No. 280 (Replaces No. 131, August 2003)

Emergency Contraception

This clinical practice guideline has been prepared by the Social and Sexual Issues Committee, reviewed by the Clinical Practice Gynaecology Committee and the Family Practice Advisory Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

PRINCIPAL AUTHORS

Sheila Dunn, MD, Toronto ON

Édith Guilbert, MD, Quebec QC

SOCIAL SEXUAL ISSUES COMMITTEE

Margaret Burnett, MD (Chair), Winnipeg MB

Anjali Aggarwal, MD, Toronto ON

Jeanne Bernardin, MD, Moncton NB

Virginia Clark, MD, Golden BC

Victoria Davis, MD, Scarborough ON

Jeffrey Dempster, MD, Halifax NS

William Fisher, PhD, London ON

Karen MacKinnon, RN, PhD, Victoria BC

Rosana Pellizzari, MD, Peterborough ON

Viola Polomeno, RN, PhD, Ottawa ON

Maegan Rutherford, MD, Halifax NS

Jeanelle Sabourin, MD, Edmonton AB

Vyta Senikas, MD, Ottawa ON

Marie-Soleil Wagner, MD, Montreal QC

Disclosure statements have been received from all members of the committee.

The literature searches and bibliographic support for this guideline were undertaken by Becky Skidmore, Medical Research Analyst, Society of Obstetricians and Gynaecologists of Canada.

Key Words: Emergency contraception, post-coital contraception, emergency contraceptive pills, post-coital copper intrauterine device, IUD

Abstract

Objective: To review current knowledge about emergency contraception (EC), including available options, their modes of action, efficacy, safety, and the effective provision of EC within a practice setting.

Options: The combined estradiol-levonorgestrel (Yuzpe regimen) and the levonorgestrel-only regimen, as well as post-coital use of copper intrauterine devices, are reviewed.

Outcomes: Efficacy in terms of reduction in risk of pregnancy, safety, and side effects of methods for EC and the effect of the means of access to EC on its appropriate use and the use of consistent contraception.

Evidence: Studies published in English between January 1998 and March 2010 were retrieved though searches of Medline and the Cochrane Database, using appropriate key words (emergency contraception, post-coital contraception, emergency contraceptive pills, post-coital copper IUD). Clinical guidelines and position papers developed by health or family planning organizations were also reviewed.

Values: The studies reviewed were classified according to criteria described by the Canadian Task Force on Preventive Health Care, and the recommendations for practice were ranked according to this classification (Table 1).

Benefits, Harms, and Costs: These guidelines are intended to help reduce unintended pregnancies by increasing awareness and appropriate use of EC.

Sponsor: The Society of Obstetricians and Gynaecologists of Canada.

Summary Statements

1. Hormonal emergency contraception may be effective if used up to 5 days after unprotected intercourse. (II-2)
2. The earlier hormonal emergency contraception is used, the more effective it is. (II-2)
3. A copper IUD can be effective emergency contraception if used within 7 days after intercourse. (II-2)
4. Levonorgestrel emergency contraception regimens are more effective and cause fewer side effects than the Yuzpe regimen. (I)
5. Levonorgestrel emergency contraception single dose (1.5 mg) and the 2-dose levonorgestrel regimen (0.75 mg 12 hours apart) have similar efficacy with no difference in side effects. (I)

J Obstet Gynaecol Can 2012;34(9):870–878

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 this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	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.[73]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[73]

6. Of the hormonal emergency contraception regimens available in Canada, levonorgestrel-only is the drug of choice. (I)
7. A pregnancy that results from failure of emergency contraception need not be terminated (I)

Recommendations

1. Emergency contraception should be used as soon as possible after unprotected sexual intercourse. (II-2A)
2. Emergency contraception should be offered to women if unprotected intercourse has occurred within the time it is known to be effective (5 days for hormonal methods and up to 7 days for a copper IUD). (II-2B)
3. Women should be evaluated for pregnancy if menses have not begun within 21 days following emergency contraception treatment. (III-A)
4. During physician visits for periodic health examinations or reproductive health concerns, any woman in the reproductive age group who has not been sterilized may be counselled about emergency contraception in advance with detailed information about how and when to use it. (III-C)

INTRODUCTION

Emergency contraception refers to all methods of contraception that are used after intercourse and before implantation. The most commonly used methods can reduce the risk of pregnancy by 75% to 89%.[1–3] The EC methods are intended for occasional use, primarily as a backup to regular methods of birth control.

