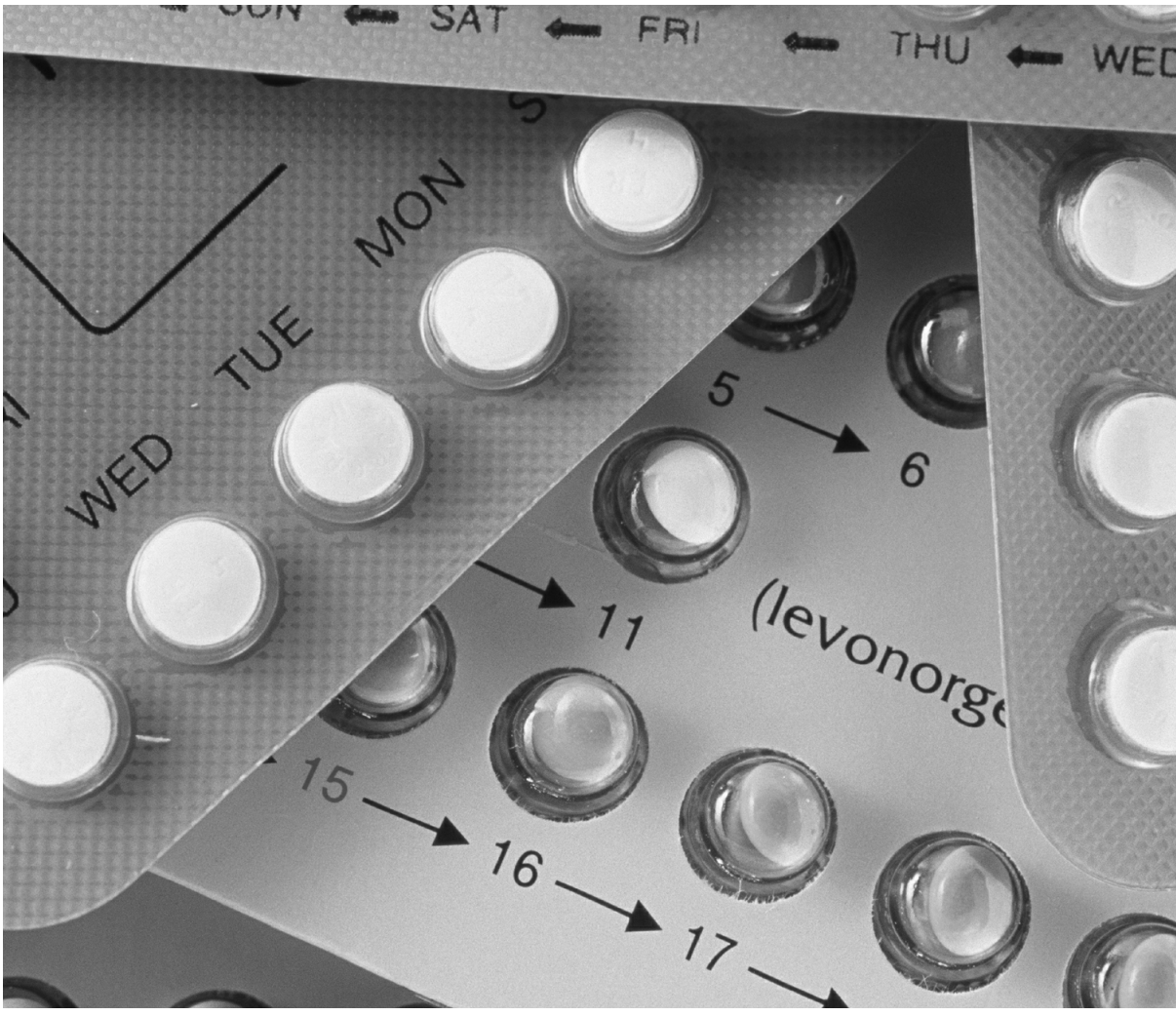
SECTION ONE

Contraceptive methods



1 COMBINED HORMONAL CONTRACEPTION

Combined oral contraception

Patient selection

QUESTION

For women who wish to use the combined oral contraceptive pill, what blood pressure measurements confer eligibility to use this method?

POPULATION: **Women with different levels of blood pressure.**
INTERVENTION: **Combined oral contraception.**
OUTCOME: **Safety.**

ANSWER

The *WHO Medical Eligibility Criteria for Contraceptive Use* advises that for women with systolic blood pressure (on more than one reading) of 140–159 mmHg or with diastolic blood pressure of 90–99 mmHg, the risks of using the combined pill generally outweigh the benefits (WHO category 3). Women with systolic blood pressure ≥ 160 mmHg, with diastolic ≥ 100 mmHg or with 'vascular disease' (which is not defined by WHO) are advised not to use the combined pill (WHO category 4).

