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UPDATE ON CONTRACEPTION (1): METHODS

- **Approximately half of unplanned pregnancies result from not using contraception, and the remainder from contraceptive failure**
- **Women should be informed about the effectiveness (of both typical and perfect use) of the different contraceptive methods**
- **Many people fail to adhere to a regular contraceptive routine, potentially resulting in contraceptive failure**
- **The choice of contraceptive method depends on the effectiveness of the method and the individual patient**

INTRODUCTION

Worldwide it is estimated that 48% of pregnancies are unintended or unplanned.[1] It is thought that family planning programmes prevent approximately 187 million unplanned pregnancies annually.[2] Adverse consequences associated with unplanned pregnancies include low birth weight, preterm birth, an increased risk of postpartum depression, psychological distress and maternal mortality.[3,4]

Approximately half of unplanned pregnancies result from not using contraception, and the remainder from contraceptive failure, usually due to incorrect/inconsistent use of contraception.[3,5,6] Reasons for not using contraception include fear of adverse effects, health concerns, lack of access to contraceptives and cultural barriers.[5,6] Healthcare professionals (HCPs) play a vital role in advising women on contraception.[7,8]

This, the first of two bulletins on contraception, outlines the various methods of contraception currently used in practice in Ireland; the second bulletin will review the use of contraception in some specific situations.

METHODS OF CONTRACEPTION

This bulletin will discuss **short-acting contraceptive methods** and **long-acting reversible contraception** (LARC). Short-acting contraceptive methods include combined hormonal contraception (CHC) (e.g. combined oral contraception [COC], combined transdermal patch ["patch"] and combined vaginal ring ["ring"]) and the oral progesterone-only pill (POP). LARC methods include intrauterine contraception (IUC) [the copper-bearing intrauterine devices (Cu-IUDs) and the levonorgestrel intrauterine systems (LNG-IUSs)], the progestogen-only implant and the progestogen-only injectable.[8] In addition, emergency contraception is available for women who have had unprotected sexual intercourse (this topic will be reviewed in our next bulletin on contraception [NMIC 2021;Vol 27:No 6]).

CONTRACEPTIVE CHOICE

The choice of a contraceptive method depends on both the effectiveness of the method and the individual patient, with consideration of factors such as age, co-morbidities, concomitant medications and preferences of the user.[6,7] Many people fail to adhere to a regular contraceptive routine, potentially resulting in contraceptive failure.[5] Table 1 outlines the failure rates associated with both "perfect" and "typical" use of contraceptive methods.

Table 1: Percentage of women experiencing an unintended pregnancy within the first year of contraceptive use[9]

Method	Typical use (%)	Perfect use (%)
No method	85	85
Female condom	21	5
Male condom	18	2
Combined hormonal contraception*	9	0.3
Progestogen-only pill	9	0.3
Progestogen-only injectable	6	0.2
Copper intrauterine device	0.8	0.6
Levonorgestrel intrauterine system	0.2	0.2
Progestogen-only implant	0.05	0.05

*includes combined oral contraception, transdermal patch and vaginal ring

Medical eligibility criteria: Most contraceptive users are medically fit and can use any available contraceptive method; however **some medical conditions are associated with risks when certain contraceptive methods are used**. The UK Medical Eligibility Criteria (MEC) (based on the WHO MEC)[10] published by the UK Faculty of Sexual and Reproductive Healthcare (FSRH), can be used by HCPs to provide guidance on who can use which contraceptive methods safely (see table 2).[11]

Table 2: Definitions of UK Medical Eligibility Criteria categories[11]

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

SHORT-ACTING CONTRACEPTION

In many countries, short-acting contraception is the most commonly used hormonal contraceptive method.[7,12-15] **Short-acting contraceptives are more user dependent in terms of adherence and are associated with higher pregnancy and lower continuation rates than LARC**.[7,9,16] Adherence (especially in those aged

<21 years) to oral contraceptives is a factor associated with higher failure rates.[2,17-19]

COMBINED HORMONAL CONTRACEPTION

The primary mechanism of CHC (i.e. COC, patch and ring) is the prevention of ovulation; secondary effects include changes to cervical mucus, endometrium and tubal motility.[7,16] **The contraceptive effectiveness of all CHC is similar and highly user dependent** (see table 1).[7,20]

