The Faculty of Sexual & Reproductive Healthcare

FSRH Guideline
Progestogen-only Pills

August 2022 (Amended July 2023) I FSRH

Faculty of Sexual & Reproductive Healthcare (FSRH) provided funding to the Clinical Effectiveness Unit (of the FSRH) to assist them in the production of this guideline, *Progestogen-only Pills* (August 2022).

Published by the Faculty of Sexual & Reproductive Healthcare.
Registered in England No. 2804213 and Registered Charity No. 1019969

*Progestogen-only Pill*s first published in March 2015.

Published in the UK.

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by the Faculty of Sexual & Reproductive Healthcare to produce this guideline. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

Information box

Title	Progestogen-only Pills August 2022 (Amended July 2023)
Author/publisher	Faculty of Sexual & Reproductive Healthcare
Publication date	August 2022
Superseded document	Progestogen-only Pills (March 2015, amended April 2019)
Review date	August 2027
Available online	https://www.fsrh.org/Public/Documents/ceu-guideline-progestogen-only-pills.aspx

From January 2019 the FSRH has published its electronic clinical guidelines on both its own website (www.fsrh.org.uk) and as an electronic supplement to the BMJ Sexual & Reproductive Health (BMJ SRH) journal. The guidelines have the same content. If a guideline is updated, the FSRH replace the version on its website and the BMJ Sexual & Reproductive Health (BMJ SRH) journal will ensure old versions of guidelines will clearly signpost the newer version.

To cite this guideline: FSRH Guideline (August 2022) Progestogen-only Pills. BMJ Sexual & Reproductive Health 2022; 48:Suppl 1. http://dx.doi.org/10.1136/bmjsrh-2022-PoP

Details of changes to original guidance document

Subsequent to the publication of this guideline in August 2022 the following amendments has been made.

Date	Revision
03 October 2022	Section 10.2 Specific considerations for DRSP POP (page 14) First paragraph text has been revised.
14 November 2022	Tables 7,9 and 10 – addition of the word 'active' in places where it is noted: "Restart/continue DRSP POP until 7 consecutive active pills taken after HFI"
10 July 2023	Table 7 updated to reflect extension of 52mg LNG-IUS license from 5 to 6 years Section 11.3 Risk of breast cancer updated to reflect newly published evidence

Abbreviations used

AUC	area under the curve
BMI	body mass index
CEC	Clinical Effectiveness Committee
CEU	Clinical Effectiveness Unit
CHC	combined hormonal contraception/contraceptive
CI	confidence interval
COC	combined oral contraception/contraceptive
Cu-IUD	copper intrauterine device
CVD	cardiovascular disease
DMPA	depot medroxyprogesterone acetate
DRSP	drospirenone
DSG	desogestrel
EC	emergency contraception
EE	ethinylestradiol
FSRH	Faculty of Sexual & Reproductive Healthcare
GDG	guideline development group
HCP	healthcare practitioner
HFI	hormone-free interval
HMB	heavy menstrual bleeding
HR	hazard ratio
LARC	long-acting reversible contraception/contraceptive
LNG	levonorgestrel
LNG-IUS	levonorgestrel-releasing intrauterine system
MI	myocardial infarction
NET	norethisterone
OR	odds ratio
PI	Pearl Index
POC	progestogen-only contraception/contraceptive
POP	progestogen-only pill
RCT	randomised controlled trial
RP	reference period
RR	relative risk
RYGB	Roux-en-Y gastric bypass
SPC	Summary of Product Characteristics
SRH	sexual and reproductive healthcare
STI	sexually transmitted infection
U&E	urea and electrolytes
UPA	ulipristal acetate
UPSI	unprotected sexual intercourse
USS	ultrasound scan
VTE	venous thromboembolism
WHO	World Health Organization

Grading of recommendations

Refer to Appendix 1 for a full explanation of the classification of evidence level and grading of recommendations.

A	**At least one meta-analysis, systematic review or randomised controlled trial (RCT) rated as 1++, and directly applicable to the target population;** ***or*** **A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.**
B	**A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results;** ***or*** **Extrapolated evidence from studies rated as 1++ or 1+.**
C	**A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results;** ***or*** **Extrapolated evidence from studies rated as 2++.**
D	**Evidence level 3 or 4;** ***or*** **Extrapolated evidence from studies rated as 2+.**
✓	**Good Practice Point based on the clinical experience of the guideline development group.**

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Key information

✓ **Contraceptive effectiveness of the progestogen-only pill (POP) relies on correct use.**

✓ **A traditional POP is considered missed if it is taken more than 3 hours late, a desogestrel (DSG) POP if it is taken more than 12 hours late, and a drospirenone (DRSP) POP if more than 24 hours late.**

How effective are POPs?

Key information

D **The risk of pregnancy during the first year of typical POP use has been estimated at about 9% If used perfectly, POPs may be more than 99% effective.**

D **The available evidence is too limited to inform whether there is a significant difference in contraceptive effectiveness between traditional POPs and DSG/DRSP POPs.**

What can affect effectiveness of the POP?

Vomiting

Key information

✓ **Contraceptive effectiveness could be affected if a POP user vomits within a few hours of pill-taking.**

Weight/BMI

Key information

D **The available evidence suggests that effectiveness of the POP is not affected by body weight or body mass index (BMI).**

Clinical recommendations

✓ **Double-dose POP for contraception is not required for individuals who are overweight or individuals with obesity.**

Bariatric surgery

Key information

D **There is insufficient evidence to inform whether contraceptive effectiveness of POPs is affected by bariatric surgery. Users may therefore wish to consider effective non-oral contraception after bariatric surgery.**

Drug interactions

Key information

✓ **Contraceptive effectiveness of POPs could be reduced by concomitant use of enzyme-inducing drugs**

Who can and cannot use POP?

All POP

Key information

D	**The FSRH supports the use of all POPs by medically eligible individuals between menarche and age 55 years.**
D	**Breast cancer, arterial thromboembolism that occurred during use of a POP, decompensated cirrhosis and hepatocellular tumours are UKMEC3 or UKMEC4 conditions for use of all POPs.**

Additional specific considerations for DRSP POP

Clinical recommendations

✓	**The manufacturer advises that the DRSP POP should not be used by individuals with severe renal insufficiency or acute renal failure.**
✓	**The guideline development group (GDG) suggests that DRSP POP should also generally be avoided by:** • **Individuals with known hyperkalaemia or untreated hypoaldosteronism (eg, Addison's disease).** • **Individuals currently using potassium-sparing diuretics, aldosterone antagonists or potassium supplements.**
✓	**The GDG suggests that DRSP POP should be used with caution by individuals with mild/moderate renal impairment or treated hypoaldosteronism (eg, treated Addison's disease).**
✓	**The GDG suggests that for individuals with significant risk factors for chronic kidney disease, measurement of urea & electrolytes (U&E) and blood pressure should be considered prior to prescription of the DRSP POP, particularly if aged over 50 years.**

What health risks are and are not associated with use of POP?

Risk of venous thromboembolism

Key information

C	**The published evidence is very limited but suggests no increase in risk of venous thromboembolic events associated with use of POPs.**

Risk of arterial thromboembolism

Key information

C	**The published evidence is very limited but suggests no increase in risk of thrombotic stroke or myocardial infarction associated with use of POPs.**

Risk of breast cancer

Key information

D	**The available evidence suggests a possible association between current or recent use of hormonal contraception (including POP) and a small increase in risk of breast cancer; absolute risk remains very small.**

Risk of ectopic pregnancy

Key information

C	**The use of all effective methods of contraception, including POPs, reduces the risk of all pregnancies (including ectopic pregnancies) compared to use of no contraception.**

What are the side effects of POP?

Change in bleeding pattern

Clinical recommendations

C	**Individuals considering use of a traditional POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use:** • **Fewer than 1 in 10 (only about 2%) LNG POP users may be amenorrhoeic.** • **About 1 in 10 LNG POP users may have infrequent bleeding (1–2 bleeding/spotting episodes).** • **About 8 in 10 LNG POP users may have normal frequency bleeding (3–5 bleeding/spotting episodes).** • **About 1 in 10 LNG POP users may have frequent bleeding (6 or more bleeding/spotting episodes).** • **Fewer than 1 in 10 LNG POP users may have prolonged bleeding (bleeding/spotting episode(s) lasting >14 days).**
C	**Individuals considering use of a DSG POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use:** • **About 4 in 10 DSG POP users may have normal frequency bleeding (3–5 bleeding spotting/episodes).** • **About 2–3 in 10 DSG POP users may be amenorrhoeic.** • **About 3 in 10 DSG POP users may have infrequent bleeding (<3 bleeding/spotting episodes).** • **Fewer than 1 in 10 DSG POP users may have frequent bleeding (6 or more bleeding/spotting episodes).** • **About 1 in 10 DSG POP users may have prolonged bleeding (bleeding/spotting episode(s) lasting >14 days).**
C	**Individuals considering use of a DRSP POP should be advised that bleeding pattern is unpredictable; they may or may not have "scheduled" bleeding/spotting during the 4-day HFI and they may or may not have "unscheduled" bleeding/spotting at other times. Both scheduled and unscheduled bleeding/spotting may reduce in frequency over the first year of use. Over a 3-month period at around 6–9 months of use:** • **The total number of days of bleeding/spotting (scheduled plus unscheduled) may be similar to the number of days of bleeding/spotting with the DSG POP.** • **About 2–3 in 10 DRSP POP users may be amenorrhoeic.** • **Fewer than 1 in 10 DRSP POP users may have frequent bleeding.** • **Fewer than 1 in 10 DRSP POP users may have bleeding episode(s) lasting >14 days.**

Mood change

Key information

C	**The available evidence does not establish a causal relationship between POP use and depression.**

Headache

Key information

D	**Evidence is too limited to confirm or exclude any causative association between POP use and headache.**

Acne

Key information

D	**A causal association cannot be confirmed or excluded by the very limited evidence relating to POP use and acne.**

Weight

Key information

D	**Whilst users of POP may gain some weight during use, there is not clear evidence that POP use *causes* significant weight gain.**

When can the POP be started?

Key information

✓	**It is established practice that traditional and DSG POP can be started on days 1–5 of a natural menstrual cycle, by day 5 after abortion or by day 21 after childbirth without requirement for additional contraceptive precautions. At any other time, traditional and DSG POP can be quick started according to Quick Starting Guidance, with advice to use additional contraceptive precautions for 2 days and to take a follow-up pregnancy test if required.**
✓	**To align with manufacturer guidance for the new DRSP POP, the GDG recommends that additional contraceptive precautions are required unless DRSP POP is started on day 1 of a natural menstrual cycle, day 1 after abortion or by day 21 after childbirth. If started at any other time, additional contraceptive precautions are required for 7 days with advice to take a follow-up pregnancy test if appropriate.**

Starting after pregnancy

Breastfeeding

Key information

A	**The available evidence indicates that progestogen-only methods of contraception have no adverse effects on lactation, infant growth or development.**

What drug interactions are important to consider?

Enzyme-inducing drugs

Clinical recommendations

✓	**Individuals using enzyme-inducing drugs should be informed that the contraceptive effectiveness of all POPs could be reduced during use of the enzyme-inducer and for 28 days after stopping the enzyme-inducer.**
✓	**Individuals using enzyme-inducing drugs should be offered a reliable contraceptive method that is unaffected by enzyme-inducers.**

Ulipristal acetate (UPA)

Key information

D	**The ability of ulipristal acetate emergency contraception (UPA-EC) to delay ovulation could be reduced if a POP is started within 5 days of taking the UPA.**
✓	**The ability of UPA-EC to delay ovulation could theoretically be reduced if a POP has been taken in the preceding 7 days.**

Clinical recommendations

✓	**Individuals should be advised to wait 5 days after taking UPA-EC before starting a POP. They should be made aware that they must use condoms reliably or abstain from sex during the 5 days waiting and then for 2 days after starting the levonorgestrel (LNG) and DSG POP and 7 days for DRSP POP.**

What should be done in an initial consultation?

Assessing suitability of POP for an individual

Clinical recommendations

✓	**Assessment of medical eligibility for POP use should include a comprehensive assessment of medical conditions and drug history.**
✓	**Individuals requesting POP should be informed about the effectiveness with both typical and perfect use of POP and other contraceptive methods, including the superior effectiveness of long-acting reversible contraception (LARC).**

Other important supporting information

Clinical recommendations

✓	**Individuals should be provided with accessible information or a link to a trusted online resource to support safe, effective POP use.**

Duration of POP prescription

Clinical recommendations

D	**A 12-month supply of traditional, DSG or DRSP POP can be provided to *medically eligible* individuals who are initiating or continuing POP, with information to seek advice if there are any changes to their medical history.**

Use of a self-completed checklist to assess medical eligibility for POP

Key information

C	**Use of suitable self-completed checklists for medical eligibility appears accurate and acceptable to users of oral contraception.**

Pharmacy provision of POP

Key information

✓	**Specific approved brands of DSG POP can now be bought by the user as Pharmacy Medicines (from a pharmacy, without a prescription, under the supervision of a pharmacist).**

Follow-up

What follow-up arrangements are appropriate?

Clinical recommendations

✓	**After initiation of POP, users should generally be reviewed annually. This can usually be achieved without an in-person consultation.**

What recommendations are there for stopping the POP?

How long can POP use be continued?

Clinical recommendations

✓	**POP can be used for contraception by medically eligible individuals until age 55 years.**

Planning pregnancy

Return of fertility

Key information

D	**The limited available evidence suggests that there is no delay in return to fertility following POP use.**

FSRH Guideline (August 2022)
Progestogen-only Pills

(Revision due by August 2027)

1 Purpose and scope

This document updates previous Faculty of Sexual & Reproductive Healthcare (FSRH) guidance and aims to summarise the available evidence and expert opinion on progestogen-only pills (POPs). The guideline is intended for use by healthcare practitioners (HCPs) providing POPs.

2 Identification and assessment of the evidence

This guideline was developed in accordance with standard methodology for developing FSRH clinical guidelines. The recommendations made within this document are based on the best available evidence and the consensus opinion of experts and the guideline development group (GDG). The methodology used in developing this guideline and a list of GDG members and other contributors can be found in **Appendix 1**.

The recommendations included should be used to guide clinical practice but are not intended to serve alone as a standard of medical care or to replace clinical judgement in the management of individual cases.

3 Introduction

This guideline will consider the progestogen-only contraceptive pills (POPs) available in the UK, namely desogestrel (DSG) 75 µg, drospirenone (DRSP) 4 mg (soon to be available in the UK) and the 'traditional' POPs levonorgestrel (LNG) 30 µg and norethisterone (NET) 350 µg.

HCPs should support individuals to make informed decisions about choosing and using POPs, ensuring that they are informed about contraceptive effectiveness, and how this compares to other contraceptive methods including long-acting reversible contraception (LARC) as well as potential risks and benefits.

4 Summary, including changes to existing guidance

In the UK there are soon to be four different POPs: desogestrel (DSG) 75 µg, drospirenone (DRSP) 4 mg (this is a new product not included in previous FSRH guidelines) and the 'traditional' POPs levonorgestrel (LNG) 30 µg and norethisterone (NET) 350 µg. (**Section 5**)

Contraceptive effectiveness. The contraceptive effect of DSG and DRSP POPs relies primarily on inhibition of ovulation. In contrast, LNG and NET POPs do not reliably suppress ovulation; their contraceptive effectiveness relies on their effect on cervical mucus, endometrium and tubal motility.

As with all oral contraception, POPs are user-dependent and rely on correct pill-taking for contraceptive effectiveness. If used perfectly, POPs may be more than 99% effective; but with typical use, risk of pregnancy during the first year has been estimated at about 9%.

Contraceptive effectiveness can also be affected by drug interactions (eg, concomitant use of enzyme-inducing drugs) and by malabsorption. (**Section 8** and **Section 9**)

How to take POP (and what to do if use has been incorrect). (Section 6 and Section 7) LNG, NET and DSG POPs are taken continuously at 24-hour intervals. The DRSP POP is taken in a regimen of 24 daily active pills followed by four hormone-free placebo pills.

All POPs should be taken at the same time each day**.** LNG and NET POPs are considered missed if taken more than 3 hours late, a DSG POP if it is taken more than 12 hours late, and a DRSP POP if more than 24 hours late.

Recommended actions after incorrect POP use are set out in Table 1, Appendix 2 and Appendix 3. Note that recommendations for DRSP POP differ from those for other POPs.

Who can and cannot use POP? All POPs can be used by medically eligible individuals between menarche and age 55 years. Contraindications to use of DSG, LNG and NET POPs as set out in UKMEC 2016 are unchanged in this guideline. Conditions for which use of POPs is UKMEC3 or UKMEC4 are set out in Table 3. Note that use of POP is UKMEC1 for individuals with history of ectopic pregnancy and ovarian cyst. UKMEC eligibility guidance for POP applies to all POPs (including DRSP POP) but there are some **additional specific considerations for use of the DRSP POP.** DRSP is an aldosterone antagonist thus there is potential risk of hyperkalaemia in susceptible individuals. The manufacturer advises that DRSP POP should not be used by individuals with severe renal insufficiency or acute renal failure. This guideline suggests that DRSP POP should also generally be avoided by individuals with known hyperkalaemia or untreated hypoaldosteronism and during use of potassium-sparing diuretics or potassium supplements. Individuals with mild/moderate renal insufficiency or treated hypoaldosteronism and those with significant risk factors for chronic kidney disease (particularly if aged over 50 years) may require assessment of urea and electrolytes (U&E) and blood pressure. **(**Section 10)

Drug interactions. Drugs that induce hepatic enzymes increase metabolism of progestogens and could reduce contraceptive effectiveness of POPs. (Section 15.1)

POPs use could reduce effectiveness of ulipristal acetate (UPA) for emergency contraception (EC). **(**Section 15.2)

Use of the DRSP POP is not recommended during use of potassium-sparing diuretics or potassium supplements due to potential risk of hyperkalaemia. Pharmacodynamic interaction between the DRSP POP and drugs such as angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists could also potentially increase risk of hyperkalaemia. **(**Section 15.3)

Health risks. Very limited evidence suggests no increased risk of venous (VTE) or arterial thromboembolism (ATE) associated with use of POPs and no significant effect on risk of endometrial cancer and ovarian cancer. There could be a small increase in breast cancer risk associated with POP use, but absolute risk remains very small.

Compared to use of no contraception, use of all effective methods of contraception, including POPs, *reduces* risk of ectopic pregnancy. (Section 11)

Side effects. Unpredictable bleeding/spotting is common with use of all POPs. Detailed recommendations in Section 12 describe bleeding patterns for all types of POP. With the DRSP POP, 'scheduled' bleeding/spotting may occur during the hormone-free interval (HFI) but 'unscheduled' bleeding/spotting is also common.

POP users with problematic bleeding should be assessed for other potential causes. Evidence to inform management of problematic bleeding during POP use is lacking. An individual could experience different bleeding patterns with different POPs, thus a change of POP could be useful for some individuals with problematic bleeding (or other side effects). For problematic bleeding during use of a DSG POP some clinicians offer use of a double dose (150 µg daily) but there is not yet robust published evidence of the effectiveness of this strategy.

Evidence is too limited to confirm or exclude any causative association between POP use and headache, acne, libido, weight gain or mood. (**Section 12**)

Non-contraceptive benefits. In practice, some clinicians offer DSG POP (or double-dose DSG POP) for management of heavy menstrual bleeding but there is not yet robust published evidence to inform effectiveness for this indication. DSG and DRSP POP could reduce dysmenorrhoea for some users. (**Section 13**)

What should be done at an initial consultation? **Section 16** provides an overview of (and a new checklist for) important aspects of a POP consultation.

Starting POP. LNG, NET and DSG POPs can be started on days 1–5 of a natural menstrual cycle, by day 5 after abortion or by day 21 after childbirth without requirement for additional contraceptive precautions. At any other time, these can be quick started with advice to use additional contraceptive precautions for 2 days and to take a follow-up pregnancy test if required.

In contrast (reflecting manufacturer guidance for the new DRSP POP) this guideline recommends that additional contraceptive precautions are required unless DRSP POP is started on day 1 of a natural menstrual cycle, day 1 after abortion or by day 21 after childbirth. If started at any other time, additional contraceptive precautions are required for 7 days with advice to take a follow-up pregnancy test if appropriate. (**Section 14**)

See **Table 5**, **Table 6** and **Table 8** for starting POP and **Table 7** for switching to POP from another contraceptive method).

Provision of POP. A 12-month supply of any POP can be provided to medically eligible individuals who are initiating or continuing POP, with information to seek advice if there are any changes to their medical history or medications. (**Section 17**)

Two specific brands of DSG POP are now available as Pharmacy Medicines. They can be bought by the user from a pharmacy under the supervision of a pharmacist without a prescription. **(Section 20**)

Follow-up. After initiation of POP, users should generally be reviewed annually. This can usually be achieved without an in-person consultation. (**Section 19** and **Section 21**)

Stopping POP. Users should be advised that after stopping POP no significant delay in return to fertility is expected. (**Section 23**) **Table 9** and **Table 10** provide guidance to support switching from POP to other contraceptive methods. It is established FSRH guidance that contraception is not required after age 55 years.

5 What are progestogen-only pills (POPs) and how do they work?

Progestogens are synthetic steroids designed to have some of the properties of progesterone. In the UK, use of LNG 30 µg, NET 350 µg and DSG 75 µg POPs is well established. A DRSP 4 mg POP will soon be available. DRSP is a potent progestogen with a similar pharmacological profile to progesterone. A spironolactone derivative, it has anti-mineralocorticoid and mild anti-androgenic activity[1] and no estrogenic or glucocorticoid activity. By opposing the effect of androgen and aldosterone, DRSP could theoretically offer benefit for acne and blood pressure, for example, although there is not yet published evidence to inform whether this is in fact the case.

The contraceptive effect of DSG and DRSP POPs relies primarily on an anti-gonadotrophic effect that inhibits ovulation.[1,2] There are additional contraceptive effects on the viscosity of cervical mucus, on the endometrium, and activity of cilia in the fallopian tube.[1]

LNG and NET POPs (often referred to as 'traditional' POPs) also affect gonadotrophins and ovarian activity, but ovulation is not reliably inhibited.[3–5] The contraceptive effectiveness of traditional POPs therefore relies on their effect on cervical mucus, endometrium (which becomes thinned)[6] and tubal motility.