Guidance from the FFPRHC on first prescription of combined oral contraception supports the WHO recommendations that women with blood pressure measurements consistently higher than 140 mmHg systolic or 90 mmHg diastolic should be advised against use of the combined pill (equivalent to a WHO category 3 recommendation).[1]

The WHO *Selected Practice Recommendations* advises that clinicians may provide up to 12 months' supply of the combined pill depending on the woman's preferences and anticipated use. An annual follow-up visit is recommended, at

which blood pressure may be measured again. The CEU considers that there are often benefits to following up more frequently than recommended by WHO and suggests a 3-month follow-up after initiation. In addition, women should be encouraged to return at any time to discuss adverse effects or problems, or if they wish to change their method of contraception.

Update to Answer

The FFPRHC has developed a UK version of the *WHO Medical Eligibility Criteria for Contraceptive Use* (published 2006). For use in the UK setting, the WHO advice on blood pressure levels has been modified. Systolic blood pressure (on more than one reading) of 140–159 mmHg or diastolic blood pressure of 90–94 mmHg is assigned to category 3; systolic blood pressure ≥ 160 mmHg or diastolic ≥ 95 mmHg is assigned to category 4.

QUESTION

For women with a body mass index (BMI) greater than 39kg/m², is combined oral contraception a safe and effective method? (Three similar enquiries.)

POPULATION: **Women with BMI greater than 39 kg/m²**
INTERVENTION: **Combined oral contraception**
OUTCOME: **Safety and efficacy.**

ANSWER

A woman with a BMI greater than 30 kg/m² is classified as clinically obese and with a BMI greater than 40 kg/m² as morbidly obese.[2] Obesity constitutes a risk factor for cardiovascular disease and venous thromboembolism (VTE). The *WHO Medical Eligibility Criteria for Contraceptive Use* categorises the use of combined oral contraceptives by women with a BMI ≥ 30 kg/m² as category 2, which means that the benefits of using the contraceptive method generally outweigh any risks to the individual. However, the *British National Formulary* (BNF) recommends that women with a BMI greater than 39 kg/m² should not use combined oral contraception.

A retrospective cohort analysis found that, after controlling for parity, women in the highest body weight quartile (≥ 70.5 kg) were at increased risk of pregnancy if prescribed low-dose (less than 35 micrograms estrogen) combined pills.[3]

The CEU advises that the WHO guidance may be followed for women with a BMI greater than 30 kg/m^2 and that they may use the combined pill. However, for women with a BMI greater than 39 kg/m^2, the CEU advises greater caution and suggests a progestogen-only or non-hormonal method of contraception.

QUESTION

For women who are former smokers, how long after smoking cessation can combined oral contraception safely be used? (Two similar enquiries.)

POPULATION: **Women who are former smokers.**
INTERVENTION: **Combined oral contraception.**
OUTCOME: **Safety.**

ANSWER

The *WHO Medical Eligibility Criteria for Contraceptive Use* does not provide guidance on former smokers but advises that non-smokers under the age of 40 years may have unrestricted use of combined oral contraception (WHO category 1). The benefits of the combined pill generally outweigh the risks (WHO category 2) for non-smokers over the age of 40 years. For women aged ≥35 years who smoke fewer than 15 cigarettes daily, the risks of the combined pill generally outweigh the benefits (WHO category 3). For women aged ≥35 years who smoke ≥15 cigarettes daily, the combined pill is **not** advised (WHO category 4).

FFPRHC guidance on contraception for women aged over 40 years[4] advises that women aged ≥35 years with no other cardiovascular risk factors who stopped smoking more than 1 year previously may consider using combined contraception (the excess risk of myocardial infarction associated with smoking falls significantly 1 year after stopping and is negligible 3–4 years later, regardless of the amount smoked).[5]

Update to Answer

The FFPRHC has developed a UK version of the *WHO Medical Eligibility Criteria for Contraceptive Use* (published 2006). For use in the UK setting, advice on former smokers has been included. This mirrors the advice in the FFPRHC guidance summarised above: a woman aged ≥35 years who stopped smoking less than 1 year ago is allocated to category 3 (risks generally outweigh benefits) whereas such a woman who stopped smoking 1 year or more ago is allocated to category 2 (benefits generally outweigh risks).

