The safety and efficacy of low-dose oral contraceptives

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Abstract

Oral contraceptives (OCs) are classified according to the dosage of ethinylestradiol (EE), the type of progestogen and whether the dosages of EE and progestogen stay the same during the cycle or change in a phasic manner. Ultimately, there is no statistically significant difference in efficacy between high-dose and low-dose OCs. There is also no difference in efficacy between monophasic and multiphasic products, which, other than lower hormone content, have no benefit over monophasic products.

Several medications, such as rifampicin, some of the anticonvulsants and certain HIV medications, may reduce the efficacy of OCs and higher dose OC preparations are recommended in patients taking these concomitant drugs.

The effectiveness of OCs with typical use is largely dependent on compliance, which is influenced by bleeding patterns and side-effects. In this regard, the composition of the OC may play a significant role. The dosage of EE and type of progestogen may relate to specific noncontraceptive benefits, such as improvement in dysfunctional uterine bleeding, dysmenorrhoea, premenstrual tension, endometriosis, iron deficiency anaemia, hyperandrogenism and acne. The 3rd generation progestogens and antiandrogens are generally regarded as more “skin friendly”.

The cardiovascular safety of OCs has long been controversial and although complications such as myocardial infarction and stroke have been reduced over the years with lower EE dosages, the risk of venous thromboembolism (VTE) has not decreased consistently. In fact, some of the low-dose products containing 3rd generation progestogens and antiandrogens may be associated with a higher risk of VTE.

Breast cancer is another controversial issue associated with OC use. Epidemiological studies do not report an increased risk, whereas other meta-analyses do. The risk may be amplified by genetic susceptibility, although data on the subject are not consistent.

An increased risk of hepatic adenoma and cervical cancer has also been noted with OC use, but the latter seems to be dependent on persistent human papilloma virus infection. On the other hand, ovarian and endometrial cancer is reduced by the use of OCs, although genetic susceptibility may also modify the risk.

As indicated by several studies on risk factors related to the safety of contraceptives, the choice of contraceptive is more complicated in patients with certain medical conditions, seeing that physiologic changes and side-effects associated with the method may increase the risk of morbidity/mortality in these women. All women requesting contraceptives should have a risk-benefit assessment before starting on any contraceptive to ensure the safety of the method. This is also true for OCs and in this regard the latest World Health Organization safety categories may be consulted.
**CLINICAL REVIEW**

**Introduction**

Contraception plays a major role in managing women’s reproductive health. Its most significant impact is to prevent pregnancies that are too early, too late, too many or too close.1

In broad terms, contraception can be defined as any method of preventing pregnancy by either hindering sperm from reaching a mature ovum or by inhibiting a fertilised egg from implanting in the endometrium.2 However, more precisely, contraception refers to the inhibition of ovulation or prevention of fertilisation of an egg cell, whereas contraception is the inhibition of implantation due to an unfavourable uterine environment. These two terms are often confused, but ultimately each mechanism plays a role in birth control and family planning.2

There are different contraceptive methods that can be used, which include barrier, hormonal and natural methods.3,4,5 In a recent article in this journal, Farrer described these methods as well as their advantages and disadvantages very elegantly.6 The methods most regularly known by both women and men are injectables, the male condom, the female condom and the oral contraceptive (OC), or so-called “pill”.1,7

In all cases where a contraceptive preparation is dispensed, the relevant information must be given to the user in order to understand the reversibility or irreversibility of the particular method, as well as possible medical risks associated with the use of it.2,3,8

Since OCs were first introduced in the 1960s the dosage of ethinyloestradiol (EE) has been reduced over the years in an attempt to lessen cardiovascular side-effects such as myocardial infarction (MI), venous thromboembolic disease, stroke and other adverse effects, yet still retaining contraceptive efficacy.8,9,10,11,12,13

This article will focus on the efficacy and safety of low-dose oral contraceptives and may give more clarity regarding the appropriate use and benefits of these drugs.