The changes in cervical mucus – reduced volume, increased viscosity and cellularity – and altered molecular structure[7–9] are unfavourable to sperm penetration into the upper reproductive tract. This 'hostile' mucus is achieved rapidly after starting a POP[9,10] even if cervical mucus is initially very favourable at the time that the POP is taken.[9] It is accepted practice that 2 days of pill-taking is sufficient to achieve this element of contraceptive protection. However, the contraceptive effect provided by changes to cervical mucus is also short-lived, unless maintained by regular pill-taking.[7] Duration of full protection conferred via cervical mucus is likely to vary according to progestogen. It has been suggested that full protection may last for less than 24 hours after a pill is taken[7,11] but a recent study found that unfavourable mucus scores were maintained 24 hours after a dose of 350 µg oral norethisterone.[9]

6 How is the POP taken?

LNG, NET and DSG POPs are taken continuously at 24-hour intervals without an HFI. The new DRSP POP is taken in a regimen of 24 daily active pills followed by four hormone-free placebo pills. The aim of the four hormone-free days is to try to establish a more predictable bleeding pattern (although the evidence suggests that this is not necessarily the case) whilst maintaining contraceptive effectiveness. In the absence of evidence for, or experience of, tailored or continuous pill-taking regimens for the DRSP POP, the GDG recommends that the manufacturer-recommended 24/4 regimen is used.

7 Incorrect POP use

Key information

✓	**Contraceptive effectiveness of the POP relies on correct use.**
✓	**A traditional POP is considered missed if it is taken more than 3 hours late, a DSG POP if it is taken more than 12 hours late, and a DRSP POP if more than 24 hours late.**

Contraceptive effectiveness of POP relies on correct use and may be reduced if a pill is missed. The more pills missed, the more likely it is that contraceptive effectiveness will be reduced. If an individual uses POP incorrectly, they should be advised that contraceptive effectiveness depends on reliable use

and be offered alternative effective contraceptive methods, including LARC (requirement for EC should of course be assessed). Users of any POP should ideally take their pill at about the same time each day. Suppression of ovulation is maintained in DSG POP users who take a pill up to 12 hours late[12] and in DRSP users who take a pill up to 24 hours late.[13] In contrast, traditional POPs do not reliably suppress ovulation (ovulation may occur in about 4 out of 10 cycles).[14] So if a traditional POP is taken more than 3 hours late (making the interval between pills more than 27 hours), the effect on cervical mucus (and thus contraceptive effectiveness) could be lost.

During correct use of a traditional POP or DSG POP, pill use is continuous without an HFI. Changes in cervical mucus prevent sperm penetration into the upper genital tract. Sperm in the **lower** genital tract do not survive for more than a few hours. It is considered, therefore, that sex that occurred **before** a missed traditional or DSG POP pill does not present a risk of pregnancy, and EC would not be required. With the DRSP POP, the contraceptive cervical mucus effect could be lost during the HFI. EC could therefore be required if pills are missed when restarting after an HFI and there has been unprotected sexual intercourse (UPSI) since the beginning of the HFI. Table 1 outlines advice for users when a POP is late or missed.

Table 1: Recommendations following incorrect progestogen-only pill use

	Traditional POP	DSG POP	DRSP POP (see also Appendix 2 and Appendix 3)
When is a pill missed?	A pill is missed if taken >3 hours late (>27 hours after last pill taken)	A pill is missed if taken >12 hours late (>36 hours after last pill taken)	A pill is missed if taken >24 hours late (>48 hours after last pill was taken or >24 hours after a new packet should have been started after an HFI)
Action if pill(s) missed	• Take the most recent missed pill as soon as possible • Take the next pill at the usual time (this may mean taking two pills in 1 day) • Use additional contraceptive precautions (eg, condoms) for 48 hours after correct pill-taking has restarted • Consider EC		• Take the most recent missed pill as soon as possible • Take the next pill at the usual time (this may mean taking two pills in 1 day) • Use additional contraceptive precautions (eg, condoms) for 7 days after correct pill-taking has restarted • Consider EC • **OMIT THE HFI (PLACEBO PILLS) IF ANY OF THE LAST 7 ACTIVE PILLS ARE MISSED**
Is EC required?	EC should be considered if there was UPSI from the time that the first pill was missed until correct pill-taking had resumed for 48 hours		EC should be considered if: • Any active pill(s) were missed and there was UPSI from the time that the first pill was missed until correct pill-taking had resumed for 7 days • Pill(s) were missed on days 1–7 of the packet and there was UPSI during the HFI or week 1 See (Appendix 2 and Appendix 3 for EC if there has been incorrect use of DRSP POP
Follow-up	Consider pregnancy test 21 days after last UPSI		

DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; HFI, hormone-free interval; POP, progestogen-only pill; UPSI, unprotected sexual intercourse.

Evidence relevant to risk of ovulation when pills are missed

In a pharmacodynamic study[12] 103 subjects taking a DSG POP for 56 days were randomised to take three tablets 12 hours late: group A on days 39, 42 and 49 or group B on days 11, 14 and 21. Only one subject (in group B) was considered to have ovulated (on the basis of a sustained elevated progesterone level). Only 87 of the subjects were fully compliant with pill-taking instructions and it is not stated whether this individual was one of them.

Data for return of ovulation were available for 99 subjects: the minimum time from last tablet intake to first post-treatment ovulation was 7 days, and the average time was 17.2±7.4 days (range 7–30 days).[12]

Evidence level 2–

A randomised controlled trial (RCT)[13] aimed to establish if inhibition of ovulation was maintained after four scheduled 24-hour delays in DRSP pill intake (in addition to the planned 4-day pill break). A total of 130 individuals with proven ovulatory cycles were randomised into two groups. Group A (n=65 with 58 subjects completing) had correct pill-taking in cycle 1 and in cycle 2 delayed tablets on days 3, 6, 11 and 22, instead taking two tablets on days 4, 7, 12 and 23. Group B (n=65 with 63 subjects completing) delayed pills as above in cycle 1 with correct use in cycle 2. One subject in group A ovulated in cycle 2. None of the subjects in group B ovulated.

In a randomised study[1] comparing the effect on ovarian activity of DSG POP and DRSP POP, 64 participants aged 18–35 years were randomised equally to take either DSG or DRSP POP for two cycles (there was no control group). Ovulation was effectively suppressed in both groups during treatment. Ultrasound scan (USS) was performed every 3 days after stopping treatment until follicular rupture, or day 27. In both treatment groups ovulation occurred at the earliest on day 9 of the post-treatment cycle: the mean ovulation day was day 13.6 (±3.8) in the DRSP group (allowing for placebo tablets, this was day 17.6 after the last active tablet) and day 18.2 (±5.5) in the DSG group.

A randomised, double-blind study[15] (investigating a new progestogen) included 13 participants aged 19–40 years with regular ovulatory cycles as a comparator group randomised to take DSG POP for 21 days. The earliest observed ovulation in the DSG POP group was on day 8 after stopping treatment (mean±SD day 20.1±12.6).

Evidence level 1–

8 How effective are POPs?

Key information

D	**The risk of pregnancy during the first year of typical POP use has been estimated at about 9% If used perfectly, POPs may be more than 99% effective.**
D	**The available evidence is too limited to inform whether there is a significant difference in contraceptive effectiveness between traditional POPs and DSG/DRSP POPs.**

Evidence from studies that consider contraceptive effectiveness of POPs is limited and Pearl Indices (PIs) and rates of ovulation vary widely between studies. If taken correctly, POPs are likely to be >99% effective for contraception. POP use is, however, very user-dependent, and it has been estimated that with typical use the risk of pregnancy during the first year of POP use may be around 9%.[16]

It has been postulated that DSG and DRSP POPs could be more effective than traditional POPs (especially with typical use) because ovulation is suppressed more consistently and there is a longer missed pill window. But because studies that consider contraceptive effectiveness of different POPs differ in design (including whether pregnancies conceived shortly after stopping the POP are considered method failure), findings are difficult to compare. As a result, there is insufficient evidence to inform whether there is, in fact, a significant difference in contraceptive effectiveness between different POPs.

The evidence

Studies with pregnancy as an endpoint

Traditional POPs

Studies that consider contraceptive effectiveness of traditional POPs are mostly of poor quality, with small sample numbers and high loss to follow-up.

A 1990 cohort study[17] included 62 non-breastfeeding subjects using ethynodiol diacetate, 189 using NET and 27 using LNG. 80 subjects switched from one POP to another during the study and there were three pregnancies over the 2-year study period (giving a PI of 0.2 per 100 person-years). All three pregnancies were in individuals who were long-term users of the POP (more than 3.5 years) and were aged 24, 29 and 36 years. It is not clear which POPs were being used when the users became pregnant.

Evidence level 2–

A double-blind phase III RCT[4] reports pregnancy data for the study arm in which 23 subjects used 0.03 mg LNG (traditional POP). Subjects were studied for one pre-treatment cycle, six treatment cycles (24 weeks) and one post-treatment cycle. There was high loss to follow-up with 15 LNG users completing the study. One individual using LNG became pregnant during the study but it should be noted that not all subjects in the study were at risk of pregnancy (some were not sexually active and others were also using condoms).

Evidence level 1–

An early comparative clinical trial[18] assigned 175 subjects aged 18–40 years to either NET 0.3 mg (n=41), norgestrel 0.05 mg (n=45), chlormadinone 0.5 mg (n=46) or megestrol acetate 0.25 mg (n=43) and followed them up for 1 year. One and three pregnancies occurred during treatment with NET and norgestrel, respectively, corresponding to pregnancy rates of 4 and 9 per 100 person-years of use. Only one of these pregnancies (in the norgestrel group) was known to have followed omission of tablets.

A small early cohort study[19] included 70 subjects using NET 0.35 mg over 2 years with the average period of use being 16.7 months. Of the six pregnancies that occurred, only two could be attributed to method failure. It was unclear how long each individual used the pills for and there was a high loss to follow-up.

Evidence level 2–

DSG POP/LNG POP

A large, double-blinded, randomised, multicentre phase III study[20] randomised 1320 individuals aged 18–45 years to take either DSG 75 µg (979 subjects) or LNG 30 µg (327 subjects) for 13 treatment cycles. Roughly one-third of the subjects in both groups were breastfeeding at the time of study start. Overall, seven pregnancies were reported during the study (three in the DSG group and four in the LNG group). After taking into account documented gross non-compliance, one in-treatment pregnancy during use of DSG and three during LNG use remained. After excluding breastfeeding subjects, the

Evidence level 1–

reported PIs were 0.17 (95% confidence interval (95% CI) 0.004–0.928) for DSG and 1.41 (95% CI 0.290–4.116) for LNG. The difference in the PI between DSG and LNG was not statistically significant.

DRSP POP/DSG POP

Palacios *et al*[21] pooled contraceptive effectiveness data from two prospective, multicentre phase III studies.[22,23] Study 1[23] included 713 subjects aged 18–46 years who used the DRSP POP for up to 13 cycles (a total of 7638 study cycles). Three pregnancies were reported (all in individuals aged ≤35 years). The PI was 0.51 (95% CI 0.11–1.49). Study 2[22] presented data from 6691 cycles in 858 subjects aged 18–45 years randomised to nine cycles of DRSP POP use. Five pregnancies were recorded (all in individuals aged ≤35 years). The PI for DRSP POP was 0.97 (95% CI 0.32–2.27). This study had a comparator arm of subjects randomised to use of the DSG POP. The PI for the DSG POP, based on 2487 exposure cycles in 332 subjects, was 0.52 (95% CI 0.01–2.91). Evidence level 2+

The pooled data from studies 1 and 2 gave an overall PI for the DRSP POP of 0.73 (95% CI 0.31–1.43). The method failure PI (based on 10 742 perfect medication cycles) was 0.97 (95% CI 0.42–1.91).[21]

In a prospective, open-label, single-arm, multicentre, phase III trial[24] non-breastfeeding subjects, most aged under 35 years and one-third with body mass index (BMI) ≥30 kg/m^2, used the DRSP POP for up to 13 treatment cycles. 993 subjects were included in the full analysis (a total of 6566 exposure cycles), of which 352 (35%) completed the study. There were 12 confirmed pregnancies, all in individuals aged ≤35 years. The reported PI was 2.9 (95% CI 1.5–5.1). It is unclear whether the subjects who became pregnant were taking their POP correctly. PIs were similar when analysed by BMI subgroup.

Studies with ovulation as an endpoint

It is noted that studies are not consistent in the criteria they use to identify ovulation, which makes comparison between outcomes for different POPs problematic.

Traditional POPs

In a double-blind RCT[4] comparing LNG POP and mifepristone, 23 subjects taking LNG POP had ovarian function assessed at baseline, 8, 16 and 24 weeks. Ovulation occurred in 30% of study participants; however, blood samples and USS were done at 8-weekly intervals and could have missed ovulation. Evidence level 1–

Literature reviews[7,14,25] identify four small studies (n=21–43) that reported wide ranges of incidence of ovulation (14%–84%) during use of a NET 300 µg POP.[26–29] Evidence level 2–

Traditional and DSG POPs

An RCT[3] randomised 71 individuals with regular cycles and confirmed ovulation at baseline to use of 75 µg DSG POP or 30 µg LNG POP for 13 28-day treatment periods. Ovarian activity was assessed by USS and serum progesterone level in treatment periods 7 and 12. Thirty subjects in the DSG group were assessed in treatment period 7 and 29 in treatment period 12; one ovulation occurred in these 59 DSG treatment periods (1.7%). 29 subjects in the LNG group were assessed in treatment period 7 and 28 in treatment period 12; 16 ovulations occurred in these 57 treatment periods (28%). Evidence level 1–

DSG POP

In an RCT[2] of 44 individuals aged 22–33 years that compared ovarian activity between subjects taking 30, 50 or 75 µg DSG for 6 months, no subjects in the 75 µg DSG group had progesterone levels indicating ovulation at any point during the trial period (USS and bloods were performed twice-weekly). This was also the case for subjects in the 50 µg group, but progesterone levels indicated ovulation in 4 of 14 subjects in the 30 µg group.

Evidence level 1–

A 2008 literature review relating to the DSG POP[14] combined the findings of the RCT mentioned earlier[3] with those from the Korver *et al* 2005 RCT[12] (see **Section 7 on missed pills**) and two other small studies[15,30] which identified no ovulations amongst a combined total of 50 subjects taking 75 µg DSG for between one and seven cycles. The review reports an overall ovulation rate of 1.25% (95% CI 0.03–6.8) of all subjects (not cycles).

As part of an RCT designed to investigate the impact of quick starting POP after ulipristal acetate emergency contraception (UPA-EC)[31], 29 subjects in the placebo arm (who had not taken UPA-EC) took 20 days of DSG POP, starting when they were approaching ovulation (with a lead follicle 14–16 mm in size). During transvaginal USS follow-up, ovulation occurred in 11 subjects (38%), all within 5 days of starting treatment. DSG started at this time inhibited ovulation in the remaining 18 subjects (62%).

DRSP and DSG POPs

An RCT[1] randomised 64 individuals aged 18–35 years with BMI between 18 and 30 kg/m^2 and ovulatory cycles to take either DRSP POP or DSG POP for two 28-day cycles; 29 subjects in each group completed the study. Despite the 4-day HFI, the DRSP POP inhibited ovulation as effectively as the DSG POP; no ovulations were observed in either group, and ovarian suppression appeared to be greater in the DRSP POP group. Ovulation did not occur before day 9 of the post-treatment cycle in either group. Mean ovulation day was 13.6 (±3.8) in the DRSP group which, allowing for placebo pills, was day 17.6 after the last active DRSP POP was taken, and day 18.2 (±5.5) in the DSG group. Cervical mucus permeability was suppressed throughout, and endometrium thinned compared to the pre-treatment cycle in both groups.

Evidence level 1–

9 What can affect effectiveness of the POP?

POP use is highly user-dependent: contraceptive effectiveness is significantly affected by non-adherence to pill-taking. Effectiveness may also be affected by vomiting or severe diarrhoea, and by use of interacting drugs.

9.1 Vomiting

Key information

✓ **Contraceptive effectiveness could be affected if a POP user vomits within a few hours of pill-taking.**

If vomiting occurs within a few hours of taking a POP, it may not be absorbed and cannot be relied upon to maintain contraception. Note that the time considered to be required for absorption varies between different POPs. See **Table 2** for manufacturer recommendations.

In this situation another pill of the same type should be taken as soon as possible. If this replacement tablet is not taken within 3 hours (traditional POP), 12 hours (DSG POP) or 24 hours (DRSP POP) of the time at which the original pill was due, missed pill rules should be followed (see **Table 1** for missed pill rules).

Table 2: Vomiting after the progestogen-only pill is taken

Type of POP	Manufacturer-recommended time after pill-taking until unaffected by vomiting
DRSP POP	3–4 hours
LNG traditional POP	2 hours
NET traditional POP	Not stated. GDG suggest 2 hours as above
DSG POP	3–4 hours

DRSP, drospirenone; DSG, desogestrel; GDG, guideline development group; LNG, levonorgestrel; NET, norethisterone; POP, progestogen-only pill.

9.2 Diarrhoea

POP users who have severe watery diarrhoea soon after taking a POP may not absorb the progestogen and should be advised to take another pill of the same type as soon as possible. There is no evidence as to how long after pill consumption severe diarrhoea would affect absorption. The time at which the ***replacement pill*** is taken determines whether additional contraceptive precautions are required as per missed pill rules (**Table 1**).

9.3 Weight/BMI

Key information

D **The available evidence suggests that effectiveness of the POP is not affected by body weight or BMI.**

Clinical recommendations

✓ **Double-dose POP for contraception is not required for individuals who are overweight or individuals with obesity.**

There is very limited evidence to inform contraceptive effectiveness of POP in individuals who are overweight or have obesity. The available data have not demonstrated an association between higher weight and/or BMI and reduced POP effectiveness.

The evidence

Traditional POP

One UK observational cohort study found no association between body weight and contraceptive failure in traditional POP users.[32] This study did, however, have significant limitations, including no report of the number of subjects with obesity or those who were overweight, lack of statistical power, and measurement of weight only at recruitment (from 1968 to 1974).

Evidence level 2–

Data from an exploratory in vitro study of 16 subjects[10] found that a single tablet of LNG 30 µg (n=8) or NET 350 µg (n=8) prevented sperm migration in samples of cervical mucus collected 12 hours after ingestion, including in the three subjects who had a BMI >35 kg/m^2. As this study only examined the impact of a single POP dose, further evidence

would be required before conclusions could be drawn about the impact of weight or BMI on the cervical mucus effect of POPs.

DSG POP

No studies have specifically examined the comparative effectiveness of the DSG POP in users of differing weights or BMIs. A 12-month study[3] of 71 subjects that compared inhibition of ovulation with use of the DSG POP and the LNG POP reported that ovulation was suppressed in all but one of 59 observed DSG cycles (weight range of subjects 46–78 kg). 16 of 57 observed LNG cycles were ovulatory. Subjects in this group weighed between 50 and 91 kg, but no analysis was carried out by weight.

Evidence level 1–

DRSP POP

In a prospective, open-label, single-arm, multicentre, phase III trial assessing safety and effectiveness of DRSP POP use for up to 13 cycles,[24] 264 subjects (26.2%) had BMI 25–30 kg/m^2 and 354 (35.2%) had BMI >30 kg/m^2 (84 had BMI >40 kg/m^2). The PI (confirmed pregnancies only) was 3.0 (95% CI 1.3–5.8) for subjects with BMI <30 kg/m^2 and 2.9 (95% CI 0.8–7.3) for BMI >30 kg/m^2.

Evidence level 2+

A study[13] of 34 subjects with BMI 25–30 kg/m^2 and 6 with BMI >30 kg/m^2 investigated suppression of ovulation if DRSP tablets were taken late. Ovulation inhibition with DRSP POP was adequate in overweight subjects, even after scheduled intake delays. The only ovulation in this study occurred in an individual with normal weight and BMI.

Evidence level 2–

Contraceptive effectiveness of DRSP POP in overweight and obese users was demonstrated by a pooled analysis of the European studies[22,23,33] of the 4 mg DRSP clinical development programme. In subjects with BMI 25–30 kg/m^2 (n=301) four pregnancies were reported (PI 1.89), whereas in subjects with BMI >30 kg/m^2 (n=71) no pregnancies were recorded (PI 0.0).

Evidence level 1+

The Summaries of Product Characteristics (SPCs) for POPs[34–37] do not advise dose adjustments based on weight or BMI.

9.4 Bariatric surgery

Key information

D **There is insufficient evidence to inform whether contraceptive effectiveness of POPs is affected by bariatric surgery. Users may therefore wish to consider effective non-oral contraception after bariatric surgery.**

There are theoretical concerns that both malabsorptive and restrictive bariatric procedures could decrease absorption of oral contraceptives.[38,39] Evidence from two recent pharmacokinetic studies[40,41] suggests that absorption of combined oral contraceptives (COCs) is not significantly affected by Roux-en-Y gastric bypass (RYGB). There is inadequate evidence to inform the effect of any type of bariatric surgery on contraceptive effectiveness of POPs.[42–44]

The evidence

A prospective study[44] of 40 patients (aged 16–44 years) who underwent biliopancreatic diversion (BPD) surgery reported two pregnancies in the 2 years following surgery amongst nine users of oral contraceptives. Both oral contraceptive users suffered long-lasting post-operative diarrhoea.

A retrospective study[43] of 215 morbidly obese individuals (aged 18–45 years) observed no pregnancies amongst an unstated number of oral contraceptive users during the 2 years after laparoscopic adjustable gastric banding bariatric surgery.