QUESTION

For women who are more than 6 months postpartum and breastfeeding, can combined oral contraception safely be used?

POPULATION: **Breastfeeding women more than 6 months postpartum.**
INTERVENTION: **Combined oral contraception.**
OUTCOME: **Safety.**

ANSWER

The *WHO Medical Eligibility Criteria for Contraceptive Use* provides guidance on the safe use of contraceptive methods. Using combined oral contraception in the early postpartum period can reduce the quantity and quality of breast milk. For breastfeeding women who are less than 6 weeks postpartum, the use of combined oral contraception is **not** advised (WHO category 4). For women who are primarily breastfeeding and are between 6 weeks and 6 months postpartum, the risks of combined oral contraception generally outweigh the benefits (category 3). However, for women who are still breastfeeding beyond 6 months, the benefits of the combined pill generally outweigh any risks (category 2). Similar advice is given in the WHO *Selected Practice Recommendations*.

The CEU supports the WHO recommendations that women may safely use combined oral contraception if more than 6 months postpartum and continuing to breastfeed.

References

1. Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. First prescription of combined oral contraception. *J Fam Plann Reprod Health Care* 2003;29:209–22.
2. Department of Health. *Prodigy Guidance Obesity*. London: DoH; 2002 [www.prodigy.nhs.uk/guidance.asp?gt=Obesity].
3. Holt VL, Cushing-Haugen KL, Daling JR. Body weight and risk of oral contraceptive failure. *Obstet Gynecol* 2002;99:820–7.
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5. Kawachi I, Colditz GA, Stampfer M, Willett WC, Manson JE, Rosner B, *et al*. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. *Arch Intern Med* 1994;154:169–75.

Choice of pill and starting regimens

QUESTION

For women who wish to use the combined oral contraceptive pill, are pills containing 20 micrograms ethinylestradiol as effective as those with higher doses of estrogen? (Three similar enquiries.)

POPULATION: Women requiring contraception.
INTERVENTION: Combined oral contraception with differing estrogen content.
OUTCOME: Efficacy.

ANSWER

The formulations of combined contraceptive pills have changed since they were originally developed. The first combined pill, in the 1960s, contained a high dose of mestranol and norethynodrel. Norethynodrel represented one of the 'first generation' of progestogens (which also includes norethisterone). A 'second generation' progestogen, levonorgestrel, was developed around 1970. From 1994, 'third generation' progestogens from the gonane class (including desogestrel, gestodene and norgestimate) were used in combined pills in an attempt to reduce androgenic and metabolic effects. Concurrent with these changes in progestogen content, the dose of estrogen in combined pills was reduced to minimise the risk of thromboembolism. The estrogen dose has been reduced stepwise from 150 micrograms to 50 micrograms and more recently to 35, 30, 20 and even 15 micrograms.[1]

Even in controlled clinical trials, it is difficult to measure the true efficacy of an oral contraceptive. Two techniques are widely used to quantify contraceptive failure rates: the Pearl index and life table analysis. The Pearl Index represents the number of failures (unintended pregnancies)/100 woman-years of exposure. A weakness of this approach is that studies of longer duration result in lower Pearl Indices, which may under-represent the true failure rate.[2–4] The CEU was unable to find any review that compared failure rates (calculated by either method) of different combined oral contraceptives.

Advice from the FFPRHC is that, when starting a combined pill for the first time, a pill containing 30–35 micrograms ethinylestradiol (with levonorgestrel or norethisterone) should generally be chosen.[5] After counselling regarding the risk of VTE, pills containing desogestrel or gestodene may be used if a woman expresses a preference. The risk of VTE does not vary with the dose of ethinylestradiol when this dose is less than 50 micrograms.

A double-blind, randomised, multicentre trial compared efficacy, cycle control and adverse effects of two combined pills (containing either 20 or 30 micrograms of ethinylestradiol with 150 micrograms desogestrel). Both formulations were found to have high contraceptive efficacy and to be well tolerated; however, cycle control was less consistent with the 20-microgram pill.[6] Another study from the same group demonstrated greater alteration in serum lipid profiles with the 30-microgram pill compared with the 20-microgram version.[7]

Thus, the CEU was unable to find any strong evidence that failure rates of combined pills increase with decreasing estrogen dose. Currently, the CEU continues to recommend a 30–35 microgram ethinylestradiol pill as a first-line choice.

QUESTION

For women using combined oral contraception, is there any evidence that certain pills are better than others in terms of certain adverse effects and sequelae? (Two similar enquiries.)