**The female reproductive cycle**

The glands and organs involved in the reproductive cycle are the hypothalamus, pituitary (adenohypophysis), ovaries, fallopian tubes, uterus and the vagina, and the cycle is regulated by hormones.3,4

Gonadotropin-releasing hormone (GnRH) is produced in the hypothalamus, thus inhibiting GnRH release and subsequent inhibition of the gonadotropin peak secretion during the midcycle. This action prevents ovulation.1,4,15 Ovulation is also prevented by the selective inhibition of pituitary function, possibly due to a decrease in responsiveness to GnRH.1,4,16

- Oestrogen inhibits the secretion of FSH by the anterior pituitary, thus no dominant follicle gets selected.2,15,17
- Progestogens, which include progesterone and synthetic progestins, suppress LH secretion from the anterior pituitary and thus suppress ovulation, but not consistently.2,8,16,17,18 Progestogen alone has the following contraceptive effects:15,16,17,18
  - It makes the endometrium less suitable for implantation
  - It makes the cervical mucus less permeable for penetration by sperm
  - It impairs normal tubal motility and peristalsis

OCs are classified as combination preparations which contain oestrogen and progestogen, and preparations that only contain progestogen (the “mini-pill”).1,2,15,16 The combined OCs contain either ethinyloestradiol (EE) or mestranol in different dosages as discussed in paragraphs to follow. However, progestogens contained in OCs vary.2,8,17 Progestogens have different gestational, oestrogenic, antioestrogenic and androgenic activity.2,12,17

These preparations are further divided in monophasic (dosages of oestrogen and progestogen are fixed), biphasic and triphasic forms (dosages of oestrogen and progestogen change once or twice during the cycle).5,8,16

The disadvantages of the bi- and triphasic preparations compared to monophasic preparations are that they cause water retention, and do not have much effect in dysmenorrhoea and premenstrual syndrome. The directions for use are more complicated and the cycle length cannot be adjusted with the multiphasic preparations.8 These products have a lower steroid content, but they have no additional clinical advantage over monophasic products.15

Oral contraceptives are also classified on the amount of ethinyloestradiol (EE) contained:

- New “ultra low-dose” preparations contain only 15–20 mcg EE.3,8,9 Some of the new OCs consist of 24 active and 4 inactive tablets, compared to traditional OCs that contain 21 active tablets and 7 inactive tablets.5,8,11 A higher occurrence of breakthrough bleeding was found with ultra low-dose preparations in some studies, however, data are limited and results inconsistent.1,9,17
- Low-dose products contain ≤ 35 mcg EE, typically ≤ 35 mcg.8,13,15,17 Folicular development is still possible with EE dosages of ≤ 35 mcg,13,15 but these products provide the same contraceptive efficacy as high-dose preparations. They may...
however have a lower risk of venous thrombosis, stroke and MI, which will be discussed in the section on safety.

- **High-dose** preparations contain 50 mcg or more EE. Because of cardiovascular side-effects, these preparations should only be used for specific indications such as:
  - Cases where dysfunctional uterine bleeding and endometriosis are not adequately controlled by low-dose preparations.
  - Patients who use hepatic enzyme-inducing agents like anticonvulsants and nevirapine.
  - Clients who get persistent breakthrough bleeding after low-dose preparations have been used for 3–6 months and other causes of bleeding have been excluded.

Table II gives an overview of the available OCs, their progestogen content and classification.

**Contraceptive efficacy**

Failure rates can be calculated by means of two methods – the Pearl index or a life table:

- The *Pearl index* is defined as the number of unintended pregnancies per 100 woman-years of use.
- *Life index* contraceptive efficacy is defined as the number of women who become pregnant using a specific contraceptive in the first year of use. For example if 100 women are using the OC and 12 women become pregnant during the first year, the first-year failure rate is calculated to be 12%.

A “perfect-use” failure rate is defined as a situation where all the rules regarding compliance and usage are followed strictly. With typical use, the failure rate is influenced by the following factors:

- Mistakes on user guidance by dispensers
- Mistakes regarding usage
- Deliberate noncompliance
- Restricted access to medication
- Drug interactions
- Vomiting and diarrhoea

Surgical sterilisation, Depo-Provera and intrauterine devices have first-year failure rates of less than one percent for perfect use; these methods are the most effective because they are not dependent on regular user action. OCs also have a theoretical first-year failure of less than one percent, but because of noncompliance or incorrect use the typical use first-year failure rates increase dramatically.

