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No. 329-Canadian Contraception Consensus Part 4 of 4 Chapter 9: Combined Hormonal Contraception

This Clinical Practice Guideline has been prepared by the Contraception Consensus Working Group; reviewed by the Family Physicians Advisory, Aboriginal Health Initiative, Clinical Practice-Gynaecology, and the Canadian Paediatric and Adolescent Gynaecology and Obstetricians (CANPAGO) Committees; and approved by the Executive and Board of the SOGC.

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Abstract

Objective: To provide guidelines for health care providers on the use of contraceptive methods to prevent pregnancy and on the promotion of healthy sexuality.

Outcomes: Overall efficacy of cited contraceptive methods, assessing reduction in pregnancy rate, safety, and side effects; the effect of cited contraceptive methods on sexual health and general well-being; and the availability of cited contraceptive methods in Canada.

Evidence: Medline and the Cochrane Database were searched for articles in English on subjects related to contraception, sexuality, and sexual health from January 1994 to December 2015 in order to update the Canadian Contraception Consensus published February-April 2004. Relevant Canadian government publications and position papers from appropriate health and family planning organizations were also reviewed.

Women have the right and responsibility to make informed decisions about their care in partnership with their health care providers. In order to facilitate informed choice, women should be provided with information and support that is evidence based, culturally appropriate, and tailored to their needs. The values, beliefs, and individual needs of each woman and her family should be sought, and the final decision about the care and treatment options chosen by the woman should be respected.

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial.	A. There is good evidence to recommend the clinical preventive action.
II-1: Evidence from well-designed controlled trials without randomization.	B. There is fair evidence to recommend the clinical preventive action.
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in the category.	D. There is fair evidence to recommend against the clinical preventive action.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	E. There is good evidence to recommend against the clinical preventive action.
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

†Recommendations included in these guidelines have been adapted from the Classification of recommendations criteria described in The Canadian Task Force on Preventive Health Care.

Values: The quality of the evidence is rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care. Recommendations for practice are ranked according to the method described in this report.

Summary Statements:

1. Although highly effective with perfect use, typical use failure rates for combined hormonal contraceptives, including the combined oral contraceptive pill, are as high as 9% (II-2).
2. The majority of qualified studies do not indicate decreased combined oral contraceptive pill efficacy in obese women; however, a small increase in contraceptive failure in women with a body mass index greater than 30 cannot be excluded (II-2).
3. Combined oral contraceptive pills are associated with a number of non-contraceptive benefits, including but not limited to decreased menstrual bleeding, decreased acne, fewer endometriosis-related symptoms, and a decreased risk of ovarian and endometrial cancers (II-2).
4. Combined oral contraceptive pills (COCs) are associated with an increased risk of venous thromboembolism (II-2). Potential differences in the risk of venous thromboembolism attributable to different progestin types and estrogen dosing in low-dose COCs do not currently justify preferential prescribing (III).
5. Low-dose combined oral contraceptive pills (containing less than 50 μg of ethinyl estradiol) are not associated with an increased risk of myocardial infarction or cerebrovascular accident in women with no additional risk factors (II-2).
6. Current epidemiological studies suggest that there is no increase in the risk of breast cancer or breast cancer mortality in women who have used combined oral contraceptive pills (COCs) compared with non-users (II-2). There may be a slight increase in breast cancer in current and/or recent COC users (II-2). The use of COCs in BRCA1/2 carriers is controversial but appears to be associated with a decreased risk of ovarian cancer and no increase in the risk of breast cancer (II-2).
7. Combined oral contraceptive pills (COCs) are associated with a decreased risk of ovarian, endometrial, and colorectal cancers (II-2). A possible association has been shown between COC use and risk of cervical cancer (II-2), but causation has not been demonstrated.
8. A blood pressure measurement is the only examination and/or investigation that is required prior to initiating combined hormonal contraception (CHC) in women who are otherwise healthy by history (II-2). Baseline weight and body mass index assessment might be helpful for monitoring changes in CHC users. Pelvic examination, Pap test, screening for sexually transmitted infections, and thrombophilia screening are not required prior to initiating CHC (III).
9. Combined oral contraceptive pills and other combined hormonal contraception (CHC) can be started at any time during the menstrual cycle provided that pregnancy or the possibility of pregnancy can be reasonably ruled out. Where there is uncertainty, the benefits of starting CHC likely outweigh any risks (III).
10. Starting combined hormonal contraception immediately (Quick Start) may improve short-term compliance and is not associated with an increase in unscheduled bleeding or other side effects (I).
11. The highest risk of ovulation occurs when the hormone-free interval is prolonged for more than 7 days, either by delaying the start of combined hormonal contraception (CHC) or by missing active hormone doses during the first or third weeks of CHC (I). Ovulation rarely occurs after 7 consecutive days of CHC use (II-2).
12. Emergency contraception (EC) and back-up contraception may be required in some instances of missed combined hormonal contraception (CHC), particularly when the hormone-free interval has exceeded 7 days. EC is rarely indicated for missed CHC in the second or third week of the cycle unless there are repeated omissions or failure to use back-up contraception after the missed doses (III).
13. Combined oral contraceptive pill exposure just prior to or during pregnancy is not associated with an increased risk of major birth defects (II-2).
14. The effectiveness of combined hormonal contraception (CHC), including combined oral contraceptive pills, may be affected by other medications, including but not limited to some anticonvulsants, some antiretrovirals, rifampicin, and griseofulvin. CHCs may affect the serum levels of other medications, including some anticonvulsants and antiretrovirals (II-2).
15. The contraceptive patch may be less effective in women with a body weight $\geq$90 kg (II-2).
16. Compared with the combined oral contraceptive pill, transdermal contraceptive patch use is associated with less breakthrough

bleeding and spotting but more breast discomfort or pain, nausea and vomiting, and dysmenorrhea (I).

17. Pharmacokinetic studies indicate that serum hormone concentrations of ethinyl estradiol and norelgestromin are maintained at ovulation inhibitory levels throughout at least 9 days of continuous transdermal contraceptive patch wear (II-2).
18. The vaginal contraceptive ring is associated with less unscheduled bleeding than the combined oral contraceptive pill and the duration of menstrual bleeding is significantly shorter than that seen with the contraceptive patch (I).
19. Serum levels of ethinyl estradiol and etonorgestrel are maintained at ovulation inhibitory levels for at least 28 days after the vaginal contraceptive ring has been inserted (II-2).
20. Continuous and/or extended regimens of combined hormonal contraception (CHCs) have similar rates of adherence and effectiveness compared with 28-day cyclic CHC regimens (I).
21. Continuous and/or extended (C/E) regimens of combined hormonal contraception (CHC) are associated with significantly less menstruation-associated symptoms than are cyclic CHC (I). Bleeding and/or spotting with C/E CHC regimens decreases with each successive cycle and is similar to or less than that with cyclic CHC (I).

ABBREVIATIONS

AED	antiepileptic drug
ART	antiretroviral therapy
BMI	body mass index
CDC	Centers for Disease Control and Prevention
C/E	continuous and/or extended
CHC	combined hormonal contraception
COC	combined oral contraceptive pill
Cu-IUD	copper intrauterine device
CYP3A4	cytochrome P450-3A4
DVT	deep vein thrombosis
E2	17 beta-estradiol
E2V	estradiol valerate
EC	emergency contraception
EE	ethinyl estradiol
ENG	etonogestrel
FPV	fosamprenavir
HDL	high-density lipoprotein
HFI	hormone-free interval
HIV	human immunodeficiency virus
HPV	human papillomavirus
IUC	intrauterine contraceptive
IUD	intrauterine device
IUS	intrauterine system
LNG	levonorgestrel
MI	myocardial infarction
PE	pulmonary embolism
PI	Pearl Index (the number of contraceptive failures per 100 women-years of use)
PK	pharmacokinetic
POP	progestin-only pill
RCT	randomized controlled trial
SHBG	sex hormone binding globulin
SOGC	Society of Obstetricians and Gynaecologists of Canada
STI	sexually transmitted infection
UPA	ulipristal acetate
UPI	unprotected intercourse
VTE	venous thromboembolism
WHO	World Health Organization
WY	women-years

Recommendations:

1. Health care providers should give clear instructions for hormonal contraceptive use, including how to manage missed hormonal contraception, as part of contraceptive counselling. Women should be provided with resources to refer to in the event of missed and/or delayed hormonal contraceptives or if they develop any signs of a serious adverse event while using hormonal contraception (III-A).
2. Health care providers should consider advising women who are initiating contraception to start their combined hormonal contraception (CHC) immediately (Quick Start) provided that they are reasonably certain that the woman is not pregnant. Back-up contraception (barrier method) or abstinence should be used for the first 7 consecutive days of CHC use unless CHC was initiated on the first day of menses (I-A).
3. Health care providers should consider the possibility of irregular pill taking, concomitant medication use, malabsorption, uterine or cervical pathology, pregnancy, or chlamydial infection in women presenting with persistent unscheduled bleeding on the combined oral contraceptive pill (III-A).
4. If 1 combined oral contraceptive pill or other combined hormonal contraception (CHC) method is missed in the first week of use, back-up contraception or abstinence should be used until the CHC method has been used for 7 consecutive days. In the case of missed CHC in the second or third week of hormones, the hormone-free interval should be eliminated for that cycle (III-A).
5. Back-up contraception should be used when 3 or more consecutive doses/days of combined hormonal contraception (CHC) have been missed in the second or third week of hormone use until the CHC has been used for 7 consecutive days. For practical reasons, the scheduled hormone-free interval should be eliminated in these cycles (I-A).
6. Health care providers should be aware of other medications being used by combined hormonal contraception users and the possibility of drug interactions that could affect serum levels and effectiveness of either medication (II-2A).
7. Health care professionals should be aware of the option of using continuous and/or extended combined hormonal contraception regimens and consider offering them to women for contraception, medical reasons, and personal preferences (III-A).
8. Women using continuous and/or extended combined hormonal contraception regimens should be counselled about expected bleeding patterns and how to manage unscheduled bleeding or spotting (III-A).
9. When a specific product has been prescribed to a woman, she should be informed if a generic substitution is being considered and her health care provider should be advised if a substitution is made. The woman should have the option to agree or disagree to the substitution and be informed about any difference in cost for a specific product (III-B).

Combined Hormonal Contraceptives

CHC refers to contraceptive methods that contain both an estrogen and a progestin. There are several forms of CHC available in Canada, including the COC, the transdermal contraceptive patch, and the vaginal contraceptive ring.

COMBINED ORAL CONTRACEPTIVE PILL

Introduction

The COC was first approved in 1960. Since then, it has undergone many evolutions in dosage, hormone type, and regimen. It has been used by more than 100 million women worldwide and has the widest geographic distribution of any method of contraception.[1] In Canada, an estimated 1.3 million women (16%) aged 15 to 49 use COCs.[2] Of Canadian women who use contraception, 43.7% use COCs.[3]

Current COC options and their compositions are listed in Appendix A.[4] Formulations may be monophasic (each tablet contains a fixed amount of estrogen and progestin) or multiphasic. Multiphasic formulations were initially developed with the intent of lowering the total steroid content of COCs and improving cycle control.[5–7]

The following 3 types of estrogen are used in COCs: Ethinyl estradiol (EE), estradiol valerate (E2V), and 7 beta-estradiol (E2). E2V is rapidly metabolized to E2. Several different progestins are used in COCs. These progestins may also have estrogenic, antiestrogenic, androgenic, antiandrogenic, or antimineralocorticoid activity. The varying progestational "potencies" attributed to different COC preparations are based on pharmacological experimental models.[8,9] Many variables affect the potency of COCs (including dosage, bioavailability, protein binding, receptor binding affinity, and interindividual variability), making it difficult to extrapolate the results of isolated experiments to provide clinically relevant information in humans.[10,11] There is no clear clinical or epidemiological evidence that compares the relative potencies of currently available COCs.

Most progestins are 19-nortestosterone derivatives. Progestins may be classified according to their chemical structure as an estrane (norethindrone, norethindrone acetate, ethynodiol diacetate) or as a gonane (LNG, desogestrel, norgestimate). In general, the gonane progestins appear to be more potent than the estrane derivatives (smaller doses can be used), but other differences between the estrane and gonane compounds are difficult to characterize.[12,13] The progestin drospirenone is derived from 17α-spirolactone and has antimineralocorticoid activity. Progestins have also been classified according to their sequence of development (first, second, third, or fourth generation), but these definitions are not universally accepted. Newer progestins (norgestimate and desogestrel) have little or no androgenic activity,[12,13] whereas other progestins (cyproterone acetate, drospirenone, and dienogest) have antiandrogenic activity.[14,15]

COCs are available in a number of different regimens with varying HFIs. Current regimens include 21/7 regimens (with a 7-day HFI), 24/4 regimens (with a 4-day HFI), 24/2/2 regimens (with 2 days of EE and a 2-day HFI), 26/2 regimens (with a 2-day HFI), and 84/7 regimens (with a 7-day HFI or 7 days of EE). COCs may also be used in an C/E fashion (off-label use) by either delaying or eliminating the HFI.

Effectiveness

The COC has a perfect use failure rate of 0.3%, but typical use failure rates are up to 9% in the first year of use.[16] Prospective, controlled, active surveillance, non-interventional cohort studies of COC users have evaluated COC effectiveness.[17,18] One study found low COC failure rates (PI 0.48, 95% CI 0.44 to 0.53) in European COC users.[18] The life-table estimates of contraceptive failure ranged from 0.75% after the first year of COC use to 1.67% (95% CI 1.61 to 1.85) after the fourth year of COC use.[18] Data from the U.S. arm of another similar study of COC users calculated an overall PI of 2.2 (95% CI 2.1 to 2.3), and the life-table estimates of contraceptive failure ranged from 3.0% (95% CI 2.8 to 3.2) after the first year of use to 6.2% (95% CI 5.8 to 6.2) after the third year of use.[17] In these studies, 42% to 46% of COC failures were associated with irregular COC intake and 9.5% to 18.3% with vomiting and/or diarrhea.[17,18]

Poor compliance limits COC effectiveness.[19] In one study, the proportion of women who reported missing

no pills was much higher than the proportion recorded electronically (53% to 59% vs. 19% to 33%).[20] According to the electronic devices, 30% of women missed 3 or more pills in the first cycle of COC use.[20] Another study found that 47% of women miss 1 or more pills and 22% miss 2 or more pills per cycle.[21] A European cohort study found that 42.2% of unplanned pregnancies occurring in COC users were associated with irregular COC intake.[18]

The effect of body weight on COC efficacy is controversial. Although some large cohort studies have demonstrated little and/or no effect of BMI and weight on COC failure,[18,22–26] one large cohort study found a slight increase in contraceptive failure in women with a BMI ≥35 kg/m^2 compared with women with a BMI <35 (HR_{adj} 1.5, 95% CI 1.3–1.8).[17] A case control study found that the odds of unplanned pregnancy in consistent COC users was higher for women with a BMI ≥27.3 (OR 2.17, 95% CI 1.38–3.41) and even higher with a BMI > 32.2 (OR 2.22, 95% CI 1.18–4.20).[27] The Food and Drug Administration conducted a meta-analysis of individual participant data from 7 phase III clinical trials of COCs and found pooled intent-to-treat PIs of 3.14 (95% CI 2.33–4.22) for women with a BMI ≥30 versus 2.53 (95% CI 1.88–3.41) in women with a BMI <30.[28] After adjusting for age and race, the overall hazards ratio suggested a higher pregnancy rate in obese women compared with non-obese women (HR_{adj} 1.44, 95% CI 1.06–1.95).[28] PK studies have found that normal-weight and obese COC users who consistently used COCs had comparable ovarian suppression during COC use,[29] and that although the peak hormone levels were lower among obese women,[30,31] the trough values were similar and there was no statistically significant difference in follicular diameter.[31]

Prospective[17] and retrospective[32] cohort studies have suggested that users of extended regimens (84/7) may have lower failure rates than users of 21/7 regimens[32] and that 24/4 regimen users may have lower failure rates than 21/7 regimen users.[17]

Summary Statements

1. Although highly effective with perfect use, typical use failure rates for combined hormonal contraceptives, including the combined oral contraceptive pill, are as high as 9% (II-2).
2. The majority of qualified studies do not indicate decreased combined oral contraceptive pill efficacy in obese women; however, a small increase in contraceptive failure in women with a body mass index greater than 30 cannot be excluded (II-2).

Mechanism of Action

COCs have multiple mechanisms of action due to both the estrogenic and progestational components. The principal mechanism of action is suppression of pituitary gonadotropin secretion, thereby inhibiting ovulation.[33] All COCs are "progestin-dominant," meaning that the progestin effects on the organs of interest exceed the estrogen component. The progestogenic component increases cervical mucus viscosity, thereby impairing sperm transport.[34] If follicle development "escapes" estrogen suppression, the progestin suppresses luteinizing hormone (LH) and impairs ovulation. Progestins have known effects on tubal transport, thereby narrowing or eliminating the potential fertilization window. Progestins have endometrial effects,[34–36] but this is not believed to be an "in vivo" mechanism of action of COCs because impaired implantation of fertilized embryos has not been demonstrated.[33] The estrogenic component impairs folliculogenesis via negative feedback on follicular-stimulating hormone, potentiates the effects of progestins (allowing for lower progestin doses to be used), and stabilizes the endometrium (improving bleeding patterns).[33]

Indications

In the absence of contraindications, the COC may be considered for any woman seeking a reliable, reversible, coitally independent method of contraception. It may be particularly suited for women who wish to take advantage of its non-contraceptive benefits. COCs do not protect against STIs. Consistent and correct use of male condoms is advised to reduce the risk of STIs, including HIV.