Two recent studies compared pharmacokinetics of a combined ethinylestradiol (EE) 30 µg/LNG COC in individuals who had undergone RYGB and matched controls who had not had bariatric surgery. De Brito *et al*[40] measured maximum plasma concentration (C_{max}), time to peak plasma level (T_{max}) and area under the curve (AUC_{0-8} and $AUC_{0-\infty}$) in 20 RYGB cases and 20 unoperated controls for 8 hours after a single dose of COC. There was no significant difference in EE pharmacokinetics. The operated group showed higher mean LNG AUC_{0-8} and $AUC_{0-\infty}$ but this was not considered clinically significant. Ginstman *et al*[41] compared 15 individuals aged 18–40 years who had undergone RYGB at least 1 year previously and reached a BMI <30 kg/m^2 with 15 BMI-matched unoperated individuals. After administration of a single dose of COC, serum LNG concentrations were determined over a 24-hour period. There were no significant differences in AUC_{0-24h}, total AUC, peak serum concentration (C_{max}), time to peak serum concentrations (T_{max}), apparent oral clearances of LNG (CL_{oral}) or terminal half-lives ($t_{½}$) between the groups.

These studies suggest that RYGB may not significantly affect EE and LNG absorption.

Victor *et al*[42] investigated the pharmacokinetics of NET 3 mg and LNG 0.25 mg in seven individuals aged 20–44 years with morbid obesity, after jejunoileal bypass. There was also a control group of non-obese subjects. Plasma concentrations of NET and LNG in the operated subjects were compared to those of the control group before and at 1, 2, 4, 6, 8 and 24 hours after ingestion of the tablet. The mean plasma levels of NET were lower in the operated patients at all times, except for the 24-hour samples, and LNG plasma levels were significantly lower in the operated patients at 2, 4 and 6 hours, but this difference could be attributable to body weight.

Evidence level 2–

9.5 Drug interactions

Key information

✓ **Contraceptive effectiveness of POPs could be reduced by concomitant use of enzyme-inducing drugs**

Drugs that induce hepatic enzymes increase the metabolism of progestogens and could reduce the contraceptive effectiveness of the POP. Contraceptive effectiveness of POPs could potentially be reduced by UPA used regularly for indications other than EC. See **Section 15**.

10 Who can and cannot use POP?

All POP

Key information

D	**The FSRH supports the use of all POPs by medically eligible individuals between menarche and age 55 years.**
D	**Breast cancer, arterial thromboembolism that occurred during use of a POP, decompensated cirrhosis and hepatocellular tumours are UKMEC3 or UKMEC4 conditions for use of all POPs.**

Additional specific considerations for DRSP POP

Clinical recommendations

✓	**The manufacturer advises that the DRSP POP should not be used by individuals with severe renal insufficiency or acute renal failure.**
✓	**The GDG suggests that DRSP POP should also generally be avoided by:** • **Individuals with known hyperkalaemia or untreated hypoaldosteronism (eg, Addison's disease).** • **Individuals currently using potassium-sparing diuretics, aldosterone antagonists or potassium supplements.**
✓	**The GDG suggests that DRSP POP should be used with caution by individuals with mild/moderate renal impairment or treated hypoaldosteronism (eg, treated Addison's disease).**
✓	**The GDG suggests that for individuals with significant risk factors for chronic kidney disease, measurement of U&E and blood pressure should be considered prior to prescription of the DRSP POP, particularly if aged over 50 years.**

UK Medical Eligibility Criteria for Contraceptive Use 2016 (UKMEC 2016)[45] indicates that there are few medical contraindications to use of POPs. Conditions that are UKMEC3 (risks generally outweigh benefits) or UKMEC4 (use represents unacceptable risk) are shown in **Table 3**.

Table 3: Medical conditions that are UKMEC3 or UKMEC4 for use of the progestogen-only pill[45]

Condition	UKMEC category for POP use	Comments
Current and history of ischaemic heart disease	UKMEC3 for continuation (UKMEC2 for initiation)	Duration of use of POP in relation to the onset of CVD should be carefully considered when deciding whether continuation of the method is appropriate (this is a precaution in case the POP somehow contributed to development of CVD)
History of stroke	UKMEC3 for continuation (UKMEC2 for initiation)	
Current breast cancer	UKMEC4	For individuals with a history of breast cancer, any decision to initiate hormonal contraception may be best made in consultation with their oncology team
Past breast cancer	UKMEC3	
Severe (decompensated) cirrhosis (associated with, eg, ascites, jaundice, encephalopathy or gastrointestinal haemorrhage)	UKMEC3	
Hepatocellular adenoma or carcinoma	UKMEC3	

Initiation: Starting a method by an individual with a specific medical condition.
Continuation: Continuing with the method already being used by anindividual who develops a new medical condition.
CVD, cardiovascular disease; POP, progestogen-only pill; UKMEC, UK Medical Eligibility Criteria for Contraceptive Use.

UKMEC	Definition of UKMEC category
Category 1	A condition for which there is no restriction for the use of the method.
Category 2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks.
Category 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.
Category 4	A condition which represents an unacceptable health risk if the method is used.

HCPs may consider discussion with or referral to a specialist sexual and reproductive health (SRH) service for an individual with a contraindication to POP use, when other methods are unsuitable.

At the time of publication of UKMEC 2016[45], the DRSP POP was not considered. On the basis of evidence now available for the DRSP POP, the GDG recommends that UKMEC 2016 recommendations relate to all POPs, but that there are ***additional*** specific considerations for use of the DRSP POP.

10.2 Specific considerations for DRSP POP

DRSP is a spironolactone derivative. As an aldosterone antagonist it opposes aldosterone activity in the distal nephron, increasing potassium reuptake and increasing sodium and water excretion. Hyperkalaemia has been observed in a few individuals during use of the DRSP POP.[24]

The SPC for the DRSP POP[36] states that use of the DRSP POP is contraindicated by severe renal insufficiency and by acute renal failure. In addition, the GDG suggests that individuals with known hyperkalaemia or untreated hypoaldosteronism (eg, Addison's disease – primary adrenal insufficiency) and those currently using potassium-sparing diuretics or potassium supplements should generally avoid use of the DRSP POP.

If use of the DRSP POP is considered by an individual with mild/moderate renal insufficiency or with treated hypoaldosteronism (eg, treated Addison's disease), the GDG suggests that monitoring of U&E and blood pressure may be required (in consultation with the individual's renal physician/endocrinologist where appropriate).

The GDG suggests that measurement of U&E and blood pressure should also be considered prior to prescription of DRSP POP for individuals with significant risk factors for chronic kidney disease (eg, hypertension, cardiovascular disease (CVD), diabetes), particularly if aged over 50 years.

10.3 Age

Although few studies have formally assessed safety of use of POP by individuals aged under 18 years, it is established practice and existing FSRH guidance that POP can be used from menarche until age 55 years.[45]

With regard to the DRSP POP, a study[46] of 111 adolescents aged 12–17 years using DRSP POP for up to 13 continuous cycles suggests no safety concerns and good toleration of DRSP. Studies of the DRSP POP do not include subjects aged over 46 years (and few were aged 35–46 years). As background risk of chronic kidney disease increases with age, the GDG suggests that measurement of U&E and blood pressure should be considered for individuals aged 50 years or over with additional risk factors for chronic kidney disease (eg, hypertension, CVD, diabetes) prior to prescription of DRSP POP. Self-taken, self-reported blood pressure is considered adequate.

See **FSRH Clinical Guideline Contraception for Women Aged Over 40 Years**[47] for information relating to use of POP during the perimenopause and with menopausal hormone therapy (hormone replacement therapy). Note that the guideline does not at present consider the DRSP POP**.**

10.4 Individuals with obesity

UKMEC indicates that obesity alone does not restrict use of POP (UKMEC1).[45] Even when obesity is in the context of other risk factors for CVD (eg, smoking, diabetes and hypertension), use of POP is UKMEC2 (benefits generally outweigh risks). The available evidence does not suggest a likely association between POP use and increased risk of CVD, but no studies have directly assessed whether POP users with raised BMI are at increased risk of CVD or venous thromboembolism (VTE) compared to non-users of hormonal contraception with raised BMI or to normal-weight POP users. **The available evidence suggests that POPs are a safe contraceptive option for individuals who are overweight and those with obesity.** See **FSRH Clinical Guideline Overweight, Obesity & Contraception**.[48]

10.5 Individuals with thrombophilia or history of venous thromboembolism

There is very limited evidence relating specifically to POP use by individuals with thrombophilia or current or previous VTE. In the general population, however, the evidence suggests no association between POP use and increased risk of VTE events. UKMEC indicates that the benefits of use of POP by individuals with thrombophilia or a history of VTE generally outweigh risks (UKMEC2).

The evidence

A 2016 prospective cohort study[49] assessed the risk of ***recurrent*** VTE associated with use of progestogen-only contraception (POC). Amongst 419 subjects who had had a first VTE event, 163 (38.9%) were exposed to POC (mostly DSG or LNG POP (43%) or levonorgestrel-releasing intrauterine system (LNG-IUS) (49%) – none used progestogen-only injectables) at some time point during follow-up. Median duration of exposure to POC was 2.5 years. In this cohort, POC did not appear to be associated with increased risk of recurrent VTE.

Evidence level 2–

10.6 Individuals with cardiovascular disease

There is no published evidence relating directly to health outcomes associated with use of POP by individuals with established CVD or significant risk factors for CVD. UKMEC[45] indicates that POP can generally be used by individuals with cardiovascular risk factors, but that risks could outweigh benefit for use by individuals who have previously had incident ischaemic heart disease or thrombotic stroke during use of POP. This reflects concern (but not evidence) that POP could have contributed to the cardiovascular event. The few studies that have considered the effect of POCs on cardiovascular risk in the general population generally suggest that there is little or no increased risk of VTE[50], no statistically significant increased risk of MI[51] and no statistically significant increased risk of stroke with POP, implants or LNG-IUS.

Studies looking at cardiovascular risk factors (eg, lipid and carbohydrate metabolism) of POC have been reassuring[52–59], with no clinically meaningful changes observed associated with POP use.

DRSP POP

Studies of the DRSP POP do not include participants with CVD. Studies evaluating the effect of DRSP POP use on haemostatic parameters are detailed in **Section 11.2**.

10.7 Individuals with breast cancer or a history of breast cancer

No studies have been conducted to assess health outcomes associated with POP use by individuals with a diagnosis of breast cancer. UKMEC[45] indicates that POP use is contraindicated during current breast cancer and that risks of POP use generally outweigh benefits for individuals with previous breast cancer.

10.8 Individuals with liver disease

No studies have been conducted to assess health outcomes associated with POP use by individuals with liver disease. UKMEC[45] indicates that risks of POP use generally outweigh benefits for individuals with severe decompensated cirrhosis or hepatocellular adenoma/adenocarcinoma.

10.9 Individuals with ovarian cysts

Current or previous ovarian cysts are not a contraindication to POP use (UKMEC1).[45] See **Section 11.7**.

10.10 Individuals with previous ectopic pregnancy

Previous history of ectopic pregnancy does not contraindicate use of POP (UKMEC1).[45] See **Section 11.8**.

11 What health risks are and are not associated with use of POP?

11.1 Risk of venous thromboembolism

Key information

C **The published evidence is very limited but suggests no increase in risk of venous thromboembolic events associated with use of POPs.**

Evidence relating to risk of VTE associated with use of POPs is limited by the small numbers of these events in individuals of reproductive age and the small numbers of POP users in the available studies. The limited available evidence does not indicate an association between POP use and risk of VTE.

The evidence

A 2018 systematic review and meta-analysis[60] pooled data relating to risk of VTE associated with use of a variety of POPs (not including the DRSP POP) from five case-control and three cohort studies. These studies included data from 500 POP users, with a total of 176 VTE events. Only one study[61] included users of the DSG POP. Compared with non-use of hormonal contraception, POP use was not associated with significantly increased risk of VTE: the adjusted pooled risk ratio for use of POP was 1.06 (95% CI 0.7–1.62). Evidence level 2+

A Swedish nationwide case-control study[62] investigating associations between combined hormonal contraception (CHC) and POC and risks of VTE contributed significantly to the pooled data in the Glisic *et al*[60] meta-analysis. The study, which included (amongst 948 cases and 902 controls) 16 case and 23 control subjects using DSG POP, 4 cases and 3 controls using NET POP and 4 cases and 8 controls using LNG POP found no increased risk of VTE associated with POP use.

A randomised, controlled, double-blind study[63] investigated in 78 healthy subjects the effects on haemostatic parameters of use of two POPs containing 75 µg DSG or 30 µg LNG. 24 subjects in the DSG group completed the treatment. Factor VII activity, plasminogen activity, prothrombin fragments 1 and 2, protein S and tissue plasminogen activator were measured. Both POPs (particularly DSG POP) had potentially favourable effects on haemostasis. Evidence level 1–

A retrospective follow-up cohort study[64] identified all Danish women aged 15–49 years between January 1995 and December 2005 from the central person registry and used information from Danish databases to identify recorded VTE events and prescribing of hormonal contraception in the cohort. Compared with non-users of oral contraceptives there was no significant increase in risk of VTE associated with current use of POP; the rate ratio for VTE in users of LNG or NET POPs was 0.59 (95% CI 0.33–1.03) and for DSG POP was 1.12 (95% CI 0.36–3.49). Evidence level 2+

A 2016 prospective cohort study[49] assessed the risk of ***recurrent*** VTE associated with use of POC. Amongst 419 subjects who had had a first VTE event, 163 (38.9%) were exposed to POC (mostly DSG or LNG POP (43%) or LNG-IUS (49%) – none used progestogen-only injectables) at some time point during follow-up. Median duration of exposure to POC was 2.5 years. In this cohort, POC did not appear to be associated with increased risk of ***recurrent*** VTE. Evidence level 2–

The evidence: drospirenone

A prospective, open-label, single-arm, multicentre phase III trial[24] evaluated contraceptive effectiveness and safety of DRSP POP use for up to 13 cycles by subjects aged 15–35 years, one-third of whom had a BMI ≥30 kg/m^2. 993 subjects and 6566 exposure cycles were included in the full analysis. No cases of VTE were reported.

Evidence level 2+

A prospective, multicentre, non-comparative phase III study[23] of 713 healthy subjects aged 18–45 years who used DRSP POP for at least 13 cycles (7638 study cycles) reported no cases of VTE.

A multicentre, open-label trial[46] assessed safety and tolerability of DRSP POP in sexually active adolescents aged 12–17 years. Of 103 subjects allocated treatment, 89 completed six cycles and 74 completed 13 cycles. There were no reported episodes of VTE related to treatment.

11.2 Risk of arterial thromboembolism

Key information

C **The published evidence is very limited but suggests no increase in risk of thrombotic stroke or MI associated with use of POPs.**

Evidence relating to risk of thrombotic stroke and MI associated with use of POPs is limited by the small numbers of these events in individuals of reproductive age and the small numbers of POP users in the available studies. The limited available evidence does not indicate an association between POP use and risk of thrombotic stroke or MI. One large observational study of DRSP POP reported a mean reduction in blood pressure amongst subjects with blood pressure ≥130/85 mmHg at baseline.

The evidence

POP (unspecified)

Two recent meta-analyses of observational studies evaluated the risk of arterial thromboembolism with POP use. The studies included related to many different POPs, and type of POP was often unspecified. A 2018 meta-analysis by Glisic *et al*[60] (which included the Heinemann *et al* case-control study[65]) found no association between POP use and MI (odds ratio (OR) 0.98, 95% CI 0.66–1.47) or stroke (OR 1.02, 95% CI 0.72–1.44), but these outcomes were based on relatively small numbers of events (n=47 for MI and n=199 for stroke). A 2015 meta-analysis by Xu *et al*[66] likewise found no association between ischaemic stroke and POP use (OR 0.99, 95% CI 0.71–1.37). It is not known how many subjects were included in the analysis, but the studies referenced in the article were small observational studies.

Evidence level 1–

A case-control study[65] that included 1058 cases of MI, thromboembolic cerebrovascular accident or VTE (181 cases were VTE) and 3808 controls found no significant increase in CVD risk associated with POP use.

Evidence level 3

A hospital-based case-control study by the World Health Organization (WHO) 1998[67] included individuals aged 15–44 years that had been admitted to a hospital over a 4-year period with VTE, stroke or MI. Compared with non-use of any hormonal contraception, current POP users were not at significantly increased risk of all CVD (adjusted odds ratio

Evidence level 1–

(aOR) 1.19, 95% CI 0.82–1.74), stroke (27 cases, 60 controls; aOR 1.07, 95% CI 0.62–1.86) or MI (3 cases, 6 controls; aOR 0.98, 95% CI 0.16–5.97). The POPs in this study were norgestrel 0.03 mg, norgestrel 0.075 mg and NET 0.35 mg.

A 2002 case-control study[68] included subjects aged 15–44 years identified from the Danish National Patient Register, who had a first-ever thrombotic stroke or transient ischemic attack over a 5-year period. Of 780 cases and 4245 controls, 4 cases and 28 controls were users of traditional POPs. The study concluded that POP use was not associated with risk of cerebral thromboembolic events but clearly the number of POP users studied was very small.

Evidence level 2+

A 1999 case-control study[69] included 9 cases of MI (2%) and 49 controls (2.8%) that were current POP users. Compared with non-users of oral contraception (386 cases and 1467 controls), the OR for MI with current POP use was 0.80 (95% CI 0.41–1.55) and aOR was 1.23 (95% CI 0.52–2.91).

Evidence level 2–

A double-blind RCT[63] compared the effect on haemostasis of POPs containing 75 µg DSG or 30 µg LNG. 25 subjects completed treatment in the DSG group and 30 in the LNG group. Observed changes were considered minor with an overall potentially favourable effect on haemostasis in both groups – reduced factor VII activity and reduced plasma concentration of the prothrombin fragments 1 and 2.

Evidence level 1–

DRSP POP

A large, multicentre, prospective, double-blind, double-dummy RCT considered safety and tolerability of DRSP POP compared to DSG POP.[70] Of a total of 1190 subjects aged 18–45 years with blood pressure <140/90 at baseline, 858 were randomised to use DRSP POP and 332 to use DSG POP for nine cycles. A wide range of biochemical, haematological, lipid/carbohydrate metabolic and haemostatic parameters were measured. No clinically relevant changes between baseline and endpoint were observed in either group.

Evidence level 1–

A large, prospective, open-label, single-arm phase III trial[24] of subjects aged 15–35 years using the DRSP POP for up to 13 treatment cycles reported data from 993 subjects in 6566 exposure cycles. 92.2% of participants were aged ≤35 years and one-third had a BMI ≥30 kg/m^2**.** 65% discontinued the study. No ***clinically relevant*** changes occurred in laboratory parameters (unspecified) other than serum potassium (see **Section 10.2 Specific considerations for DRSP POP**), blood pressure or heart rate.

The group of subjects with baseline systolic/diastolic blood pressure ≥130/85 mmHg had a mean ***reduction*** from baseline in blood pressure at study exit; there was no mean change in blood pressure amongst those subjects with lower baseline blood pressures.

Evidence level 2+

A prospective, non-comparative phase III study[23] of 713 healthy subjects aged 18–45 years using a DRSP POP for at least 13 cycles found no clinically relevant changes in “laboratory parameters” (no indication given as to what these were), blood pressure or heart rate over the study period.

Evidence level 2+

A comparative study[71] evaluated and compared haemostatic parameters (activated protein C (APC) resistance, antithrombin III, protein C reactivity, factor VII, factor VIII and D-dimer) during use of DRSP or DSG POP. 39 subjects used DRSP and 29 used DSG for nine complete cycles. There was a significantly greater reduction (from a higher baseline) in factor VII in the DSG group than the DRSP group, but a significantly greater reduction (from a higher baseline) in protein C activity in the DSG group than the DRSP group. D-dimers increased in the DSG but reduced in the DRSP group. Other parameters did not change significantly from baseline. The authors concluded that there were no meaningful changes in haemostatic parameters associated with use of DRSP POP.

Evidence level 1–

11.3 Risk of breast cancer

Key information

D **The available evidence suggests a possible association between current or recent use of hormonal contraception (including POP) and a small increase in risk of breast cancer; absolute risk remains very small.**

The limited available evidence shows no consistent evidence of an association between POP use and breast cancer risk. All available evidence is from observational studies with small numbers of POP users and non-significant findings.[7,72–77,143,144]

The evidence

Evidence to inform the effect of POP use on risk of breast cancer is limited and conflicting. The available evidence derives from observational studies, some of which have found no effect of progestogen-only pill use on breast cancer risk while others have reported a small increased risk (although absolute risk of breast cancer remains very small).

Evidence level 2+

The number of incident breast cancers amongst women of reproductive age is very small, which makes effect of hormonal contraception on risk difficult to study. The observational, database-based nature of the studies that we *do* have means that findings could be affected by confounding factors that are not recorded or not considered. For example, a group of individuals that choose to use hormonal contraception may make other choices (eg lifestyle choices) that are different to those made by people that choose not to use hormonal contraception. There may be prescribing bias based on individuals' other risks. Individuals currently or recently using a given contraceptive method could have been using a different method prior to that and this is not always accounted for. Studies do not always distinguish between progestogens.

A case-control study[143] using UK database data for the period 2007-2018 compared current or recent use of hormonal contraception by individuals aged <50 years with incident breast cancer with use by matched controls. 1308 people with incident breast cancer were currently using or had recently used POP. The study reported a small increased relative risk of breast cancer amongst current or recent POP users (they could previously have used other hormonal contraceptives) compared with people who had not used hormonal contraception during the study period (adjusted OR 1.26, 95% CI 1.16-1.37). Adjustment was made for time since last birth, number of recorded births, BMI, and alcohol intake. This effect on risk was similar in size to that with the other progestogen-only methods investigated.

A cohort study[144] using the Swedish nationwide register included women aged 15-34 in 2005 and those that turned 15 thereafter, until the end of 2017 or age 45. During 172,132 person years of progestogen-only pill use (any type), 78 breast cancers occurred. Compared to individuals that did not use hormonal contraception during the study period, current users of a progestogen-only pill (any type) had an adjusted relative risk of incident breast cancer (invasive or in situ) of 1.40 (95% CI 1.26-1.56; p<0.01). For the desogestrel POP, the adjusted relative risk was 1.37 (95% CI 1.22-1.53; p<0.01). Adjustment was made for age, education, place of birth, parity, age at first term pregnancy, but not for factors such as BMI, smoking and alcohol. Relative risk appeared to be highest during the first 10 years of use of progestogen-only contraception (RR 1.74 (95% CI 1.44-2.10) at 1-5 years and RR 1.26 (95% CI 1.06-1.49) at 5-10 years and to be no longer apparent 10 years after stopping.