Emergency contraception has been available in Canada for almost 30 years, but as of 2002 only 57% of Canadian women were familiar with it.[4] Forty to fifty percent of pregnancies in Canada remain unplanned despite the wide availability of contraceptive methods,[5,6] and in 2006, 91 310 abortions were performed in Canada.[7] The appropriate use of EC may reduce the number of unintended pregnancies.

ABBREVIATIONS

EC emergency contraception

EE ethinyl estradiol

LNG levonorgestrel

METHODS OF EMERGENCY CONTRACEPTION

There are 2 methods of emergency contraception available in Canada: hormonal methods, also known as emergency contraceptive pills, and post-coital insertion of a copper intrauterine device.

Three products, Plan B, NorLevo, and Next Choice, are approved in Canada as hormonal EC. The first 2 consist of 2 tablets of levonorgestrel 750 μg taken as a single dose. The third consists of 2 tablets of levonorgestrel 750 μg taken 12 hours apart. All are now available in participating Canadian pharmacies without a prescription.[8]

The other hormonal EC, known as the Yuzpe method,[1] has been in use since the 1970s, and consists of 2 tablets of Ovral (50 μg of ethinyl estradiol and 250 μg of levonorgestrel) taken orally and repeated 12 hours later. Occasionally, an antiemetic is also required. Other contraceptive pills can be substituted if they are more readily available, as they are

considered to offer equivalent efficacy,[9] although they may not deliver an exactly equivalent dose (Table 2). None of these combined hormonal products have been approved for use as EC in Canada. Nonetheless, they may still be used for this purpose as they are readily available (on prescription) and economical.

The antiprogestin mifepristone (RU 486) has been shown to be a highly effective post-coital contraceptive,[10–14] but this product is unlikely to be available to Canadian women in the near future. Another antiprogestin, ulipristal acetate, has been found to be at least as effective as levonorgestrel emergency contraception and was approved in 2010 by the United States Food and Drug Administration but has not yet been approved by Health Canada.[15,16]

The insertion of a copper IUD within 5 days of unprotected intercourse has been shown to prevent pregnancy.[17–19] The use of a post-coital copper IUD between 5 and 7 days after unprotected intercourse is less well studied, although some trials have extended the treatment window to 7 days.[18,20] If successful in preventing pregnancy, the copper IUD may remain in place to provide ongoing contraception. Flexi-T and Nova-T are the 2 copper-bearing IUDs currently licensed for contraceptive use in Canada. Both are prescription products and may used "off-label" for EC. The levonorgestrel intrauterine system (Mirena intrauterine system) is not currently recommended for use as EC.[21]

MECHANISM OF ACTION OF EMERGENCY CONTRACEPTION

The exact mechanisms of action of emergency contraceptives are unclear, but EC could theoretically interfere with follicle maturation, the ovulatory process, cervical mucus, sperm migration, corpus luteum sufficiency, endometrial receptivity, fertilization, or zygote development, transport, or adhesion.[22] The mechanism of action may differ not only with the different EC regimens, but also within each regimen, depending upon when it is given relative to the time of both intercourse and ovulation.[22]

Statistical evidence of the effectiveness of hormonal EC agrees with clinical data, suggesting that the main mechanism of action is related to interference with ovulation.[22–28] When given before ovulation, the Yuzpe EC, levonorgestrel-only EC, and mifepristone appear to suppress or delay ovulation[22–26]; if ovulation does occur, it appears to be dysfunctional.[23,25,26] When EC is given at the time of or after ovulation, no effect on ovulation is seen.[23,24,26] Recent data show that LNG-EC prevents pregnancy only when taken before fertilization of the ovum has occurred.[29,30] It appears unlikely that EC has an effect on the luteal phase.[22–26,30]