Contraindications

WHO and the CDC have developed guidelines that categorize medical conditions into 1 of 4 categories based on their level of risk (Table 2).[37,38] The following recommendations for CHC are made based on the existing literature and the recommendations of the CDC and WHO.

Category 4

- <4 weeks postpartum (breastfeeding)
- <21 days postpartum (not breastfeeding)[39–41]
- Smoker >35 years (>15 cigarettes/day)
- Vascular disease
- Hypertension (systolic ≥160 mmHg or diastolic ≥100 mmHg)
- Acute DVT/PE
- History of DVT/PE, not receiving anticoagulant therapy, with higher risk for recurrent VTE (history of

Table 2. Categories of Medical Eligibility Criteria for Contraceptive Use[37,38]

Category	Recommendation
Category 1	A condition for which there is no restriction for the use of the contraceptive method.
Category 2	A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
Category 3	A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
Category 4	A condition that represents an unacceptable health risk if the contraceptive method is used. The method should not be used.

estrogen-associated DVT/PE, pregnancy-associated DVT/PE, idiopathic DVT/PE, known thrombophilia including antiphospholipid syndrome, active cancer with the exception of non-melanoma skin cancer, history of recurrent DVT/PE)

- Major surgery with prolonged immobilization
- Known thrombophilia
- Current and/or history of ischemic heart disease
- History of stroke
- Complicated valvular heart disease (pulmonary hypertension, risk of atrial fibrillation, history of subacute bacterial endocarditis)
- Systemic lupus erythematosus with positive (or unknown) antiphospholipid antibodies
- Migraine with aura (as defined by the International Headache Society[42])
- Peripartum cardiomyopathy with moderately/severely impaired cardiac function
- Peripartum cardiomyopathy with normal/mildly impaired cardiac function <6 months
- Current breast cancer
- Severe decompensated cirrhosis
- Hepatocellular adenoma
- Malignant hepatoma
- Complicated solid organ transplantation (graft failure, cardiac allograft vasculopathy)

It should be noted that even though one study found that among women with superficial venous thrombosis, the risk of VTE was higher in COC users than in non-users,[43] it is not a contraindication to CHC use (WHO category 2). Women with varicose veins can use CHC without restriction (category 1).

Category 3

Women with a category 3 medical condition may benefit from expert consultation prior to advising against the method.

- 4 to 6 weeks postpartum (breastfeeding with other risk factors for VTE such as aged ≥35, previous VTE, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, Cesarean delivery, preeclampsia, or smoking)[39]
- 3 to 6 weeks postpartum (not breastfeeding with other risk factors for VTE)
- DVT/PE on established anticoagulation therapy with no other risk factors for VTE (history of estrogen-associated DVT/PE, pregnancy-associated DVT/PE, idiopathic DVT/PE, known thrombophilia including antiphospholipid syndrome, active cancer excluding non-melanoma skin cancer, history of recurrent DVT/PE) [44,45]
- History of DVT/PE with lower risk of recurrent DVT/PE (no other risk factors for VTE)
- Multiple sclerosis with prolonged immobility
- Smoker aged ≥35 (<15 cigarettes per day)
- Multiple risk factors for arterial cardiovascular disease (e.g., older age, smoking, diabetes hypertension, low HDL, high low-density lipoprotein, or high triglyceride levels (category according to severity of conditions)
- Adequately controlled hypertension (blood pressure can be evaluated)
- Hypertension (systolic 140 to 159 mmHg or diastolic 90 to 99 mmHg)
- Peripartum cardiomyopathy with normal/mildly impaired cardiac function >6 months
- History of breast cancer and no evidence of disease for 5 years
- Symptomatic gallbladder disease (current or medically treated)
- Acute or flare of viral hepatitis (for COC initiation only; category should be assessed according to severity of condition)
- Diabetes with nephropathy/retinopathy/neuropathy, other vascular disease, or diabetes of >20 years duration (category should be assessed according to severity of the condition)
- Past COC-related cholestasis
- History of malabsorptive bariatric procedures (Roux-en-Y gastric bypass, biliopancreatic diversion)

- Certain anticonvulsant use (phenytoin, oxcarbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, lamotrigine)
- Rifampicin or rifabutin therapy
- FPV ART therapy[46]

Non-Contraceptive Benefits

In addition to providing effective contraception, the COC has a number of non-contraceptive benefits[47] secondary to its mechanisms of action, in particular ovulation inhibition, local progestin effects on the endometrium, and antiandrogenic effects. These include the following:

- Cycle regulation with predictable withdrawal bleeds
- Decreased menstrual flow[48–52]
- Decreased anemia[53]
- Increased bone mineral density, particularly during the later reproductive years[54–57]
- Decreased dysmenorrhea[58,59]
- Decreased perimenopausal symptoms[60–62]
- Decreased acne[63–66]
- Decreased hirsutism[67]
- Decreased endometrial cancer[68–73]
- Decreased ovarian cancer[68,71,72,74–79]
- Decreased risk of fibroids[80–83]
- Fewer functional ovarian cysts[84] due to impaired folliculogenesis (although not effective for treatment of preexisting functional cysts)[85]
- Lower risk of benign breast disease[86]
- Decreased colorectal carcinoma[71,73,87–90]
- Decreased incidence of salpingitis[91,92]
- Decreased incidence or severity of premenstrual symptoms and premenstrual dysphoric disorder[93–97]
- Reduced pelvic pain and less recurrence of dysmenorrhea and endometriomas associated with endometriosis[98–100]

Summary Statement

3. Combined oral contraceptive pills are associated with a number of non-contraceptive benefits, including but not limited to decreased menstrual bleeding, decreased acne, fewer endometriosis-related symptoms, and a decreased risk of ovarian and endometrial cancers (II-2).

Side Effects

Side effects of COCs are common in the first 3 months and are often self-limiting.[101] Inadequate counselling about side effects increases the likelihood of pill discontinuation.[101] Proactive counselling and reassurance about expected side effects and addressing myths and misperceptions may help enhance compliance.[102–104] Common reasons for COC discontinuation include abnormal uterine bleeding (12%), nausea (7%), weight gain (5%), mood changes (5%), breast tenderness (4%), and headache (4%).[102]

Changes in bleeding patterns

The rates of unscheduled bleeding reported in COC clinical trials vary widely. Unscheduled bleeding may occur in up to 30% of women in the first month of COC use,[105–107] is slightly more common in lower-dose preparations,[101,108] may be affected by the progestin component,[109] and is a common reason for COC discontinuation.[108] Comparisons of unscheduled bleeding rates among formulations are difficult because they are defined inconsistently; however, unscheduled bleeding generally improves with time.[110–112] Risk factors for unscheduled bleeding include inconsistent pill use and smoking.[113–115] Unscheduled bleeding in a woman who previously had good cycle control warrants further investigation, including STI screening.[116]

The available evidence is insufficient to determine whether there are significant differences in bleeding patterns between multiphasic and monophasic pills.[7,117]

Being progestin dominant, COCs are associated with a decrease in duration and amount of menstrual bleeding, and some women will have no withdrawal bleeding during the HFI.[48–52,118] Amenorrhea is more common with COCs that contain $\leq$20 μg EE and in regimens with shorter HFIs.[118–120]

Breast tenderness and nausea

Placebo-controlled studies have not demonstrated an increased odds of breast pain in COC users compared with placebo.[121] Breast tenderness and nausea may occur but generally improve with time. These symptoms may occur less often in women who use COCs containing lower doses of estrogen.[101,118]

Weight gain

Placebo-controlled trials have failed to show any association between COCs and weight gain.[122,123] Women concerned about weight gain may benefit from being weighed at the first consultation and at a follow-up visit.

Mood changes

Although reports of mood changes are not uncommon among COC users,[124,125] small studies show inconsistent effects on mood.[126] Placebo-controlled trials have not

demonstrated a significantly increased risk of mood changes in COC users compared with placebo users,[121] and there is some evidence that COCs may be protective for mood.[127] An epidemiological study of 6654 women in the United States showed that, compared with non-hormonal or non-users, women using COCs had lower concurrent depressive symptoms and were less likely to report recent suicide attempts.[127] COCs, particularly those containing drospirenone, have been shown to improve premenstrual dysphoric disorder symptoms.[97]

Sexual function

COC users may experience effects on sexual function, although the evidence on the nature of the effect is conflicting.[128,129] Some studies have found no change in sexual function,[128–132] others have found a negative effect,[128,129,133,134] and others have found improved sexual function with COC use.[128,129,131] Potential adverse effects include low libido and vaginal dryness.[134] Desire and coital frequency naturally increase around ovulation and premenstrually, and COC-associated ovulation inhibition and cycle regulation may blunt this effect.[132,135] COCs are also associated with a decrease in circulating androgens that may be associated with changes in libido. Switching to another COC may provide some benefit, but there is no clear difference between androgenic or non-androgenic progestins.[136] Dehydroepiandrosterone supplementation may restore androgen levels in COC users, but there is minimal evidence that this correlates with improved sexual functioning.[137]

Vaginal dryness is likely related to suppression of endogenous estrogen production and may improve by using a COC with a higher estrogen dose, the vaginal contraceptive ring, or switching to a POP or non-hormonal method.[134]

If a long-time COC user develops new onset of decreased libido, an appropriate assessment and investigation are recommended to examine other potential causes of decreased libido.

Headache

COC users may experience headaches, although placebo-controlled studies have not demonstrated a significant increase in headaches with COCs compared with placebo.[122] Women who experience menstrual migraines without aura may have reduced migraine frequency by reducing or eliminating the HFI with the use of extended COC regimens.[138–141] If a woman reports headaches during COC use, the timing of the headaches is important as is the presence of migraines, aura,[42] or focal neurological deficits. Women experiencing migraines with aura should discontinue COCs and consider non–estrogen-containing methods of contraception.[142] Women with migraine without aura or other headaches on COCs may find that switching to a lower-dose formulation or progestin-only method may improve symptoms.[143–145]

Chloasma

Chloasma, a darkening of facial skin pigmentation, is rare but may occur during COC use.[146,147] If chloasma occurs, changing to another pill will not help.[148] The hyperpigmentation may never completely disappear. The use of sunscreen may help to prevent further pigmentation.

Risks

VTE

COC users have a 2- to 3-fold increase in the risk of VTE compared with non-users.[149–151] In comparison, the relative risk of VTE during pregnancy and in the postpartum period is 6.7 (95% CI 5.7 to 7.8) and 115.1 (95% CI 96.4 to 137.0), respectively.[152] Modern data obtained through prospective, active surveillance have found that non-pill users of reproductive age have a background rate of VTE of 4 to 5 per 10 000 WY and that COC users have an approximate rate of up to 10 per 10 000 WY.[149,150] The incidence of confirmed PE in COC users is estimated to be up to 4 per 10 000 WY compared with 1.6 per 10 000 WY in non-users.[150] The risk of VTE in the first year of COC use appears to be higher than in subsequent years of use.[149,150,153]

Various studies of uneven quality have examined the effect of different progestins and estrogen doses on the risk of VTE. Even though several case control and retrospective cohort studies performed using administrative databases have supported an increased risk of VTE in women using COCs containing third- and fourth-generation progestins,[154–157] well-designed prospective cohort studies have failed to find an increased risk of VTE associated with specific progestins.[149,150] A recent study found that CHC use was not associated with an increased risk of recurrent VTE in women receiving therapeutic anticoagulation.[44]

Summary Statement

4. Combined oral contraceptive pills (COCs) are associated with an increased risk of venous thromboembolism (II-2). Potential differences in the risk of venous thromboembolism attributable to different progestin types and estrogen dosing in low-dose COCs do not currently justify preferential prescribing (III).

Cerebrovascular accident (stroke) and MI

The overall risk of arterial thrombosis does not appear to be increased in COC users compared with non-users, with the exception of women using COCs containing 50 μg EE

and more[158–160] (which are no longer available in Canada). The risk does not appear to vary significantly with progestin type.[160] The baseline risk of MI in reproductive age women with no other risk factors is low, with an incidence of 0.001 per 10 000 women aged 20 to 24, but increases sharply after age 35 to an incidence of 0.2 per 10 000 per year.[158,161] Both smoking and age over 35 compound this risk.[158,159,162] A number of studies, including a Cochrane review, have found no significant increase in the risk of MI with COCs containing less than 50 μg EE.[71,72,151,160,163]

A significantly increased risk of stroke has been documented in users of COCs containing 50 μg EE and more.[160,164] One meta-analysis found no increase in hemorrhagic stroke but did report an increased risk of ischemic stroke in women using CHC (OR 1.9, 95% CI 1.24 to 2.9), with the risk being significantly higher in 50 μg COC users compared with those using lower-dose COCs (OR 2.37, 95% CI 1.05 to 5.38).[151] However, a 2015 Cochrane review found no increase in the risk of ischemic stroke in COC users (OR 1.0, 95% CI 0.9 to 1.1), although the risk seemed to increase with higher doses of estrogen.[160]

Summary Statement

5. Low-dose combined oral contraceptive pills (containing less than 50 μg of ethinyl estradiol) are not associated with an increased risk of myocardial infarction or cerebrovascular accident in women with no additional risk factors (II-2).

Gallbladder disease

COC use increases the secretion of cholic acid in bile and decreases gallbladder motility, potentially leading to a higher incidence of gallstone formation.[165] However, in general, there does not appear to be an increase in gallbladder disease in COC users.[166,167] Whereas one cohort study found a slight increase in symptomatic gallstones in women who had used COCs for 15 years or longer (RR 1.5, 95% CI 1.10 to 2.20),[168] a case control study found no association between COC use and gallbladder disease (LNG-COC: OR 1.0, 95% CI 0.9 to 1.1; drosperinone (DRSP)-COC: OR 0.9, 95% CI 0.7 to 1.1).[167] The progestin type does not appear to have a clinically significant effect on the development of symptomatic gallstones.[167,169]

Breast cancer

Data on risk of breast cancer with use of contraceptive hormones have been conflicting, but more recent data are reassuring. A large meta-analysis from 1996 suggested that current COC users were at a slightly increased risk of breast cancer (RR 1.24, 95% CI 1.15 to 1.33) and that the risk decreased slowly to baseline in the 10 years following discontinuation.[170] A subsequent meta-analysis found that COC use was associated with an increased risk of premenopausal breast cancer in general (OR 1.19, 95% CI 1.09 to 1.29).[171] A 2013 meta-analysis also showed a small increased risk of breast cancer in COC users (OR 1.08, 95% CI 1.00 to 1.17), with more recent use (within the last 5 years) associated with a higher risk (OR 1.21, 95% CI 1.04 to 1.41).[73] The risk was no longer significant 5 years or more after discontinuing the COC, and there were no significant risk differences with different durations of COC use.[73] One prospective cohort study with over 1.2 million person-years of follow-up found that past COC use was not significantly associated with an increased risk of breast cancer (RR 1.12, 95% CI 0.95 to 1.33), although current COC use was associated with a marginally increased risk (RR 1.33, 95% CI 1.03 to 1.73).[172] Put into perspective, the cumulative likelihood of breast cancer before 39 years is approximately 4 per 1000 women.[173] If 1000 women were using COCs, and if the associated relative risk of breast cancer risk was 1.33, there would be 5 cases of breast cancer by the age of 39 rather than 4 cases. It is unclear whether this small increase in breast cancer risk is related to the COC itself or to delaying the first full-term birth.[170,171,174–176] A 2014 nested case control study found that COC use within the previous year was associated with an increased breast cancer risk compared with never use or former use (OR 1.5, 95% CI 1.3 to 1.9).[177]

Many epidemiological studies have failed to demonstrate an increased risk of breast cancer or breast cancer mortality in COC users.[68,71,72,175,176,178–180] The final report of the Oxford Family Planning Association study found that in a cohort of over 17 000 women, COC use did not increase the risk of breast cancer in terms of ever use or total duration of use (RR 1.0, 95% CI 0.9 to 1.1).[180] These findings were similar to those of the Nurses' Health Study, which found that women under 35 who used COCs for more than 10 years did not have an increased risk of breast cancer (RR 1.07, 95% CI 0.70 to 1.65).[179]

Data on the risk of breast cancer in BRCA1/2 carriers who use COCs are inconsistent, although there does appear to be a decrease in ovarian cancer.[68,77] Even though some studies have demonstrated an increased risk of breast cancer with COC use in BRCA1/2 carriers,[181,182] 3 recent meta-analyses did not find an increased risk with ever use of COCs.[77,183]

Summary Statement

6. Current epidemiological studies suggest that there is no increase in the risk of breast cancer or breast cancer mortality in women who have used combined oral

contraceptive pills (COCs) compared with non-users (II-2).
There may be a slight increase in breast cancer in current and/or recent COC users (II-2). The use of COCs in BRCA1/2 carriers is controversial but appears to be associated with a decreased risk of ovarian cancer and no increase in the risk of breast cancer (II-2).