Evidence level 2+

Other studies have found no association between POP and breast cancer.

A prospective cohort study by Mørch *et al*[72] included 1.8 million women followed for an average of 10.9 years (a total of 19.6 million person-years). There were 11 517 incident cases of breast cancer of which 78 were during or within 6 months of use of NET POP, 16 were during or within 6 months of use of LNG POP, and 42 during or within 6 months of use of DSG POP. Compared with never-use of hormonal contraception, there was no significant increase in breast cancer risk associated with current or recent use of NET POP (relative risk (RR) 1.0, 95% CI 0.80–1.25) or DSG POP (RR 1.18, 95% CI 0.87–1.6). There was, however, a statistically significant increased relative risk in this study of 1.93 (95% CI 1.18–3.16) associated with current or recent use of a LNG POP.

A systematic review by Samson *et al*[73] identified six studies relating to progestogens and breast cancer risk, two of which included POP.75,78 One of the relevant studies (Marchbanks *et al*[78]) included individuals aged 35–64 years in a matched case-control study, and found that 0.5% of 4575 cases and 4682 controls (32 breast cancer cases and 39 controls) had used POC at some time. The study found no increased risk of breast cancer amongst individuals who currently or had previously used a POC compared to those who had never used an oral contraceptive (OR 0.9). The second study (Kumle *et al*[75]) included 103 027 individuals aged 30–49 years in an 8-year prospective cohort study. A total of 1008 primary invasive breast cancers were diagnosed; 3435 subjects had only ever used POP: 29 of these were diagnosed with breast cancer. Compared with never-use of hormonal contraception, ever-use of POP by individuals who had never used other hormonal contraceptives was not significantly associated with risk of breast cancer (adjusted relative risk (aRR) 1.1, 95% CI 0.8–1.7).

A prospective Norwegian national population-based cohort[74] included 74 862 women aged 30–53 years and observed 1245 incident premenopausal breast cancer diagnoses during 58 017 person-years of follow-up. 171 breast cancers were in ever-users of POP. After adjustment for confounding factors, no statistically significant association was observed between estrogen receptor-defined breast cancer and ever, current or former POP use for <5 years. For ≥5 years of POP use, however, a slight increase in risk of all breast cancers (adjusted hazard ratio (aHR) 1.45, 95% CI 1.08–1.95) and estrogen receptor-positive breast cancer (aHR 1.59, 95% CI 1.09–2.32) was observed. It is unclear if participants in this study using POP had previously used another type of hormonal contraception.

A case-control study[77] included 464 subjects aged 25–56 years with breast cancer and 542 age-matched controls. They were interviewed about history of oral contraceptive use, identifying POP use by 9 cases and 10 controls (type of POP unspecified). In this analysis of a small number of subjects there was no statistically significant increased risk of breast cancer associated with POP use.

Evidence level 2+

Meta-analysis by the Fitzpatrick *et al*[143] which combined data from their study with data from 5 other observational studies (including 4 of those described above *al*[72,74,75,144] suggests a small but statistically significant increased breast cancer risk for current or recent users of POP compared to non-users of hormonal contraception (RR 1.29, 95% CI 1.21-1.37). This was similar to risk associated with other hormonal contraceptives, and decreased with time after stopping POP. As the number of cases of breast cancer is very small amongst people aged under 50, the absolute risk of breast cancer remained very low amongst users of hormonal contraception, including the POP. The authors estimated that 5 years of use of combined or progestogen-only oral contraception between age 16 and 20 might result in a total increase in breast cancer risk during the 5 years of use and the subsequent 10 years of non-use from 0.084% to 0.093%. For 5 years of use between age 25 and 29, the 15 year risk might increase from 0.50% to 0.57%, and for 5 years of use between age 35 and 39, from 2.0% to 2.2%.

11.4 Risk of endometrial cancer

The extremely limited available data from studies[7,79–82] including only small numbers of POP users suggest either no association between POP use and endometrial cancer or a possible protective effect.

The evidence

An open-label study[83] included 21 subjects (17 completed the study) aged 18–40 years who used DRSP POP for 13 cycles. The primary outcome was endometrial safety during DRSP use; endometrial thickness was a secondary outcome. After 13 cycles of 28 days of DRSP POP use, endometrial biopsy results amongst study completers were not significantly different from pre-treatment biopsies. Mean endometrial thickness in the 17 study completers reduced from 8.2 mm pre-treatment to 5.6 mm at study completion.

Evidence level 2+

A cohort study[82] using data from Danish national databases identified 549 incident endometrial cancers in individuals aged 15–49 years between 1995 and 2014 (over 21 million person-years of observation). The study demonstrated a significantly lower risk of endometrial cancer amongst current or recent users of any hormonal contraceptive compared to non-users. There was no significant effect compared to non-use of hormonal contraception of current or recent use of POC on risk of endometrial cancer before age 50 years for POCs other than the LNG-IUS (RR 0.61 (95% CI 0.27–1.37)). Data specific to POPs are not available.

11.5 Risk of ovarian cancer

Large observational studies[84–86] that included POP users have found no association between POP use and ovarian cancer. However, these studies are limited by their observational nature as well as by the very small numbers of POP users and/or very small numbers of ovarian cancers.

The evidence

A cohort study[84] using data from Danish national databases identified 1249 incident ovarian cancers in individuals aged 15–49 years between 1995 and 2014 (over 21 million person-years of observation). The study demonstrated a significantly lower risk of ovarian cancer by age 50 years amongst current or recent users of POCs (RR 0.72 (95% CI 0.55- 0.95)) and ever-users of any hormonal contraceptive (RR 0.66 (95% CI 0.58-0.76)) compared to non-users of hormonal contraception. Data specific to POPs are not available.

Evidence level 2+

A 2013 population-based, case-control study[85] included 554 Danish subjects aged 35–79 years with ovarian cancer between 1995 and 1999, and a random sample of 1564 controls aged 35–79 years from the general population. The same percentage (1.8%) of both cases and controls exclusively used POP (n=10 cases, n=28 controls). No significant effect of exclusive POP use on risk of ovarian cancer was found (OR 0.97; 95% CI 0.45–2.14).

A 2004 prospective, cohort study[86] included 103 551 subjects aged 30–49 years in 1991–1992 from the Norwegian-Swedish Women's Lifestyle and Health Cohort Study who were followed up until 2000. A total of 214 incident cases of epithelial ovarian neoplasia occurred during the study, 6 of them amongst the 4438 subjects who had ever-used POP and had not used COC. The RR of ovarian cancer with ever-use of POP compared to never-use of hormonal contraception was 0.5 (95% CI 0.2–1.2). No association was found from these small numbers between ever-use of POP and risk of ovarian cancer.

11.6 Risk of cervical cancer

No studies were identified that assessed the risk of cervical cancer associated with POP use. UKMEC recommends no restriction on use of POP by individuals with cervical cancer (UKMEC1).[45]

11.7 Risk of ovarian cysts

As with non-users of hormonal contraception, the evidence suggests that it is not uncommon for users of POP to experience ovarian cysts; these are very often asymptomatic, incidental findings that require no treatment. Thus ovarian cysts observed during use of POP may not be caused by the POP.

Management of ovarian cysts in POP users is the same as the management for non-POP users. Ovarian cysts are categorised as UKMEC1 for use of POP, meaning that current or previous ovarian cysts do not contraindicate use of POP.[45]

The evidence

Randomised trials

A randomised, double-blind, group comparative study[3] allocated 71 participants to use of DSG POP (n=35) or LNG POP (n=36), and 29 DSG POP users and 28 LNG users completed 12 months of use. Transvaginal USS and serum estradiol, progesterone, luteinising hormone and follicle-stimulating hormone measurements were performed throughout the 7th and 12th 28-day treatment periods. In the DSG group, 20% of subjects had an ovarian cyst >30 mm at 7 months and 14% at 12 months. In the LNG group, 17% had an ovarian cyst at 7 months and 25% at 12 months. None of the persistent follicles or cysts caused any clinical symptoms and they resolved spontaneously. There was no control group.

Evidence level 1–

A double-blind, randomised, group comparative trial[20] included individuals aged 18–45 years with regular menstrual cycles, observed during 13 consecutive treatment cycles of 28 days. 989 subjects were randomised to DSG POP and 331 to LNG POP (there was no control group). Four "serious adverse events" that were considered to be possibly related to the use of the POP occurred in the DSG POP group, all related to ovarian cysts. Two "serious adverse events" in the LNG group, one ovarian cyst (0.2%) and one ectopic pregnancy (0.2%), were considered to be possibly related to the use of LNG. The study did not mention if any of the ovarian cysts were symptomatic. There was a high discontinuation rate in this study (44.8% in the DSG group; 39.4% in the LNG group).

Evidence level 1–

An open-label study[1] randomised 64 subjects aged 18–35 years with BMI 18–30 kg/m^2 and proven ovulatory cycles to receive either DRSP POP or DSG POP for two cycles. Follicle-like structures >13 mm were common in both groups; mean diameter was smaller in the DRSP POP group. The maximum diameter observed was 27.8 mm in the DRSP POP group and 34.9 mm in the DSG group. No persistent large follicle-like structures were recorded during the two study cycles and all but two subjects in each group returned to ovulation within the month following treatment cessation.

Observational

A total of 335 Swedish women aged 25–40 years, randomly selected from the population register, took part in a study[76] in which they underwent pelvic USS. Twelve subjects were using LNG-POP, 41 LNG-IUS, 81 COC and 197 no hormonal contraception. Three of the 12 subjects using LNG POP (25%) had an ovarian cyst ≥25 mm on USS, compared with 12 of the 197 subjects (6%) who were not using hormonal contraception: clearly evidence is limited by the small number of POP users included. In this study, 82% of ovarian cysts seen on the USS at study entry were no longer present at 3 months.

Evidence level 2–

An observational study[87] included three groups of participants. Group 1 (n=15) had been using a POP for at least 6 months (either LNG or NET), group 2 (n=17) had been using a COC for at least 6 months and group 3 (n=10) were a control group who had not been using any hormonal contraceptive for at least 6 months. USS taken over the course of 3 months demonstrated small ovarian follicles (10–30 mm diameter) in all three groups. There was a higher incidence of enlarged ovarian follicles (diameter >30 mm) in the POP group than in the other two groups (the numbers were too small to reach significance) but none of these persisted for more than two cycles (thus none were classified as functional ovarian cysts) and none were symptomatic.

An observational study[5] recruited 21 participants using POP (6 LNG POP, 8 NET POP, 7 ethynodiol diacetate) who all reported regular bleeds during POP use, and 21 similar controls using no hormonal contraception (all with regular cycles). Ultrasound scanning over the course of a month demonstrated a functional ovarian cyst (defined as a fluid-filled structure >30 mm in diameter which failed subsequently to rupture and produce a corpus luteum) at any time in 12 POP users (57%) but in only 4 control subjects (19%). Some POP users with functional cysts reported pain when they were directly questioned; and 29% of POP users and 81% of control subjects ovulated.

Other

(Note that this study does not include POP users but provides useful context.) An observational study[88] included 428 healthy subjects of whom 147 had not used any contraception other than barrier methods within the previous 3 months, 211 had used COC for at least the last 3 months and 70 had been using the copper intrauterine device (Cu-IUD) for more than 6 weeks. Overall, 29 (7%) were found to have ovarian cysts (defined as >30 mm diameter) which resolved spontaneously in 18 subjects. Cysts were observed in 9.5% of subjects using barrier methods, 2.4% of COC users and 14.3% of Cu-IUD users (prevalence was significantly lower in COC users (p<0.001)).

Evidence level 2–

11.8 Risk of ectopic pregnancy

Key information

C **The use of all effective methods of contraception, including POPs, reduces the risk of all pregnancies (including ectopic pregnancies) compared to use of no contraception.**

The degree of protection that a contraceptive method provides against ectopic pregnancy may depend on the degree to which it prevents ovulation, as well as on correct use. Contraceptive methods that suppress ovulation could be associated with a lower overall rate of ectopic pregnancy than those that do not.

The incidence of ectopic pregnancy associated with POP use is difficult to determine due to the small numbers of ectopic pregnancies that occur and the inability to adequately control for factors that may influence risk. Many of the available studies are old and therefore included only POPs that relied upon cervical mucus effect, rather than anovulation, as the primary mechanism of contraceptive action.

It is noted that a previous history of ectopic pregnancy is a condition for which UKMEC 2016 does not place any restrictions on the use of POPs.[45]

The evidence

A 1998 double-blind RCT[20] randomised 1320 subjects aged 18–45 years 3:1 to use of DSG POP or LNG POP for 13 months. Seven in-treatment pregnancies were reported during the study, three in the DSG POP group and four in the LNG POP group. One pregnancy in the LNG group was ectopic (0.2%).

A 1982 randomised, double-blind study[89] included 518 participants aged 18–38 years using either a COC or a NET or LNG POP. Amongst 258 POP users the study reported two ectopic pregnancies (one ectopic pregnancy per 1115 person-years of observation).

Evidence level 1–

A 1987 multicentre, prospective, open study[90] included 435 individuals aged 16–47 years (72% aged 16–34 years and 28% aged 35–47 years) using ethynodiol diacetate 0.5 mg POP. Over 15 months, five pregnancies were reported, three of which were a result of incorrect use. The net pregnancy rate at 1 year for method failure was 0.5%. No ectopic pregnancies were reported.

Evidence level 2–

Pooled data[21] from two prospective, multicentre phase III studies[22,23] demonstrated eight pregnancies (none of them ectopic) amongst 1571 study participants (14 329 exposure cycles).

Evidence level 1–

In a prospective, open-label, single-arm, multicentre, phase III trial[24] which included 993 participants using DRSP POP for up to 13 treatment cycles (a total of 6566 exposure cycles) there were 12 confirmed pregnancies (none of them ectopic).

Evidence level 2+

11.9 Effect on bone mineral density

There are no published studies that directly measure the effect of POP use on bone mineral density. The SPCs for the DSG POP[37] and DRSP POP[36] state that during use, estradiol levels correspond to those in the early follicular phase of the menstrual cycle. It is not known whether this has any clinically relevant effect on bone mineral density. Suppression of estradiol levels by DSG and DRSP POP is, however, significantly less than with depot medroxyprogesterone acetate (DMPA) use and the GDG suggest that although evidence is limited, it is unlikely that there is a clinically relevant effect for most users.

The evidence relating to serum estradiol levels during use of different POCs

In a randomised study,[1] 64 healthy subjects aged 18–35 years with BMI of 18–30 kg/m^2 and proven ovulatory cycles were randomised to use of DSG POP or DRSP POP for two 28-day cycles. In both treatment cycles, serum estradiol levels were lower in the DRSP POP group (184.34±92.53 pmol/L cycle 1 and 184.97±85.57 pmol/L cycle 2) than the DSG POP group (374.95±284.03 pmol/L cycle 1 and 255.68±146.58 pmol/L cycle 2), reflecting greater ovarian suppression in the DRSP group. The authors concluded that in both groups estradiol levels were not profoundly suppressed and remained comparable to normal early or mid-follicular phase levels.

Similarly, a study that investigated suppression of ovulation in 71 healthy subjects randomised to use of DSG 75 µg or LNG 30 µg POPs[3] demonstrated mean serum estradiol levels of 333 pmol/L at 7 months and 272 pmol/L at 12 months in the DSG POP group. In the LNG POP group, mean serum estradiol was higher (505 pmol/L at 7 months and 539 pmol/L at 12 months).

Evidence level 1–

In a 2019 review article, Hadji *et al*[91] compared mean serum estradiol levels during use of different POCs. The review indicates serum estradiol levels as above during use of POPs and of around 330 pmol/L during use of the etonogestrel-releasing implant (ENG-IMP) and between 94 and 129 pmol/L during use of DMPA.

Evidence level 2–

12 What are the side effects of POP?

12.1 Change in bleeding pattern

Clinical recommendations

C	**Individuals considering use of a traditional POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use:**[20] • **Fewer than 1 in 10 (only about 2%) LNG POP users may be amenorrhoeic.** • **About 1 in 10 LNG POP users may have infrequent bleeding (1–2 bleeding/spotting episodes).** • **About 8 in 10 LNG POP users may have normal frequency bleeding (3–5 bleeding/spotting episodes).** • **About 1 in 10 LNG POP users may have frequent bleeding (6 or more bleeding/spotting episodes).** • **Fewer than 1 in 10 LNG POP users may have prolonged bleeding (bleeding/spotting episode(s) lasting >14 days).**
C	**Individuals considering use of a DSG POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use:**[20] • **About 4 in 10 DSG POP users may have normal frequency bleeding (3–5 bleeding spotting/episodes).** • **About 2–3 in 10 DSG POP users may be amenorrhoeic.**[22,92] • **About 3 in 10 DSG POP users may have infrequent bleeding (<3 bleeding/spotting episodes).** • **Fewer than 1 in 10 DSG POP users may have frequent bleeding (6 or more bleeding/spotting episodes).** • **About 1 in 10 DSG POP users may have prolonged bleeding (bleeding/spotting episode(s) lasting >14 days).**
C	**Individuals considering use of a DRSP POP should be advised that bleeding pattern is unpredictable; they may or may not have "scheduled" bleeding/spotting during the 4-day HFI and they may or may not have "unscheduled" bleeding/spotting at other times. Both scheduled and unscheduled bleeding/spotting may reduce in frequency over the first year of use. Over a 3-month period at around 6–9 months of use:**[22,92] • **The total number of days of bleeding/spotting (scheduled plus unscheduled) may be similar to the number of days of bleeding/spotting with the DSG POP.** • **About 2–3 in 10 DRSP POP users may be amenorrhoeic.** • **Fewer than 1 in 10 DRSP POP users may have frequent bleeding.** • **Fewer than 1 in 10 DRSP POP users may have bleeding episode(s) lasting >14 days.**

See **Section 22 Management of problematic bleeding with POP use**.

Overall summary

Bleeding patterns with POCs vary depending upon the progestogen used, the dose at which it is given, the circulating endogenous estradiol levels, and ovulation suppression.[2] Irregular bleeding is commonly cited as a reason for discontinuation of POP.[20,89] For any individual, bleeding pattern during use of any type of POP is unpredictable.

Traditional POPs

Reported incidence of different bleeding patterns during use of traditional LNG or NET POPs varies considerably between studies, many of which are older and small, with high discontinuation rates. High rates of "normal frequency bleeding", "mostly regular bleeding" or "no menstrual disturbance" are generally reported in studies of traditional POP use and rates of amenorrhoea are low.

DSG POP

In general, studies suggest that bleeding becomes less frequent and less prolonged over the first year of DSG POP use, with about half the subjects reporting either amenorrhoea or infrequent bleeding/spotting, and low rates of frequent or prolonged bleeding/spotting after a year of use. About one-quarter to one-third of study subjects report amenorrhoea after 9–12 months of use.

DRSP POP

Studies indicate that users of DRSP POP may have "scheduled" bleeding/spotting (starting during the 4-day HFI) but "unscheduled" bleeding/spotting is also common. An individual may have both scheduled and unscheduled bleeding. The bleeding is often reported as light or moderate, and both scheduled and unscheduled bleeding may reduce over the first year of use. About one-quarter to one-third of study subjects report amenorrhoea after 9–12 months of use, with low rates of frequent or prolonged bleeding.

The evidence

Studies do not all categorise bleeding patterns in the same way or report patterns for the same time periods, making overall findings for any one POP type difficult to establish and bleeding patterns with different POP types difficult to compare. It is unclear how changes in bleeding pattern over time that are reported by studies are affected by high rates of study discontinuation.

The evidence: traditional POPs

A 1982 randomised, double-blind study[89] of healthy subjects aged 18–38 years with regular menstrual cycles (some of them breastfeeding) allocated subjects to use for up to 2 years of one of two COCs or one of two POPs (LNG POP, n=128 and NET POP, n=130). Discontinuation rates were high (about 50% at 1 year and 75% at 2 years), many subjects citing irregular bleeding as a reason for discontinuation. The study reported low rates of "amenorrhoea" and >50% "frequent bleeding" amongst POP users in the first 3 months of use (note that definitions of the various bleeding patterns are quite different from those described in later studies). Rates of "frequent" and "irregular" bleeding in POP users reduced by the end of the first year of use, but this could reflect high rates of discontinuation amongst those with irregular bleeding.

Evidence level 1–

A 1990 retrospective notes review[17] including 189 individuals using a NET POP and 27 using a LNG POP for various lengths of time reported "mostly regular" bleeding in 39% of subjects, "mostly irregular" bleeding in 24%, "mostly amenorrhoea" in 8% (amenorrhoea being defined as >3 months without bleeding) and mixed irregular bleeding, regular bleeding and amenorrhoea in 22%.

Evidence level 2–

A 1988 comparative analysis of bleeding patterns in individuals using various methods of contraception observed 52 NET POP users and 44 LNG POP users over four consecutive 90-day reference periods (a total of 360 days).[93] In the four reference periods, 52%–69% of NET POP users and 61%–75% of LNG POP users reported no menstrual disturbance. No amenorrhoea was reported.

Evidence level 2–

The evidence: traditional versus DSG POP

A 1998 double-blind, randomised, multicentre trial[20] randomised healthy subjects aged 18–45 years who had regular menstrual cycles and weight between 80% and 130% of "ideal body weight" to use of either DSG 75 µg (n=989) or LNG 30 µg (n=331) for 13 consecutive treatment periods of 28 days. One-third of the cohort was breastfeeding at enrolment. In this study, 'spotting' was defined as requiring a maximum of one pad or tampon per day; 'bleeding' required two or more. The standard definitions of bleeding patterns were used: 'amenorrhoea' was defined as no bleeding in a 90-day reference period, 'infrequent' bleeding/spotting as 1–2 bleeding/spotting episodes per 90-day reference period, 'normal frequency' bleeding/spotting as 3–5 bleeding/spotting episodes per 90-day reference period and 'frequent' bleeding/spotting as 6 or more bleeding/spotting episodes per 90-day reference period. 'Prolonged' bleeding/spotting was defined as an episode lasting for more than 14 days.