Studies of the effects of combined EC and levonorgestrel-only EC (LNG-EC) on the endometrium are not consistent; however, most recent studies have failed to show major alterations in the mechanisms associated with endometrial receptivity.[22,23,25–27,30] Since the effect on ovulation may not explain the total effectiveness of hormonal EC,[31,32] more clinical data are required to assess the contribution of other mechanisms of action.

EFFICACY

Hormonal Regimens

The Yuzpe and levonorgestrel-only regimens have been shown to reduce the risk of pregnancy by about 75% to 89%, respectively,[1–3,33] but this does not mean that up to 25% of women using the Yuzpe regimen will become pregnant. Theoretically, if 100 women had unprotected intercourse once during the second or third week of their cycle, about 8 would become pregnant; following treatment with the Yuzpe regimen, only 2 would become pregnant, a reduction of 75%.[34] However, recent studies using statistical estimation of the effectiveness of hormonal EC suggest that the risk reduction may not be this great.[35,36] The World Health Organization reports a pregnancy rate of 1.1% with the levonorgestrel-only regimen compared with 3.2% for the Yuzpe regimen.[1]

Two randomized trials[1,3] compared levonorgestrel given twice 12 hours apart with the Yuzpe regimen, and both showed that levonorgestrel only had higher efficacy (85% vs. 57% for typical use and 89% vs. 76% for perfect use).[1]

In 2002, 2 large randomized trials[37,38] showed that a single dose of 1.5 mg of levonorgestrel was as effective as the standard 2-dose levonorgestrel regimen.

In a randomized controlled trial,[39] a 1-dose regimen of Ovral was less effective than the 2-dose regimen, but the difference was not significant (54% vs. 67% for typical use and 62% vs. 73% for perfect use). In a study that assessed effect of Ovral on ovulation,[25] it appeared that a single dose of Ovral did not suppress ovulation as efficiently as 2 doses.

Although mifepristone is not available in Canada, it is worth noting that it is 6 times more effective than the Yuzpe regimen,[11] even at low doses,[11–14] and that very low-dose mifepristone (unidose of 10 mg) is as effective as levonorgestrel only.[37] Mifepristone 25 mg to 50 mg is superior to all hormonal regimens currently in use in Canada.[40]

Copper Intrauterine Device

A meta-analysis of 20 published papers[41] showed that copper IUDs inserted within 5 days of unprotected intercourse are significantly more effective than hormonal EC, with an efficacy of 98.7%. There were no pregnancies in 2 studies: 1 comparing 14 emergency users of copper IUD with 219 mifepristone users,[13] and another following a cohort of 1963 women obtaining a copper IUD within 120 hours of unprotected sexual intercourse.[19] Only 1 pregnancy occurred in another descriptive study of 1013 women using copper IUDs post-coitally.[18] The 2008 Cochrane Review supported the conclusion that the copper IUD is an excellent EC with efficacy close to 99%. [40]

Timing

Effectiveness of EC appears to decline with increasing delay between unprotected intercourse and initiation of treatment. Levonorgestrel prevented 95% of pregnancies when taken ≤ 24 hours after intercourse, 85% within 25 to 48 hours, and 58% within 49 to 72 hours. The corresponding figures for the Yuzpe regimen were 77%, 36%, and 31%.[1] These findings were replicated in several studies,[11,38,42] although this timing–efficacy relationship was not universally seen.[37,43]

Although their use has generally been recommended only up to 72 hours after intercourse, the Yuzpe regimen[43,44] and the 1 double-dose and 2-dose levonorgestrel regimens[37,38] have been shown to be effective when taken between 72 and 120 hours after unprotected intercourse.