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**Table I: Summary of the reproductive cycle**

| Day 1 | Menstrual bleeding begins
|       | Levels of GnRH and FSH start to increase gradually and a new cycle starts
|       | This phase is characterised by the development of follicles in the ovaries
|       | Smooth muscle contractions in uterus increase
| Day 2 | LH starts to increase
| Day 5/6| Oestrogen levels increase
|       | The new endometrium starts proliferation
|       | Production of the cervical mucus also starts
| Day 12| As the FSH levels decline, only one (or occasionally two) of the follicles is selected for maturation
|       | In addition to oestrogen (oestrogen reaches peak levels), the primary follicle also produces progesterone and prostaglandin
| Day 13| The ovulatory phase starts with the surge of LH which causes the complete maturation of the dominant follicle
|       | Oestrogen decreases
|       | FSH increases again and peaks somewhat
| Day 14| Ovulation
|       | In this phase the follicle that released the oocyte becomes the corpus luteum and secretes progesterone and oestradiol
|       | LH and FSH decrease
|       | The cervical mucus becomes thin and easily permeable
|       | Body temperature rises because of increasing progesterone
| Day 21| Oestrogen declines again
|       | Progesterone promotes the thickening of the endometrium, causing it to fill with fluids and nutrients in order to support implantation, should fertilisation occur
|       | Smooth muscle contraction decreases
|       | Cervical mucus becomes impermeable
|       | If the oocyte is not fertilised, the corpus luteum deteriorates for the next seven days
| Day 28| The deterioration of the corpus luteum causes a decrease in progesterone which causes degeneration of the endometrium and ultimately menstruation

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Table II: Progestogens in oral contraceptives and classification8,15,17,18

<table>
<thead>
<tr>
<th>Progestogens</th>
<th>Progestogen generation/class</th>
<th>Product examples</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desogestrel</td>
<td>3rd generation</td>
<td>Marvelon 150/30®, Mercilon®</td>
<td></td>
</tr>
<tr>
<td>Drospirenone</td>
<td>Antiandrogen and antimineralocorticoid</td>
<td>Yates®, Yaz®</td>
<td></td>
</tr>
<tr>
<td>Gestodene</td>
<td>3rd generation</td>
<td>Femodene ED®, Melodene®, Minesse®, Minulet®, Mirelle®</td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>2nd generation</td>
<td>Nordette®, Loette®</td>
<td></td>
</tr>
<tr>
<td>Norgestimate</td>
<td>3rd generation</td>
<td>Ovral®</td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>2nd generation</td>
<td>Nordiol®</td>
<td>High-dose monophasic combined</td>
</tr>
<tr>
<td>Norgestimate</td>
<td>3rd generation</td>
<td>Tricilest®</td>
<td></td>
</tr>
<tr>
<td>Levonogestrel</td>
<td>2nd generation</td>
<td>Logynon ED®, Triphasil®</td>
<td>Low-dose triphasic</td>
</tr>
<tr>
<td>Norethisterone</td>
<td>1st generation</td>
<td>*Norinyl-1/28®</td>
<td></td>
</tr>
<tr>
<td>Norgestrel</td>
<td>2nd generation</td>
<td>Ovral®</td>
<td></td>
</tr>
<tr>
<td>Gestodene</td>
<td>3rd generation</td>
<td>Tri-Minulet®, Triodene ED®</td>
<td></td>
</tr>
<tr>
<td>Levonogestrel</td>
<td>2nd generation</td>
<td>Logynon ED®, Triphasil®</td>
<td></td>
</tr>
<tr>
<td>Norethisterone</td>
<td>1st generation</td>
<td>Trincovum®</td>
<td></td>
</tr>
<tr>
<td>Norgestimate</td>
<td>3rd generation</td>
<td>Tricilest®</td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>2nd generation</td>
<td>Biphasil®</td>
<td>High-dose biphasic</td>
</tr>
</tbody>
</table>

*Norinyl-1/28® contains mestranol, whereas all other products contain ethinyloestradiol. Mestranol is metabolised to EE in the liver.8

The actual failure rates for combination and progestogen-only pills are at least 5-8%, mostly due to missed pills or not resuming therapy after the pill-free interval.15,17,18 Some authors report the actual failure rate of progestogen-only products to be slightly higher than that of combined OCs.3,6,18 The “mini-pill” must be taken at the same time every day to maximise the contraceptive effect.6,8,17,18

Preparations with 20 mcg EE were compared to 35 mcg EE products in a number of studies and no differences in efficacy were recorded.9,15 Overall, the Pearl index for women taking products with 20 mcg EE ranged from 0.2 to 1 in these studies.9