Evidence level 1–

Bleeding generally became less frequent and less prolonged over time in the DSG POP group. Amongst the 325 non-breastfeeding DSG POP users continuing the study drug in the last 90 days of the trial there were higher rates of amenorrhoea and infrequent bleeding/spotting episodes and lower rates of normal frequency, frequent and prolonged bleeding in the final 90 days of the study (reference period 4 – 'RP4') than there were amongst the 484 non-breastfeeding DSG users in the 90 days starting on day 29 of the study treatment (shifted reference period 1 – 'RP1'). It is noted, however, that 23% of all DSG POP discontinuers (including those in the breastfeeding group) cited irregular bleeding as a reason for discontinuation.

Bleeding patterns did not change significantly over time in the LNG POP group. There were similar, high rates of "normal frequency" bleeding/spotting, and similar, low rates of all other bleeding patterns and prolonged bleeding in 'RP1' (n=167) and in 'RP4' (n=111). Irregular bleeding was cited as a reason for discontinuation by 18% of all LNG POP discontinuers.

Comparing non-breastfeeding DSG POP users with non-breastfeeding LNG POP users, in the final 90-day reference period of the study ('RP4') ending at 12 months of use:

- About 2 in 10 DSG POP users and fewer than 1 in 10 (about 2%) LNG POP users were amenorrhoeic.
- About 3 in 10 DSG POP users and about 1 in 10 LNG POP users had 1–2 bleeding/spotting episodes (infrequent bleeding).
- About 4 in 10 DSG POP users and about 8 in 10 LNG POP users had 3–5 bleeding/spotting episodes (normal frequency bleeding).
- Fewer than 1 in 10 DSG POP users and about 1 in 10 LNG POP users had 6 or more bleeding/spotting episodes (frequent bleeding).
- About 1 in 10 DSG POP users and fewer than 1 in 10 LNG POP users had bleeding/spotting episode(s) lasting >14 days (prolonged bleeding).

A 2013 Cochrane Review of RCTs relevant to POP effectiveness, acceptability and continuation rates identified no additional studies providing useful information about bleeding patterns. The review suggested that the DSG POP caused more bleeding problems than the LNG POP (the difference was not statistically significant) and that discontinuation because of irregular bleeding was more common with the DSG POP than the LNG POP (rate ratio 1.32; 95% CI 0.99–1.78).[94]

Evidence level 1–

The evidence: DRSP versus DSG

An open-label, randomised, phase II trial[1] compared ovarian activity during use of DRSP POP (n=32) and DSG POP (n=32) for two 28-day cycles by healthy subjects aged 18–35 years with BMI 18–35 kg/m^2 and proven ovulatory cycles at baseline. The study reported that 74.1% (n=20) of the DRSP group had scheduled bleeding (bleeding associated with the HFI and lasting for up to 8 days). The reported median number of bleeding or spotting days was 9 days in the DRSP POP group and 18 days in the DSG POP group. With both POPs, the bleeding intensities most frequently reported were spotting and slight bleeding.

Evidence level 1–

A multicentre, double-blind, randomised trial[22,92] designed to compare bleeding with DRSP and DSG POPs randomised 1312 subjects aged 18–45 years to use of DRSP POP or DSG POP for nine 28-day cycles. 858 subjects contributed to data for 6691 DRSP POP treatment cycles (by treatment cycle 9, data are reported for 442 subjects in the DRSP arm) and 332 subjects contributed to data for 2487 DSG POP treatment cycles (by treatment cycle 9, data are reported for 161 subjects in the DSG arm).

The study considered bleeding/spotting in each of study cycles 2–9 and cumulatively for cycles 2–4 (reference period (RP) 1) and cycles 7–9 (RP3). Scheduled bleeding was defined as any bleeding that occurred during the DRSP POP HFI, persisting for up to eight consecutive days. Unscheduled bleeding was unrelated to the HFI. Thus bleeding during use of the DRSP POP could be scheduled or unscheduled but any bleeding occurring during use of the DSG POP was unscheduled. The authors noted that amongst bleeding and spotting days "spotting days prevailed".

In both the DRSP and DSG study groups, over time (see **Table 4**):

- The percentage of subjects with ***(any)*** bleeding or spotting decreased (there was no significant difference between groups in RP3 (cycles 7, 8 and 9). 27% of subjects in the DRSP group and 32% in the DSG group were amenorrhoeic in RP3.
- The mean number of days of ***(any)*** bleeding or spotting decreased (there was no significant difference between groups in RP3 – 10 days DRSP, 11 days DSG).
- The percentage of subjects with ***unscheduled*** bleeding decreased (there was no significant difference between groups in RP3 – 65% DRSP, 68% DSG).
- The mean number of days of ***unscheduled*** bleeding or spotting decreased (significantly fewer days for the DRSP group (7 days) than the DSG group (11 days) in RP3).
- The percentage of subjects with frequent bleeding decreased (there was no significant difference between groups in RP3 – 5% DRSP, 4% DSG).
- The percentage of subjects with prolonged bleeding (>14 consecutive days) decreased (significantly lower for the DRSP group than the DSG group in RP3 – 3% DRSP, 11% DSG).

Table 4: Comparison of drospirenone progestogen-only pill (POP) and desogestrel POP bleeding patterns[22,92]

Parameter	Reference period	DRSP	DSG	P value
Percentage of subjects with any bleeding or spotting during:	RP1 (cycles 2–4)	79.9%	86.5%	0.032
	RP3 (cycles 7–9)	73.3%	67.9%	NS
Mean (median) days of bleeding or spotting during:	RP1 (cycles 2–4)	13.1 (10)	16.9 (12)	0.015
	RP3 (cycles 7–9)	9.7 (6)	10.8 (7)	NS
Percentage of subjects with ***unscheduled*** bleeding/spotting during:	RP1 (cycles 2–4)	67.9%	86.5%	<0.0001
	RP3 (cycles 7–9)	65.0%	67.9%	NS
Mean (median) days of ***unscheduled*** bleeding or spotting during:	RP1 (cycles 2–4)	9.6 (5)	16.9 (12)	<0.0001
	RP3 (cycles 7–9)	7.2 (4)	10.8 (7)	0.028
Percentage of subjects with frequent bleeding during:	RP1 (cycles 2–4)	9.1%	7.2%	NS
	RP3 (cycles 7–9)	5.3%	4.4%	NS
Percentage of subjects with prolonged bleeding (>14 consecutive days) during:	RP1 (cycles 2–4)	12.1%	16.7%	NS
	RP3 (cycles 7–9)	2.9%	10.9%	0.0003
Percentage of subjects with amenorrhoea* during:	RP1 (cycles 2–4)	20.1%	13.5%	
	RP3 (cycles 7–9)	26.7%	32.1%	

*Extrapolated from data for percentage of subjects with any bleeding/spotting in these reference periods.
DSG, desogestrel; DRSP, drospirenone; NS, not significant; RP, reference period.

Significantly fewer subjects discontinued because of bleeding problems in the DRSP group (3.2%, 27 subjects) than in the DSG group (6.6%, 22 subjects) (p<0.05).

The evidence: DRSP alone

An open-label study,[83] designed to examine endometrial safety during use of DRSP POP for 13 28-day cycles, included 21 subjects aged 18–40 years with regular cycles at baseline. Bleeding pattern was assessed as a secondary outcome. Seventeen subjects completed the study. The principal study author is medical director of the DRSP POP manufacturer Exeltis.

Evidence level 2–

71.4% of subjects reported unscheduled bleeding/spotting in cycle 2 and 47.1% in cycle 13; between these times, percentages varied between 2.4% and 52.4%. The mean number of days of ***unscheduled*** bleeding/spotting was 4.1 days during cycle 2, 2 days during cycle 13 and varied between 3.5 and 0.5 days in cycles 3–12. The percentage of subjects with ***scheduled*** bleeding/spotting decreased from 76.2% in cycle 2 to 47.1% in cycle 13; the mean number of days of ***scheduled*** bleeding/spotting was 5 days in cycle 2, varied between 1.4 and 2.9 days in cycles 3–12 and was 1.8 days in cycle 13. Mean number of days on which there was ***any*** bleeding/spotting (scheduled or unscheduled) was 9.1 in cycle 2 and 3.8 in cycle 13.

A multicentre, open-label trial[46] assessed safety, tolerability and bleeding pattern with use of DRSP POP for six 28-day cycles by female adolescents aged 12–17 years, with a seven-cycle voluntary extension (patient choice). 102 subjects commenced the study treatment, 89 completed six cycles and 74 completed 13 cycles.

The study reported that over time:

- **The percentage of subjects with both scheduled and unscheduled bleeding/spotting decreased.** 50% of subjects experienced ***scheduled*** bleeding/spotting at the end of cycle 1, reducing to 38% at the end of cycle 6. The percentage of subjects with **only *scheduled*** spotting/bleeding decreased with time. The percentage of subjects with **no *scheduled*** bleeding/spotting but with ***unscheduled*** bleeding/spotting generally increased with time.
- **The number of bleeding/spotting days decreased.** The median ***overall*** number of bleeding/spotting days was 14 in cycles 2–4 and 11 in cycles 11–13. The median number of ***scheduled*** bleeding/spotting days was 4 in cycles 2–4 and 0 in cycles 11–13. The median number of ***unscheduled*** bleeding/spotting days fluctuated between 5 and 6 in cycles 2–4, reaching a maximum of 8 in cycles 11–13.
- **The percentage of subjects with amenorrhoea increased.** 19% of subjects had no bleeding/spotting during cycle 2 compared with 31% during cycle 4.
- **Bleeding became lighter** (throughout the study about half the bleeding/spotting episodes were spotting only) and
- **Bleeding episodes became shorter.**

In questionnaire responses at study exit (after 6 cycles, 13 cycles or at early discontinuation):

- 61% of subjects reported that their bleeding had become more predictable over the course of treatment (18% considered predictability unchanged)
- 70% of subjects reported shorter duration of bleeding (20% considered duration unchanged)
- 76% reported reduced volume of bleeding (18% considered volume unchanged).

Five subjects (4.9%) left the trial due to irregular bleeding, and one subject due to amenorrhoea.

Evidence level 2–

A prospective, multicentre, non-comparative, phase III study[23] included 713 healthy subjects aged 18–45 years who used DRSP POP for up to 13 28-day cycles, contributing data for 7638 study cycles. The primary outcome was contraceptive effectiveness and the secondary outcome was bleeding pattern.

Evidence level 2+

The proportion of subjects reporting ***bleeding*** decreased from 72.7% in cycle 1 to 32.1% in cycle 13 (***spotting*** was reported by 87.1% of participants in cycle 1, decreasing to 44.7% in cycle 13). >90% of bleeding days were classified as slight or moderate. No bleeding episodes were reported by 14.4% of subjects during cycles 2–4, increasing to 26.6% during cycles 11–13.

Scheduled bleeding during the HFI was reported by 47.9% of subjects in cycle 1, reducing to 24.4% in cycle 13.

Unscheduled bleeding was reported by 49.1% of subjects in cycle 1, reducing to 22.8% in cycle 13. Incidence of unscheduled spotting decreased from 69.6% in cycle 1 to 35.1% in cycle 13. The mean number of days of unscheduled bleeding decreased from 1.9 in cycle 1 to 0.7 in cycle 13 and the mean number of unscheduled spotting days decreased from 3.4 in cycle 1 to 1.2 days in cycle 13.

Mean bleeding duration decreased over time (2.9 days in cycle 1, 1 day in cycle 13). Prolonged bleeding (>14 days of bleeding/spotting) was reported by 6.5% of participants during cycles 2–4 decreasing to 4.2% during cycles 11–13.

Evidence level 2+

The study reported that 4.2% of subjects discontinued due to irregular bleeding.

A prospective, open-label, single-arm, multicentre, phase III trial[24] which evaluated contraceptive effectiveness and safety of DRSP POP included participants aged 15–35 years for up to 13 treatment cycles. A total of 352 participants (35%) completed the trial, and 269 of the original 1006 subjects were lost to follow-up.

In cycles 2–4 (data for 609 subjects):

- 44% reported scheduled bleeding (mean number of days of scheduled bleeding 1.8)
- 41.5% reported scheduled spotting (mean number of days of scheduled spotting 1.1)
- 57% reported unscheduled bleeding (mean number of days of unscheduled bleeding 4.9)
- 61.2% reported unscheduled spotting (mean number of days of unscheduled spotting 3.9).

In cycles 11–13 (data for 310 subjects):

- 29% reported scheduled bleeding (mean number of days of scheduled bleeding 1.2)
- 25.8% reported scheduled spotting (mean number of days of scheduled spotting 0.8)
- 41.6% reported unscheduled bleeding (mean number of days of unscheduled bleeding 3.2)
- 41.9% reported unscheduled spotting (mean number of days of unscheduled spotting 2.3).

Percentage of subjects with amenorrhoea increased from 23.3% in cycles 2–4 to 35.8% in cycles 11–13. Few (1.9%) participants discontinued due to bleeding (although data are not available for those lost to follow-up).

The authors concluded that the frequency of both scheduled and unscheduled bleeding reduced with time, the number of unscheduled bleeding days decreased over time, and mean duration of all bleeding/spotting episodes decreased over time with a trend towards fewer recording prolonged bleeding/spotting. Over time, a greater proportion reported amenorrhoea.

12.2 Mood change

Key information

C **The available evidence does not establish a causal relationship between POP use and depression.**

It is important to acknowledge that some individuals report mood change during use of hormonal contraception whether the hormonal contraception is the cause of these changes or not. HCPs should ensure an individualised approach to managing signs and symptoms of depression and explore other possible contributing factors whilst considering offering alternative contraception if an individual

considers that their mood has been adversely affected by POP use. Current or previous depression does not contraindicate use of POPs (UKMEC1).

The evidence

A 2018 systematic review of studies that used externally validated measures of depression[95] concluded that the identified data did not support a clear, general association between POCs and depression scores or incident depression diagnoses. This review included the following two studies relating to POP.

Evidence level 2+

A prospective RCT published in 1995[96] randomised 150 subjects at centres in Scotland and Philippines to receive a combined EE/LNG COC (n=50), LNG POP (n=50) or placebo (n=50). Self-reported depression scores were lower, across centres, in the LNG POP group compared to placebo and COC groups at months 2, 3 and 4.

Evidence level 1–

A Danish population-based cohort study[97] used information from Danish databases to identify use of hormonal contraception and incident diagnosis of depression or first use of antidepressants by women aged 15–34 years between 2000 and 2013. Data were available relating to 40 069 person-years of use (or recent use within 6 months) of DSG POP, 33 182 person-years of use or recent use of NET POP, 1289 person-years of use or recent use of LNG POP and 3 041 595 person-years of non-use of hormonal contraception.

Evidence level 2+

From these observational data (which could be significantly affected by unmeasured confounding factors) there is an apparent small but statistically significant increase in risk of first prescription of antidepressants associated with use of all three POP types (adjusted RRs for first use of antidepressants associated with use/recent use of DSG POP, NET POP and LNG POP were 1.4 (95% CI 1.30–1.46), 1.3 (95% CI 1.18–1.37) and 1.7 (95% CI 1.18–2.38), respectively). A small statistically significant increase was reported in risk of first diagnosis of depression associated with use of DSG POP, whereas increase in risk of first diagnosis of depression was not significantly associated with use of NET or LNG POP (adjusted RRs for first diagnosis of depression were 1.2 (95% CI 1.06–1.42) for DSG, 1.1 (95% CI 0.88–1.29) for NET and 1.5 (95% CI 0.54–3.86) for LNG). For both first use of antidepressant and first diagnosis of depression, observed risk compared to non-users of hormonal contraception was greater for 15–19-year-old POP users than for older POP users.

A Swedish study[98,99] used data from nationwide registers to examine prescription of antidepressant drugs in relation to use of hormonal contraceptives between 2005 and 2008 by all Swedish women aged 16–31 years (n=917 993). The study population was divided into individuals who had not used hormonal contraceptives at all (n=377 744), those who had used solely one formulation (n=385 784) and those who had changed from one formulation to another (switched within, as well as between, the CHC and POC groups) (n=154 465).

8.5% of the Swedish women used antidepressants during the study. Compared to non-users of hormonal contraception, the odds ratio for use of antidepressants during the 3-year study period by individuals prescribed DSG POP during the same 3-year period (n=15 045) was slightly elevated (OR 1.11, 95% CI 1.08–1.14); risk was highest for 16–19-year-olds. For the small number of NET POP users (n=220), the associated increase in

odds ratio was not statistically significant (OR 1.03, 95% 0.94–1.13) except amongst 16–19-year-olds. Formulation-specific analyses suggest that antidepressant drug use was generally higher amongst users of non-oral hormonal contraceptives than users of oral contraception. Significant unmeasured confounding factors may affect findings and causality cannot be determined.

Evidence level 2+

An observational prospective cohort study[97] designed to assess the effect of use of hormonal contraception on risk of suicide attempt and suicide extracted information from Danish national databases relating to the period 1996–2013, for the 475 802 women who attained the age of 15 years during the study period and had no prior use of hormonal contraception or antidepressant use and no psychiatric history.

During the 3.9 million person-years considered, there were 6999 suicide attempts and 71 suicides. The study included 25 580 person-years of use of DSG POP and 13 236 person-years of use of NET POP. Use of any POP was positively associated with risk of suicide attempt (HR compared with never-use of hormonal contraception was 2.29 (95% CI 1.77–2.95 – not statistically significantly different from the risk with COCs). DSG POP conferred a HR for first suicide attempt of 2.01 (95% CI 1.44–2.81) and NET POP conferred a HR of 2.77 (95% CI 1.89–4.05) compared to never-use of hormonal contraception. Significant unmeasured confounding factors could affect these findings.

A recently published study[100] extracted information from Swedish national databases relevant to the period August 2006–December 2013 for all women who attained the age of 15 years during that time. Of these, 216 702 individuals aged 15–22 years for whom almost 900 000 person-years of data were available**,** 69 507 (32%) had no record of hormonal contraceptive use, 97 515 (45%) used only COCs during the observation period, 23 468 (11%) used only POPs and 26 212 (12%) used both COCs and POPs. The outcome of interest was the first instance of suicidal behaviour (suicide attempt or suicide death). During the observation period there were 1359 non-fatal attempts and 36 deaths, corresponding to 15.5 suicidal events per 10 000 person-years. Mean age at suicidal event was 16.9 years. The rate of suicidal events was higher amongst individuals using POPs at the time of suicidal event (23.1 per 100 person-years) than for those who had never used hormonal contraception (14.9 per 100 person-years) and those using COCs at the time of suicidal event (15.1 per 100 person-years). There is significant risk of confounding by unmeasured factors.

Drospirenone

A multicentre, open-label trial[46] to assess the safety, tolerability and bleeding pattern of DRSP POP over six cycles in female adolescents, with a seven-cycle extension phase, included 89 subjects who completed six cycles and 74 who completed 13 cycles. Nine participants dropped out due to side effects; 63.7% (n=65) experienced side effects, of which one of the most frequently reported was mood disturbance.

Evidence level 2+

To date there is no published evidence specific to the effect of use of DRSP POP on mood or premenstrual syndrome symptoms.

12.3 Headache

Key information

D **Evidence is too limited to confirm or exclude any causative association between POP use and headache.**

Headache is a condition that commonly affects individuals of reproductive age. Some individuals do report headache during use of hormonal contraception, but often it is not possible to confirm whether the contraception is the cause. In clinical studies[20,23,24] headache is reported by fewer than 1 in 10 subjects during use of LNG, DSG and DRSP POP. Evidence is too limited to establish the effect of POP on risk of headache or identify differences between different POPs in this regard.

Evidence level 2+

The GDG advises that HCPs should ensure an individualised approach to managing headache that occurs during use of hormonal contraception and explore other possible contributing factors whilst considering offering alternative contraception if an individual considers that use of POP has contributed to their headaches.

A history of headache does not contraindicate use of POP (UKMEC1).[45]

12.4 Acne

Key information

D **A causal association cannot be confirmed or excluded by the very limited evidence relating to POP use and acne.**

In studies, fewer than 1 in 10 users report acne as a potential side effect – the progestogen may or may not be the cause. Evidence is inadequate to inform the effect of any POP on incidence of acne or to compare the different POPs in this regard.

The GDG advises that HCPs should ensure an individualised approach to managing acne which occurs during POP use, explore other possible contributing factors, and consider offering alternative contraception if an individual considers that use of POP has negatively affected their skin.

The evidence

Amongst 979 subjects using DSG POP and 327 using LNG-POP for up to a year in a large comparative study[20] 3.1% of DSG-POP users and 4.0% of LNG-POP users reported acne as a side effect.

Evidence level 1–

A prospective, multicentre, non-comparative, phase III study[23] investigating effectiveness of DRSP POP reported acne as a potential side effect in 6.3% of 713 subjects who contributed data for 7638 study cycles.

Evidence level 2+

If an individual considers that they have new acne or worsening of existing acne related to use of a POP, whether the POP is in fact the cause or not, they may wish to switch to alternative contraception and they should be supported by HCPs to choose an effective alternative method.

Effect of POP on existing acne/hirsutism

Evidence relating to the effect of use of POP on pre-existing acne is extremely limited. One RCT[101] randomised 20 individuals with acne and 20 with hirsutism to use of a COC or traditional LNG POP (LNG 0.03 mg) for 6 months. Compared to a control group of individuals without acne or hirsutism, those with acne or hirsutism had significantly higher serum free testosterone at baseline, that was reduced after 6 months of use of either COC or LNG POP (the reduction was significantly greater with COC than with POP in the acne group, but not in the hirsutism group). Acne and hirsutism scores reduced significantly after 6 months of use of either the COC or the LNG POP; improvement in acne was significantly greater in the COC group than the LNG POP group, but reduction in hirsutism scores was similar in both groups. The study did not report effect of COC or LNG POP on serum free testosterone or incident acne in the control group.

Evidence level 1–

In a study designed to compare effects of DSG 75 µg and LNG 30 µg on lipid metabolism,[53] 81 healthy subjects randomised to use of either DSG 75 µg or LNG 30 µg for seven 28-day treatment periods had a reduction in serum hormone-binding globulin that was slightly greater for the LNG group than the POP group. This contrasts to the effect of CHC which increases serum hormone binding globulin and can thus be beneficial for acne.

The DRSP POP (which has anti-androgenic activity) might be expected to be beneficial for existing acne/hirsutism but has not been specifically studied.