Other Factors

Hormonal EC is less effective in women who do not take it according to instructions (non-perfect use) and in those who have unprotected intercourse again after taking it.[1,12,37–39]

Repetitive use of hormonal EC as a regular contraceptive has not been found to provide adequate contraceptive efficacy.[45] In 1 study,[45] women were asked to take levonorgestrel 0.75 mg within 1 hour of each act of intercourse. The overall pregnancy rate over the 6-month period was 6 per 100 women-years, which was twice the failure rate for combined oral contraceptives. Irregular bleeding was a major drawback of this method, as it was experienced by 70% of the participants.[45]

AVAILABILITY

PlanB and NorLevo are the only products currently approved by Health Canada for emergency contraception. Neither product requires a prescription, but availability depends on the pharmacist's willingness to stock these items. A 2006 study of Ontario pharmacies found that, province-wide, levonorgestrel emergency contraception was available in 93% of pharmacies.[46] The combined oral contraceptive and copper IUD are licensed in Canada and may be prescribed "off-label" for EC use.

Table 2. Ovral and substitutions

Brand	Pills/ 2 doses	EE Dose, µg	LNG Dose, µg
Ovral	2	100	500
Allesse	5	100	500
Triphasil	4 yellow	120	500
Triquilar	4 yellow	120	500
Minovral	4	120	600

INDICATIONS

Hormonal EC should be considered for any woman who presents within 5 days of unprotected or inadequately protected sexual intercourse and who does not wish to be pregnant. Insertion of a copper IUD can be considered up to 7 days after the unprotected intercourse. Unprotected intercourse may occur because of the following:

- failure to use a contraceptive method
- condom breakage or leakage
- dislodgement of a diaphragm or cervical cap
- 1 missed birth control pill in the first week of combined oral contraception (SOS [Stay on Schedule] algorithm)[47]
- 3 or more missed birth control pills in the second or third week of combined oral contraception (SOS algorithm)[47]
- missed progestin-only pill (SOS algorithm)[47]
- detachment of the contraceptive patch (SOS algorithm)[47]
- withdrawal of the contraceptive vaginal ring (SOS algorithm)[47]
- Depo-Provera injection over 2 weeks late (SOS algorithm)[47]
- ejaculation on the external genitalia
- mistimed fertility awareness
- sexual assault, when the woman is not using reliable contraception.

Because it is difficult to determine with certainty the fertile time of a woman's cycle,[48–50] EC should be provided regardless of the cycle day on which exposure occurs if a woman is concerned about her risk of pregnancy. Although hormonal EC is not recommended as a regular form of contraception, repeat use poses no known health risks and should not be a reason for denying women access to treatment.[51]

CONTRAINDICATIONS

There are no absolute contraindications to the use of emergency hormonal contraception except known pregnancy, and this is only because it is ineffective. The research is reassuring that these drugs are not teratogenic. A recent study of pregnancy outcomes after LNG-EC failure found no associated risk of malformation or other adverse pregnancy outcomes in exposed pregnancies.[52,53] Studies of pregnancies in which the fetus has been exposed to oral contraceptives have shown no evidence of teratogenecity,[54] and exposure, therefore, is not an indication for termination of pregnancy.

The WHO found no contraindications for hormonal or IUD emergency contraception use in breastfeeding women,[55] and there are no known medical contraindications to the use of hormonal EC, except allergy to 1 of the constituents.[55] Data from the United Kingdom on more than 4 million prescriptions of the Yuzpe regimen showed only 6 serious adverse events (3 venous thrombosis and 3 cerebrovascular events); in none of these was the relationship between the administration of hormonal EC and the event clearly determined.[56] Women who have contraindications to the daily use of oral contraceptives, such as smokers over the age of 35, can safely use either of the hormonal methods of EC, as the duration of hormonal use is very brief.[57] No substantial increased risk for developing venous thromboembolism has been found with combined EC, but studies of safety have frequently excluded women who have contraindications to oral contraception.[58] As the levonorgestrel-only regimen carries no theoretical risk, it may be a preferable option for women who have strong contraindications to estrogen, such as women with known thrombophilia, history of stroke, heart attack, or active migraine with neurological symptoms.[59] There has been concern that an excess risk of ectopic pregnancy may exist should the progestin-only EC fail to prevent pregnancy,[60] as is seen with other progestin-only contraceptives.[61] Although a few case reports of ectopic pregnancies associated with hormonal EC have been published, a recent review concludes that the rate of ectopic pregnancy when treatment with emergency contraceptive pills fails does not exceed the rate observed in pregnancies in the general population. Because emergency contraceptive pills are effective in lowering the risk of pregnancy, their use will reduce the chance that an act of intercourse will result in ectopic pregnancy.[62]