In the absence of contraindications to its use, CHC is suitable for the majority of women up to age 50 years.[7] Contraindications for CHC include women aged ≥35 years who smoke, systolic blood pressure (BP) ≥140 mmHg or diastolic BP ≥90 mmHg, history of or current venous thromboembolism (VTE), current and history of ischaemic heart disease (IHD) or stroke, current breast cancer, migraine with aura, positive antiphospholipid antibodies, multiple risk factors for cardiovascular disease and body mass index (BMI) ≥35 kg/m^2;[11] see the full UKMEC accessed at www.fsrh.org (note that women with conditions categorised as UKMEC 3 and 4 should avoid CHC). A family history of breast cancer is not a contraindication to use of CHC.[7,21]

Different types of CHC: The majority of COCs in Ireland contain the synthetic estrogen, ethinylestradiol (EE) in doses between 20 and 35 microgram (other formulations contain estradiol and estradiol valerate).[22-33] The different types of progestogens include levonorgestrel, norgestimate, desogestrel, gestodene, drospirenone, dienogest and nomegestrol, which may be classified by "generation" (first, second, third and other), according to when they were first marketed.[7] The patch contains EE and norelgestromin, and the ring contains EE and etonogestrel.[34,35]

The majority of COCs in Ireland are monophasic, i.e. all the pills in the pack contain the same dose of hormones,[22-31] however there are some multiphasic preparations available.[32,33] There is currently insufficient evidence to suggest that there is a significant difference between monophasic and multiphasic preparations.[7,16,36,37]

Standard use of CHC involves the administration of 21 days of hormones followed by a 7 day hormone-free interval (HFI) (21 + 7 regimen) (see table 3).[38] Note that there are two COC products authorised as a 24 + 4 regimen and one as a 26 + 2 regimen.[30,31,33] The HFI results in a withdrawal bleed, which has no health benefits.[7,38,39] The first 7 days of hormones inhibit ovulation and the remaining 14 days of hormones maintain anovulation.[7] **Contraceptive protection is maintained during the HFI as long as the user has consistently adhered to correct administration.** The incorrect use of CHC (missing pills or making mistakes with patches or rings) may result in ovulation with subsequent contraceptive failure.[7] The Summary of Product Characteristics (SmPC) of each individual product and the FSRH have guidance on what to do in the event of incorrect use of CHC.

Tailored regimens: There is evidence that CHC regimens with an extended hormone treatment period and shorter HFI (so called "tailored regimens") could reduce the risk of pregnancy, especially if CHC use around the HFI is imperfect.[7,38-43] The UK FSRH supports the CHC tailored regimens as shown in table 3. Tailored regimens are an acceptable alternative to standard CHC regimens for many women, who should be informed that this use is off-label.[7,44-48]

Table 3: Standard and tailored regimens for use of CHC[7,16,21]

Type of regimen	Period of CHC use	HFI
Standard use	21 days (21 active pills or 3 patches or 1 ring)	7 days
Tailored use		
Shortened HFI	21 days (21 active pills or 3 patches or 1 ring)	4 days
Extended use (tricycling)	9 weeks (3 x 21 active pills or 9 patches or 3 rings used consecutively)	4 days
Flexible extended use	Continuous use (≥21 days) of active pills, patches or rings until breakthrough bleeding occurs for 3-4 days	4 days
Continuous use	Continuous use of active pills, patches or rings	None

CHC- combined hormonal contraception; HFI-hormone free interval

Tailored regimens reduce the frequency of withdrawal bleeding and associated symptoms (e.g. headache, breast tenderness and mood change).[7,39,45,49] Bleeding patterns are similar or improved with tailored regimens;[7,44,45,48-50] there may be an increase in breakthrough bleeding (BTB) during the first few months, which decreases in frequency and intensity with time.[7,38,45,50] Some women may report BTB after several months of continuous CHC use.[38,51] Current data regarding the safety of tailored CHC regimens is reassuring.[39,44,49,52-54] **Tailored regimens can only be offered for monophasic preparations that are licensed as a 21/7 regimen;[7,38] multiphasic COCs should not be used.**[7]