12.5 Weight

Key information

D **Whilst users of POP may gain some weight during use, there is not clear evidence that POP use *causes* significant weight gain.**

The GDG advises that HCPs should ensure an individualised approach to weight management and explore other possible contributing factors whilst considering offering alternative contraception if an individual considers that use of POP has negatively affected their weight.

The evidence

Evidence relating to the effect of POP use on weight is extremely limited. A retrospective cohort study[102] used data from 380 patient records to compare weight at baseline with that after 12 months of use of various contraceptive methods. The 52 subjects using POP (type not recorded) gained an average of 1.3 kg, whilst the 15 subjects using Cu-IUDs gained an average of 0.5 kg and the 26 subjects using condoms gained an average of 0.64 kg. The study is, however, small and subject to bias resulting from subject selection and factors influencing choice of contraceptive, and it relates to a Malaysian population.

Evidence level 2–

One small prospective cohort study[103] compared body composition changes in 42 perimenopausal subjects using a DSG POP and 26 perimenopausal subjects not using hormonal contraception. At 12 months the mean weight increase in the groups was not significantly different (+0.3 kg in POP vs –0.2 kg in controls) but POP users had a statistically significant increase in fat mass of 2.8% compared with –0.5% in controls. The study is limited by its small size and its observational nature and relates to a perimenopausal population.

No further evidence has been found since the release of the **FSRH CEU Statement Contraception and Weight Gain.**[104]

12.6 Libido

There is inadequate evidence to inform the effect of POP use on libido and whether different POPs affect libido differently. It is recognised that there are many factors that affect libido and other contributing factors should be explored. The GDG advises that an individualised approach is important if an individual considers that a POP is adversely affecting their libido; they may wish to consider trying a different effective contraceptive method.

13 What are the non-contraceptive benefits of POP?

13.1 Management of heavy menstrual bleeding

In practice some clinicians offer DSG POP or double-dose DSG POP (150 µg) for management of heavy menstrual bleeding (HMB) but there is not yet robust published evidence to inform the effect of use of any POP for this indication.

Alternative contraceptive options with proven benefit for management of HMB and supported by **National Institute for Health and Care Excellence (NICE) guidance**[105] include the **LNG-IUS**[106] and **CHC**.[107]

The evidence

Three systematic reviews relating to HMB and use of progestogens do not include evidence relevant to contraceptive POPs and are therefore not relevant to this guideline.[108–110]

Interestingly, a prospective, non-interventional study[111] that included 592 individuals who chose to switch from a COC to a POP (>80% used a DSG POP) reported a reduction in the proportion of subjects with heavy bleeding from 15.4% at baseline on the COC to 4.3% at 6–12 months after starting the DSG POP.

Evidence level 2+

A published service evaluation[112] based in a UK tertiary paediatric centre considered the effect of single- and double-dose DSG POP (75 µg or 150 µg DSG daily) on bleeding amongst 129 adolescent girls (aged 10–18 years) with adolescent menstrual dysfunction (AMD). 69% were prescribed the double dose – the decision to use single- or double-dose was based on clinician and patient preference. At follow-up (median 5 months, range 3–8 months) 49% of the 87 double-dose DSG users reported amenorrhoea and light spotting compared to 18% of the 40 single-dose DSG users (p=0.001). Significantly fewer subjects in the double-dose group reported bleeding-related side effects (45% vs 70%, p=0.008) and discontinuation rates were lower in the double-dose group (51% vs 88%, p<0.001). The findings are limited by significant potential confounding and the lack of standardised definitions of “amenorrhoea and light spotting”.

13.2 Dysmenorrhoea

The limited available evidence suggests that use of DSG and DRSP POP could reduce dysmenorrhoea for some users.

The evidence

A prospective, non-comparative, observational study[113] observed the effects of DSG POP in subjects with cyclical symptoms, including dysmenorrhoea. 406 subjects with dysmenorrhoea took the DSG POP for three or four 28-day cycles. At baseline, 49.5% of subjects reported moderate dysmenorrhoea and 34.7% reported severe dysmenorrhoea. By the end of the study, the incidence of moderate/severe dysmenorrhoea decreased to 7% (39% reported mild dysmenorrhoea, and dysmenorrhoea was absent in 51%). Overall, dysmenorrhoea resolved or improved in 93% of subjects and worsened in only one case (0.2%). Correspondingly, use of analgesics dropped from 70% of subjects at baseline to 8% at study end.

Evidence level 2+

An open-label trial[46] included 102 adolescents of whom 89 completed six cycles of DRSP POP use and 74 completed 13 cycles. At baseline, 47 subjects reported recent dysmenorrhoea (21.3% severe, 48.9% moderate and 29.8% mild). By the end of cycle 6, amongst the 47 subjects with dysmenorrhoea at baseline 4.3% reported severe dysmenorrhoea, 6.4% moderate and 19.1% mild; 66% reported no dysmenorrhoea (data were missing for 4.3%). By the end of cycle 13, dysmenorrhoea was reported as severe by 4.3%, moderate by 2.1% and mild by 10.6%, and 57.4% had no dysmenorrhoea (data were, however, missing for 25.5%).

In studies dysmenorrhoea is an uncommonly reported side effect of POP use.[1,20,24]

13.3 Other

As DRSP has anti-androgenic activity, the DRSP POP might theoretically be expected to offer benefit for users with acne or hirsutism. Similarly its diuretic effect might be postulated to be beneficial for weight. Effect of DRSP POP on acne, hirsutism, weight (and mood/premenstrual syndrome) has not however been specifically studied.

The FSRH Clinical Effectiveness Unit (CEU) is regularly asked about induction of withdrawal bleeding in individuals with polycystic ovary syndrome who are amenorrhoeic during use of progestogen-only contraception. Studies have not specifically assessed the effect of POPs on the endometrium in individuals with polycystic ovary syndrome, but in the general population use of POCs is associated with reduced endometrial thickness. It is established practice that induction of withdrawal bleeding is not required in individuals with polycystic ovary syndrome during use of a POP even if they are amenorrhoeic.

14 When can the POP be started?

Key information

✓ **It is established practice that traditional and DSG POP can be started on days 1–5 of a natural menstrual cycle, by day 5 after abortion or by day 21 after childbirth without requirement for additional contraceptive precautions. At any other time, traditional and DSG POP can be quick started according to Quick Starting Guidance, with advice to use additional contraceptive precautions for 2 days and to take a follow-up pregnancy test if required.**

✓ **To align with manufacturer guidance for the new DRSP POP, the GDG recommends that additional contraceptive precautions are required unless DRSP POP is started on day 1 of a natural menstrual cycle, day 1 after abortion or by day 21 after childbirth. If started at any other time, additional contraceptive precautions are required for 7 days with advice to take a follow-up pregnancy test if appropriate.**

14.1 Standard start

Starting POP at the beginning of a natural menstrual cycle

It is established practice that the traditional POP and DSG POP can be started on days 1–5 of a natural menstrual cycle without the need for additional contraceptive precautions (see **Table 5**). DRSP POP can be started on day 1 of a natural menstrual cycle without the need for additional contraceptive precautions.

14.2 Quick start

Starting traditional/DSG POP after day 5 of a natural menstrual cycle or DRSP POP after day 1

So long as a pregnancy test is negative (or it is certain that there has been no UPSI), traditional/DSG POP can be quick started after day 5 of a natural menstrual cycle and DRSP POP after day 1, even if very early pregnancy cannot be absolutely excluded because of UPSI in the last 21 days. Additional contraceptive precautions (eg, condom use) should be advised for the first 2 days of traditional/DSG POP use (or for the first 7 days of DRSP POP use) and a follow-up pregnancy test taken if appropriate.

From the very limited available evidence there is no indication that use of POP in very early pregnancy is associated with adverse pregnancy outcomes. See **FSRH Clinical Guideline Quick Starting Contraception**[114] and **Table 6**. For guidance when quick starting POP after oral EC see **Section 14.7**.

Table 5: Starting the progestogen-only pill: no recent hormonal contraception

Current situation		Last UPSI	PT now?	Consider EC?	Start POP now?	Additional contraceptive precaution required? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)	Follow-up
No recent contraception (or expired Cu-IUD) Check that LMP was a typical bleed at expected time (or consider PT)	Days 1–5 of natural cycle **(day 1 only for DRSP POP)**	N/A	No	No	Yes	No	None
	After day 5 of natural cycle **(after day 1 for DRSP POP)** or amenorrhoeic	Before start of LMP	No	No	Yes	Yes	None
		Since start of LMP **and** ≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		Since start of LMP **and** <21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT at 21 days after UPSI
Cu-IUD in situ (in date) Check that LMP was a typical bleed at expected time (or consider PT)	Days 1–5 of natural cycle **(day 1 only for DRSP POP)**	N/A	No	No	Yes	No	None
	After day 5 **(after day 1 for DRSP POP)**	≥7 days ago	No	No	Yes	Yes	None
		<7 days ago	No	No	Yes	Yes AND retain Cu-IUD for 7 days after last UPSI	None

*Unless ulipristal acetate oral EC is given.

Cu-IUD, copper intrauterine device; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; IUD, intrauterine device; LAM, lactational amenorrhoea method; LMP, last menstrual period; N/A, not applicable; POP, progestogen-only pill; PT, pregnancy test; UPSI, unprotected sexual intercourse.

Table 6: Starting the progestogen-only pill after pregnancy

Current situation		Last UPSI	PT now?	Consider EC?	Start POP now?	Additional contraceptive precaution required? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)	Follow-up
After childbirth	<Day 21	N/A	No	No	Yes	No	None
After childbirth **(if LAM does not apply)** If menstrual cycle is re-established, follow advice for "no recent contraception" **(Table 5)**	≥Day 21	After day 21 **and** ≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		After day 21 **and** <21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT at 21 days after UPSI
After childbirth **(if LAM applies** and continues until POP becomes effective)	Up to 6 months after delivery	N/A	No	No	Yes	No	None
<6 weeks after miscarriage, ectopic or abortion	Days 1–5 **(day 1 only for DRSP POP)**	N/A	No	No	Yes	No	None
	After day 5 **(after day 1 for DRSP POP)**	No UPSI since day 5 (day 1 for DRSP)	No	No	Yes	Yes	None
		UPSI after day 5 (day 1 for DRSP)	PT may remain positive for about 6 weeks after miscarriage, ectopic or abortion. Consider requirement for immediate and follow-up PT and EC		Yes*	Yes	Follow-up PT required (follow local protocol)

*Unless ulipristal acetate oral EC is given.

Cu-IUD, copper intrauterine device; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; IUD, intrauterine device; LAM, lactational amenorrhoea method; LMP, last menstrual period; N/A, not applicable; PT, pregnancy test; UPSI, unprotected sexual intercourse.

14.3 Starting after pregnancy

Starting POP after childbirth

Any POP can be started at any time after childbirth including immediately after delivery.[115] Contraception is required from day 21 after childbirth if the individual wishes to avoid pregnancy. If any POP is started by day 21 after delivery it will be effective immediately with no requirement for additional contraception. If any POP is quick started on day 21 or later, unless the criteria for lactational amenorrhoea are met, risk of existing pregnancy should be assessed prior to starting and additional contraception (eg, condom use) is required (2 days for traditional/DSG POP, 7 days for DRSP POP) after starting. See **FSRH Clinical Guideline Contraception After Pregnancy**[115] and **Table 5**.

Breastfeeding

Key information

A	**The available evidence indicates that progestogen-only methods of contraception have no adverse effects on lactation, infant growth or development.**

14.4 Starting POP after abortion, miscarriage or ectopic pregnancy

POP can safely be started at any time after medical or surgical abortion, miscarriage or ectopic pregnancy.[115] The evidence indicates that POP can be started at the time of mifepristone administration without affecting the effectiveness of medical abortion.[115] If a traditional or DSG POP is initiated within 5 days after abortion, miscarriage or ectopic pregnancy or a DRSP POP is initiated on day 1, it will be effective immediately with no requirement for additional contraception. If quick started thereafter, risk of existing pregnancy should be assessed prior to starting and additional contraception (eg, condom use) is required for 2 days (traditional/DSG POP) or 7 days (DRSP POP). See **FSRH Clinical Guideline Contraception After Pregnancy**[115] and **Table 6**.

14.5 Switching to POP from another contraceptive method

Evidence is lacking for maintenance of contraceptive effect when switching from other hormonal contraception to POP. Established FSRH guidance is given in **Table 7**. This may be more cautious than advice given in the SPCs for POP.[34–37] For switching from a Cu-IUD see **Table 5**.

Table 7: Switching to the progestogen-only pill from another hormonal contraceptive method

Current situation		Last UPSI	PT now?	Consider EC?	Commence POP now?	Additional contraceptive protection required? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)	Follow-up
Correctly taken CHC	Days 1–2 of HFI	N/A	No	No	Yes	No	None
	Days 3–7 of HFI	Before HFI	No	No	Yes	Yes	None
		Since start of HFI	No	No	No	Restart CHC until 7 consecutive pills taken after HFI then switch (with no additional precautions required)	None
	Week 1	Before HFI	No	No	Yes	Yes	None
		Since start of HFI	No	No	No	Continue CHC until 7 consecutive pills taken after HFI then switch (with no additional precautions required)	None
	Weeks 2–3 (and later weeks of continuous CHC use)	N/A	No	No	Yes	No	None
Incorrectly taken CHC		≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT 21 days after UPSI
ENG-IMP (in situ ≤3 years)		N/A	No	No	Yes	No	No
ENG-IMP (expired)	In situ 3–4 years	≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	No	Yes, if PT negative	Yes	Consider PT 21 days after UPSI
	In situ >4 years	≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT 21 days after UPSI

(Table continues on next page)

Table 7: Switching to the progestogen-only pill from another hormonal contraceptive method (continued)

Current situation		Last UPSI	PT now?	Consider EC?	Commence POP now?	Additional contraceptive protection required? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)	Follow-up
DMPA (≤14 weeks since last injection)		N/A	No	No	Yes	None	None
DMPA (>14 weeks since last injection)		Before 14 weeks	No	No	Yes	Yes	None
		After 14 weeks and ≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		After 14 weeks and <21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT 21 days after UPSI
Traditional POP (if taken correctly to date)		N/A	No	No	Yes	No for other traditional or DSG POP Condoms for 7 days for DRSP POP	None
DSG POP (if taken correctly to date)		N/A	No	No	Yes	No	None
DRSP POP (if taken correctly to date)	During HFI (placebo pills days 25–28) or days 1–7 (active pills) after HFI	Since start of HFI	No	No	No	Restart/continue DRSP until seven consecutive active DRSP pills have been taken, then switch as below	None
		Before start of HFI	No	No	Yes	Yes	None
	Days 8–24 (active pills)	N/A	No	No	Yes	No	None
Incorrectly taken POP		≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	Yes	Yes*, if PT negative	Yes	PT 21 days after UPSI

(Table continues on next page)

Table 7: Switching to the progestogen-only pill from another hormonal contraceptive method (continued)

Current situation		Last UPSI	PT now?	Consider EC?	Commence POP now?	Additional contraceptive protection required? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)	Follow-up
LNG-IUS (in date)		≥7 days ago	No	No	Yes	Yes	None
		<7 days ago	No	No	Yes	Yes AND retain IUS for 7 days after last UPSI	None
52 mg LNG-IUS (expired)	In situ 6–7 years	≥7 days ago	Yes	No	Yes, if PT negative	Yes	Consider PT 21 days after UPSI
		<7 days ago	Yes	No	Yes, if PT negative	Yes AND retain IUS for 7 days after last UPSI	Consider PT 21 days after UPSI
	In situ >7 years	≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	Yes	Yes, if PT negative	Yes (consider also retaining IUS if UPSI ≤7 days ago)	PT 21 days after UPSI
Other LNG-IUS (expired)		≥21 days ago	Yes	No	Yes, if PT negative	Yes	None
		<21 days ago	Yes	Yes	Yes, if PT negative	Yes (consider also retaining IUS if UPSI ≤7 days ago)	PT 21 days after UPSI

*Unless ulipristal acetate oral EC is given.

CHC, combined hormonal contraception; DMPA, depot medroxyprogesterone acetate; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; HFI, hormone-free interval; ENG-IMP, etonogestrel implant; IUS, intrauterine system; LNG-IUS, levonorgestrel-releasing intrauterine system; POP, progestogen-only pill; PT, pregnancy test; UPSI, unprotected sexual intercourse.

14.6 Starting POP after oral emergency contraception

POP can be started immediately after LNG-EC. Additional contraception (eg, condom use) is required for 2 days (traditional/DSG POP) or 7 days (DRSP POP) after starting and a pregnancy test should be taken 21 days after the last UPSI. POP start should be delayed for 5 days after UPA-EC to avoid affecting the effectiveness of the UPA-EC. Additional non-hormonal contraception (eg, condom use) is required until POP is started and then for a further 2 days (traditional/DSG POP) or 7 days (DRSP POP). A pregnancy test is required 21 days after the last UPSI. See **FSRH Clinical Guideline Emergency Contraception**[116] and **Table 8**.

Table 8: Starting the progestogen-only pill: after emergency contraception

At time of EC			
EC type	**Start POP now?**	**Additional precautions? (condoms for 2 days for traditional or DSG POP, condoms for 7 days for DRSP POP)**	**Follow-up**
Levonorgestrel oral emergency contraception	Yes	Yes	PT 21 days after last UPSI
Ulipristal acetate oral emergency contraception (UPA-EC)	No. Delay start for 5 days after UPA-EC	Condoms until POP start and then: ▶ Condoms for a further 2 days after traditional/DSG POP start ▶ Condoms for a further 7 days after DRSP POP start	PT 21 days after last UPSI
Copper intrauterine device (Cu-IUD)	Cu-IUD is effective for long-term contraception	Retain Cu-IUD until PT 21 days after Cu-IUD insertion	

Cu-IUD, copper intrauterine device; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; POP, progestogen-only pill; PT, pregnancy test; UPA, ulipristal acetate; UPSI, unprotected sexual intercourse.

15 What drug interactions are important to consider?

15.1 Enzyme-inducing drugs

Clinical recommendations

✓ **Individuals using enzyme-inducing drugs should be informed that the contraceptive effectiveness of all POPs could be reduced during use of the enzyme-inducer and for 28 days after stopping the enzyme-inducer.**

✓ **Individuals using enzyme-inducing drugs should be offered a reliable contraceptive method that is unaffected by enzyme-inducers.**

Drugs that induce hepatic enzymes increase the metabolism of progestogens and could reduce the contraceptive effectiveness of the POP. Individuals in this situation should be offered an effective contraceptive method that is unaffected by enzyme-inducing drugs (DMPA, the Cu-IUD or the LNG-IUS are suitable options if the individual is medically eligible) (see **FSRH Clinical Guidance Drug Interactions with Hormonal Contraception).**[117] If an individual declines these methods and opts to use a POP for contraception during use of an enzyme-inducing drug, they should be advised that contraceptive effectiveness may be reduced and condoms should be used consistently and correctly in addition.

15.2 Ulipristal acetate (UPA)

Key information

D	**The ability of UPA-EC to delay ovulation could be reduced if a POP is started within 5 days of taking the UPA.**
✓	**The ability of UPA-EC to delay ovulation could theoretically be reduced if a POP has been taken in the preceding 7 days.**

Clinical recommendations

✓	**Individuals should be advised to wait 5 days after taking UPA-EC before starting a POP. They should be made aware that they must use condoms reliably or abstain from sex during the 5 days waiting and then for 2 days after starting the LNG and DSG POP and 7 days for DRSP POP.**

UPA is a selective progesterone receptor modulator. Biomedical studies[31,118] have demonstrated that starting a DSG POP or a COC soon after UPA 30 mg given for EC (UPA-EC) reduces the ability of UPA-EC to delay ovulation and could therefore reduce the effectiveness of the EC. The **FSRH Clinical Guideline Emergency Contraception**[116] recommends that after UPA-EC, commencement of POP (and other hormonal contraceptives) is delayed for at least 120 hours after UPA-EC has been given. This ensures that the UPA-EC is as effective as possible in preventing pregnancy resulting from the episode(s) of UPSI for which it was taken. Condoms should be used during the 5 days waiting. After the 5 days waiting, the POP can be started with advice to use additional contraceptive precautions for the following 2 days when starting the LNG and DSG POPs and for 7 days when starting DRSP POP.

Evidence level 2–

EC may be indicated if an individual has UPSI in the time after quick start POP commencement during which additional condom use is required. In this situation, the ability of UPA-EC to delay ovulation could theoretically be reduced by the recently taken POP.

Limited biomedical evidence[31] suggests that the contraceptive effectiveness of the DSG POP is not reduced by concomitant use of single-dose UPA-EC. Theoretically there could be an interaction between the POP and UPA taken regularly for other indications.

Evidence level 2–

15.3 Other potential interactions

Contraceptive hormones could affect the activity of other drugs taken concomitantly. Potential interactions should be checked at **BNF drug interaction checker**.[119] See **FSRH Clinical Guidance Drug Interactions with Hormonal Contraception).**[117]

Drug interactions specific to DRSP POP

Use of the DRSP POP is not recommended during use of potassium-sparing diuretics or potassium supplements. Pharmacodynamic interaction between the DRSP POP and drugs such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists could also potentially increase risk of hyperkalaemia; consider checking U&E during the first cycle of concomitant use (see **BNF drug interaction checker**[119]**)**.

16 What should be done in an initial consultation?

16.1 Suggested checklist prior to POP start or continuation

It is suggested that a contraceptive provider initiating or continuing POP should ensure that (as a minimum) the following criteria are met:

1 Individual assessed as medically eligible (see **Section 16.2**)
2 Checked no interacting drugs or herbal remedies (see **Section 15**)
3 Checked no allergies to POP content (note that some DSG POP preparations contain soya and may cause cross-reaction in individuals allergic to peanuts)
4 Checked for any existing risk of pregnancy, requirement for EC, requirement for additional contraceptive precautions, requirement for follow-up pregnancy testing
5 Individual advised about:
   - Contraceptive effectiveness (perfect and typical use)
   - How to take pills
   - Any requirement for initial additional contraception
   - Management of late/missed pills
   - Interaction with medicines/herbal remedies
   - Potential bleeding patterns
   - Other potential side effects
   - Alternative contraceptive methods, including LARC.

   Also consider:
   - Sexually transmitted infection (STI) risk assessment
   - Checking cervical screening status.