Cervical cancer

HPV is the major risk factor for cervical cancer.[184] Studies that have controlled for plausible confounders have shown that prolonged COC use is not associated with an increased risk of cervical intraepithelial neoplasia;[185,186] however, a recent cohort study that adjusted for oncogenic HPV status found that oral contraceptive (OC) use for ≥20 months combined with heavy cigarette smoking significantly increased the risk of cervical intraepithelial neoplasia.[187] Although not all studies have controlled for HPV status, several studies have found that the risk of cervical cancer appears to be increased in COC users compared with non-users.[180,188–190] Whereas one study suggested long-term COC use increased the risk of cervical cancer in HPV-positive women but not in HPV-negative women,[188] a systematic review of 28 studies found that the risk was still increased after adjusting for number of sexual partners, HPV status, smoking, histology, and use of barrier methods.[189] A subsequent re-analysis of 24 studies found that the risk of invasive cervical cancer increased with duration of COC use (RR 1.90, 95% CI 1.69 to 2.13 for ≥5 years of COC use) but that the risk declined after discontinuation to the baseline risk by 10 years.[190] The results of a large cohort study found that the relative risk of ever use compared with never use was 3.4 (95% CI 1.6 to 8.9); the risk increased with duration of COC use and declined steadily with interval since last COC use.[180] Based on Canadian data, approximately 1 of 149 (0.7%) women will be diagnosed with cervical cancer in their lifetime.[191] If the relative risk of cervical cancer in COC users was 1.9, and without accounting for additional cervical screening in COC users or the use of HPV immunization strategies, 1 of 75 (1.33%) women using COCs would be at risk of being diagnosed with cervical cancer in their lifetime. Although a possible association has been demonstrated, this does not imply causation.

Myths and Misperceptions

1. COC users should take periodic "pill breaks."

   Fact: This is unnecessary. Pill breaks place a woman at risk for unintended pregnancy and cycle irregularity.[192,193] In addition, the risk of VTE is highest not only in the first year of starting COCs but also when a woman restarts after a period of non-use of at least 1 month.[149,153] Provided there are no other contraindications and a woman is tolerating the COC, it can be continued until contraception is no longer required, an alternative method is desired, or the non-contraceptive benefits are no longer required.

2. The COC has a negative effect on future fertility.

   Fact: Fertility is quickly restored (usually within 1 to 3 months) to a woman's baseline fertility once the COC is discontinued.[192,194] Overall, 1-year pregnancy rates following discontinuation of COCs, implants, or intrauterine contraceptives are comparable, ranging from 79% to 96%.[195] A cohort study of 3727 women aged 18 to 40 did not find an adverse effect on fecundability after stopping long-term COC use, although there was a short-term delay compared with barrier methods.[194] Longer-term COC use was associated with higher fecundability compared with COC use of less than 2 years,[196] possibly due to a beneficial effect of long-term COC use on the inhibition of follicle depletion and postponement of natural menopause.[197,198]

3. The COC causes birth defects if a woman becomes pregnant while taking it.

   Fact: There is no evidence that COCs cause birth defects if they are taken inadvertently during pregnancy.[199,200]

4. The COC must be stopped in all women over 35.

   Fact: Healthy, non-smoking women may continue to use the COC provided they have no contraindications or other medical conditions that may significantly elevate the absolute risk of an adverse event.[60,142,201–203] However, there is limited evidence in women over 45 regarding the safety of COCs containing EE and whether COCs containing ≤20 μg EE or formulations containing EV2 or E2 are safer for women in their later reproductive years than those containing >20 μg EE.[203] Hence the contraceptive needs of women over 35 should be reassessed regularly, and health care providers may wish to consider changing from CHC methods to another method of contraception at age 50.[204]

5. The COC causes acne.

   Fact: Acne improves in most women using the COC due to a decrease in circulating free androgens.[63,205,206] Some COCs (e.g., those that contain drospirenone or cyproterone acetate) also exhibit a direct antiandrogenic effect.[65,66] (Note: The combination pill containing cyproterone acetate and EE is approved for the indication of moderate to severe acne but is also known to be a contraceptive.[63])

6. The COC causes cancer.

   Fact: The combined relative risk of cancer of the uterus, ovary, and cervix is decreased in women who have ever used COCs compared with those who have never used COCs (RR_{adj} 0.7, 95% CI 0.5 to 0.8).[207] COC use protects against ovarian and uterine cancer.[68–72,74–77,180] The risk of ovarian cancer is reduced by at least half in women who have ever used COCs (RR 0.5, 95% CI 0.4 to 0.7) and possibly as much as 75%,[76–78] even if initiated at an older age.[208] The risk of endometrial cancer is also reduced by at least 50% (RR 0.5, 95% CI 0.3 to 0.7) after 49 to 72 months of COC use.[180] Protection against both of these cancers appears to increase with increasing duration of use and wanes with increasing interval since last use but is still present for 20 years or more after discontinuation.[70,72,73,79,180,209] The effect appears to be independent of estrogen dose or progestin type[209] and has also been demonstrated in BRCA1/2-positive women.[68,77] Past COC use is also associated with longer survival in women with ovarian cancer.[210] COCs may also have a protective effect against colorectal cancer.[71,73,88] A recent meta-analysis found a decreased risk of colorectal cancer in ever users of COCs versus never users (RR 0.81, 95% CI 0.72 to 0.92).[88] Myths and misperceptions regarding CHC are listed in Appendix B.

Summary Statement

7. Combined oral contraceptive pills (COCs) are associated with a decreased risk of ovarian, endometrial, and colorectal cancers (II-2). A possible association has been shown between COC use and risk of cervical cancer (II-2), but causation has not been demonstrated.

Initiation

Initial assessment

Prior to prescribing a COC or any CHC, a thorough history should be taken, including potential contraindications, smoking history, and current medications. Few examinations or tests are required prior to COC initiation among otherwise healthy women.[211] A blood pressure assessment should be performed because of a greater risk of MI and ischemic stroke in women with hypertension.[159,212,213] A pelvic examination and Pap test are important aspects of well-woman care but are not required prior to initiating hormonal contraception because they do not identify conditions for which the use of hormonal contraceptives would be unsafe.[211] Testing for STIs is not required, although testing should be considered per the Canadian STI guidelines.[214] Urine polymerase chain reaction (PCR) testing or vaginal self-swabs for chlamydia and gonorrhea may be performed rather than using cervical swabs. A baseline weight and BMI assessment may help to monitor changes in COC users over time.[211] Screening for hyperlipidemia, liver disease, and clinical breast examination is not required because of the low prevalence of undiagnosed lipid disorders, liver disease, and breast cancer among reproductive-aged women.[211] Universal screening for thrombophilias is not recommended because of the high cost of screening and the rarity of the conditions.[215–217]

Summary Statement

8. A blood pressure measurement is the only examination and/or investigation that is required prior to initiating combined hormonal contraception (CHC) in women who are otherwise healthy by history (II-2). Baseline weight and body mass index assessment might be helpful for monitoring changes in CHC users. Pelvic examination, Pap test, screening for sexually transmitted infections, and thrombophilia screening are not required prior to initiating CHC (III).

Counselling

In a Cochrane review, only 1 of 8 eligible studies found a benefit of strategies to encourage adherence and continuation of hormonal contraceptives (repeated structured information increased depot medroxyprogesterone acetate continuation rates),[103] although another Cochrane review found an increase in consistent contraceptive use with theory-based counselling.[218] Regardless, adequate counselling prior to COC initiation is needed to ensure that women make a truly informed choice about their contraception and to improve adherence and continuation. Counselling should include the following:

- Instructions on taking the COC, including when to start and the importance of never having more than a 7-day HFI
- Non-contraceptive benefits
- Potential side effects and risks
- Common myths and misconceptions
- Risks and danger signs, including when and where to seek medical care
- Instructions on what to do if pills are missed, including when to consider EC
- Emphasizing dual protection (COC with condoms to protect against STIs and HIV)

Recommendation

1. Health care providers should give clear instructions for hormonal contraceptive use, including how to manage missed hormonal contraception, as part of contraceptive counselling. Women should be provided with resources to refer to in the event of missed and/or delayed hormonal contraceptives or if they develop any signs of a serious adverse event while using hormonal contraception (III-A).

Selecting and initiating

The choice of a COC should take into account the prescriber's clinical judgement, medical conditions, concurrent medications, and the woman's preferences, including preferences for withdrawal bleeding and non-contraceptive benefits. The preparation of choice for the COC user is the one that provides effective contraception, acceptable cycle control, and the fewest side effects for that individual.

In the absence of contraindications, CHC, including COCs, can be initiated at any time, provided that pregnancy or the possibility of pregnancy can be reasonably excluded.[211] Although product monographs usually state that the COC should be started on the first day of menstrual bleeding or on the first Sunday after the start of menstruation, waiting for the next menstrual period is not necessary and may put a woman at increased risk of an unintended pregnancy. When the possibility of pregnancy is uncertain, the benefits of starting the COC likely exceed any risk; thus the COC can be started immediately and a follow-up pregnancy test arranged in 2 to 4 weeks.[211] COCs can be started immediately after a surgical abortion or medical abortion.[37,38,211]

The Quick Start method refers to starting the COC or any other CHC immediately once pregnancy has been ruled out.[219,220] Ovulation is effectively inhibited after 7 consecutive days of CHC use so back-up contraception (barrier method) and/or abstinence should be used for the first 7 consecutive days of CHC use, unless it is initiated on the first day of menses. The Quick Start method may improve short-term compliance, particularly among adolescents, and is not associated with an increased incidence of breakthrough bleeding or other side effects.[220–223]

To improve continuation rates and enhance a woman's abilities to obtain her contraception when she needs it, health care providers should prescribe up to a 1- or 2-year supply of COCs at the initial and return visits.[211,224] A systematic review found that dispensing a greater number of pill packs was associated with increased continuation rates.[224]

A follow-up visit is suggested to review the COC user's satisfaction, concerns, adherence, any changes in her medical condition, and a blood pressure assessment. Weight may be measured if a woman is concerned about weight changes. Certain women may require or benefit from earlier or more frequent follow-ups, including adolescents and women with other medical conditions.[211]

Health care providers may apply to compassionate programs on behalf of women who are unable to afford their medications and are not covered by a private insurance plan or government assistance. Public health units and sexual health/youth clinics may provide contraception at a reduced cost. Most COCs are covered under the Non-Insured Health Benefits Program for First Nations and Inuit.[225] Several COC manufacturers have compassionate programs, and the SOGC currently administers a National Compassionate Contraception Assistance Program (http://compassion.sogc.org/).

Summary Statements

9. Combined oral contraceptive pills and other combined hormonal contraception (CHC) can be started at any time during the menstrual cycle, provided that pregnancy or the possibility of pregnancy can be reasonably ruled out. Where there is uncertainty, the benefits of starting CHC likely outweigh any risks (III).
10. Starting combined hormonal contraception immediately (Quick Start) may improve short-term compliance and is not associated with an increase in unscheduled bleeding or other side effects (I).

Recommendation

2. Health care providers should consider advising women who are initiating contraception to start their combined hormonal contraception (CHC) immediately (Quick Start) provided that they are reasonably certain that the woman is not pregnant. Back-up contraception (barrier method) or abstinence should be used for the first 7 consecutive days of CHC use unless CHC was initiated on the first day of menses (I-A).

Switching from another method of contraception

Women may switch from one method to another during the first 5 days of their menses. However, they do not have to wait until their next menses to do so. Table 3[226,227] shows how a woman can switch from one contraceptive method to another. These instructions are conservative and may ensure effectiveness of both the initial and the new method.

Table 3. Switching from one method of contraception to another

	Switching to							
Initial method	COC	Contraceptive patch	Contraceptive vaginal ring	POP	Injectable Progestin	Implant	LNG-IUS	Cu-IUD
COC	No interruption. Take the first tablet of the new pack of COC the day after taking any tablet of the initial COC	Apply the patch for 1 week and take 1 COC tablet the same day and 1 the next day	No interruption. Insert the day after taking any tablet of the initial COC	Take 1 tablet of POP and COC for 2 days at the same time	Inject DMPA and take 1 COC tablet daily for 7 days	Insert and take 1 COC tablet daily for 7 more days	Insert and take 1 COC tablet daily for 7 days	Insert up to 5 days after taking the last COC tablet
Contraceptive patch	Take the first tablet 1 day before taking the patch off.		No interruption. Insert the ring and remove the patch the same day	Take the first tablet of POP 2 days before taking the patch off	Inject DMPA at least 7 days before removing the patch	Insert 7 days before removing the patch	Insert 7 days before removing the patch	Insert up to 5 days after removing the patch
Contraceptive vaginal ring	Take the first COC tablet 1 day before removing the ring	Apply the patch 2 days before removing the ring		Take the first POP tablet 2 days before removing the ring	Inject DMPA 7 days before removing the ring	Insert 7 days before removing the ring	Insert 7 days before removing the ring	May insert up to 5 days after removing the ring
POP	Take 1 COC tablet and 1 POP tablet daily for 7 days	Apply the patch and take 1 POP daily for 7 days	Insert the ring and take 1 POP tablet daily for 7 days		Inject DMPA and take 1 POP tablet daily for 7 additional days	Insert and take 1 POP tablet daily for 7 days	Insert and take 1 POP tablet daily for 7 days	Insert up to 5 days after taking a POP tablet
Progestin injectable	Take the first COC tablet no later than 13 weeks after the last injection	Apply the patch no later than 13 weeks after the last injection	Insert the ring no later than 13 weeks after the last injection	Take the first POP tablet no later than 13 weeks and 5 days after the last injection		Insert no later than 13 weeks after the last injection	Insert no later than 13 weeks after the last injection	Insert no later than 14 weeks and 5 days after the last injection
Implant	Take 1 COC tablet per day for 7 days before removing the implant	The patch should be applied for at least 7 consecutive days prior to removing the implant	Insert the ring for at least 7 days before removing the implant	Take 1 POP tablet daily for 2 days before removing the implant	Inject DMPA at least 7 days prior to removing the implant		Insert at least 7 days before removing the implant	Insert up to 5 days after removing the implant
LNG intrauterine system	Take 1 COC tablet daily for 7 days before removing the LNG-IUS	The patch should be applied for at least 7 consecutive days prior to removing the LNG-IUS	Insert the ring for at least 7 days before removing the LNG-IUS	Take 1 POP tablet daily for 2 days before removing the LNG-IUS	Inject DMPA at least 7 days before removing the LNG-IUS	Insert at least 7 days before removing the LNG-IUS	Insert the new LNG-IUS on the same day that the previous LNG-IUS is removed	Insert the Cu-IUD on the same day that the LNG-IUS is removed

Continued

Table 3. Continued

Initial method	Switching to							
	COC	Contraceptive patch	Contraceptive vaginal ring	POP	Injectable Progestin	Implant	LNG-IUS	Cu-IUD
Cu-IUD	Take 1 COC tablet daily for at least 7 consecutive days before removing the Cu-IUD	The patch should be applied for at least 7 consecutive days prior to removing the Cu-IUD	The ring should be inserted at least 7 days before removing the Cu-IUD	Take 1 POP tablet daily for at least 2 days before removing the Cu-IUD	Inject DMPA at least 7 days before removing the Cu-IUD	Insert at least 7 days before removing the Cu-IUD	Remove the Cu-IUD and insert the LNG-IUS on the same day. Condoms should be used for at least 7 days before the Cu-IUD is removed and for another 7 days after the LNG-IUS is inserted	Insert the new Cu-IUD on the same day that the initial Cu-IUD is removed

DMPA: depot medroxyprogesterone acetate; IUS: intrauterine system.

Note. The delay between the initial method and Cu-IUD insertion takes into account the post-coital effect of the Cu-IUD.

Table adapted from the Reproductive Health Access Project[226] (www.reproductiveaccess.org) by le Comité d'experts en planning familial de l'Institut national de santé publique du Québec[227] (www.inspq.qc.ca/contraception).

If a woman wishes to switch from an IUC to the COC (or any CHC), it is suggested that she starts the COC at least 7 days before the IUC is removed. This is due to the theoretical concern of residual sperm being present in the genital tract and possible fertilization if ovulation occurs.[211] If a woman had UPI within the previous 5 days and asks to have her IUC removed and switch to the COC afterwards, her risk of having an unplanned pregnancy is increased and must be explained to her. In such a situation, there are 2 options:

1. The COC is started immediately, and IUC removal is postponed for 1 week. Once the COC has been taken for 7 consecutive days, the IUC can be removed. No back-up contraception is required.
2. The IUC is removed and EC is given immediately (preferably LNG-EC). The COC is started the same day or the day after, and a back-up method of contraception or abstinence should be used for the first 7 days of COC use.

With either option, if no withdrawal bleeding occurs during the planned subsequent HFI, a pregnancy test should be performed.

If a woman does not understand the switching instructions, they may be simplified by advising her to use condoms for at least 7 days before discontinuing her first method and for the first 7 days after switching to her new method. Breakthrough bleeding may occur at the time of switching. If symptoms of pregnancy occur or there is uncertainty about the risk of pregnancy, a pregnancy test should be performed.

Continuous or Extended Use of COC

Women may choose to use COCs in a C/E regimen for either medical or personal reasons. Rather than having a 28-day cycle with an HFI and withdrawal bleed, a woman may choose to avoid the HFI and a withdrawal bleed by skipping the placebo pills in the pill pack and immediately starting the active hormone-containing pills in the next pill pack. Some COCs are available in an extended regimen. More information is available in the Continuous or Extended Use of COC section discussed later.