Health risks associated with CHC: Women should be informed of the health risks associated with CHC; the recommendations that apply to COC are usually extrapolated to include the patch and ring.[7]

Current use of CHC is associated with an increased risk of VTE compared with non-use, however the absolute risk of VTE is small.[7,55] This increased risk varies with different CHCs and depends on the dose of EE and the progestogen type; current data indicates that CHCs with higher doses of EE are associated with a higher risk and those containing levonorgestrel, norethisterone or norgestimate have the lowest risk (see table 4).[7,55-57] An increased risk of VTE is also associated with EE and cyproterone acetate (licensed for moderate to severe acne); this is similar to the risk of drospirenone, gestodene and desogestrel-containing COCs.[56,58,59] **The risk of VTE is highest in the months immediately after initiation of CHC or when restarting after a break of ≥1 month;**[7] **unnecessary breaks in CHC use should be avoided.**

Table 4: Risk of venous thromboembolism with CHC[55]

Combined hormonal contraception (CHC)	Venous thromboembolism (per 10,000 women per year of use)
Non-pregnant women not using CHC	2
Women using CHC containing levonorgestrel, norethisterone or norgestimate	5 - 7
Women using CHC containing etonogestrel or norelgestromin	6 – 12
Women using CHC containing drospirenone, gestodene or desogestrel	9 - 12
Women using CHC containing dienogest or nomegestrol	Not yet known

There is a small increased risk of breast and cervical cancer in patients on CHC; this risk reduces with time after stopping CHC.[7,60-62] There is also a very small increased risk of myocardial infarction (MI) and ischaemic stroke, which is increased with higher doses of estrogen;[7,57,63] CHC should be avoided in women with other risk factors for cardiovascular disease (CVD).[7] Adverse effects associated with CHC include mood change, headache and unscheduled bleeding.[7] There is no evidence that use of CHC is associated with subsequent long-term reduction in fertility.[7]

Non-contraceptive benefits of CHC include reduced heavy menstrual bleeding and menstrual pain, improved acne, reduction of pre-menstrual symptoms, reduction of symptoms associated with polycystic ovary syndrome, reduced recurrence of endometriosis after surgery and reduced risk of endometrial, ovarian and colorectal cancer.[7,60,64,65]

Drug interactions of CHC are important to consider. The effectiveness of CHC may be reduced by concomitant use of other medicines (e.g. enzyme-inducing drugs [EIDs]), while CHC itself may affect other medicines resulting in a potential for adverse effects (e.g. lamotrigine),[7] an alternative form of contraception may be more appropriate for women on such medicines (see the next bulletin for more information on drug interactions [NMIC 2021;Vol 27:No.6]).

Choice of CHC: A first-line CHC option would be a COC containing EE ≤30 microgram combined with either levonorgestrel.[7] The FSRH advises that CHCs containing EE can be started up to and including day 5 of a natural menstrual cycle (day 1 for estradiol-containing COC) without the need for additional contraceptive protection;[7] additional contraceptive precautions are required outside of this time frame.[7]

ORAL PROGESTOGEN-ONLY CONTRACEPTION

Progestogen-only pills (POPs) are an oral contraceptive option for women who are not considered eligible for CHC or who prefer to avoid estrogen. There are two POPs currently marketed in Ireland; norethisterone and desogestrel.[66,67] **POPs primarily act by altering cervical mucus and preventing sperm penetration**. However POPs may also inhibit ovulation, particularly in older women; **studies suggest that desogestrel inhibits ovulation in 97% of women.**[16,68,69] POPs that are used consistently and correctly are >99% effective (see table 1).[68]

Contraindications for POPs include current breast cancer;[11] the full list of contraindications is available in UKMEC accessed at www.fsrh.org (note that women with conditions categorised as UKMEC 3 and 4 should avoid POPs).