16.2 Assessing suitability of POP for an individual

Clinical recommendations

✓	**Assessment of medical eligibility for POP use should include a comprehensive assessment of medical conditions and drug history.**
✓	**Individuals requesting POP should be informed about the effectiveness with both typical and perfect use of POP and other contraceptive methods, including the superior effectiveness of LARC.**

Medical eligibility

See also **Section 10 Who can and cannot use POP?**.

Traditional and DSG POPs

FSRH recommends that traditional and DSG POPs can be used by medically eligible individuals from menarche until age 55 years. Few medical conditions contraindicate use of traditional and DSG POP. The UK Medical Eligibility Criteria for Contraceptive Use 2016 (UKMEC 2016)[45] recommend that:

- POP should not be used by individuals who currently have breast cancer (UKMEC4).
- Potential health risks associated with use of POP generally outweigh contraceptive benefits (UKMEC3) for individuals who have had breast cancer, those who have had an arterial thrombotic event during use of POP and those with severe decompensated cirrhosis, hepatocellular adenoma or hepatocellular carcinoma (see **Table 3**). Note that UKMEC Category 3 does not absolutely contraindicate the method: use may be considered if safer effective contraceptive methods are unavailable or unacceptable. Discussion with a specialist SRH service may be considered.

DRSP POP

In addition to the above UKMEC3 and UKMEC4 conditions for use of any POP, the DRSP POP should not be used by individuals with severe impairment of renal function or acute renal failure. Use of the DRSP POP is not recommended in the presence of hyperkalaemia, hypoaldosteronism and during use of potassium-sparing diuretics or potassium supplements. For considerations relating to use of the DRSP POP by individuals with mild/moderate impairment of renal function, risk factors for chronic kidney disease, and age over 50 years see **Section 10.2**.

Investigations

No clinical examination or laboratory investigations are routinely required prior to starting traditional or DSG POP. For the DRSP POP, if an individual has mild/moderate impairment of renal function or significant risk factors for chronic kidney disease (particularly if aged over 50 years), consider U&E and blood pressure check prior to prescription. In some cases U&E and blood pressure check after a month of use may be appropriate (see **Section 10.2**).

STI risk assessment and screening should be considered.

16.3 Assessment of factors that could affect contraceptive effectiveness

Drug interactions

A drug history should identify any prescribed or non-prescribed drug that could affect the contraceptive effectiveness of POP or could itself be affected by POP (see **Section 15**).

Note also that use of the DRSP POP is not recommended during use of potassium-sparing diuretics or potassium supplements. Pharmacodynamic interaction between the DRSP POP and drugs such as ACE inhibitors and angiotensin II receptor antagonists could potentially increase risk of hyperkalaemia; consider checking U&E during the first cycle of concomitant use (see **BNF drug interaction checker**[119]**)**.

Malabsorption

The contraceptive effectiveness of POP could be reduced by malabsorption resulting from, for example, vomiting and severe diarrhoea (see **Section 9)**, use of weight management drugs that induce malabsorption, bariatric surgery, small bowel resection or active inflammatory bowel disease. See **FSRH Guideline Sexual and Reproductive Health for Individuals with Inflammatory Bowel Disease**.[120]

16.4 Individuals for whom POP is unsuitable

Individuals assessed as medically ineligible for POP should be told why, and the risk to their health should be explained. Alternative contraceptive methods that can be safely used should be discussed and offered. People with medical conditions or using medications that could reduce contraceptive effectiveness should be given advice regarding (and where possible provided with) alternative methods that would be effective for them.

16.5 Choosing which POP to use

Selecting which POP to use will be an individual choice for each user, which may depend on prior experience of POP side effects including bleeding pattern. The wider window for pill-taking with DRSP and DSG POPs could make these easier than traditional POP to use perfectly. Choice may be influenced by local prescribing formularies.

16.6 Other important supporting information

Clinical recommendations

✓	**Individuals should be provided with accessible information or a link to a trusted online resource to support safe, effective POP use.**

It is important that users are offered the opportunity to ask questions. Users should be provided with the following information regarding use of their chosen POP:

- When to start the method (see **Section 14**), highlighting whether additional contraceptive precautions are required before the contraceptive effect of POP can be relied upon.
- What to do when the method is used incorrectly or inconsistently (see **Section 7**) and when EC may be indicated.
- Significant new health events that should prompt them to review their contraceptive method (eg, diagnosis of breast cancer).
- Advice that they should check with the prescriber of any new medication or with their contraceptive provider whether any new prescribed or non-prescribed drug could affect the contraceptive effectiveness of POP.
- Arrangements for subsequent prescription of POP and follow-up (see **Section 21**).
- What to do if they wish to discontinue POP or change their contraception (see **Section 23.2**).
- Verbal information-giving should be supported by a comprehensive leaflet or direction to a trusted website.

17 Duration of POP prescription

Clinical recommendations

D	**A 12-month supply of traditional, DSG or DRSP POP can be provided to *medically eligible* individuals who are initiating or continuing POP, with information to seek advice if there are any changes to their medical history.**

In line with the World Health Organization Selected Practice Recommendations[121] the GDG advises that provision of up to a 1-year supply of POP may be appropriate depending on the individual's preference and anticipated use. Restriction of the length of supply could result in unwanted discontinuation of the method and increased risk of pregnancy. Although there could be some potential wastage, cost and use of resource associated with frequent follow-up appointments are avoided.

Some users will require review earlier than 1 year. This may include DRSP POP users with risk factors for hyperkalaemia, who could also require U&E check.

The evidence

A systematic review[122] suggested that provision of a greater number of packs of ***COC*** was associated with increased rates of continuation. Studies that compared provision of 1 versus 12 packs, 1 versus 12 or 13 packs, or 3 versus 7 packs found increased continuation of pill use amongst subjects provided with more pill packs.[123–125] Provision of more pill packs was associated with fewer pregnancy tests, fewer pregnancies and lower costs for users. However, a greater number of pill packs (ie, 13 vs 3 packs) was also associated with increased pill wastage in one study.[123]

Evidence level 2–

18 Use of a self-completed checklist to assess medical eligibility for POP

Key information

C **Use of suitable self-completed checklists for medical eligibility appears accurate and acceptable to users of oral contraception.**

Medical contraindications to use of POP are uncommon. Use of a suitable self-completed checklist is appropriate for identifying personal characteristics/medical conditions that could affect medical eligibility for POP or use of a drug that could affect contraceptive effectiveness.

The evidence

In a study that compared self-screening using a checklist with provider-screening[126], 1271 female US shoppers aged 18–49 years were given a checklist of contraindications to POP use (including medical contraindications and use of common interacting drugs) and asked to mark whether they had any of the conditions listed. After completing the checklist, subjects were screened for these same conditions by a nurse practitioner. Only 0.4% of participants failed to identify a contraindication to POP use that was identified by the nurse practitioner: the negative predictive value (the probability that an individual who identified no contraindication in fact had no contraindication) was 99.6% (95% CI 99.0%–99.8%). Only 0.6% of subjects indicated a contraindication to POP use on the checklist but did not have a true contraindication.

Evidence level 2–

Four studies (two from the USA[127,128] and one each from the UK[129] and Tanzania[130]) compared assessment of medical eligibility for CHC using questionnaires self-completed by subjects with clinical assessment by trained providers. The studies reported high levels of agreement between study subjects and HCPs. All four studies found that subjects were more likely than providers to identify contraindications. The UK study[129] concluded that no clinically important information relevant to a particular individual's use of CHC was missed and none of the subjects would have been wrongly prescribed CHC based only on their self-completed questionnaires.

If self-assessment checklists are used they should be developed and validated to ensure that they are effective.

19 Remote prescribing

The General Medical Council (GMC) recommends that if a clinician has adequate knowledge of the patient's health and is satisfied that the medicine will serve the patient's needs, remote prescribing is acceptable.[131] The Joint British Association for Sexual Health and HIV (BASHH)/FSRH Standard for Online and Remote Providers of Sexual and Reproductive Health Services[132] advises that when prescribing remotely, prescribers must satisfy themselves that they can make an adequate and reliable assessment which does not compromise service user care.

Different individuals have different requirements and preferences regarding remote versus in-person contraceptive consultation. For some users, remote provision of POP can facilitate access to effective contraception. The GDG recommends that an in-person consultation is not required to achieve safe POP prescribing.

Validated self-completed assessment forms could be used to exclude health conditions categorised as UKMEC3 or UKMEC4 for use of POP, risks for hyperkalaemia if DRSP POP is to be offered and to identify any relevant drug interactions. As with in-person provision of POP, remote prescribers should ensure that the user is made aware of the failure rate of user-dependent contraception and advised about more effective LARC methods and how to access them. The user must be signposted to clear information to support safe, effective use of their contraception and advised how to access further supplies and to obtain advice if they encounter problems with the contraception or develop new health problems.

20 Pharmacy provision of POP

Key information

✓ **Specific approved brands of DSG POP can now be bought by the user as Pharmacy Medicines (from a pharmacy, without a prescription, under the supervision of a pharmacist).**

Progestogen-only contraceptive pills have previously always been Prescription-Only Medicines. In 2021, however, the Medicines and Healthcare products Regulatory Agency (MHRA) approved two new brands of DSG 75 µg POP as Pharmacy Medicines.

Pharmacy Medicines can be bought by the user from a pharmacy under the supervision of a pharmacist, without a prescription. A 3-month supply of DSG POP can be sold to new users and a 12-month supply to current or recent users aged 18 years and over (supply is limited to 3 months for users aged under 18 years). These products are not on the General Sales List and are not, therefore, available off the shelf in pharmacies or other retail outlets.

The manufacturers of the DSG POP brands approved for pharmacy provision have developed comprehensive packages of materials to support pharmacy provision, including pharmacy training guides, pharmacy checklists, pharmacy supply algorithms and pregnancy exclusion tools. Both brands are supplied with comprehensive patient information.

It is recognised that a contraception consultation is an opportunity for safeguarding, for offering more effective LARC methods and for provision of wider sexual and reproductive health care, advice and information. Crucially, contraception remains available on National Health Service (NHS) prescription without charge to the user. However, accessing existing contraceptive services can, for some individuals, be a barrier to achieving effective contraception. Buying a DSG POP from a pharmacy is an additional option.

Pharmacists already have training and experience in giving contraceptive advice and providing oral EC. As well as supporting identification of medical contraindications to DSG POP use and relevant drug interactions, the pharmacy training guides and pharmacy checklists support safeguarding, provision of information about alternative contraceptive methods, safer sex, cervical screening, identification of vaginal bleeding that may require investigation, and breast awareness and screening. The provision of comprehensive patient information supports safe, effective use.

21 Follow-up

What follow-up arrangements are appropriate?

Clinical recommendations

✓ **After initiation of POP, users should generally be reviewed annually. This can usually be achieved without an in-person consultation.**

Annual review is recommended for most POP users. Clinicians may consider that more frequent follow-up is required for some individuals but frequent review has not been shown to improve correct use or continuation of short-acting contraception.[133,134] If review cannot be achieved within a year, this should not be a barrier to continuation of the method.

All POP users should be advised to seek professional advice at any time if they are experiencing troublesome side effects, have a significant new health event, start new medication, wish to discontinue POP or to discuss alternative methods.

At follow-up, medical eligibility should be rechecked, drug history updated, method adherence and method satisfaction assessed, and alternative contraceptive options considered (including LARC). Users should be reminded about health events and changes in medication that should prompt them to seek medical review.

22 Management of problematic bleeding with POP use

Irregular, unpredictable bleeding is common with use of POP, but HCPs should always consider other causes.

Evidence to inform management of problematic bleeding during POP use is lacking.

When there is problematic bleeding during use of a DSG POP some clinicians offer use of a double dose (150 µg daily) to try to improve bleeding. There is not yet robust published evidence of effectiveness of this strategy for this indication, although one small study[112] with significant potential confounding factors suggested that 150 µg DSG could be superior to 75 µg DSG for management of bleeding in adolescents with dysfunctional bleeding. Study evidence is not available to inform safety of use of double-dose DSG POP (but it is acknowledged that 150 µg DSG is the dose used in COC preparations).

There is no evidence that changing type of POP will improve problematic bleeding. An individual could, however, experience different bleeding patterns with different POP preparations and a change of POP could be useful for some individuals. A Cochrane Review[135] concluded that there was no evidence that bleeding pattern with one POC predicted bleeding pattern with another.

Strategies such as estrogen supplementation or use of mefenamic acid, naproxen or tranexamic acid are often used to reduce bleeding induced by POCs in the short term, but there is no evidence to inform longer-term strategies. See **FSRH Clinical Guideline Problematic Bleeding with Hormonal Contraception**.[136]

The evidence

A 2013 Cochrane systematic review[135] reviewed the evidence for management of vaginal bleeding irregularities induced by POCs. The review identified a 2002 study[137] in which 103 subjects started a DSG POP on the first day of menstruation and were randomised to receive either 150 mg of a novel anti-progestogen not available in the UK (Org 31710) or placebo tablets once every 28 days, for four to seven treatment cycles. The study reported that subjects in the anti-progestogen group developed a cyclical bleed-free interval and also reported significantly fewer bleeding/spotting days, and shorter duration of bleeding episodes than the placebo group. It appeared, however, that this beneficial effect on bleeding might reduce with time and, importantly, increased ovarian activity observed in the anti-progestogen group suggested that contraceptive effectiveness could potentially be affected.

Evidence level 1–

A 2017 literature review[138] identified no studies specific to unscheduled bleeding with POP. The authors suggested that "although mefenamic acid was tested only in DMPA and implant users and naproxen in LNG IUD users, it is reasonable to try these therapies in other progestin-only methods".

No other studies relating to management of problematic bleeding during use of POP were identified: this is an area of recommendation for future study.

23 What recommendations are there for stopping the POP?

23.1 How long can POP use be continued?

Clinical recommendations

✓ **POP can be used for contraception by medically eligible individuals until age 55 years.**

There is no maximum length of time for which POP can be used by medically eligible individuals. Contraception is not required after age 55 years.

23.2 Advice after stopping POP

When POP is stopped, users should be provided with the following information:

- Immediate return to underlying fertility
- Requirement for alternative contraception as soon as POP is discontinued (if the individual does not wish to become pregnant)
- Options for (and access to) ongoing contraception.

23.3 Switching from POP to another method of contraception

Individuals who wish to switch from POP to a different method of contraception should be advised whether additional contraceptive precaution (ie, barrier methods/abstinence) is required, and for how long (see **Table 9** and **Table 10**). See **FSRH Guidance Switching or Starting Methods of Contraception**.[139]

Table 9: Switching from the progestogen-only pill to a hormonal method of contraception

Situation		Starting CHC	Starting another POP	Starting DMPA	Starting IMP	Starting IUS
Traditional POP (if taken correctly to date)		Start immediately Condoms for 7 days	Start immediately No additional precautions for traditional or DSG POP Condoms for 7 days for DRSP POP	Start immediately Condoms for 7 days	Start immediately Condoms for 7 days	Start immediately Condoms for 7 days
DSG POP (if taken correctly to date)		Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions
DRSP POP (if taken correctly to date)	During HFI (placebo pills, days 25–28) **OR** Days 1–7 (active pills) after HFI **AND** No UPSI since start of HFI	Start immediately Condoms for 7 days	Start immediately Condoms for 2 days for DSG/ traditional POP	Start immediately Condoms for 7 days	Start immediately Condoms for 7 days	Start immediately Condoms for 7 days
	During HFI (placebo pills, days 25–28) **OR** Days 1–7 (active pills) after HFI **AND** UPSI since start of HFI	Restart/ continue DRSP POP until 7 consecutive active pills taken **THEN** Switch as for days 8–24	Restart/ continue DRSP POP until 7 consecutive active pills taken **THEN** Switch as for days 8–24	Start immediately **AND** Restart/ continue DRSP POP until 7 consecutive active pills taken	Start immediately **AND** Restart/ continue DRSP POP until 7 consecutive active pills taken	Start immediately **AND** Restart/ continue DRSP POP until 7 consecutive active pills taken
	Days 8–24 (active pills)	Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions	Start immediately No additional precautions

(Table continues on next page)

Table 9: Switching from the progestogen-only pill to a hormonal method of contraception (continued)

Situation		Starting CHC	Starting another POP	Starting DMPA	Starting IMP	Starting IUS
ANY POP (taken incorrectly)	PT negative **AND all UPSI ≥21 days ago**	Start immediately Condoms for 7 days	Start immediately Condoms for 2 days DSG/ traditional POP Condoms for 7 days DRSP POP	Start immediately Condoms for 7 days	Start immediately Condoms for 7 days	Insert immediately (PT **MUST** be negative) Condoms for 7 days
	PT negative **but UPSI within the last 21 days**	Consider EC Start immediately (or after 5 days if UPA-EC given) Condoms until 7 days after starting new method PT 21 days after last UPSI	Consider EC Start immediately (or after 5 days if UPA-EC given) Condoms for 2 days DSG/ traditional POP Condoms for 7 days DRSP POP PT 21 days after last UPSI	Consider EC Consider bridging with CHC/POP/ ENG-IMP If bridging unacceptable or unsuitable, start DMPA immediately (or after 5 days if UPA-EC given) Condoms for 7 days after DMPA given PT 21 days after last UPSI	Consider EC Start immediately (or after 5 days if UPA-EC given) Condoms until 7 days after starting new method PT 21 days after last UPSI	Consider EC Delay insertion until pregnancy excluded by negative PT 21 days after last UPSI and consider bridging with CHC/POP/ ENG-IMP (or DMPA if other methods unacceptable or unsuitable)

CHC, combined hormonal contraception; DMPA, depot medroxyprogesterone acetate; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; ENG-IMP, etonogestrel-releasing implant; HFI, hormone-free interval; LNG-IUS, levonorgestrel-releasing intrauterine system; N/A, not applicable; POP, progestogen-only pill; PT, pregnancy test; UPA, ulipristal acetate; UPSI, unprotected sexual intercourse.

Table 10: Switching from the progestogen-only pill to a non-hormonal method of contraception

Situation			Starting Cu-IUD	Starting condoms
Traditional POP (if taken correctly to date)			Insert immediately No additional precautions	Start immediately No additional precautions
DSG POP (if taken correctly to date)			Insert immediately No additional precautions	Start immediately No additional precautions
DRSP POP (if taken correctly)	During HFI (placebo pills, days 25–28) **OR** Days 1–7 (active pills) after HFI	No UPSI since start of HFI	Insert immediately No additional precautions	Start immediately No additional precautions
		UPSI since start of HFI	Insert immediately No additional precautions	Start immediately AND Restart/continue DRSP POP until 7 consecutive active pills taken after HFI
	Days 8–24 (active pills)		Insert immediately No additional precautions	Start immediately No additional precautions
POP (taken incorrectly) **DSG, traditional and DRSP**	PT negative **AND all UPSI ≥21 days ago**		Insert immediately (PT MUST be negative) No additional precautions	Start immediately No additional precautions
	PT negative **but UPSI within the last 21 days**	All UPSI either ≥21 days ago or <5 days ago	Insert immediately	Consider EC Start immediately PT 21 days after last UPSI
		UPSI between 5 and 21 days ago	Delay insertion until pregnancy excluded by negative PT 21 days after last UPSI Consider oral EC (if also UPSI in last 5 days) Consider bridging with CHC/POP/ENG-IMP (or DMPA if other methods unsuitable or unacceptable)	Start immediately Consider EC (if also UPSI in last 5 days) PT 21 days after last UPSI

CHC, combined hormonal contraception; Cu-IUD, copper intrauterine device; DMPA, depot medroxyprogesterone acetate; DRSP, drospirenone; DSG, desogestrel; EC, emergency contraception; ENG-IMP, etonogestrel-releasing implant; HFI, hormone-free interval; LNG-IUS, levonorgestrel-releasing intrauterine system; POP, progestogen-only pill; PT, pregnancy test; UPSI, unprotected sexual intercourse.

23.4 Planning pregnancy

Return of fertility

Key information

D **The limited available evidence suggests that there is no delay in return to fertility following POP use.**

Individuals who wish to conceive after stopping contraception should be advised that after stopping POP no significant expected delay in return to fertility is expected.[1,12,15] Folic acid and vitamin D supplementation can be started prior to stopping POP.

The evidence

All studies investigating return of ovulation after POP use investigate only short-term use of DSG or DRSP POP (up to 56 days).

Evidence level 1–

A randomised study[1] comparing the effect on ovarian activity of DSG POP and DRSP POP included return of ovulation as a study outcome. 64 participants aged 18–35 years were randomised equally to take either DSG or DRSP POP for two cycles (there was no control group). USS was performed every 3 days after treatment until follicular rupture, or day 27. In each group return of ovulation was documented for all but two subjects by 27 days post-treatment. In both treatment groups ovulation occurred at the earliest on day 9 of the post-treatment cycle, the mean ovulation day was day 13.6 (±3.8) in the DRSP group (allowing for placebo tablets, this was day 17.6 after the last active tablet) and day 18.2 (±5.5) in the DSG group.

A randomised, open-label, pharmacodynamic study[12] investigated the maintenance of ovulation inhibition with DSG POP after scheduled 12-hour delays in pill-taking. Subjects aged 19–40 years, with confirmed ovulation, took DSG POP for 56 days. They were randomised to take either pills 11, 14 and 21 or pills 39, 42 and 49 12 hours late. Serum progesterone levels were measured every 2 days, looking for evidence of ovulation. Data for return of ovulation were available for 99 subjects: the minimum time from last tablet intake to first post-treatment ovulation was 7 days, and the average time was 17.2±7.4 days (range 7–30 days).

A randomised, double-blind study[15] investigating a new progestogen included 13 participants aged 19–40 years with regular ovulatory cycles as a comparator group randomised to take DSG POP for 21 days. The return of ovulation after treatment was confirmed in 12 of 13 participants in the DSG group within about a month by twice-weekly USS and endocrine measurements. The earliest observed ovulation in the DSG POP group was on day 8 after stopping treatment (mean±SD day 20.1±12.6).

23.5 Preconception care

Refer to the **FSRH Clinical Statement Preconception Care**.[140]

23.6 Unplanned pregnancy during POP use

There is no indication from drug safety monitoring that use of POP during pregnancy is associated with fetal abnormality or adverse pregnancy outcomes.[114] POP use should be stopped if a user is found to be pregnant.