Troubleshooting

1. **Breakthrough bleeding**

   Rates of unscheduled bleeding reported by women in COC clinical trials and surveys vary widely (15% to 30%).[107,228] Unscheduled bleeding will often improve with time[111,112,118,120,229–231]; therefore, new COC users should be encouraged to continue with the expectation that unscheduled bleeding will subside, rather than switching to another COC. Initial reassurance and a reminder of the

usually transient nature of irregular bleeding are essential.[232,233] A Pap test, STI testing, or a pregnancy test may be performed if indicated. COCs containing ≤20 μg EE may have higher rates of bleeding pattern disruptions in the first months of use and early discontinuation for irregular bleeding.[108] Theoretically, variations in cycle control with COCs may be related to progestin half-lives, the estrogen:progestin ratio, and individual metabolic differences.[234,235]

If the bleeding persists after the third cycle of use or has a new onset, other causes of bleeding should be ruled out with history taking and appropriate physical examination and/or investigations. Possible reasons for irregular bleeding in COC users include irregular pill taking[115]; smoking[114,236]; uterine or cervical pathology; malabsorption; pregnancy; use of concomitant medications (e.g., anticonvulsants, rifampin, St. John's Wort or other herbal medicines[237]); and infection.[116] New onset of irregular bleeding in long-term COC users may be a marker for chlamydia infection; up to 29% of these women may have a positive chlamydia test.[116]

Recommendation

3. Health care providers should consider the possibility of irregular pill taking, concomitant medication use, malabsorption, uterine or cervical pathology, pregnancy, or chlamydial infection in women presenting with persistent unscheduled bleeding on the combined oral contraceptive pill (III-A).

Once other causes of unscheduled bleeding have been ruled out, several empirical regimens have been suggested, but there is limited evidence to support any of these. In the case of persistent or new onset bleeding, a therapeutic trial of another COC may be offered. It may be helpful to switch to a COC containing a higher dose of estrogen, with a higher estrogen:progestin ratio, with a different type of progestin (i.e., from a gonane to an estrane progestin or vice versa), or a progestin with a longer half-life (drospirenone, dienogest, desogestrel).[238,239] There is limited, consistent evidence that one COC preparation is less likely than others to cause ongoing unscheduled bleeding.[228] A short course of oral estrogen in addition to the COC may be helpful, such as 1.25 mg of conjugated estrogen or 2 mg of E2 daily for 7 days. Consistent pill use and smoking cessation should be emphasized. If the bleeding is problematic for the woman, alternative methods of contraception should also be discussed.

Women who experience unscheduled bleeding or spotting while using an C/E COC regimen and want treatment may be advised to discontinue the COC for 3 to 4 days, provided that she has taken the COC for at least 21 consecutive days previously.[240] With this interruption of pill-taking, flow is usually transiently increased and then decreases abruptly 7 to 8 days later.[241] A 3- to 4-day HFI is not recommended more than once per month because contraceptive effectiveness may be decreased.

2. Missed pills

Advice for missing COCs will depend on whether the dose is "late" (<24 hours since a pill should have been taken), "missed" (>24 hours since the last pill was taken), how many pills were missed, timing in the pill pack, and whether UPI has occurred (Figure 1).[242] The HFI should never exceed 7 days, and missing pills at the beginning or end of a 21-day cycle has the effect of lengthening the HFI and increasing the risk of ovulation and unintended pregnancy.[242] Eliminating the HFI when 1 or more COCs are missed in week 2 or 3 will reduce the risk of unplanned pregnancy.

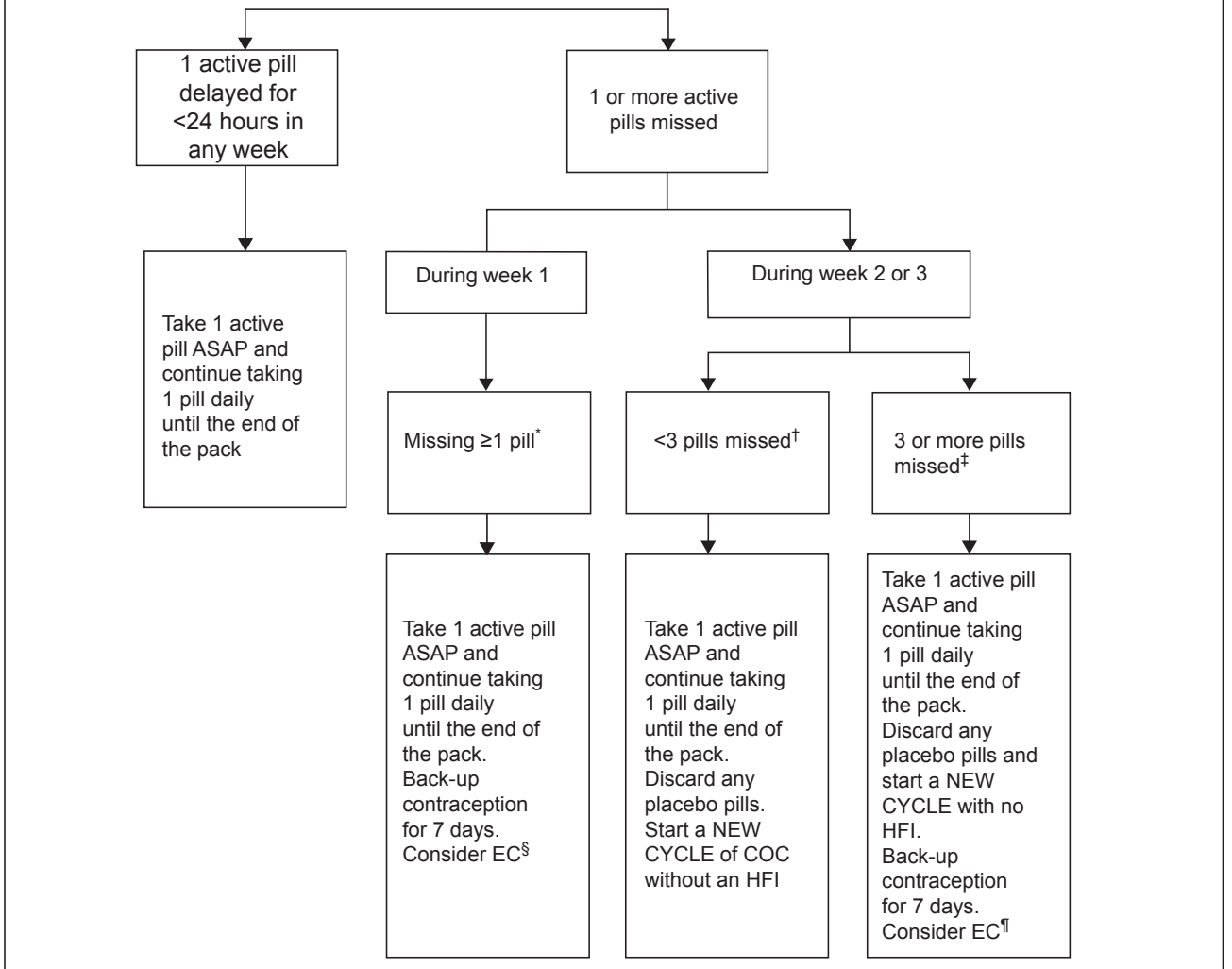
Due to concerns about potential drug interaction between UPA-EC and CHC, LNG-EC is recommended when EC is required for missed COCs (or any CHC), particularly when a woman plans to continue using the COC as her method of contraception. CHC can be restarted the same day or the day after LNG-EC is taken. A barrier contraceptive method or abstinence should be used for the first 7 days of CHC use. If EC is indicated and a woman uses UPA-EC rather than LNG-EC, she should wait 5 days before restarting her CHC. She should use a barrier contraceptive method or abstain from intercourse for the first 5 days after taking UPA-EC and for the first 7 days after starting CHC (i.e., when UPA-EC is used and CHC is restarted, back-up contraception and/or abstinence is required for a total of 12 days after UPA-EC ingestion) (see Addendum to the Canadian Consensus On Contraception: Emergency Contraception[243]).

Many women and health care providers have difficulty understanding missed pill instructions.[244] Graphics-based missed pill instructions or interactive apps (e.g., SOGC's Stay on Schedule app at http://www.sexandu.ca/games-and-apps/s-o-s-stay-on-schedule, Appendix C) may help to improve comprehension. Local Telehealth services may also be a resource for health advice. Women who frequently miss COCs should consider less user-dependent methods of contraception.

Summary Statements

11. The highest risk of ovulation occurs when the hormone-free interval is prolonged for more than 7 days, either by delaying the start of combined hormonal contraception (CHC) or by missing active hormone doses during the first or third weeks of

Figure 1. Missed combined oral contraceptives.



*During the first week of use (week 1), delay in taking 1 pill ≥24 hours (i.e., missing one or more pills) increases the HFI and may allow ovulation during this week. Missing 1 active pill before ovulation is effectively inhibited (achieved after taking 1 active pill daily × 7 consecutive days) may also allow ovulation during this week. If intercourse occurred during the day of pill omission or in the 5 days prior, consider EC.

†Missing fewer than 3 pills in a row during week 2 or 3 is the same as having a short HFI after achieving effective inhibition of ovulation during the preceding week (1 pill daily × 7 consecutive days). Therefore, efficacy is not expected to be reduced, although breakthrough bleeding may occur. Eliminating the HFI may reduce the risk of unintended pregnancy when pills are missed in week 3. Eliminating the HFI when pills are missed in week 2 is proposed to simplify this algorithm.

‡Missing 3 or more pills in a row during week 3 is likely to impair contraceptive effectiveness because the HFI comes immediately after week 3. Eliminating the HFI and using a back-up method until 7 consecutive days of pills are taken should reduce the risk of unintended pregnancy. EC can be considered if unprotected intercourse has occurred during the interval of missed pills up until 7 consecutive pills have been taken. The same recommendation is proposed for week 2 to simplify the algorithm.

§If unprotected intercourse within the last 5 days.

¶If repeated or prolonged omission.

CHC (I). Ovulation rarely occurs after 7 consecutive days of CHC use (II-2).

12. Emergency contraception (EC) and back-up contraception may be required in some instances of missed combined hormonal contraception (CHC), particularly when the hormone-free interval has exceeded 7 days. EC is rarely indicated for missed CHC in the second or third week of the

cycle unless there are repeated omissions or failure to use back-up contraception after the missed doses (III).

Recommendations

4. If 1 combined oral contraceptive pill or other combined hormonal contraception (CHC) method is missed in the first week of use, back-up contraception or abstinence should be used until the CHC method has been used for 7 consecutive days. In the case of missed CHC in the second or third week of hormones, the hormone-free interval should be eliminated for that cycle (III-A).
5. Back-up contraception should be used when 3 or more consecutive doses/days of combined hormonal contraception (CHC) have been missed in the second or third week of hormone use until the CHC has been taken for 7 consecutive days. For practical reasons, the scheduled hormone-free interval should be eliminated in these cycles (I-A).

3. Vomiting or severe diarrhea while using COCs

There is a lack of evidence addressing acute, short-term vomiting or severe diarrhea in COC users. Theoretically, COC effectiveness may be decreased,[211] and studies have reported contraceptive failures in COC users who reported episodes of diarrhea and/or vomiting.[17,18] A reasonable approach would be to follow the same recommendations as for missed pills. If the vomiting or diarrhea occurs and continues within 24 to 48 hours of taking a COC, a woman should continue taking pills daily at the usual time (if possible). If the vomiting/diarrhea occurred in the first week of COC use, a woman should use back-up barrier contraception or abstain from sexual intercourse until the COC has been used for at least 7 consecutive days after the vomiting/diarrhea has resolved.[211] EC should be considered if UPI occurred in the previous 5 days.

Although not specifically studied in these instances, vaginal COC administration has been studied.[245–247] Theoretically, vaginal administration may avoid "first pass" metabolism by the liver and help decrease COC side effects and improve tolerance. One large multicenter study of 1055 women using the COC vaginally found 1-year pregnancy rates of 2.78% with a 50 μg COC (50 μg EE/250 μg LNG) and 4.54% with a 30 μg COC (30 μg EE/150 μg desogestrel) (no significant difference).[245] Failure rates were not compared directly with orally administered COCs. Small studies comparing vaginal and oral administration of EC found that vaginal administration may require a higher dose than standard oral doses to achieve equivalent systemic LNG concentrations.[248]

4. Amenorrhea

COCs are progestin-dominant, and some women will have no withdrawal bleeding during the HFI. Amenorrhea is more common with COCs that contain ≤20 μg EE and in regimens with shorter HFIs.[118–120] Provided that a woman has been taking her pill consistently and has no symptoms of pregnancy, pregnancy is unlikely; however, pregnancy should be ruled out in any COC user who develops new onset of amenorrhea. Amenorrhea in women taking COCs is not dangerous. If amenorrhea is unacceptable to the woman, switching to another COC preparation (e.g., one with a higher estrogen dose) may result in resumption of menses.

5. Breast pain (mastalgia) and galactorrhea

Mastalgia often resolves after several cycles of COC use.[249] Decreasing caffeine intake does not appear to be helpful in treating mastalgia.[250] Decreasing the estrogen content of the COC may be helpful.[101,118] Galactorrhea during COC use is rare, and other possible causes should be investigated.

Nausea

Although placebo-controlled studies have found no increase in nausea in COC users compared with placebo,[121] nausea is a commonly reported side effect during the first cycles of COC.[251,252] It usually decreases with time.[249] Switching to a COC with a lower estrogen dose may be helpful[101] and taking the COC at bedtime may be suggested. If new onset nausea occurs in a long-time pill user, pregnancy must be ruled out.

6. Pregnancy

If pregnancy occurs in a COC user, she should stop taking the pill immediately. However, there does not appear to be an increased risk of birth defects as a result of inadvertent COC use during pregnancy.[199,200]

Summary Statement

13. Combined oral contraceptive pill exposure just prior to or during pregnancy is not associated with an increased risk of major birth defects (II-2).

Drug Interactions

A drug can be a substrate, an inhibitor, or an inducer of metabolizing enzymes. Drug interactions occur when a drug alters the PKs of another drug or its metabolites. EE is metabolized in several different sites. EE is sulphated in the intestinal wall, then it is hydroxylated in the cytochrome

P450-3A4 (CYP3A4) pathway of the liver, after which it is conjugated with glucuronides and passes into the enterohepatic circulation.[253–256] Intestinal bacteria can unconjugate the estrogen compounds, allowing them to be reabsorbed. Free EE in the liver increases production of SHBG and activates the CYP3A4 system. The majority of progestins are metabolized by CYP3A4, UDP-glycosyltransferase, and sulfotransferases, but the relative contribution of CYP3A4 is not known.[256] Progestins are well absorbed, undergo extensive metabolism in the liver, and do not undergo enterohepatic recirculation. These processes may vary among women and may be affected by other medications.[257] Drug interactions may occur via alterations in absorption, serum protein binding, receptor binding, or in hepatic metabolism.[258,259] The COC is a moderate inhibitor of CYP1A2 and a weak inhibitor of CYP3A4, CYP2D6, and CYP219. The clinical significance of many of the COC interactions is questionable, and it has been suggested that less than 5% of drug interactions with COCs result in pregnancy.[259] Nevertheless, due to the widespread use of COCs, health care professionals must be aware of concurrent medication use and the potential for drug interactions.

AEDs, such as phenytoin, phenobarbital, carbamazepine, felbamate, topiramate, oxcarbazepine, and primidone, induce CYP3A4, leading to enhanced metabolism of either/both the estrogenic and progestogenic component of COCs, thereby reducing their efficacy.[260,261] Although some have suggested using a 50 μg EE COC in COC users taking enzyme-inducing AEDs,[262,263] there is limited evidence to support this practice, and 50 μg COCs are no longer available in Canada. Valproic acid inhibits CYP3A4 and thus does not affect COC efficacy.[261] COCs have been shown to reduce lamotrigine plasma levels, thus it is advisable to monitor lamotrigine levels in women who initiate or discontinue COCs.[260,264,265]

The evidence regarding COC use with antidepressants or antipsychotics is limited. There may be concern for those with a narrow therapeutic window; however, selective serotonin reuptake inhibitors have a wide therapeutic window and thus are a WHO/CDC category 1.[37,38] St. John's Wort is a moderate CYP3A4 inducer, and small studies have found an increase in breakthrough bleeding and ovulation and a decrease in progestin levels in COC users taking St. John's Wort,[237,266–268] but there is no published data on pregnancies. Hence, St. John's Wort is in category 2.[37]

Of the ARTs available, small studies of the nucleoside/nucleotide reverse transcriptase inhibitor efavirenz have suggested a possible clinically relevant interaction between efavirenz and COCs (more ovulation, lower progestin levels).[269–271] Protease inhibitors boosted with ritonavir, including atazanvir/r, darunavir/r, fosamprenavir/r, tipranavir/r, and saquinavir/r, have been associated with a decrease in EE and/or norethindrone levels.[271] HIV-positive women using COCs and these ARTs should use a back-up method of contraception.[270,271] Latex condom use is advised. Interactions between FPV and hormonal contraceptives may decrease FPV levels, thereby diminishing its effectiveness; for this reason, FPV has been assigned to category 3 for CHC use.[37,46]

The effect of antibiotic use on the effectiveness of COCs has been controversial, but the evidence suggests that most broad-spectrum antibiotics do not affect the effectiveness of the COC. A significant PK interaction between COCs and antibiotics, apart from rifampicin and griseofulvin, has not been proven.[272–274] Surveys of COC failures in women exposed to antibiotics report failure rates of 1.2% to 1.6% that are well within the 1% to 9% failure rate reported with typical use of COCs.[16,272] If an interaction does exist, it is likely that it occurs in a small number of predisposed individuals, but it is not possible at this time to predict who is at risk for potential interaction.