POPs should be taken on a daily basis at the same time; if norethisterone is >3 hours late or desogestrel is >12 hours late, the delayed/missed pill should be taken immediately, the remaining tablets taken normally and additional barrier methods of contraception used for 7 days.[66-68]

Women should be informed that users of POPs may experience altered bleeding patterns including irregular bleeding and oligomenorrhoea, which may resolve with long-term treatment.[16,68] Current evidence suggests that POPs are not associated with an increased risk of CVD or breast cancer (the evidence is limited and an increased risk of breast cancer cannot be completely excluded).[68] **The efficacy of POPs is reduced by EIDs and an alternative method of contraception is recommended for women on EIDs.**[66-68]

Of note, another POP has recently been authorised (currently not marketed) in Ireland, which consists of 4mg drospirenone in a 24 day active/4 day placebo regimen;[70] evidence suggests that it has similar efficacy to CHC, and an improved cycle control compared to traditional POPs.[71-74]

LONG-ACTING REVERSIBLE CONTRACEPTION

LARC includes intrauterine contraception (IUC) [Cu-IUDs and LNG-IUSs], the progestogen-only implant and the progestogen-only injectable.[17,75] **LARC is usually acceptable to most women (including young women), is not user dependent, has lower failure rates and higher continuation rates than the shorter-acting methods.**[2,6,17,76] The proportion of LARC users has increased in recent years, however it is smaller than those using short-acting methods.[14,15] It is anticipated that increasing the uptake of LARC will reduce the numbers of unplanned pregnancies.[8,17] **Barriers to use of LARC include a lack of information about the methods, limited access and limited resources.**[5,17,77] There are relatively few contraindications for LARC, which can be used by many women for whom short-acting methods are not suitable; see www.fsrh.org for the full UKMEC for each LARC method (note that women with conditions categorised as UKMEC 3 and 4 should avoid the specific LARC method). HCPs require appropriate training and experience in the insertion of IUC and progestogen-only implants.[8] Women requesting contraception (including LARC) should be informed that the consistent and correct use of condoms is an effective means of protecting against HIV and other sexually transmitted infections (STIs). Table 5 summarises the types of LARC currently available in Ireland.

Intrauterine contraception (IUC) (i.e. Cu-IUDs and LNG-IUSs) are highly effective methods of contraception,[21,76] and for most women there are few long-term risks associated with their use.[76] The use of intrauterine methods of contraception should not be restricted based on parity or age.[17,76] Contraindications to IUC include postpartum and post-abortion sepsis and current pelvic infection; the full list of contraindications is available in UKMEC accessed at www.fsrh.org.[11] **Screening for STIs should be considered in those at risk, prior to insertion of IUC** and is suggested for patients <25 years.[17,76] There is a risk of ectopic pregnancy with the use of IUC, which is less than the overall risk of ectopic pregnancy in women not using any contraception.[76] Users should be informed of the symptoms and **an ectopic pregnancy excluded if pregnancy occurs in an IUC user.**[16,76]

Copper intrauterine devices: A wide range of Cu-IUDs are available; the FSRH recommends use of Cu-IUDs with a total of 380 mm² of copper.[76] An intrauterine ball which comprises of a number of copper beads in a flexible alloy frame is a novel Cu-IUD, with similar safety and efficacy to other Cu-IUDs.[21,86] The Cu-IUD may be associated with a reduced risk of endometrial and cervical cancer.[76]

Levonorgestrel intrauterine system: **The LNG-IUS has become increasingly popular for long-term contraception.**[87,88] There are three types of LNG-IUSs

Table 5: Long-acting reversible contraceptives [8,17,75,76,78-85]

Type of LARC method (Mode of action)	Duration of use	Effects on menstrual cycle	Risk/precautions with use include*:
Copper containing intrauterine device (primarily prevents fertilisation and also inhibits implantation)	5-10 years depending on type of device	Heavier bleeding +/- dysmenorrhoea	**Expulsion** < 1 in 20 women (most common in the first year) **PID:** <1% in women at low risk of STI **Uterine perforation** up to 2 in 1000 (increased risk with breastfeeding)
Levonorgestrel intrauterine system 52mg 19.5mg 13.5mg (prevents fertilisation and endometrial suppression)	 6 years 5 years 3 years	Irregular bleeding and spotting may occur up to one year after insertion Oligomenorrhoea or amenorrhoea likely by end of first year** (the 52mg LNG-IUS is also authorised for heavy menstrual bleeding)	**Expulsion** < 1 in 20 women (most common in the first year) **PID:** <1% in women at low risk of STI **Uterine perforation** up to 2 in 1000 (increased risk with breastfeeding) Increased **risk of ovarian cysts**; mainly asymptomatic and resolve spontaneously **Adverse effects** e.g. acne, breast tenderness, headaches, mood changes
Progestogen-only implant ENG-IMP 68mg (primarily prevents ovulation)	3 years	Unpredictable bleeding including amenorrhoea (25%), irregular uterine bleeding/spotting, which may persist	Complications with removal and insertion uncommon (rare complications include intravascular insertion and distant migration) **Reduced efficacy with EIDs and other potential drug interactions***
Progestogen-only injectable DMPA (primarily prevents ovulation)	Every 12-13 weeks	Amenorrhoea common (may benefit women with menstrual problems) Persistent bleeding may occur	**Weight gain** – especially in women <18 years with BMI ≥30kg/m^2 Reversible **reduction in BMD** (May be **delayed fertility** of 1 year [however pregnancy can occur on discontinuing]) **Not affected by EIDs however reduced efficacy with ulipristal acetate**