24 Cost-effectiveness of the POP

Costs associated with contraceptive use include not only the cost of the contraceptive method itself, but also the cost of the consultation and assessment for prescribing and management of any subsequent method-associated problems. When assessing cost-effectiveness of a contraceptive method, these costs are weighed against costs associated with unplanned pregnancy, taking into account any non-contraceptive benefits.

Cost-effectiveness of POP use in the current UK setting relative to other effective methods of contraception is difficult to estimate accurately.

There is a lack of recently published figures; data from 2008 and 2009 suggest that oral contraception use may be more cost effective in the short-term, but that LARC methods are superior in cost-effectiveness beyond 12–24 months of continued use.[141,142]

Cost-effectiveness of oral contraception depends on user adherence to correct use, which is difficult to study in the real-world setting. Cost-effectiveness of LARC is highly dependent on continuation. Reported LARC continuation rates vary widely between studies, which reflect diverse healthcare settings and different populations across different time periods and do not necessarily reflect continuation rates for LARC in the current UK setting. It is therefore very difficult to accurately compare cost-effectiveness of POP with that of other effective contraceptive methods. It is, however, noted that user acceptability contributes to method continuation and provision of contraceptive choice for the user is important in reducing risk of unwanted pregnancy.

Recommendations for future research

- Effectiveness of double-dose DSG-POP (150 µg daily) for management of problematic bleeding
- Impact of bariatric surgery on effectiveness of POPs
- Contraceptive effectiveness of DRSP POP started on days 2–5 of the menstrual cycle without additional contraceptive precautions
- Bleeding pattern with continuous-use DRSP POP
- Effect of use of DRSP on androgenic symptoms (eg, acne/hirsutism) and on premenstrual syndrome
- Health outcomes in DRSP POP users aged >45 years
- Time to onset of contraceptive cervical mucus effect of DRSP POP (and DSG POP)
- UK usage and continuation data for DSG and DRSP POP
- Uptake of pharmacy provision of DSG POP (to include user demographic, acceptability (user and pharmacist), continuation).

Considerations for implementation of this guideline

The FSRH CEU produces a range of resources (summaries, webinars, lectures) to facilitate dissemination of guideline content and raise awareness of any changes to recommended practice. Changes in FSRH guidance are highlighted in FSRH emails to its membership and via social media platforms and are incorporated into FSRH training and educational materials. The FSRH CEU supports and facilitates national audit relevant to the key auditable standards for each FSRH guideline.

The introduction of the new DSRP POP will necessitate new Patient Group Direction (PGD) documents for this drug and education of clinical staff around use of the new product. FSRH products (including national PGDs and educational products) will support this.

Useful link

- Family Planning Association (FPA): the sexual health company. Your guide to the Progestogen-only Pill (leaflet). Available online **here**.

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APPENDICES

Appendix 1: FSRH Clinical Guideline development process

Who has developed the guideline?

This guideline is produced by the Clinical Effectiveness Unit (CEU) with support from the Clinical Effectiveness Committee (CEC) of the Faculty of Sexual & Reproductive Healthcare (FSRH). The FSRH is a registered charitable organisation which funds the development of its own clinical guidelines. NHS Lothian is contracted to host the CEU in the Chalmers Centre and to provide the CEU's services using ring-fenced funding from the FSRH. No other external funding is received. Chalmers Centre supports the CEU in terms of accommodation, facilities, education, training and clinical advice for the members' enquiry service. As an organisation, NHS Lothian has no editorial influence over CEU guidelines, although staff members may be invited to join the CEU's multidisciplinary guideline development groups (GDGs), in an individual professional capacity.

Development of the guideline was led by the secretariat (CEU staff) and involved the intended users of the guidelines (contraception providers) and patient/service user representatives as part of a multidisciplinary group. The scope of the guideline was informed by a scoping survey conducted amongst members of the FSRH and amongst service users from three sexual and reproductive health services across the UK. The first draft of the guideline was produced based on the final scope of the guideline agreed by the GDG. The first draft of the guideline (version 0.1) was reviewed by the GDG and a revised draft guideline (version 0.2) was produced in response to comments received, after which it was sent to international and UK-based external independent reviewers suggested by the GDG at the face-to-face meeting. A further revision generated a version of the draft guideline (version 0.3) which was placed on the FSRH website for public consultation between 06/06/2022 and 04/07/2022. The revised draft guideline (version 0.4) was sent to the GDG for final comments and to reach consensus on the recommendations (details of this process are given later).

Listed below are the contributors involved in the development of this clinical guideline.

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Dr Sarah Hardman	CEU Co-Director
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Multidisciplinary Guideline Development Group (GDG)

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Dr Madeleine Crow	Community Sexual and Reproductive Health Specialty Registrar (Leeds Sexual Health, UK); CSRH Trainee Representative
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Gemma Middlemass	Patient Representative
Dr Helen Munro	Vice President FSRH; Consultant in Community Sexual Health (Hywel Dda University Health); Clinical Effectiveness Committee Representative
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Independent reviewers

Professor Deborah Bateson	Professor of Practice (The Daffodil Centre, Faculty of Medicine and Health, The University of Sydney, Australia)
Dr Anitra Beasley	Associate Professor, Obstetrics and Gynecology (Baylor College of Medicine, Houston, Texas, USA)
Professor Oskari Heikinheimo	Professor, Chief Physician (Department of Obstetrics and Gynecology, University of Helsinki, Finland)
Dr Kate Weaver	Associate Specialist, Sexual and Reproductive Health (Chalmers Sexual Health Centre, Edinburgh, UK)

Declaration of interests

***Professor Deborah Bateson*:** I have provided education to general practitioners (GPs) on POPs (including the drospirenone POP) which have been sponsored by Besins Healthcare and Bayer, and have attended an advisory board for Besins Healthcare as part of my previous role as Medical Director of Family Planning NSW but have never received any personal remuneration for these services.

***Professor Oskari Heikinheimo*:** I serve occasionally on advisory boards for Bayer Healthcare, and Gedeon Richter, and designed and lectured at educational events connected with these companies.

***Dr Anitra Beasley*:** I serve/have served as the site Principal Investigator (PI) for studies with Medicines 360 and Mithra Pharmaceuticals. All funds were received by the institution/organisation where the studies are/were conducted. I am not a consultant or scientific advisor to any medical or pharmaceutical company.

Patient involvement

Service users from three sexual and reproductive health services (Leeds Sexual Health, Nottingham University Hospitals NHS Trust Integrated Sexual Health Services and Chalmers Sexual Health Centre Edinburgh) across the UK were involved in providing feedback on the scope of the guideline.

Two patient representatives were involved consistently throughout the development process. They provided valuable feedback on multiple drafts of the guideline; their input informed and supported content and the development of recommendations.

Public consultation contributors

We would like to thank the contributors who provided their valuable feedback during the public consultation. We would also like to thank the Royal College of General Practitioners (RCGP) for supporting the public consultation of this guideline.

Guideline development methodology

This FSRH guideline was developed in accordance with the standard methodology for developing FSRH clinical guidelines (outlined in the FSRH's *Framework for Clinical Guideline Development* which can be accessed here). The methodology used in the development of this guideline has been accredited by the National Institute for Health and Care Excellence (NICE).

Systematic review of evidence

A systematic review of the literature was conducted to identify evidence to answer the clinical questions formulated and agreed by the GDG. Searches were performed using relevant medical subject headings and free-text terms using the following databases: PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and POPLINE®. Further, the National Guideline Clearinghouse (NGC) and Scottish Intercollegiate Guideline Network (SIGN) were also used to identify relevant guidelines produced by other organisations; these guidelines were checked to identify missing evidence. No language restrictions were applied to the searches.

Search date: The databases were initially searched up to 17/05/2021. The evidence identified up to this point was used to develop the first draft of the guideline. Any evidence published after this date was not considered for inclusion.

Search strategy: The literature search was performed separately for the different subcategories covered in this clinical guideline.

Articles identified from the search were screened by title and abstract and full-text copies were obtained if the articles addressed the clinical questions relevant to the guideline. A full critical appraisal of each article was conducted. Studies that did not report relevant outcomes or were not relevant to the clinical questions were excluded.

Synthesis of evidence and making clinical recommendations

The recommendations are graded (A, B, C, D and Good Practice Point) according to the level of evidence upon which they are based. The highest level of evidence that may be available depends on the type of clinical question asked. The CEU adopts the comprehensive methodology developed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) (http://www.gradeworkinggroup.org/) to assess the strength of the evidence collated and for generating recommendations from evidence.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels		Grades of recommendations	
1++	High-quality systematic reviews or meta-analysis of randomised controlled trials (RCTs) or RCTs with a very low risk of bias.	A	At least one systematic review, meta-analysis or RCT rated as 1++, and directly applicable to the target population; *or* A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.
1+	Well-conducted systematic reviews or meta-analysis of RCTs or RCTs with a low risk of bias.		
1–	Systematic reviews or meta-analysis of RCTs or RCTs with a high risk of bias.		
2++	High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal.	B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1++ or 1+.
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal.	C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2++.
2–	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.	D	Evidence level 3 or 4; *or* Extrapolated evidence from studies rated as 2+.
3	Non-analytical studies (eg, case report, case series).		
4	Expert opinions.	✓	Good Practice Points based on the clinical experience of the guideline development group.*

*On the occasion when the GDG finds there is an important practical point that they wish to emphasise but for which there is not, nor is there likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. It must be emphasised that these are NOT an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

Considerations when making recommendations

FSRH clinical guidelines are produced primarily to recommend safe and appropriate clinical practice in relation to the provision of different contraceptive methods. Therefore, when formulating the recommendations, the GDG takes into consideration the health benefits, side effects and other risks associated with implementing the recommendations, based on the available evidence and expert opinion. Further, the GDG takes into consideration the different financial and organisational barriers that clinicians and services may face in the implementation of recommendations to ensure that the recommendations are realistic and achievable.

Reaching consensus on the recommendations

When further revisions based on public consultation feedback have been made, members of the GDG were asked to complete a form to indicate whether they agree or disagree with the recommendations proposed. The consensus process is as follows:

- Consensus will be reached when 80% of the GDG members agree with the recommendation.
- Recommendations where consensus is not reached will be redrafted in light of any feedback.
- The recommendation consensus form will be sent again for all recommendations. Consensus will be reached when 80% of the GDG members agree with the recommendation.
- If consensus is not reached on certain recommendations, these will be redrafted once more.
- If after one more round of consultation consensus is still not reached, the recommendation will be taken to the CEC for final decision.
- Any group member who is not content with the decision can choose to have their disagreement noted within the guideline.

Updating this guideline

Clinical guidelines are routinely due for update 5 years after publication. The decision as to whether update of a guideline is required will be based on the availability of new evidence published since its publication. Updates may also be triggered by the emergence of evidence expected to have an important impact on the recommendations. The final decision on whether to carry out a full or partial clinical guideline update is taken by the CEU in consultation with the CEC of the FSRH.

Appendix 2: Recommendations following incorrect use of the drospirenone progestogen-only pill

- In each packet there are 24 active drospirenone progestogen-only pills (DRSP POP), followed by 4 placebo pills. Packets are taken consecutively with no breaks.
- Users should be encouraged to take pills correctly. If not used correctly, there is a potential risk of pregnancy, even if these recommended actions are followed.
- If any pill is taken <24 hours late, contraceptive effectiveness is not reduced.
- A "missed pill" is a pill taken ≥24 hours late (≥48 hours since the last pill was taken).
- If any active pill is "missed" (taken ≥24 hours late), contraceptive effectiveness may be reduced.
- The more active pills that are missed, the more likely it is that contraceptive effectiveness will be reduced.
- If an individual uses DRSP POP incorrectly, they should be made aware that contraceptive effectiveness depends on reliable use. Offer alternative effective contraceptive methods, including LARC.

Timing of pill(s) missed	Is EC required?	Additional advice for user	Follow-up
1 or more pill(s) missed in days 1–7 (active pills)	Consider* if there was UPSI in the HFI or days 1–7 of pill-taking	1 Take the last pill that was missed 2 Continue taking subsequent white active pills as normal 3 Use condoms/abstain until pills have been taken for 7 consecutive days	Advise PT 3 weeks after last UPSI
1 or more pill(s) missed in days 8–17 (active pills)	Consider* if there was UPSI since the first pill was missed or if incorrect pill use earlier in the packet	1 Take the last pill that was missed 2 Continue taking subsequent active pills as normal 3 Use condoms/abstain until pills have been taken for 7 consecutive days	Consider PT 3 weeks after last UPSI
1 or more pill(s) missed in days 18–24 (active pills)	Consider* if there was UPSI since the first pill was missed or if incorrect pill use earlier in the packet	1 Take the last pill that was missed 2 Continue taking subsequent white active pills as normal 3 Use condoms/abstain until pills have been taken for 7 consecutive days 4 **Omit HFI (placebo pills)**	Consider PT 3 weeks after last UPSI
1 or more pill(s) missed in days 25–28 (placebo pills)	No	1 Dispose of missed pill(s) 2 Continue to take remainder of pills as normal 3 Ensure next packet of pills is started on time 4 If next packet of pills is not started on time, follow rules for missed pills in days 1–7	None required

EC, emergency contraception; HFI, hormone-free interval; PT, pregnancy test; UPSI, unprotected sexual intercourse.
*See **Section 7 Incorrect POP use**.

Appendix 3: Considerations for emergency contraception following incorrect use of the drospirenone progestogen-only pill

There is insufficient evidence to accurately inform risk of pregnancy if any specific combination of pills is missed. **In addition to following the missed pill rules for drospirenone progestogen-only pill (DRSP POP)**, the need for emergency contraception (EC) will need to be evaluated on a case-by-case basis, considering the following:

- The more pills that are missed, the higher the risk of decreased contraceptive protection.
- **Missed pills during days 1–7 after the hormone-free interval (HFI) (placebo pills)**
  - If one or more pills are missed during days 1–7 AND there was unprotected sexual intercourse (UPSI) in the HFI or later there could be significant risk of pregnancy and EC should be considered.
- **Missed pills during days 8–17**
  - ***Provided that all other pills in the packet have been taken correctly*** the risk of pregnancy is likely to be low if pills are missed on **up to 4 consecutive** days from day 8 to day 17. EC can be considered, but the priority is restarting correct DRSP pill-taking.
  - If any other combination of pills is missed during days 8–17 or if pills were missed earlier in the packet, EC should be considered.
- **Missed pills during days 18–24**
  - ***Provided that all other pills in the packet have been taken correctly*** the risk of pregnancy is likely to be low if pills are missed on **up to 4 consecutive** days from day 18 to day 24. EC can be considered, but the priority is restarting correct active DRSP pill-taking and omitting the HFI.
  - If any other combination of pills is missed during days 18–24 or if pills were missed earlier in the packet, EC should be considered.

What method of EC should I choose?

- If EC is indicated after missed DRSP POP, levonorgestrel EC can be used within 96 hours of UPSI to delay ovulation **and the DRSP POP restarted immediately**.
- Use of UPA in the missed pill situation is generally not recommended because:
  - The ability of ulipristal acetate (UPA) to delay ovulation could be reduced if DRSP pill-taking is restarted within 5 days. But if DRSP pill-taking is delayed for 5 days, this increases the number of missed pills and thus the risk of ovulation.
  - The ability of UPA to delay ovulation could theoretically be reduced by residual progestogen from previously taken pills.
- **Assuming correct use in the previous packet**, a copper intrauterine device (Cu-IUD) can be inserted for EC:
  - Within 5 days after the first missed DRSP pill in the packet **OR**
  - Within 5 days after the first UPSI since the start of this packet **whichever occurs later.**

For further information about EC see **FSRH Clinical Guideline Emergency Contraception**.[116]

Questions for continuing professional development

1 What is the estimated typical use failure rate for the progestogen-only pill (POP)?
   a) 0.3%
   b) 1%
   c) 3%
   d) 9%
   e) 13%

2 What is primary mode of action of the desogestrel (DSG) POP and drospirenone (DRSP) POP?
   a) Changes to the endometrium
   b) Reduction in activity of cilia
   c) Suppression of ovulation
   d) Thickening of cervical mucus

3 Which of the following statements about age and POP use is true?
   a) DSG POP cannot be used by individuals aged <18 years
   b) DSG POP should not be used after age 50 years
   c) DRSP POP would not be suitable for a 16-year-old
   d) DRSP POP could be suitable for an individual aged 52 years
   e) DRSP POP would not be suitable for a smoker aged 47 years

4 How long since the last norethisterone (NET) POP is taken is a pill considered missed?
   a) 3 hours
   b) 27 hours
   c) 24 hours
   d) 36 hours
   e) 48 hours

5 How long since the last DSG POP is taken is a pill considered missed?
   a) 3 hours
   b) 27 hours
   c) 24 hours
   d) 36 hours
   e) 48 hours

6 How long since the last DRSP POP is taken is a pill considered missed?
   a) 3 hours
   b) 27 hours
   c) 24 hours
   d) 36 hours
   e) 48 hours

7 When quick starting POP after levonorgestrel oral emergency contraception, condoms should be advised for:
   a) 2 days for DSG POP and 7 days for DRSP POP
   b) 2 days for DSG POP and 2 days for DRSP POP
   c) 7 days for DSG POP and 2 days for NET POP
   d) 2 days for NET POP and 7 days for DSG POP
   e) 2 days for NET POP and 2 days for DRSP POP

8 Which of these drugs is not expected to affect (or potentially affect) the contraceptive effectiveness of the DRSP POP?
   a) Carbamazepine
   b) Efavirenz
   c) Spironolactone
   d) Phenobarbital
   e) Topiramate

9 Which one of the following conditions is UKMEC3 or UKMEC4 for starting POP?
   a) A history of myocardial infarction
   b) A history of breast cancer
   c) Hypertension (blood pressure ≥160/100 mmHg)
   d) A history of ovarian cysts
   e) A history of ectopic pregnancy

10 In relation to bleeding during use of the POP, which of the following statements is true?
   a) Traditional POP does not affect bleeding pattern
   b) Doubling the dose of DSG POP reliably improves bleeding
   c) Dysmenorrhoea is a common side effect of POP
   d) Bleeding with the DRSP POP is predictable
   e) Unpredictable bleeding is common with DSG and DRSP POPs

11 An individual presents complaining of reduced libido and weight gain on a POP – what do you advise?
   a) POP does not affect weight – you should continue POP
   b) POP causes weight gain – you should consider another method
   c) POP does not affect libido – you should continue POP
   d) If you think that your POP is causing side effects you should avoid other POPs
   e) If you think that POP is causing side effects you could consider another contraceptive option

12 Which of the following would contraindicate use of DRSP POP?
   a) Severe renal impairment
   b) Age >45 years
   c) Obesity
   d) Uncomplicated hypertension
   e) History of venous thromboembolism

Auditable standards

Every FSRH clinical guideline includes a set of auditable standards. These reflect some of the recommendations made in the guideline that are key to making good prescribing decisions and achieving safe, effective contraception for the user. Some of the auditable standards may relate to key guidance that is new in the guideline; others are based on important aspects of already established guidance.

It is important for clinicians and services to collect information about whether they are practising according to recognised guidelines at a given point in time, use the information gathered to inform whether changes to their practice/protocols are indicated and review at a later time point whether any changes implemented have led to improvement in adherence to guidelines.

The auditable standards accompanying FSRH guidelines are a tool that can be used by clinicians and services when undertaking audit of their practice in the field of contraception. FSRH CEU offers additional materials and support for services to undertake National Benchmarking Audit (NBA). NBA facilitates review of current practice in a service as compared to guidance, comparison of the service's practice to that in other similar services, and evaluation of any changes made by the service designed to align practice with guidelines.

Suggested auditable standards

The following auditable standards are provided to accompany the FSRH 2022 Progestogen-only Pills Guideline. When collecting data for audit, services may wish to gather other useful information (suggestions are made alongside the auditable standards).

1 Assessment of suitability of a POP for an individual should include a comprehensive drug history (standard 100%)

Some drugs (Prescription, Pharmacy, General Sales List, herbal or recreational), when used alongside a POP, have potential to affect its contraceptive effectiveness. Conversely, POP could affect activity of other drugs or interact with them to cause undesirable effects. It is crucial to safe, effective use of POP that any drug interactions are identified. It is good practice to document that this has been undertaken.

- Services may wish also to collect data regarding instances in which a POP interaction with another drug is missed.
- Services may wish also to collect data regarding duration of POP prescription and reasons for providing a supply of POP for less than a year to inform service efficiency.

2 Individuals using an enzyme-inducing drug should be offered effective contraception that is not affected by the enzyme-inducer (standard 100%)

Enzyme-inducing drugs may reduce contraceptive effectiveness of POPs (as well as combined hormonal contraception and the etonogestrel implant). Individuals in this situation who require contraception should be offered an intrauterine contraceptive or progestogen-only injectable, if medially eligible (these are unaffected by induction of hepatic enzymes).

3 POP users should be informed about its contraceptive effectiveness with both typical and perfect use (standard 100%)

When used perfectly, contraceptive effectiveness of POPs is high. With typical use, however, the risk of pregnancy during the first year of use has been estimated at about 9% (this compares to <1% with typical use of LARC methods). It is considered that this is crucial information to inform user choice of method and to highlight the importance of correct use. It is good practice to document that this information has been provided.

- Services may wish also to collect information about whether alternative contraceptive options are offered.

4 Individuals should be given advice – and directed to reliable, accessible information – about how to take their POP correctly and what to do if use is incorrect (standard 100%)

Having opted to use a user-dependent method of contraception, it is crucial that the user is then given adequate information to support effective use. It is good practice to document that this has been undertaken.

- Services may wish also to collect information about how access to patient information is provided.
- Services may wish also to collect data as to documented discussion about bleeding patterns during use of POP.

Comments and feedback on published guideline

All comments on this published guideline can be sent directly to the Clinical Effectiveness Unit (CEU) of the Faculty of Sexual & Reproductive Healthcare (FSRH) via the FSRH website (www.fsrh.org). The CEU may not respond individually to all feedback. However, the CEU will review all comments and provide an anonymised summary of comments and responses, which are reviewed by the Clinical Effectiveness Committee and any necessary amendments made subsequently.