As stated above, not resuming therapy after the pill-free interval is one of the reasons for higher failure rates with typical use.15 This pill-free interval may cause increased and even rebound ovarian activity, which may lead to contraceptive failure. Legro et al conducted a study (n = 62) to compare the effects of continuous and cyclic oral contraception. In the cyclic OC group there were 11 suspected ovulatory cycles out of 60 cycles vs only one ovulatory cycle in the continuous OC group over a study period of 168 days; these differences approached statistical significance (p = 0.054), but there were no pregnancies in either group.21 In another study (n = 641) with a continuous OC regimen compared to a cyclic OC product, one woman became pregnant on the continuous OC compared to 3 pregnancies in the cyclic comparator group, but the significance of this difference is not clear.22

A study (n = 1417) was also done to compare the contraceptive efficacy, cycle control, compliance, and safety of a weekly transdermal contraceptive patch and a daily OC. The overall and method failure Pearl indexes were 1.24 and 0.99 respectively for the patch, compared to 2.18 and 1.25 for the OC. Although the patch was numerically superior, the differences were not of any statistical significance. There was an 88.2% perfect compliance in the patch group as opposed to only 77.7% in the OC group. One conclusion from this study was that the lower compliance rate with OCs could have resulted in the numerically higher actual failure rates compared to the patch.20

**Drug interactions**

Several medications may alter active ingredient levels of OCs, which may subsequently alter efficacy:

- Enzyme-inducing agents such as anticonvulsants (e.g. carbamazepine, oxcarbazepine, phenytoin, phenobarbital and topiramate) accelerate the metabolism of the contraceptive hormones. Sodium valproate, lamotrigine, gabapentin and levetiracetam, however, do not seem to reduce the efficacy of OCs.8,15,23
- Reports of OC failure due to broad spectrum antibiotics are somewhat conflicting and anecdotal, but rifampicin reduces hormone levels of OCs quite dramatically.4,8,15,23
- Nevirapine and HIV protease inhibitors also cause drug interactions with oral contraceptives.8,15,23
- In a study done to determine the effects of St John's Wort (SJW) on desogestrel-containing OC therapy, no statistically significant differences were found in follicle maturation and serum oestradiol or progesterone levels between the three cycles (control cycle = OC alone, Cycle A = OC and SJW twice a day, Cycle B = OC and SJW three times per day). However, the area under curve (AUC, 0.24h) of 3-ketodesogestrel decreased significantly in cycles A and B compared to the control cycle and the incidence of intracyclic bleeding increased from 35% to 78% and 88% during cycles A and B, respectively. Although there was no evidence of
ovulation during concomitant use of the OC and SJW, it was concluded that bleeding irregularities may cause a decrease in compliance and together with the decrease in serum concentrations of 3-ketodesogestrel, the risk of unintended pregnancies may increase.15,24

Noncontraceptive benefits of OCs
Oral contraceptives also have indications other than contraception, such as management of:

• Menorrhagia and dysfunctional uterine bleeding: Progestogens prevent endometrial proliferation and oestrogen provides stability to the endometrium.9,17 OCs that contain 19-nor progestogens and lower dosages of oestrogen tend to cause more glandular atrophy and usually, less bleeding.16
• Dysmenorrhoea: Patients who experience this condition should take preparations with a higher progestogen component.17 Suppression of ovulation may be followed by painless periods.4,16,23
• Endometriosis: In this case the patient should use a product that has a higher progestogen and a low oestrogen component.17 Continuous OC use should also be considered in these patients, as long term administration of progestogen or combination therapy prevents the periodic breakdown of endometrial tissue.15,16,17
• Premenstrual tension and/or premenstrual dysphoric disorder (PMDD): Monophasic 24/4 regimes and continuous OCs reduce hormonal fluctuations.8,15,19,22 Although it is very difficult to determine the effect of OCs on behaviour and mood, they are being used successfully in the treatment of these syndromes, likely due to the oestrogen component.8,15,16,17 Yas® (0.02 mg EE and 3 mg drospirenone) has been registered for the treatment of the emotional and physical symptoms of PMDD.13,15,19
• Hyperandrogenism and hirsutism: OCs are successfully used in women with hyperandrogenism (mostly due to polycystic ovary syndrome) because of their overall antiandrogenic effect.15,17 Both oestrogen and progestogen inhibit gonadotropin secretion, which decreases ovarian androgen secretion. OCs also decrease the serum free androgen concentrations by increasing plasma levels of sex hormone binding globulin (SHBG) and inhibit adrenal androgen secretion.15,16,17,25 In addition, progestogens inhibit 5α-reductase, resulting in decreased dihydrotestosterone (DHT).17,25 Preparations that contain levonorgestrel must be avoided in women with hyperandrogenism, because it may aggravate the problem.15 To the contrary, the 3rd generation progestogens may be more effective than older generation progestogens in reducing hirsutism and acne in women with hyperandrogenism, although this has not been clinically proven.15,17
• Acne: OCs may improve acne by blocking the androgen receptor and/or causing a decrease in bioavailable testosterone, which in turn leads to lower sebum production.5,16,26 The “skin friendly” progestogens (3rd generation) with low androgenic action and the antiandrogens may be particularly useful.4,15,17,25 There is some speculation that drospirenone formulations are the most effective contraceptive products in the treatment of acne and hirsutism.26 However, in a comparative trial with Diane-35® (n = 125), the median reduction in total facial acne lesions was 62% with Yasmin® and 59% with Diane-35® after 9 cycles; the difference was not statistically significant.25 Therefore, superiority is not proven and more head-to-head trials are needed.15,25