Table 4 shows potential drug interactions with COCs. Some medications may result in contraceptive failure if used concomitantly with COCs.[275,276] Some medications may increase COC activity,[259,275] although these do not necessarily represent a contraindication. COCs may also increase or decrease the clearance of other medications, thereby affecting their activity.[259,275,276] Other drug interactions may occur but are not included in Table 4 because of a lack of scientific documentation or questionable clinical significance.

Summary Statement

14. The effectiveness of combined hormonal contraception (CHC), including combined oral contraceptive pills, may be affected by other medications, including but not limited to some anticonvulsants, some antiretrovirals, rifampicin, and griseofulvin. CHCs may affect the serum levels of other medications, including some anticonvulsants and antiretrovirals (II-2).

Recommendation

6. Health care providers should be aware of other medications being used by combined hormonal contraception users and the possibility of drug interactions that could affect serum levels and effectiveness of either medication (II-2A).

Table 4. Drug interactions with COCs

Medications whose interaction may cause contraceptive failure	Medications that may increase COC activity	Medications whose effect may be altered by COCs
Antiepileptic drugs (AEDs) (e.g. barbiturates, carbamazepine, clobazam, fosphenytoin, phenytoin, oxcarbazepine, perampanel, primidone, rufinamide, topiramate)	Acetaminophen	Anastrozole
Bile acid sequestrants (cholestyramine, colestipol, colesevelam)	Amiodarone	Anticoagulants
Bosentan	Estrogenic herbs (alfalfa, black cohosh, bloodroot, ginseng, hops, kudzu, licorice, red clover, saw palmetto, soybean, thyme, wild yam, yucca)	Benzodiazepines (alprazolam, chlordiazepoxide, diazepam, midazolam, triazolam)
Dabrafenib	Antifungals (fluconazole, voriconazole)	Beta-blockers (acebutolol, propranolol)
Deferasirox	Erythromycin	Caffeine
Exenatide	Grapefruit juice	Corticosteroids
Fosaprepitant	Progestogenic herbs (bloodroot, chasteberry, damiana, oregano, yucca)	Cyclosporine
Hepatitis C protease inhibitors (boceprevir, telaprevir)	Rosuvastatin	Fosamprenavir (FPV)[46]
HIV protease inhibitors (atazanavir, darunavir, FPV, lopinavir/ritonavir, nelfinavir, ritonavir, darunavir, tipranavir)	Serotonin reuptake inhibitors (fluoxetine, fluvoxamine, sertraline)	Lamotrigine[265]
Modafinil	Vitamin C	Mifepristone
Mycophenolic acid		Phenytoin
Purcalopride		Ropinirole
Rifampin		Selegiline
St. John's Wort[268]		Theophylline
Ulipristal acetate		Thyroid products
		Tizanidine
		Tranexamic acid
		Tricyclic antidepressants (amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline)
		Ursodiol
		Ulipristal Acetate (UPA)
		Voriconazole
		Zolmitriptan

TRANSDERMAL CONTRACEPTIVE PATCH

Introduction

The contraceptive patch was approved for use in Canada in 2002 and became available for use in January 2004. The contraceptive patch is a 20-cm^2 square matrix system that delivers 200 μg of norelgestromin (the primary active metabolite of norgestimate) and 35 μg of EE daily to the systemic circulation.[277] Following the first application of the patch, serum hormone levels increase gradually over the first 48 to 72 hours, reach a plateau, and then remain constant during the remainder of the 21-day period.[278] Compared with the COC, plasma hormone levels remain constant and the peak levels are lower because first-pass hepatic metabolism and gastrointestinal enzyme degradation are avoided. Although peak levels are lower, the area under the curve, which represents overall EE exposure, is higher.[278,279]

One patch is applied weekly for 3 consecutive weeks, followed by 1 patch-free week. The patch is placed on 1 of 4 sites: the buttocks, upper outer arm, lower abdomen, or upper torso, excluding the breast.

Effectiveness

The patch has a perfect use failure rate of 0.3% and a typical use failure rate of 9%.[16] It is as effective as COCs.[231,251,280,281]

Clinical studies found that the PI with perfect use of the contraceptive patch was 0.7 (95% CI, 0.31 to 1.10), whereas with typical use the PI was 0.88 (95% CI, 0.44 to 1.33).[231,280,282] A subgroup of women weighing more than 90 kg may have an increased risk of pregnancy while using the patch.[280,282,283] In one study, 4 of 6 pregnancies that occurred were in women weighing at least 90 kg[280]; in a pooled analysis, 5 of the 15 pregnancies that occurred in patch users were in women weighing more than 90 kg.[282]

Compliance affects contraceptive effectiveness, and patch users may be more compliant than users of COCs.[251,282,284] Compared with COC, the odds of perfect compliance with the patch are 2.05 to 2.76 times higher (95% CI 1.83 to 2.29 and 2.35 to 3.24, respectively).[231,251,281] However, early discontinuation rates may be higher compared with the COC, and patch users are more likely to discontinue due to adverse events than are COC users.[231,251,285]

Summary Statement

15. The contraceptive patch may be less effective in women with a body weight $\geq$90 kg (II-2).

Mechanism of Action

The mechanism of action is similar to that of the COC.

Indications

In the absence of contraindications, the contraceptive patch may be considered for any woman seeking a reliable, reversible, coitally independent method of contraception. It may be especially suited for women seeking a less compliance-demanding method of contraception, shift workers, those who have difficulty swallowing pills, or those who have medical conditions that are associated with decreased gastrointestinal absorption such as inflammatory bowel disease. The patch does not protect against STIs. Consistent and correct use of male condoms is advised to reduce the risk of STIs, including HIV.

Contraindications

WHO and the CDC have developed guidelines that categorize medical conditions into 1 of 4 categories based on their level of risk (Table 2).[37,38,286] Contraindications to use of the contraceptive patch are generally the same as those for the COC (see the Combined Oral Contraceptive Pill section). The exception is a history of malabsorptive bariatric procedures, which is not a contraindication to contraceptive patch use (category 1).[37]

Although obesity is not a contraindication to use of the patch,[142] studies have suggested that the patch may be less effective in women with a body weight of ≥90 kg compared with women with lower body weights.[282] The patch can still be used in obese women provided they are aware of a potential small decrease in effectiveness.

Non-Contraceptive Benefits

Although non-contraceptive benefits are assumed to be similar to those seen with the COC, few studies have specifically addressed other potential benefits of the patch. Cycle control is comparable to the COC.[231,251,280,282] Although the patch has been shown to reduce pain symptoms in women with endometriosis, it is not as effective as the vaginal contraceptive ring in women with rectovaginal endometriotic lesions.[287] Due to the increase in SHBG and decreases in free testosterone and dehydroepiandrosterone sulfate that occur during patch use, the patch is likely associated with improvements in hyperandrogenic symptoms such as acne and hirsutism.[278,288]

Side Effects

The patch has similar side effects to the COC with the exception of application site reactions.[231,251,280] Compared with the COC, patch use is reportedly associated with less breakthrough bleeding and spotting but more breast discomfort or pain, dysmenorrhea, and nausea and vomiting.[251] The most frequently reported side effects with the patch are breast symptoms (22%), headache (21.1%), nausea (17%), and application site reactions (17.4%).[289] The patch does not appear to be associated with clinically significant weight gain.[121,289]

Irregular bleeding/spotting

The overall incidence of breakthrough bleeding and spotting is similar to that seen with COC users.[251,282,290] Compared with COC users, patch users may have significantly higher rates of spotting during cycles 1 and 2 (18.3% vs. 11.4%)[231] but lower rates of breakthrough bleeding and spotting at cycle 13.[281] The incidence of breakthrough bleeding and/or spotting tends to decrease with time.[282] Amenorrhea with the contraceptive patch is rare.[280]

Local skin reaction

Up to 20% of women experience an application site reaction.[231,251,281,289] Most application site reactions are mild in severity (92%), and only 2% of patch users in clinical studies discontinued it for this reason.[289] The frequency of application site reactions does not increase over time.[231]

Breast symptoms and headache

Breast symptoms, including discomfort, engorgement, or pain, and headache are the most common side effects reported with patch use (22% and 21%, respectively).[289] Breast symptoms are more common with the patch than with the COC, particularly in the first 2 cycles of patch use,[251,281,289] but by cycle 3, there does not appear to be a significant difference between the 2 groups.[231] Most breast symptoms are either mild or moderate (86%) and tend to decrease with continued patch use, down to 0% of women at 13 months.[231] In a pooled analysis, only 1.9% of women discontinued patch use due to breast symptoms and 1.1% due to headaches.[289]

Summary Statement

16. Compared with the combined oral contraceptive pill, transdermal contraceptive patch use is associated with less breakthrough bleeding and spotting but more breast discomfort or pain, nausea and vomiting, and dysmenorrhea (I).

Risks

Cardiovascular risk

All CHC methods are associated with an increased risk of VTE due to prothrombotic effects on coagulation factors.[285,291] In 5 clinical trials, the estimated frequency of VTE in patch users was 5.3 per 10 000 women (95% CI 0.1 to 29.4).[251] Several retrospective database studies, including a large study sponsored by the Food and Drug Administration,[153] found no significant increased risk of VTE in patch users compared with COC users (OR 1.23,

95% CI 0.86 to 1.77)[292–294]; conversely, another case-control database study showed a significantly higher risk of VTE in patch users compared with COC users (OR 2.2, 95% CI 1.2 to 2.4).[295] In case control studies[295] and historical cohort studies,[296] there does not appear to be a significantly increased risk of stroke or MI in patch users.

Myths and Misconceptions

1. The patch won't stay on during exercise; in hot, humid weather; while swimming; or while in the shower.

   Fact: The patch has excellent adhesive properties under a wide range of conditions and climates, including bathing, sauna, and whirlpool use; treadmill activity; or cool-water immersion.[297] Patch detachment is rare[251]; in clinical trials, approximately 1.9% of patches required replacement due to complete detachment.[231,280] The incidence of patch detachment may decrease as the patch user becomes more familiar with the application technique. Although detachment is rare, patch users should check daily to ensure that their patch is adequately attached.

2. Because of the transdermal delivery system, the patch will have less effect on the lipid profile than will the COC.

   Fact: A slight increase in serum total cholesterol and triglyceride levels is seen in users of both the patch and the COC.[231,289] A randomized, placebo-controlled trial found that patch users had a small increase from baseline in total cholesterol, HDL cholesterol, and total triglycerides and a mean decrease in low-density lipoprotein/HDL. These changes were within normal limits and consistent with the lipid effects of a COC.[298]

Initiation

How to start and to use the patch

The transdermal contraceptive patch is approved for a 28-day regimen with a new patch being applied every week for 3 weeks and a fourth patch-free week. Every new patch should be applied on the same day of the week ("patch change day").[277] Withdrawal bleeding usually occurs during the patch-free interval. The patch-free interval should not exceed 7 days. Once a medical history has ruled out any contraindications to its use, the only examination required prior to initiating the patch is a blood pressure measurement.[211] An initial weight and BMI may be helpful for follow-up.

Although the product monograph states that the patch should be applied on the first day of menstrual bleeding or on the first Sunday after her period starts (Sunday Start),[277] the patch can in fact be applied at any time in the menstrual cycle (Quick Start), provided that it is reasonably certain that a woman is not pregnant.[211] If the patch is applied on the first day of menses, no backup method of contraception is required. If the patch is initiated at any other time of the menstrual cycle, back-up contraception or abstinence should be used for 7 days. Quick Start does not appear to be associated with any increase in side effects, including bleeding problems.[223]

The patch should be applied to clean, dry, healthy, intact skin. The patch may be applied at 1 of 4 sites: the buttock; the abdomen; the upper outer arm; or the upper torso, but not directly to the breast. These 4 sites are therapeutically equivalent.[299] Patch users should be advised to check daily that their patch is adhering well.

A follow-up appointment is suggested to assess the patch user's satisfaction with the method, discuss any side effects, ensure that it is being used correctly, assess blood pressure, and answer questions.

Switching from another method of contraception to the patch

Women may switch from one method to another during the first 5 days of their menses. However, they do not have to wait until their next menses to do so. Table 3 shows how a woman can switch from one contraceptive method to another. These instructions are conservative and may ensure effectiveness of both the initial and the new method.

If a woman wishes to switch from an IUC to the patch, it is suggested that she starts the patch at least 7 days before the IUC is removed. This is due to the theoretical concern of residual sperm being present in the genital tract and possible fertilization if ovulation occurs.[211] If a woman had UPI within the previous 5 days and asks to have her IUC removed and switch to the transdermal contraceptive patch afterwards, her risk of having an unplanned pregnancy is increased and must be explained to her. In such a situation, switching instructions are the same as for the COC (see the Combined Oral Contraceptive Pill section).

C/E use of the contraceptive patch

Women may choose to use the patch in a C/E regimen for either medical or personal reasons. Rather than having a patch-free week after 3 weeks of patch use, a woman can avoid an HFI and associated withdrawal bleed by immediately applying a new patch. Compared with cyclic use, extended use of the patch is associated with significantly fewer bleeding days.[300] Although there are some concerns regarding C/E patch use because of increasing serum EE levels over time before the patch free-week,[279] at this time there is no evidence to support an increased risk of VTE or other adverse events in extended-cycle patch users compared with extended cycle vaginal ring or COC

users.[301] See the Continuous or Extended Use of CHC section for more information.

Troubleshooting

1. **The patch partially or completely detaches**
   Patch detachments are rare. In clinical studies, 5% of the patches required replacement due to complete or partial detachment.[231] Advice for a patch detachment will depend on how long the patch has been off (<24 hours, 24 to 72 hours, or ≥72 hours); the timing in the cycle; and whether UPI has occurred. Advice is based on the following assumptions: ovulation is effectively inhibited after 7 consecutive days of CHC use[223]; the HFI should never exceed 7 days; and having the patch off for longer than 24 hours at the beginning or end of a 21-day cycle has the effect of lengthening the HFI and increasing the risk of ovulation and unintended pregnancy.[242] Eliminating the HFI when a patch has been off for more than 72 hours in week 2 or 3 of the cycle will reduce the risk of unplanned pregnancy (Figure 2).

   If the patch has either partially or completely detached for less than 24 hours, the woman should attempt to reattach the patch. If this is not successful, a new patch should be applied. The patch change day would remain the same. If the patch has been completely or partially detached for more than 24 hours or the timing is uncertain, a new patch should be applied (Figure 2). Back-up contraception and EC should be considered, depending on timing in the cycle and the duration of patch detachment.[242]

2. **Forgetting to apply, change, or remove the patch**
   PK studies indicate that the hormone reservoir in the contraceptive patch maintains serum concentrations of EE and norelgestromin at ovulation inhibitory levels throughout 9 days of wear, which is 2 days past the approved time for use.[302] Extended wear past 9 days results in falling hormone levels in week 2, 3, or 4 of the cycle.

   Extended wear of the third and final patch in the cycle falls into the planned HFI (week 4) and will not decrease patch effectiveness unless it is worn past the start of the next patch cycle. If a woman forgets to remove the third patch during week 4, she should remove it as soon as she remembers. The next patch is applied on the usual patch change day and this will be the start of her next cycle. Back-up contraception is not required (Figure 2).

   For extended wear of the first or second patch, the same rule as for missed COCs in weeks 2 and 3 applies. Missing COC for less than 3 days or extended patch wear for less than 12 days (i.e., 9 days of therapeutic levels with patch plus 3 hormone-free days) should not decrease contraceptive effectiveness as long as the HFI is not extended. If the first or second patch is left on for fewer than 12 days, the woman should remove it as soon as she remembers and apply a new patch immediately. The patch change day can be kept the same. The woman should finish her current cycle of patches, omit the HFI, and then immediately start a new cycle of 3 patches. If the patch is left on for more than 12 days, the same steps should be taken; in addition, back-up contraception should be used for 7 days and EC should be considered.[242] If a patch user forgets to apply her first patch in week 1, she should apply a new patch as soon as she remembers. Back-up contraception is recommended for 1 week, and EC should be considered if UPI occurred within the previous 5 days. The patch user can either keep the same patch change day or have a new patch change day.

Summary Statement

17. Pharmacokinetic studies indicate that serum hormone concentrations of ethinyl estradiol and norelgestromin are maintained at ovulation inhibitory levels throughout at least 9 days of continuous transdermal contraceptive patch wear (II-2).

3. A woman would like to change her patch-change day

A new cycle should be started by placing the first patch of the new cycle on the new desired patch change day during the patch-free week. The patch-free interval should not exceed 7 days.