POPULATION: Women requiring contraception.
INTERVENTIONS: Combined oral contraceptives with differing formulations.
OUTCOME: Adverse-effect profile.

ANSWER

Our literature search identified very few studies that compare different types of combined pill. Based on the scant evidence identified, the following conclusions were drawn:

- Breakthrough bleeding is significantly more frequent in women using a 20-microgram ethinylestradiol pill compared with a 30-microgram pill.[6]
- There is some evidence that pills containing desogestrel or gestodene may carry a lower risk of myocardial infarction compared with pills containing levonorgestrel.[8] Nevertheless, evidence is conflicting and a 1999 case–control study did not confirm this finding.[9]
- Compared with non-users of combined contraception, women using pills containing levonorgestrel or norethisterone have a three-fold elevation in risk of VTE and women using pills containing desogestrel or gestodene have a five-fold elevation in risk.[10]
- Little evidence is available on the risk of VTE associated with pills containing norgestimate (Cilest®, Janssen-Cilag).[11,12] However, as

norgestimate is metabolised to levonorgestrel such pills may carry a risk similar to that of pills containing levonorgestrel.[13,14]

- There is insufficient evidence to estimate the risk of VTE associated with pills containing drospirenone (Yasmin®, Schering Health).[15]
- Compared with users of pills containing levonorgestrel, women using pills containing cyproterone acetate (the anti-acne pill, Dianette®, Schering Health) have a four-fold elevation in risk of VTE.[16]
- Risk of VTE does not appear to be related to the dose of ethinylestradiol in the pill formulation.[17]
- Small randomised trials have shown significant reductions in acne lesions with pills containing gestodene, desogestrel or levonorgestrel.[18–20]

Considering the body of evidence as a whole, the CEU advises that, generally, a woman choosing her first pill should choose one with the lowest risk of VTE: that is, one containing levonorgestrel or norethisterone. Nevertheless, if a woman favours a different formulation for any one of a range of possible reasons, she may be offered her own choice after appropriate counselling. Experience of adverse effects differs among individuals and decisions regarding changing from one pill to another must be governed by a clinician's experience and a woman's preferences.

Update to Answer

2006 guidance from the CEU on first prescription of combined oral contraception alerts clinicians to a statement from the Committee on Safety of Medicines which suggests that the risk of VTE with drospirenone-containing combined pills does not appear to differ from that with other combined pills.

QUESTION

Which combined oral contraceptive would provide greatest efficacy, safety and acceptability for a woman with a previous 'pill failure'

POPULATION:	**Women who have experienced unintended pregnancy while using combined oral contraception.**
INTERVENTION:	**Combined oral contraceptives of various formulations.**
OUTCOMES:	**Efficacy, safety, acceptability.**

ANSWER

The risk of failure of any contraceptive method, including combined oral contraception, is determined by method, user and provider factors.[21] Evidence indicates that there is little to choose between the various modern, low-dose combined pills in terms of efficacy.[22,23] Formulations containing 35 micrograms ethinylestradiol appear to be no more effective than those containing 20 micrograms.[24] Paradoxically, a 20-microgram formulation may prove more effective in practice if a lower incidence of adverse estrogenic effects improves compliance and continuation.

User factors are the most important determinants of efficacy with a user-controlled method such as combined oral contraception. A woman who has experienced unintended pregnancy while using a combined pill should therefore be counselled regarding alternative methods such as progestogen-only injectables or implants and intrauterine contraception. If such methods are unacceptable to a woman (for example due to unacceptable adverse effects) then the combined pill must be resumed.

Provider factors are important in optimising compliance and continuation for a woman with a previous 'pill failure'. Although modern low-dose pills can be as effective as their high-dose predecessors, there appears to be less margin for error in pill-taking.[25,26] Counselling, backed up by clear written information, on the importance of regular pill-taking routines is of fundamental importance.

In summary, the CEU advises that a woman who has experienced unintended pregnancy while using combined oral contraception should be re-started on a different monophasic formulation (possibly even one with a lower estrogen content to minimise adverse effects while maintaining efficacy) and should be meticulously counselled about pill-taking routines (if alternative methods are unacceptable).

QUESTION

What is the risk of ovulation for women starting hormonal contraception up to and including day 5 of the menstrual cycle, without additional contraceptive protection? (Two similar enquiries.)

POPULATION: Women requiring contraception.
INTERVENTION: Starting hormonal contraception up to day 5 of the menstrual cycle.
OUTCOME: Risk of ovulation.