OCs may also have the additional benefit of protecting women against:

• Iron-deficiency anaemia: The reduction in blood loss caused by progestogens may be useful in iron deficiency anaemia.15,16,23 An increase in serum iron and total iron binding capacity has been noted in clients who use OCs.16
• Ovarian cysts and cancer: The risk of ovarian cysts is reduced by products that contain high oestrogen dosages.15,17 Ovarian cancer may be prevented for 10–30 years after the OC has been discontinued. It is suggested that OCs protect against ovarian cancer because of their ovulation-suppressing effects, thereby reducing the chance that DNA damaged cells within the ovaries will multiply. Less stimulation of the ovaries by gonadotropin and progestogen-induced apoptosis are also possible mechanisms of protection.15,17,27,28 Low-dose OCs seem to be as effective as high-dose OCs in preventing ovarian cancer.12 Depending on how long OCs were used, they can give a 30–60% reduction in the risk of ovarian cancer.27 Although OCs may decrease the risk of ovarian cancer in some women, it may also increase the risk of breast cancer in certain cases, even to the point that it should not be used.17,28 This risk will be discussed in the section on safety.
• Endometrial cancer: The reduction in the risk of endometrial cancer is most likely due to suppression of endometrial proliferation by progestogen.3,12,15,17,23

OCs also decrease the risk and incidence of benign breast disease, ectopic pregnancy and pelvic inflammatory disease.4,9,15,17,22 Combined hormonal contraceptives have little effect on bone health, but may preserve bone mass in the perimenopause.22 OCs may prevent postmenopausal hip fractures in women who used them in their 30s.9,15,17

Safety
Cardiovascular (CV) disease
The reduction of EE dose in OCs from 50 mcg to 30 mcg has decreased cardiovascular-related death in OC users by 60%. It was thought that reducing EE to 20 mcg will further decrease these incidents, however, data are still inconclusive5 and this fact is demonstrated in paragraphs to follow:

• Hypertension: OCs can cause a mild increase in blood pressure within the normal range, however there have been some cases of overt hypertension reported. In the Nurses’ Health Study only 41.5 hypertensive cases per 10,000 person-years could be attributed to OC use; this risk decreased after cessation of therapy.12 Hypertensive OC users have an increased risk of MI and stroke.12,23
• Myocardial infarction (MI): It has been previously suggested...
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Venous thromboembolic disease (VTE):

- Factors: In these women the risk of MI outweighs the risk of VTE. Older women who smoke or those with other CV risk factors. In these women the risk of MI outweighs the risk of VTE. Older women who smoke or those with other CV risk factors. In these women the risk of MI outweighs the risk of VTE.

- Older women who smoke or those with other CV risk factors.

- The newer, 3rd generation OCs (i.e. containing desogestrel, norgestimate and gestodene) have better effects on the lipid profile than 2nd generation progestogens, however, this does not directly translate to lower MI risk. While some studies suggest no difference between the MI risk related to 2nd and 3rd generation progestogens, others suggest that 3rd generation progestogens may have a lower risk. Data are still inconclusive.

- Stroke: A higher ischaemic stroke risk has been reported in most studies, but not in all. In two meta-analyses, it was concluded that the results of studies cast doubt on the true association between oral low-dose OCs and stroke risk.