Drug Interactions

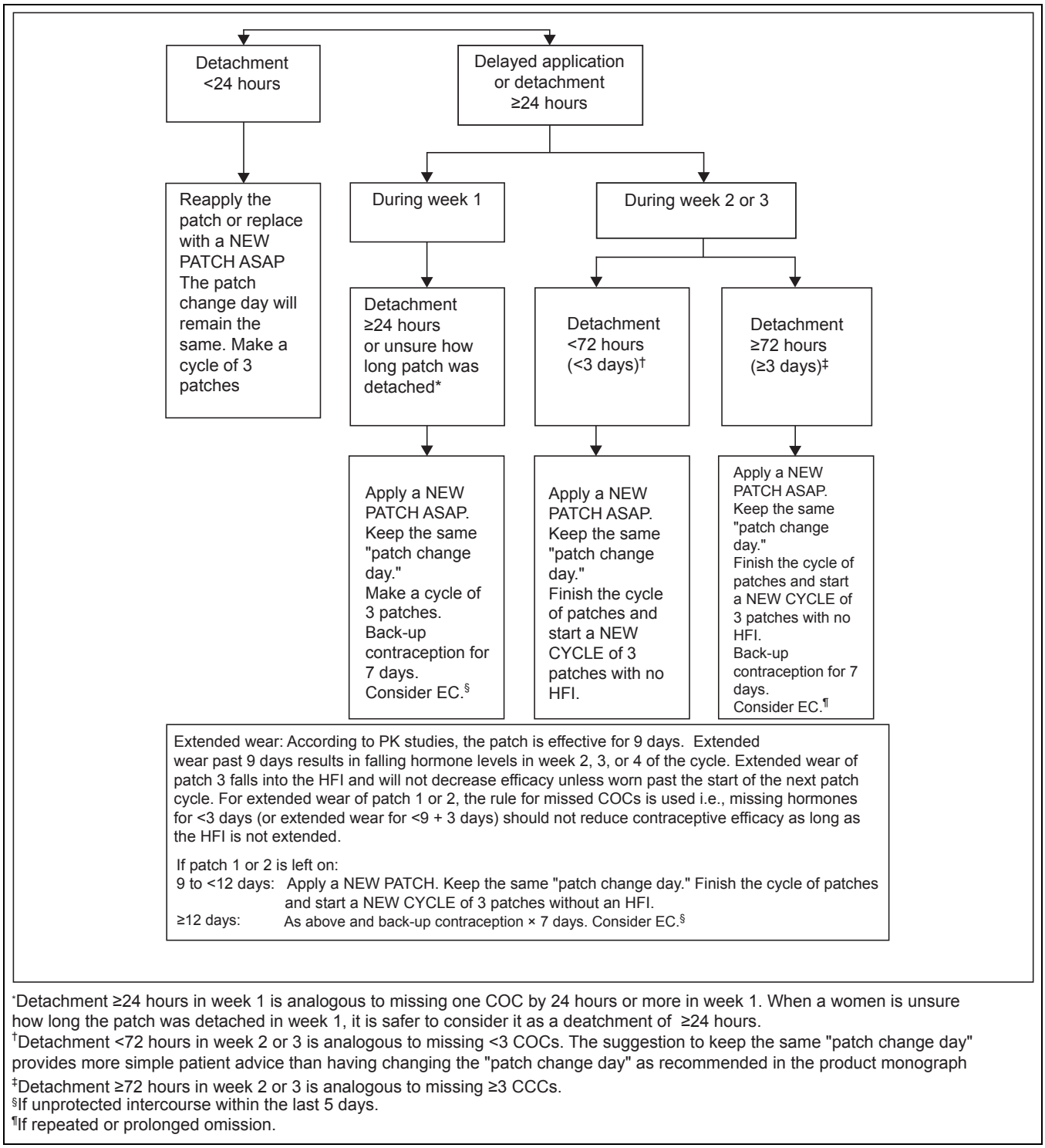
Few drug interactions have been specifically studied with the contraceptive patch; therefore, drug interactions that occur with COC use are assumed also to occur with the patch (Table 4). PK studies have shown no significant interaction between tetracycline and the patch.[303]

VAGINAL CONTRACEPTIVE RING

Introduction

The vaginal contraceptive ring (NuvaRing) was approved by Health Canada in 2004. It is a flexible, soft, transparent ring made of the copolymer ethylene vinyl acetate and measures 54 mm in outer diameter and 4 mm in cross-sectional diameter.[304] The ring releases 15 μg of EE and 120 μg of the progestin ENG (the active metabolite of desogestrel) per day, which is absorbed through the vaginal epithelium.[304,305] Serum hormone levels increase immediately after ring insertion and then decrease slowly over the cycle.[279] Each

Figure 2. Missed contraceptive patch.



*Detachment ≥24 hours in week 1 is analogous to missing one COC by 24 hours or more in week 1. When a women is unsure how long the patch was detached in week 1, it is safer to consider it as a deatchment of ≥24 hours.
†Detachment <72 hours in week 2 or 3 is analogous to missing <3 COCs. The suggestion to keep the same "patch change day" provides more simple patient advice than having changing the "patch change day" as recommended in the product monograph
‡Detachment ≥72 hours in week 2 or 3 is analogous to missing ≥3 CCCs.
§If unprotected intercourse within the last 5 days.
¶If repeated or prolonged omission.

ring is inserted into the vagina and removed by the woman herself. After 3 weeks of continuous use, the woman removes the ring and has 1 ring-free week, during which time withdrawal bleeding usually occurs. A new ring is used for each cycle.[304] Vaginal administration of contraceptive hormones avoids gastrointestinal absorption and the hepatic first-pass effects.[306] The NuvaRing is the only vaginal contraceptive ring currently available in Canada.

Effectiveness

The ring has a perfect use failure rate of 0.3% and a typical use failure rate of 9%.[16] In studies of several thousand

cycles of ring use, the PI with perfect use of the ring was between 0.40 (95% CI 0.08−1.16)[307] and 0.77 (95% CI 0.37−1.40).[308,309] In the same studies, the intention-to-treat PI was between 0.65 (95% CI 0.24−1.41)[307] and 1.18 (95% CI 0.73−1.80).[308] Ring users may be more compliant than users of COCs.[251] Perfect compliance was reported in 86% to 91% of ring users.[307,308] The ring is as effective as the COC, with comparative clinical trials demonstrating a PI of 0.25 to 1.23 for the ring compared with 0.99 to 1.19 for the COC.[251,310,311]

Mechanism of Action

The ring has multiple mechanisms of action similar to the COC.[312−315]

Indications

In the absence of contraindications, the vaginal contraceptive ring can be considered for any woman seeking a reliable, reversible, coitally independent method of contraception. It may be suitable for women who prefer a less compliance-demanding method of contraception, have difficulty swallowing pills, have medical conditions that are associated with decreased gastrointestinal absorption such as inflammatory bowel disease, or who may benefit from its non-contraceptive effects. Some women may find that the ring is a more discrete and private method of contraception. The ring does not protect against STIs. Consistent and correct use of male condoms is advised to reduce the risk of STIs and HIV.

Contraindications

WHO and the CDC have developed guidelines that categorize medical conditions into 1 of 4 categories based on their level of risk (Table 2).[37,38,286] Contraindications to use of the ring are the same as those for the COC. The exception is a history of malabsorptive bariatric procedures, which is not a contraindication to vaginal contraceptive ring use (category 1).[37]

Although not contraindications to use of the ring, women with significant pelvic relaxation, vaginal stenosis, or obstruction (if they prevent retention of the ring); conditions that make the vagina more susceptible to irritation or ulceration; or an inability or unwillingness to touch their genitals may not be good candidates for the ring.[148] Women with a history of genital herpes (herpes simplex virus) may still use the ring.

Non-Contraceptive Benefits

Although the non-contraceptive benefits of the ring are likely similar to those seen with the COC, there are few studies specifically for the ring. One randomized controlled trial found that the ring was associated with a reduction in menstrual blood loss and an improvement in duration of menses and in hemoglobin and ferritin levels after 3 cycles of treatment.[316] Other studies have reported a reduction in dysmenorrhea,[317−322] premenstrual syndrome,[319,320,322] menstrual headaches and migraines,[322,323] hirsutism and hyperandrogenemia,[324] and endometriotic nodule volume.[325]

Side Effects

The ring has similar side effects as the COC, with the exception of more vaginal symptoms (e.g., vaginitis, leukorrhea, and ring-related problems).[134,310,311,326] Ring use reportedly is associated with less nausea, acne, and emotional lability than the COC.[251] The most frequently reported side effects with the ring are headache (5.8%), vaginitis (5.6%), and leukorrhea (4.8%).[308] Other hormonal side effects include nausea (3.2%) and breast tenderness (2.6%).[308] Non-comparative studies and studies comparing the ring with the COC have found that the ring is not associated with clinically significant weight gain.[307,308,317,318,320,327,328]

Unscheduled bleeding

Withdrawal bleeding occurs in 98.5% of cycles, starts within a median time of 3 days after ring removal, has a mean duration of 4.5 to 5.2 days, and continues into the next cycle in 24% of cycles.[307,308] Early bleeding (i.e., bleeding starting just before the ring-free period) occurs in 6% of cycles,[308] and unscheduled bleeding, mostly spotting, occurs in up to 6% of cycles.[308,329] Unscheduled bleeding does not appear to be significantly higher in first cycles of use compared with later cycles.[307,308] In randomized trials, the ring was associated with less unscheduled bleeding than the COC[251,320,326,327,330] and significantly shorter duration of menstrual bleeding than the patch.[331]

Summary Statement

18. The vaginal contraceptive ring is associated with less unscheduled bleeding than the combined oral contraceptive pill and the duration of menstrual bleeding is significantly shorter than that seen with the contraceptive patch (I).

Vaginal symptoms

The most common local side effects with ring use are vaginitis (1.8% to 5.6%) and leukorrhea (5%).[307,308,310,311,326,327,329] *Candida* was specified as the cause of vaginitis in only one study.[310] These side effects usually do not lead to discontinuation.[308] There are no major changes in the vaginal

ecosystem with the use of the ring,[332–334] although an in vitro study showed that *Candida* yeasts adhere to the ring surface.[335] Compared with the COC, the ring is reportedly associated with more vaginal wetness and less dryness.[134,332]

One study found that 85% of women rarely or never felt the ring and 71% of their partners rarely or never felt the ring; 94% of partners did not object to use of the ring.[336] Although women or their partners may be aware of the device, only 2.5% of ring users discontinued the ring due to foreign body sensation, coital problems, or expulsion in clinical studies.[308] Ring expulsion may occur spontaneously, although the reported expulsion rates vary. In one study, 20.4% of women reported that the ring was expelled at least once during any 3-week period.[331] Another study found that the ring slipped in 9% of women at least once a week, whereas in 72% of women it never slipped.[332]

Sexual effects

Some studies have shown an improvement in sexual function in ring users, including an increase in sexual desire, fantasy, and satisfaction.[134,337–339] One of the studies reported that overall sexual desire was either unchanged or increased in 91.4% of ring users.[337] Conversely, other studies have found more sexual dysfunction (feeling the ring during intercourse, negative partner reaction) with the ring compared with the patch[340] and a reduction in sexual function scores.[341]

Risks

Cardiovascular risk

All CHC methods are associated with an increased risk of VTE. Two retrospective database studies found that ring users had an increased risk of VTE compared with women using COCs containing LNG (RR 1.9, 95% CI 1.33 to 2.71)[342] and an increased risk of thrombotic stroke compared with non-use of hormonal contraception (RR 2.49, 95% CI 1.41–4.41); [296] but no increased risk of MI (RR 2.08, 95% CI 0.67–6.48).[296] Conversely, another retrospective database study found that new users of the ring did not have an increased risk of VTE or arterial thromboembolism compared with older generation COCs.[153] A large international, prospective cohort, active surveillance study of 33 295 new users of the ring or COC was conducted to compare the cardiovascular risks of the 2 methods.[343] In that study, there was no significant difference in the incidence of VTE between ring users and COC users (8.3/10 000 vs. 9.2/10 000 WY; HR_{adj} 0.8, 95% CI 0.5–1.5) and no difference in the incidence of arterial thromboembolism (HR_{adj} 0.7, 95% CI 0.2–2.3). When discussing the cardiovascular risk of CHC, including the vaginal ring, one should consider the quality of studies, level of evidence, and potential confounders and biases.

The majority of studies have shown that the ring is not associated with significant changes in blood pressure.[307,308,310,311,317,318,321,327]

Metabolic effects

The ring is associated with minimal changes in carbohydrate metabolism.[344–348] Studies examining the effect of the ring on lipid metabolism have found minimal effects[321,348,349] or changes similar to those seen with the COC.[347,350] There is minimal effect on adrenal or thyroid function.[344]

The ring appears to have a minimal effect on hemostatic variables.[326,351] Some studies have shown that the ring is associated with a greater increase in SHBG (a surrogate marker for thrombosis) than the COC,[348,349,352] whereas others have not.[353] Although one study found that switching from the COC to the ring was beneficial for thrombosis biomarkers (no change in SHBG, increase in protein S, no change in activated Protein C resistance [APC-r]) compared with the patch,[354] another study found that both the patch and ring had greater activated protein C resistance than the COC.[352]

Cervical effects

The ring has not been associated with major changes in cervical cytology.[308] In one study, only a minority of women had changes in their cytology results, with 1.3% changing from normal to a low-grade squamous intraepithelial lesion and 0.4% from normal to a high-grade squamous intraepithelial lesion.[308]

Myths and Misconceptions

1. The vaginal contraceptive ring is less effective in obese women.

   Fact: There is limited evidence regarding the effect of weight on the efficacy of the ring. However, 2 PK studies compared hormone levels and ovarian suppression during a 28-day cycle and an extended 6-week regimen of the ring in obese (up to a BMI of 39.9) and normal-weight women. In both groups, ovarian follicular development was suppressed and no ovulation occurred.[355,356] This would support the ring's effectiveness in obese women. A prospective cohort study did not show an increased risk of contraceptive failure in overweight and obese women using the ring.[26]

2. A women's partner will feel the ring during intercourse and object to its use.

   Fact: In a randomized controlled study comparing the effect of the ring and the COC on sexual function, 89% of women and 69% of partners never felt the ring during

vaginal intercourse.[337,357] In clinical studies, even if some partners felt the ring during intercourse, the majority of them (more than 80%) did not object to use of the ring.[307,308] The ring does not need to be removed during intercourse, although some women may choose to do so. If it is removed, it should be reinserted within 3 hours.

3. A woman who uses the vaginal ring cannot use tampons.

   Fact: Women who use a ring can use tampons. Studies have shown no evidence of interactions between the ring and tampons, spermicides, or antimycotics.[358–360]

Initiation

How to start and use the ring

The vaginal contraceptive ring is approved for 3 weeks of continuous use and then is to be removed for 1 ring-free week, although the product monograph states that there is contraceptive protection for an additional week of ring use (28 days total).[304] Withdrawal bleeding usually occurs during the ring-free interval. The ring-free interval should not exceed 7 days. Once a medical history has ruled out any contraindications to its use, the only examination required prior to initiating the ring is a blood pressure measurement.[211] An initial weight and BMI may be helpful for follow-up. The ring is "one size fits all" and does not need to be fitted.

Although the product monograph states that the ring should be inserted on the first day of menstrual bleeding,[304] the ring can in fact be inserted at any time in the menstrual cycle (Quick Start) provided that it is reasonably certain that a woman is not pregnant.[211] If the ring is inserted on the first day of menses, no back-up method of contraception is required. If the ring is initiated at any other time of the menstrual cycle, back-up contraception (i.e., condoms) or abstinence should be used for the first 7 consecutive days of ring use. Use of the Quick Start method of CHC is associated with greater compliance at 3 months and no increase in unscheduled bleeding compared with conventional starts.[220,221,361] Quick Start with the ring is associated with high satisfaction and greater likelihood of continuation.[362]

Some women may choose to insert the ring on the first day of the month and remove it on the 28th day of each month, thereby decreasing the HFI to 1 to 4 days per month (off-label use).

Switching from another method

Women may switch from one method to another during the first 5 days of their menses. However, they do not have to wait until their next menses to do so. Table 3 shows how a woman can switch from one contraceptive method to another. These instructions are conservative and may ensure effectiveness of both the initial and the new method. If a woman wishes to switch from an IUC to the vaginal ring, it is suggested that she start the vaginal ring 7 days before the IUC is removed. This is due to the theoretical concern of residual sperm being present in the genital tract and possible fertilization if ovulation occurs.

If a woman wishes to switch from the IUC to the ring but has had UPI within the previous 5 days, the risk of having an unplanned pregnancy is increased if the IUC is removed. Switching options for the ring are similar to those for the COC or the patch (Table 3).