* the Summary of Product Characteristics should be consulted for full prescribing information, **amenorrhoea may be less likely with 13.5mg and 19.5mg LNG-IUS; LARC – long-acting reversible contraception, IUD – intra-uterine device, PID – pelvic inflammatory disease, STI – sexually transmitted infection, LNG – levonorgestrel, ENG-IMP-etonogestrel implant, EID-enzyme-inducing drugs; DMPA - depot medroxyprogesterone acetate, BMD – bone mineral density

currently available in Ireland (see table 5) with similar efficacy and safety;[79-82] the 19.5mg and 13.5mg LNG-IUSs have narrower diameters and are reported to be significantly easier to insert with less pain on insertion than the 52mg LNG-IUS.[83] Additional contraindications for LNG-IUS specifically include breast cancer; the full list of contraindications is available in UKMEC accessed at www.fsrh.org.[11] Evidence does not support a link between LNG-IUS and increased risk of VTE, MI or breast cancer.

Progestogen-only implant: The etonogestrel implant (ENG-IMP) is a single non-biodegradable, subdermal rod (see table 5), which is recommended for use in medically eligible women between menarche and age 55 years.[78] **Women should be informed of the risk of irregular, unpredictable bleeding which commonly occurs with the implant and may lead to discontinuation.**[17,75,89,90] Limited evidence suggests that the risk of pregnancy is likely to be low in the fourth year of implant use, however routine extended use is not recommended.[78] Contraindications for the progestogen-only implant include breast cancer; the full list of contraindications is available in UKMEC accessed at www.fsrh.org).[11] The limited evidence available does not suggest an increased risk of VTE, arterial thromboembolic events or breast cancer (however the evidence is too limited to completely exclude an association with breast cancer).[78] Non-contraceptive benefits of the implant include reduced dysmenorrhoea.[78]

Progestogen-only injectable: Depot medroxyprogesterone acetate (DMPA) is given intramuscularly every 12 to 13 weeks (see table 5).[75] DMPA is a contraceptive option for women with sickle cell disease as it may reduce the severity of sickle crisis pain.[16,75] Due to reversible reduced bone mineral density (BMD) associated with DMPA, it should only be considered for women aged <18 years when other methods of contraception are inappropriate and women aged ≥45 years should be advised to switch to another method.[21,75] **Users of DMPA should be reviewed every two years to assess the risks and benefits of continuing use of the method.**[73] Contraindications to the progestogen-only injectable include breast cancer; the full list of contraindications is available in UKMEC accessed at www.fsrh.org).[11] There is a weak association between DMPA use and cervical and breast cancer.[75] A causal association has not been established between DMPA and VTE or human immunodeficiency virus (HIV), and due to the limited evidence available it is not possible to confirm or exclude an association between DMPA and MI or stroke.[75]

SUMMARY

Women requesting contraception should be informed about the effectiveness of the various contraceptive methods as outlined in this bulletin (see table 1). The choice of contraceptive method depends on the effectiveness of the method and the individual patient, considering factors such as age, co-morbidities, concomitant medications and preferences of the user. The next contraceptive bulletin (NMIC 2021;Vol 27:No.6) will review contraception in specific populations.

List of references available on ePublication on www.nmic.ie. Date of publication: December 2021

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