- The risk of VTE is higher in first-time users in the first 6 months to a year of starting the OC. The VTE risk disappears after 1–3 months of discontinuation of OCs.

Effects on liver

Changes in bile acid components may cause an increase in symptomatic gall bladder disease and jaundice associated with the use of OCs. An increased risk of hepatic adenomas has also been noted, but the risk of hepatocellular carcinoma is not affected.

Carbohydrate metabolism

High-dose OCs may give abnormal glucose tolerance test results compared to low-dose OCs that render normal results. However, low-dose OCs may cause insulin resistance. In addition, the more potent progestogens such as norgestrel may cause progressive decreases in carbohydrate metabolism over years of use. Progestogen-only OCs must be used with caution in women with a history of gestational diabetes mellitus, seeing that it may lead to type 2 diabetes.

Cervical cancer

Women who used OCs may have a higher risk of developing cervical cancer, especially if infected with human papilloma virus (HPV). In a systematic review of 24 epidemiological studies that included 16 573 women, a positive correlation was found between women using combined OCs and the length of time therapy was used. The risk of in situ, as well as invasive carcinoma was increased with OC use of more than 5 years.

Breast cancer

There is conflicting evidence with respect to the risk of breast cancer and OC use. Epidemiologic studies have generally not shown any relationship between OC use and the occurrence of breast cancer later in life. To the contrary, a small but significant increase in the overall relative risk (RR) of breast cancer was observed in some meta-analyses. However, because OC users are young this represented a very small increase in the absolute risk.

Because of the uncertainty of the risk of breast cancer in women with a family history of breast cancer, a historical cohort study was conducted to determine whether the use of OCs in these women relates to a higher risk of breast cancer. The RR of breast cancer in the entire study population was 1.4 and did not differ according to the duration of OC use. In sisters and daughters of persons that were previously diagnosed with breast cancer, the risk increased significantly in those who had ever used OCs compared to never users (RR = 3.3). The increased risk was not seen in granddaughters, nieces or marry-ins. The increased risk seems to be more prominent in subjects who had used older formulations, containing higher dosages of oestrogen and progestogen.

In another study involving users and former users of OCs, the risk in women age 35–44 years who had a family history of breast cancer were higher, but not significantly, compared to users in the same age group without such family history.
In this study, the RR did not increase consistently with higher dosages of oestrogen or with longer periods of use.26

Incidental use during pregnancy
Accidental OC use during early pregnancy is not connected to an elevated risk of congenital anomalies, however there may be an increase in the incidence of congenital urinary tract abnormalities.12,23

Absolute contraindications
The following absolute contraindications and warnings related to combined OCs must be noted:23,3,8,15,23

- A history of arterial or venous thrombosis or thrombogenic mutation (factor V Leiden, prothrombin mutation, protein S, protein C and antithrombin deficiencies)
- Coronary or ischaemic heart disease, structural heart disease with complications and severe hypertension
- Smoking or CV disease (including migraine with aura or focal symptoms of transient ischaemia) in women over 35 years
- Migraine with aura in women of any age and even simple migraine in women of 35 years and older
- A history of oestrogen-dependent tumour
- Oestrogen-containing products should be stopped 4 weeks before major surgery (because of the risk of thromboembolic events) and alternative contraceptive methods should be used
- Active liver disease
- Hypertriglyceridaemia, diabetes for > 20 years or diabetes with nephropathy, neuropathy or retinopathy
- Undiagnosed abnormal uterine bleeding
- Pregnancy and lactation (< 6 weeks postpartum)

The World Health Organization (WHO) developed categories for scenarios where combination OCs should not be used, or be used with extreme caution, as well as situations where advantages generally outweigh disadvantages and where no restrictions on use should apply.2,5,23

The WHO tables can be found at http://whqlibdoc.who.int/publications/2009/9789241563888_eng.pdf.

Conclusion
Over the last few decades there have been noteworthy advances in the development of new contraceptive products, including a change from high-dose to low-dose to ultra low-dose combined OCs, containing different progesterogens.8,12,23

While the different combined OCs are equally effective in preventing pregnancy, the choice of product requires a trade-off among the advantages and disadvantages of each formulation. The choice is strongly influenced by the individual’s medical history and preferences.5,17,23

By counselling clients on the benefits, side-effects and risks of OC use and on how to take the tablets correctly and complianly, low-dose OCs can have a significant impact on the lives of women by preventing unwanted pregnancies.1,2,24

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