C/E use of the vaginal ring

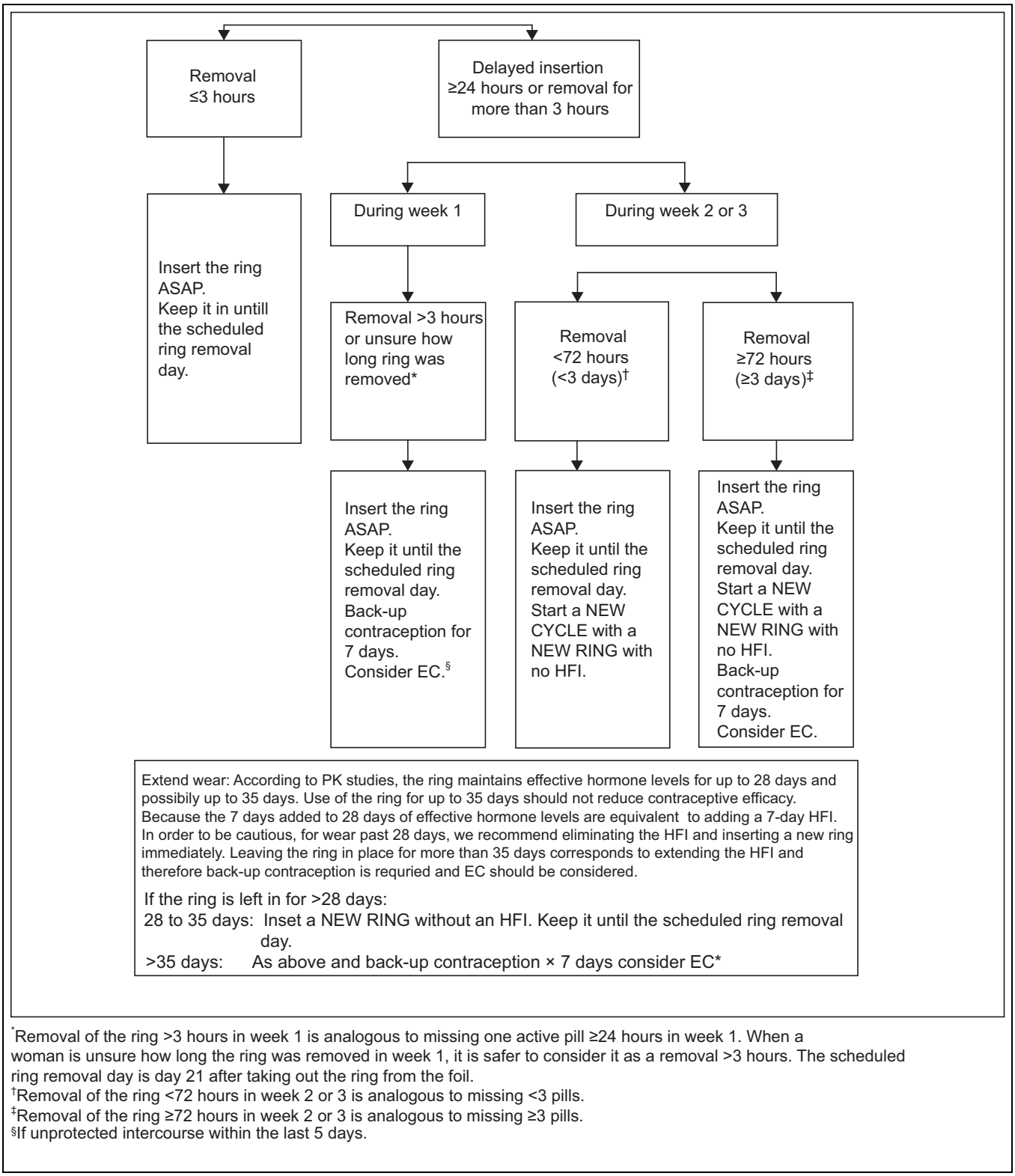
As with the COC and the patch, the ring can be used in a C/E regimen or with a shortened HFI. The ring may be removed and a new one inserted immediately every 21 to 28 days. There is no limit to the number of times a woman may do this, and some woman may choose to suppress their cycles/menstruation in this fashion indefinitely.

An RCT comparing 3 extended ring regimens (49-day, 91-day, and 364-day cycles) with the conventional 28-day cycle found less unscheduled bleeding with the 28-day cycle.[363] Satisfaction was higher for the shorter cycles (28-day and 49-day cycles), and more women discontinued in the 91-day and 364-day cycle groups.[363] A prospective study of the ring in an 84-day cycle found that 86% had adequate menstrual patterns at 1 year.[364] Only 4% discontinued the ring because of irregular bleeding.

Troubleshooting

1. **The ring interferes with intercourse**
   Ring removal during intercourse is not recommended. However, if the ring bothers a woman or her partner during intercourse, she may remove it and then reinsert it after intercourse. The ring should not be left out of the vagina for more than 3 hours and should be reinserted as soon as possible. Before reinserting, it should be rinsed in lukewarm water.
2. **Missed ring**
   Vaginal ring expulsion and delayed removal and/or insertion are considered as missed or incorrect use. Advice will depend on whether the ring was expelled, how many hours the ring has been out of the vagina, the timing in the cycle, and whether UPI has occurred (Figure 3). The HFI should never exceed 7 days, and a delay in inserting the ring in week 1 has the effect of lengthening the HFI and increasing the risk of ovulation and unintended pregnancy.[242] As with other CHC

Figure 3. Missed contraceptive ring.



*Removal of the ring >3 hours in week 1 is analogous to missing one active pill ≥24 hours in week 1. When a woman is unsure how long the ring was removed in week 1, it is safer to consider it as a removal >3 hours. The scheduled ring removal day is day 21 after taking out the ring from the foil.
†Removal of the ring <72 hours in week 2 or 3 is analogous to missing <3 pills.
‡Removal of the ring ≥72 hours in week 2 or 3 is analogous to missing ≥3 pills.
§If unprotected intercourse within the last 5 days.

methods, ovulation is effectively inhibited after 7 consecutive days of ring use.

If the ring is out of the vagina for less than 3 hours, it should be reinserted as soon as possible. It should remain in the vagina until the next scheduled ring removal day. No back-up contraception is required. In week 1, if ring insertion was delayed by more than 24

hours or the ring was out of the vagina for more than 3 hours, the ring should be inserted as soon as possible and back-up contraception or abstinence should be used until the ring has been in place for 7 consecutive days. If UPI occurred within the previous 5 days, EC should be considered (Figure 3).

In week 2 or 3, if the ring was out of the vagina for less than 3 days (72 hours), the ring should be inserted as soon as possible and left in the vagina until the next scheduled ring removal day. On the scheduled ring removal day, a new cycle should be started by inserting a new ring immediately and eliminating the HFI.

If during week 2 or 3 the ring was out of the vagina for more than 72 hours, the ring should be reinserted and left in the vagina until the next scheduled ring removal day. On the scheduled ring removal day, the woman would remove the ring, skip the HFI, and insert a new ring. Back-up contraception or abstinence should be used for the first 7 days of consecutive ring use and EC should be considered if UPI occurred in the previous 5 days or during the first 7 consecutive days of ring use.

3. **Delayed ring removal**

Ovulation inhibitory levels of hormones are maintained with extended wear of the ring up to 28 days.[305] If the ring is left in for more than 28 days but less than 35 days, the old ring should be removed and a new ring should be inserted immediately, with no HFI.

If the ring was left in for more than 35 days, the old ring should be removed and a new ring inserted immediately. In addition, back-up contraception or abstinence should be used for 7 days and EC should be considered if UPI occurred within the previous 5 days or during the first 7 days of new ring use.

Summary Statement

19. Serum levels of ethinyl estradiol and etonorgestrel are maintained at ovulation inhibitory levels for at least 28 days after the vaginal contraceptive ring has been inserted (II-2).

Drug Interactions

There does not appear to be an interaction between the ring and antimycotics (miconazole), amoxicillin, doxycycline, spermicides, or tampons.[358–360,365] There are limited data on other specific drug interactions with the ring. Although the ring does bypass the first-pass metabolism, medications that are CYP-enzyme enhancers (e.g., some AEDs) may affect hormone levels and thus affect the ring's effectiveness. Similarly, the ring and other CHC may affect levels of other medications. Until there is additional data specifically for the ring, the same potential drug interactions as for the COC should be assumed (Table 4).

CONTINUOUS OR EXTENDED USE OF CHC

Continuous use of COCs was first studied in 1977 using 50 μg EE pills.[366] Since that time, low-dose COCs, the transdermal contraceptive patch, and the vaginal contraceptive ring have all been used and studied in a C/E fashion.[367] CHC used in a C/E fashion may have advantages, including decreased incidence of pelvic pain, headaches, bloating/swelling, and breast tenderness for women who experience these symptoms during the pill-free interval[367,368]; improved control of endometriosis symptoms[369–372] and polycystic ovarian syndrome[373]; and greater convenience due to fewer withdrawal bleeds per year. Disadvantages include little information on long-term safety (although there are long-term data for comparable total estrogen-progestin doses per month[367,374]), possible delay in the recognition of pregnancy, unscheduled bleeding and spotting,[363,367,375,376] and a slightly higher cost for medications (an extra 3 pill packages per year for a 91-day cycle). Potential disadvantages must be weighed against the likely reduction in the cost of sanitary supplies, pain medication, and time off work or school.[367] Pregnancy rates may be significantly lower with extended 84/7 regimens.[32]

Attitudes Towards C/E CHC Regimens

Surveys have found that women have favorable views on C/E use of CHCs.[367,377–381] In a national survey in Spain, 24.5% of women aged 18 to 45 were interested in C/E COC regimens, and this percentage increased to nearly 50% in women under 25.[379] A convenience sample of 1111 Brazilian women reported that 64.3% disliked menstruation and 86.1% would use COCs to induce amenorrhea.[380] A Dutch national sample found that 73% of COC users had at one point skipped pill-free intervals and 38% did so regularly, even if it was not actively promoted.[381] In a recent study among college and university students in Quebec, 25.7% of CHC users were taking them in a C/E fashion.[382] In a survey of 1700 female students at the University of Oregon, 17% of COC users delayed or skipped their scheduled bleeding for convenience or personal choice; 47% of them had learned about C/E regimens from health care professionals, whereas 30% learned from family or friends.[383]

Health professionals have adjusted their prescribing patterns for CHC.[367] Eighty percent of Brazilian

gynaecologists said they prescribed extended COC regimens to induce amenorrhea,[384] and 97% of female gynaecologists in Germany and Austria prescribed extended regimens, mostly for medical reasons (cycle-related headaches or complaints, dysmenorrhea, and hypermenorrhea).[385] In the United States, 92% of 799 health care professionals attending continuing medical education conferences have recommended extended regimens, mostly an 84/7 regimen (84 days of active pills followed by a 7-day HFI).[386]

Clinical Outcomes and Continuation Rates with C/E CHC Regimens

Clinical outcomes of C/E regimens for a variety of CHCs have been compared with cyclic regimens in several RCTs. Most extended regimens were multiples of the conventional "21 days" (e.g., 42, 63, 84, 168 days), followed by a conventional 7-day HFI.[300,363,375,376,387–392] More recent studies[393–396] have focused on flexible or tailored regimens in which active COC tablets are taken for a minimum of 21 or 24 days until either bleeding/spotting occurs for a certain number of days (3 to 7 days) or until a certain limit of days (e.g., 120 days) followed by a 3- or 4-day HFI.

In these RCTs, study discontinuation rates ranged from 7% to 42% for C/E CHC regimens and from 6% to 45% for cyclic regimens.[300,363,375,376,387–396] In all but 3 of the RCTs,[363,376,391] there was no overall difference in study discontinuation rates in the C/E group compared with the cyclic group.[397] In 6 of the 14 RCTs, there were more discontinuations due to bleeding problems in the C/E cycle arms.[363,375,376,391,392,395] In 6 studies in which treatment adherence was defined and measured, there was no significant difference in unscheduled bleeding between C/E and cyclic regimens.[300,363,376,387,389,397]

Most prospective studies have not demonstrated a significant difference in the risk of pregnancy between regimens,[300,363,375,376,387–396] except one trial in which COC regimens were used intravaginally. In that trial, women in the C/E regimen group had fewer pregnancies.[247] However, a recent retrospective study of American pharmacy claims found that 1-year pregnancy rates were significantly lower with 84/7 regimens than with 21/7 (4.4% vs. 7.3%; $P < 0.0001$) and 24/4 (4.4% vs. 6.9%; $P < 0.0001$) regimens.[32]

Bleeding and Other Events with C/E CHC Regimens

Most RCTs have demonstrated either no difference in bleeding or less bleeding/spotting with C/E regimens compared with traditional cyclic regimens.[397] Adding low-dose estrogen (e.g., 10 μg EE daily for 7 days), to the HFI of an extended regimen may improve the bleeding profile.[398] An RCT comparing 3 extended ring regimens (49-day, 91-day, and 364-day cycles) to the conventional 28-day ring cycle found less unscheduled bleeding with the 28-day cycle.[363] Satisfaction was higher for the shorter cycles (28-day and 49-day cycles), and more women discontinued in the 91-day and 364-day cycle groups.[363] In several RCTs reporting data on menstruation-associated symptoms,[363,375,376,387,390,392,395,396] the C/E arms showed benefit on headache frequency,[375,387,392,396] genital irritation,[387] tiredness,[387] bloating,[376] breast tenderness,[391,396] menstrual pain,[376,390,392] behavioural change,[390] nausea,[391,392] and acne.[392] Except for one study, in which the weight gain was significantly lower in the C/E regimen group,[247] most RCTs reported no significant differences regarding weight between C/E and cyclic regimens.[375,376,387,389–391,395] Investigations concerning the effects of C/E regimens on blood pressure and lipid or carbohydrate metabolism revealed no differences compared with the conventional regimen or according to the route of administration.[346,399] Assessment of the endometrium using ultrasound and/or endometrial biopsy in 4 RCTs revealed no significant differences in endometrial thickness or tissue histology between groups.[363,388–390,397]

Two RCTs[400,401] and 1 cohort study[402] compared various C/E regimens and different routes of administration. In the first RCT, 120 women were randomly assigned to a 42/7 regimen of either drospirenone/EE30 COC, the contraceptive norelgestromin/EE patch, or the ENG/EE vaginal ring for 1 year.[401] Compared with baseline, all groups experienced fewer bleeding days and less mastalgia and menstrual pain. Although there was an increase in spotting days with all 3 methods, it decreased with each successive cycle, and satisfaction was high with all 3 methods, especially with the patch. In the second RCT, 172 women were randomly assigned to continuous use of the vaginal contraceptive ring or a 20 μg COC (LNG/EE) over 12 months on a flexible regimen that required women to remove the ring or stop their pill if a bleeding/spotting episode persisted beyond 4 days and to restart after a 4-day interval.[400] There was a significant reduction in the mean number of bleeding/spotting days from the first 3-month reference period of the study (ring 14.2 $\pm$ 10; COC 16.6 $\pm$ 10.9) to the fourth reference period (ring 8.8 $\pm$ 9.6; COC 8.8 $\pm$ 9.1). Amenorrhea or infrequent bleeding was experienced by 15% of ring users versus 4% of COC users. If bleeding occurred, a 4-day HFI usually led to a cessation of the bleeding episode. In a cohort study involving 150 women, half of the women used the vaginal ring and the other half used a 30 μg desogestrel-containing COC in a

84/7 regimen for 1 year.[402] The total number of scheduled bleeding and spotting days decreased significantly during the year for both methods but more so for COC users. Unscheduled bleeding and spotting also decreased significantly with both methods with time, more so for ring users ($P = 0.003$).

Initiation and Counselling for a C/E CHC Regimen

When initiating C/E CHC, the overall concept should be explained and differences between C/E and cyclic regimens discussed. Provided there are no contraindications to CHC use, a woman can decide with her health care provider which CHC to use in a C/E fashion and when to have an HFI, if at all. It is important to discuss possible side effects, including unscheduled bleeding and/or spotting and how to manage them. C/E CHC may be started at any time in the cycle, provided pregnancy can be excluded. If using the Quick Start method, back-up contraception should be used for the first 7 days of use. A minimum of 21 consecutive days of hormonal CHC should be taken before having an HFI. At no time should the HFI exceed 7 days.

Follow-up and troubleshooting are comparable for C/E and for cyclic CHCs. If unscheduled bleeding or spotting occurs after a woman has taken at least 21 consecutive days of active pills, she can either continue to use the contraceptive method or take a 3- to 4-day HFI and then restart her CHC.[211,403] A systematic review found that taking a short HFI when unscheduled bleeding occurs during C/E CHC use may reduce unscheduled bleeding days compared with women who continued using their method without an HFI.[240] An HFI is not recommended more than once per month. If a woman is concerned about the possibility of pregnancy and presents with pregnancy symptoms, a pregnancy test should be performed. If unscheduled bleeding persists, incorrect usage, pregnancy, STI, gynecological pathology, or systemic illness should be ruled out.

Missed Hormonal Contraception in Women Using CHC in a C/E Regimen

The following recommendations apply to women using a C/E CHC regimen who have had UPI either in the 3 days before they missed their contraception or during the time of missed contraception:

- If omission occurs within the first week of C/E CHC use, apply the rules related to omission of CHC (COC, patch, or ring) in the first week of cyclic use.
- If omission occurs in any week after the first week of C/E CHC use, apply the rules related to omission in the second or third week for cyclic use of CHC (Figures 1–3).
- If CHC is not taken for at least 7 consecutive days, it is equivalent to extending the HFI. If UPI has occurred, EC should be taken as soon as possible (preferably LNG-EC if CHC is to be restarted due to concerns about potential drug interaction between UPA and CHC). CHC can be restarted in a C/E regimen the same day or the day after LNG-EC is taken. A barrier contraceptive method or abstinence should be used for the first 7 days of CHC use. If EC is indicated and UPA-EC is used rather than LNG-EC, the woman should wait 5 days before restarting her CHC and use a barrier contraceptive method or abstain from intercourse for the first 5 days after taking UPA-EC and for the first 7 days after starting CHC (i.e., if a woman uses UPA-EC and restarts CHC, back-up contraception and/or abstinence is required for a total of 12 days after UPA-EC ingestion).
- If CHC is missed for $\leq$7 consecutive days, she is safe provided that she has been taking CHC for at least 21 consecutive days prior to missing her doses.
- If the C/E CHC is omitted for $\leq$7 consecutive days, any new omission within the next 21 days must follow the rules related to omission for cyclic use.

