. *Gut* 2012; 62: 1153-1159.
  62. Dhiman RK, Chawla YK. Is there a link between oestrogen therapy and gallbladder disease? *Expert Opin Drug Saf* 2006; 5: 117-129.
  63. Gallo MF, Lopez LM, Grimes DA, Carayon F, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. *Cochrane Database Syst Rev* 2014; (1): CD003987.
  64. Gallo MF, Nanda K, Grimes DA, Lopez LM, Schulz KF. 20 microg versus >20 microg estrogen combined oral contraceptives for contraception. *Cochrane Database Syst Rev* 2011; (1): CD003989.
  65. Oddsson K, Leifels-Fischer B, de Melo NR, et al. Efficacy and safety of a contraceptive vaginal ring (NuvaRing) compared with a combined oral contraceptive: a 1-year randomized trial. *Contraception* 2005; 71: 176-182.
  66. McCann MF, Potter LS. Progestin-only oral contraception: a comprehensive review: mode of action. *Contraception* 1994; 50(6 Suppl 1): S13-S195.
  67. Duijkers IJM, Heger-Mahn D, Drouin D, Colli E, Skouby S. Maintenance of ovulation inhibition with a new progestogen-only pill containing drospirenone after scheduled 24-h delays in pill intake. *Contraception* 2016; 93: 303-309.
  68. Vessey MP. Progestogen only oral contraception. Findings in a large

- prospective study with special reference to effectiveness. *Br J Fam Plann* 1985; 10: 117-121.
69. Apter D, Colli E, Gemzell-Danielsson K, Peters K. Multicenter, open-label trial to assess the safety and tolerability of drospirenone 4.0 mg over 6 cycles in female adolescents, with a 7-cycle extension phase. *Contraception* 2020; 101: 412-419.
70. Sheth A, Jain U, Sharma S, et al. A randomized, double-blind study of two combined and two progestogen-only oral contraceptives. *Contraception* 1982; 25: 243-252.
71. Grimes DA, Lopez LM, O'Brien PA, Raymond EG. Progestin-only pills for contraception. *Cochrane Database Syst Rev* 2010; (1): CD007541.
72. Korver T. A double-blind study comparing the contraceptive efficacy, acceptability and safety of two progestogen-only pills containing desogestrel 75 µg/day or levonorgestrel 30 µg/day: collaborative study group on the desogestrel-containing progestogen-only pill. *Eur J Contracept Reprod Health Care* 1998; 3: 169-178.
73. Palacios S, Colli E, Regidor PA. Multicenter, phase III trials on the contraceptive efficacy, tolerability and safety of a new drospirenone-only pill. *Acta Obstet Gynecol Scand* 2019; 98: 1549-1557.
74. Archer DF, Ahrendt HJ, Drouin D. Drospirenone-only oral contraceptive: results from a multicenter noncomparative trial of efficacy, safety and tolerability. *Contraception* 2015; 92: 439-444.
75. Palacios S, Colli E, Regidor PA. Bleeding profile of women using a drospirenone-only pill 4 mg over nine cycles in comparison with desogestrel 0.075 mg. *PLoS One* 2020; 15: e0231856.
76. Faculty of Sexual and Reproductive Healthcare (FSRH). FSRH guideline: contraception for women aged over 40 years. London: FSHR; 2017 (updated 2019). Available online at: <https://www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/> (accessed November 2021).
77. Berenson AB, Rahman M. Changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio associated with injectable and oral contraceptive use. *Am J Obstet Gynecol* 2009; 200: 329.e1-8.
78. Clark MK, Sowers M, Levy B, Nichols S. Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. *Fertil Steril* 2006; 86: 1466-1474.
79. 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: 90-99.
80. Harel Z, Johnson CC, Gold MA, et al. Recovery of bone mineral density in adolescents following the use of depot medroxyprogesterone acetate contraceptive injections. *Contraception* 2010; 81: 281-291.
81. Berenson AB, Rahman M, Breitkopf CR, Bi LX. Effects of depot medroxyprogesterone acetate and 20-microgram oral contraceptives on bone mineral density. *Obstet Gynecol* 2008; 112: 788-799.
82. Kyvernitakis I, Kostev K, Nassour T, Thomasius F, Hadji P. The impact of depot medroxyprogesterone acetate on fracture risk: a case-control study from the UK. *Osteoporos Int* 2017; 28: 291-297.
83. Lopez LM, Chen M, Mullins Long S, Curtis KM, Helmerhorst FM. Steroidal contraceptives and bone fractures in women: evidence from observational studies. *Cochrane Database Syst Rev* 2015; (7): CD009849.
84. Dorney E, Botfield JR, Robertson S, McGeechan K, Bateson D. Acceptability of the copper intrauterine device as a form of emergency contraception in New South Wales, Australia. *Eur J Contracept Reprod Health Care* 2020; 25: 114-119.
85. Faculty of Sexual and Reproductive Healthcare (FSRH). FSRH guideline: emergency contraception. London: FSRH; 2017 (updated 2020). Available online at: <https://www.fsrh.org/documents/ceu-clinical-guidance-emergency-contraception-march-2017/fsrh-guideline-emergency-contraception03dec2020.pdf> (accessed November 2021).
86. Piaggio G, Kapp N, von Hertzen H. Effect on pregnancy rates of the delay in the administration of levonorgestrel for emergency contraception: a combined analysis of four WHO trials. *Contraception* 2011; 84: 35-39.
87. Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet* 2010; 375: 555-562.
88. Festin MP, Peregoudov A, Seuc A, Kiarie J, Temmerman M. Effect of BMI and body weight on pregnancy rates with LNG as emergency contraception: analysis of four WHO HRP studies. *Contraception* 2017; 95: 50-54.
89. Jatlaoui TC, Riley H, Curtis KM. Safety data for levonorgestrel, ulipristal acetate and Yuzpe regimens for emergency contraception. *Contraception* 2016; 93: 93-112.
90. Brache V, Cochon L, Deniaud M, Croxatto HB. Ulipristal acetate prevents ovulation more effectively than levonorgestrel: analysis of pooled data from three randomized trials of emergency contraception regimens. *Contraception* 2013; 88: 611-618.
91. Australian product information. EllaOne (ulipristal acetate) 30 mg tablet. Melbourne: Brand Solutions: Australia, 2021. Available online at: <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2021-PI-02212-1&d=20211126172310101> (accessed November 2021).