Summary Statements

20. Continuous or extended regimens of combined hormonal contraception (CHC) have similar rates of adherence and effectiveness compared with 28-day cyclic CHC regimens (I).
21. Continuous and/or extended regimens of combined hormonal contraception (CHC) are associated with significantly less menstruation-associated symptoms than are cyclic CHC (I). Bleeding and/or spotting with C/E CHC regimens decreases with each successive cycle and is similar to or less than that with cyclic CHC (I).

Recommendations

7. Health care professionals should be aware of the option of using continuous or extended combined hormonal contraception regimens and consider offering them to women for contraception, medical reasons, and personal preferences (III-A).
8. Women using continuous or extended combined hormonal contraception regimens should be counselled about expected bleeding patterns and how to manage unscheduled bleeding or spotting (III-A).

GENERIC HORMONAL CONTRACEPTION FORMULATIONS

In Canada, several generic versions of COCs, POPs, injectable progestins, and LNG EC have been approved by Health Canada. These generic formulations have the potential to increase women's access to contraception by lowering the cost. Generic products must contain the same active ingredients in the same doses as the original brand name product and they must demonstrate bioequivalence.[404] Generic versions are deemed to be bioequivalent if the 90% confidence interval of the mean rate and extent of absorption is within 80% to 125% of the brand name product.[405] In addition, generic formulation manufacturing processes and facilities must meet Health Canada standards for Good Manufacturing Practices.[406] Generic products are not required to, and have not had, the safety, side effect, and efficacy trials that have been done for the original branded products. There is no evidence that generic oral contraceptive pills are either equally or less effective or safe compared with their brand name equivalents.

Recommendation

9. When a specific product has been prescribed to a woman, she should be informed if a generic substitution is being considered and her health care provider should be advised if a substitution is made. The woman should have the option to agree or disagree to the substitution and be informed about any difference in cost for a specific product (III-B).

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APPENDIX

Appendix A. Composition of Hormonal Contraceptives[4]

Type	Product name	Estrogen dose per tablet (μg)	Progestin dose per tablet (μg)	Regimen
Combination monophasic pills, patches, and rings				
EE/LNG	Alesse 21	20	100	21/7
	Alesse 28	20	100	21/7
	Alysena 21*	20	100	21/7
	Alysena 28*	20	100	21/7
	Aviane 21*	20	100	21/7
	Aviane 28*	20	100	21/7
	Esme 21*	20	100	21/7
	Esme 28*	20	100	21/7
	Lutera 21*	20	100	21/7
	Lutera 28*	20	100	21/7
	Min-Ovral 21	30	150	21/7
	Min-Ovral 28	30	150	21/7
	Ovima 21*	30	150	21/7
	Ovima 28*	30	150	21/7
	Portia 21*	30	150	21/7
	Portia 28*	30	150	21/7
EE/desogestrel	Marvelon 21	30	150	21/7
	Marvelon 28	30	150	21/7
	Apri 21*	30	150	21/7
	Apri 28*	30	150	21/7
	Freya 21*	30	150	21/7
	Freya 28*	30	150	21/7
	Mirvala 21*	30	150	21/7
	Mirvala 28*	30	150	21/7
	Reclipsen 21*	30	150	21/7
	Reclipsen 28*	30	150	21/7
EE/norethindrone	Minastrin 1/20, 21 day	20	1000	21/7
	Minastrin 1/20, 28 day	20	1000	21/7
	Lo Loestrin 1.5/30, 21 day	30	1500	21/7
	Lo Loestrin 1.5/30, 28 day	30	1500	21/7
	Brevicon 0.5/35, 21 day	35	500	21/7
	Brevicon 0.5/35, 28 day	35	500	21/7
	Brevicon 1/35, 21 day	35	1000	21/7
	Brevicon 1/35, 28 day	35	1000	21/7
	Ortho 0.5/35, 21 day	35	500	21/7
	Ortho 0.5/35, 28 day	35	500	21/7
	Ortho 1/35, 21 day	35	1000	21/7
	Ortho 1/35, 28 day	35	1000	21/7
	Select 1/35, 21 day	35	1000	21/7
	Select 1/35, 28 day	35	1000	21/7
EE/norgestimate	Cyclen 21	35	250	21/7
	Cyclen 28	35	250	21/7
	Previfem 21*,†	35	250	21/7
	Previfem 28*,†	35	250	21/7
	Sarensis 21*,†	35	250	21/7
	Sarensis 28*,†	35	250	21/7
EE/norethindrone acetate	Lolo	10 × 24 days 10 × 2 days	1000 × 24 days	24/2/2
EE/ethynodiol diacetate	Demulen 30, 21 day	30	2000	21/7
	Demulen 30, 28 day	30	2000	

Continued

Appendix A. Continued

Type	Product name	Estrogen dose per tablet (μg)	Progestin dose per tablet (μg)	Regimen
EE/drospirenone	Yaz	20	3000	24/4
	Yaz Plus‡	20	3000	24/4
	Mya*	20	3000	24/4
	Nikki*,†	20	3000	24/4
	Yasmin 21	30	3000	21/7
	Yasmin 28	30	3000	21/7
	Yasmin Plus†,‡	30	3000	21/7
	Drospirenone and EE 21*,†,§	30	3000	21/7
	Drospirenone and EE 28*,†,§	30	3000	21/7
	Qismette 21*,†	30	3000	21/7
	Qismette 28*,†	30	3000	21/7
	Zarah 21*	30	3000	21/7
	Zarah 28*	30	3000	21/7
	Zamine 21*	30	3000	21/7
	Zamine 28*	30	3000	21/7
EE/norelgestromin (NGM)	Evra transdermal patch	600 (releases 35 μg EE/day)	6000 (releases 200 μg Norelgestromin/day)	21/7
EE/ENG	NuvaRing vaginal ring	2600 (15 μg/day)	11 400 (120 μg/day)	21/7
EE/cyproterone acetate	Diane 35§	35	2	21/7
	CLÉO-35*,§	35	2	21/7
	Cyestra-35§	35	2	21/7
	Novo-Cyproterone/EE*,§	35	2	21/7
	Ran-cyproterone/EE*,§	35	2	21/7
Estradiol (E2)/ nomegestrol acetate	Zoely¶	1500	2500	24/4
Combination biphasic pills				
EE/norethindrone	Synphasic 21	35	500/1000	21/7
	Synphasic 28	35	500/1000	21/7
Combination triphasic pills				
EE/desogestrel	Linessa 21	25	100/125/150	21/7
	Linessa 28	25	100/125/150	21/7
EE/norethindrone	Ortho 7/7/7/ 21 day	35	500/750/1000	21/7
	Ortho 7/7/7/ 28 day	35	500/750/1000	21/7
EE/norgestimate	Tri-Cyclen 21 day	35	180/215/250	21/7
	Tri-Cyclen 28 day	35	180/215/250	21/7
	Centrisa 21*,†	35	180/215/250	21/7
	Centrisa 28*,†	35	180/215/250	21/7
	Tri-Lena 21*,†	35	180/215/250	21/7
	Tri-Lena 28*,†	35	180/215/250	21/7
	Tri-Previfem 21*,†	35	180/215/250	21/7
	Tri-Previfem 28*,†	35	180/215/250	21/7
	Tri-Cyclen Lo 21 day	25	180/215/250	21/7
	Tri-Cyclen Lo 28 day	25	180/215/250	21/7
	Centrisa Lo 21*,†	25	180/215/250	21/7
	Centrisa Lo 28*,†	25	180/215/250	21/7
	Tricira Lo 21*	25	180/215/250	21/7
	Tricira Lo 28*	25	180/215/250	21/7
EE/LNG	Triquilar 21	30/30/40	215/50/75	21/7
	Triquilar 28	30/30/40	215/50/75	21/7
Combination multiphasic pills				
E2V/dienogest	Natazia†	3 mg × 2/2 mg × 5/2 mg × 17/1 mg × 2	2 mg × 5/3 mg × 17 × 2	26/2
Combination extended regimen pills				
EE/LNG	Seasonale	30	150	84/7
	Indayo*,†	30	150	84/7
EE/LNG	Seasonique	30 × 84 days 10 × 7 days	150	84/7

Continued

Appendix A. Continued

Type	Product name	Estrogen dose per tablet (μg)	Progestin dose per tablet (μg)	Regimen
Progestin-only contraception: pills, injectables, intrauterine systems, implants				
LNG	Jaydess (intrauterine system)		Releases average of 6 μg/day (contains 13.5 mg LNG)	Approved for up to 3 years of use
	Mirena (intrauterine system)		Releases up to 20 μg/day (contains 52 mg LNG)	Approved for up to 5 years of use
	Kyleena (intrauterine system)		Releases up to 17.5 mcg/day (contains 19.5 mg LNG)	Approved for up to 5 years of use
Norethindrone	Micronor (mini-pill)		350	28
	Jencycla*		350	28
	Movisse*		350	28
Medroxyprogesterone acetate	Depo-Provera injection		150 mg/mL	91
	Medroxyprogesterone acetate injectable suspension USP		150 mg/mL	91
ENG	Implanon NXT/Nexplanon¶		68 mg (releases up to 70 μg/day initially then gradually decreases to ≈30 μg/day at end of third year)	Up to 3 years of use
EC				
LNG	Plan B		750	
	Plan B		1500	
	BackUp Plan*,†		750	
	BackUp Plan Onestep 1.5 mg*,†		1500	
	Contingency 0.75 mg*,†		750	
	Contingency One 1.5 mg*,†		1500	
	Next Choice*		750	
	Norlevo*		750	
	Norlevo*,†		1500	
	Option 2*		750	
Ulipristal acetate	Ella		30 mg‖	

*Generic.

†Approved by Health Canada, not yet marketed.

‡Contains 0.451 mg levomefolate calcium/tablet.

§Approved in Canada for the treatment for moderate to severe acne, not for contraception.

¶Not currently approved in Canada.

‖Selective progesterone modulator.

Appendix B. CHC Myths and Facts

Myth		Fact
1	COC users should take periodic "pill breaks"	Periodic pill breaks are unnecessary. Stopping and restarting COCs may put a woman at increased risk of unintended pregnancy, cycle irregularity, and VTE.[146,153,192,193]
2	The COC has a negative effect on future fertility	Fertility is quickly restored (usually within 1 to 3 months) to a woman's baseline fertility once the COC is discontinued.[192,194–196]
3	The COC causes birth defects	There is no evidence that COCs cause birth defects if they are taken inadvertently during pregnancy.[199,200]
4	The COC must be stopped in all women over 35	Healthy, non-smoking women may continue to use the COC provided they have no contraindications or other medical conditions that may significantly elevate the absolute risk of an adverse event.[60,142,201–203]
5	The COC causes acne	Acne improves in most women using the COC due to a decrease in circulating free androgens.[63,205,206]
6	The COC causes cancer	COC use protects against ovarian and uterine cancer.[68–72,74–77,180] COCs may also have a protective effect against colorectal cancer.[71,72,88] The risk of cervical cancer may be increased in COC users compared with non-users.[180,188–190]
7	The COC causes weight gain	Placebo-controlled trials have failed to show any association between COCs and weight gain.[122,123]
8	The patch will not stay on during exercise; in hot, humid weather; while swimming; or while in the shower	The patch has excellent adhesive properties under a wide range of conditions and climates.[297] Patch detachment is rare.[251]
9	Because of the transdermal delivery system, the patch will have less effect on the lipid profile than the COC	A slight increase in serum total cholesterol and triglyceride levels is seen in users of both the patch and the COC.[231,289] These changes are within normal limits and consistent with the lipid effects of a COC.[298]
10	Because the patch is a hormonal method of contraception, women who use the patch will gain weight	There does not appear to be an association between the contraceptive patch and weight gain compared with placebo.[122] In a pooled analysis of patch users, 78.5% of women remained within 5% of their baseline weight while using the contraceptive patch.[289]
11	The vaginal contraceptive ring is less effective in obese women	A prospective cohort study did not show an increased risk of contraceptive failure in overweight and obese women using the ring.[26]
12	A women's partner will feel the ring during intercourse and object to its use	Most women (89%) and men (69%) do not feel the ring during vaginal intercourse.[337,357] Even if some partners feel the ring during intercourse, the majority do not object to its use.[307,308]
13	A woman who uses the ring cannot use tampons	Women who use a ring can use tampons. Studies have shown no evidence of interactions between the ring and tampons, spermicides, or antimycotics.[358–360]

Appendix C.

ALGORITHM : MISSED COMBINED HORMONAL CONTRACEPTIVES
Combined oral contraceptives (COC), patch, ring

Key points :
- The hormone-free interval (HFI) should not exceed 7 days.
- Ovulation is effectively inhibited after 7 days of consecutive use of combined hormonal contraceptives.
- A missed dose is defined as either taking of initiating the combined hormonal contraceptive 24 hours or more after the scheduled time.
- Patch : detachment or delayed removal or application are considered as missed or incorrect use of the patch.
- Ring : expulsion or delayed removal or insertion of the ring are considered as missed or incorrect use of the ring.
- The 1st week of use is crucial.
- Missing doses for more than one day means missing doses for several consecutive days.
- When unsure how long the method was missed or non consecutive missing doses opt for the safest approach.
- Emergency contraception is rarely useful during 2nd and 3rd week unless omission is repeated or prolonged.

During which week did the missing occurred?

Week 1

COC delayed < 24 h
Patch < 24 h
Ring ≤ 3 h

AS SOON AS POSSIBLE (ASAP) :
- COC : take 1 active pill ASAP and continue taking one pill daily until the end of the pack.
- Patch : reapply or replace with a NEW patch ASAP. Keep the same patch change day. Make a cycle of 3 patches.
- Ring : insert the ring ASAP and keep it until the scheduled ring removal day.

COC ≥ 1 pill
Patch ≥ 24 h
Anneau > 3 h

1) Same as for COC < 24 h and for Ring ≤ 3 h.
2) Patch: Apply a NEW patch ASAP. Keep the same patch change day. Make a cycle of 3 patches.

AND

1) Back-up contraception x 7 days.
2) Consider Emergency contraception (EC) *.

Week 2 or 3

COC < 24 h
Patch < 24 h
Ring ≤ 3 h

AS SOON AS POSSIBLE :
- COC : take 1 active pill ASAP and continue taking one pill daily until the end of the pack. Discard any placebo pills. Start a new cycle of COC without a HFI.
- Patch : apply a NEW patch ASAP. Keep the same patch change day. Finish the cycle of patches and start a new cycle of 3 patches with no HFI.
- Ring : insert the ring ASAP and keep it until the scheduled ring removal day. Start a new cycle with a new ring with no HFI.

COC ≥ 1 pill and < 3 pills
Patch ≥ 24 h and < 3 days
Ring > 3 h and < 3 days

COC ≥ 3 pills
Patch ≥ 3 days
Ring ≥ 3 days

1) Same as for COC ≥ 1 and < 3 pills, Patch ≥ 24 h and < 3 days and Ring > 3 h and < 3 days. No HFI for the three methods.

AND

1) Back-up contraception x 7 days.
2) Consider EC **.

* If unprotected intercourse within the last 5 days
** If repeated or prolonged omission

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Source : Institut national de santé publique du Québec (INSPQ). Avis du Comité d'experts en planning familial. 2007 et/ou Guilbert E, Black A, Dunn S. Missed hormonal contraceptives : New recommandations – Committee opinion. J Obstet Gynaecol Can. 2008 Nov;30(11) :1050-77.

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ALGORITHM : EXTENDED WEAR OF THE PATCH AND THE RING

Key points :
- Extended wear means that the method is left in place longer than expected.
- Patch : forgiveness period of 2 days if the patch is left in place.
- Ring : forgiveness period of 2 weeks if the ring is left in place.

Extended wear of the ring

28-35 days

1) Insert a new ring without a HFI.
2) Keep the ring it until the scheduled ring removal day.

> 35 days

1) Same as for 28-35 days.

AND

1) Back-up contraception x 7 days.
2) Consider Emergency contraception (EC) *.

Extended wear of the patch

Patch 1 or 2

9 à < 12 days

1) Apply a NEW patch.
2) Keep the same patch change day.
3) Finish the cycles of patches.
4) Start a new cycle of 3 patches without a HFI.

≥ 12 days

1) Same as for 9 to < 12 days.

AND

1) Back-up contraception x 7 days.
2) Consider Emergency contraception (EC) *.

Patch 3

Extended wear of patch 3 falls into the HFI and will not decrease efficacy unless worn past the start of the next patch cycle.

Keep the same patch change day.

* If unprotected intercourse within the last 5 days

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