If a copper IUD is considered the following should be taken into account:

- A pre-existing pregnancy must be excluded. This may require a urine pregnancy test or serum hCG test, especially in women who have had sexual intercourse at the beginning of their cycle.
- There should be no history of recent pelvic inflammatory disease and no apparent vaginal or cervical infection on examination.
- At the time of insertion, consider obtaining endocervical specimens to test for gonorrhea and Chlamydia.
- Although a 2001 Cochrane Review concluded that prophylactic antibiotics at the time of IUD insertion were not routinely warranted, the use of antibiotic prophylaxis in populations at higher risk for sexually transmitted infections was shown to reduce subsequent pelvic infection by one third.[63,64] Antibiotics such as a single dose of azithromycin (1g) or doxycycline 200 mg should be considered in women at high risk to reduce the risk of pelvic infection.[64]
- If the copper IUD fails to prevent pregnancy the device should be removed immediately once the diagnosis of pregnancy is made. It is also important to rule out ectopic pregnancy.

ASSESSMENT

Very little information is required to determine whether EC is indicated. History taking must determine that unprotected intercourse occurred within the time frame when EC is effective. The woman's risk for having a pre-existing pregnancy should be assessed by determining the timing of her last menstrual period, that it was normal, and that she is not currently overdue for her expected period. Rarely will a urine pregnancy test be necessary to rule out pregnancy. A woman who has had unprotected intercourse earlier in the cycle may be at risk of pregnancy because the EC therapeutic period has passed, but she should not be denied EC if she has also had unprotected intercourse within the 5-day window during which it is likely to be effective.

When seeing women for consideration of EC, health care providers should address related sexual health concerns such as whether the unprotected act was coerced, risks for sexually transmitted infections, and need for ongoing birth control. Appropriate counselling, testing, and treatment should be offered. Women should be informed about the potential side effects and potential failure of EC and should be advised that hormonal EC will not prevent pregnancy from unprotected intercourse in the days or weeks following treatment. A barrier method such as the condom can be used for the remainder of the cycle and a different method initiated at the beginning of the next cycle if the woman desires. If a woman with no contraindications wishes to start oral contraceptives, she can be provided with a prescription to start the next day following the use of hormonal EC or with her next period.[65] A condom should be used until she has taken the contraceptive pill for 7 consecutive days.[61]

FOLLOW-UP

Women should be advised to have a pregnancy test if they do not experience normal menstrual bleeding by 21 days following EC treatment or by 28 days if an oral contraceptive was started after taking hormonal EC. If indicated, a follow-up appointment can be made to address ongoing birth control or to test for sexually transmitted infections.

SIDE EFFECTS

The 2-dose levonorgestrel regimen has a significantly lower incidence than the Yuzpe regimen of nausea (23.1% vs. 50.5%), vomiting (5.6% vs. 18.8%), dizziness (11.2% vs. 16.7%), and fatigue (16.9% vs. 28.5%).[1] In the studies comparing the 2-dose levonorgestrel regimen with the 1 double-dose regimen, the occurrence of side effects was similar.[37,38]

An antiemetic has been demonstrated to reduce the risk of nausea by 27% and vomiting by 64% when taken 1 hour before the first dose of the Yuzpe regimen.[66] Expert opinion suggests that if the woman vomits within the first 2 hours after taking hormonal EC, the dose should be repeated and consideration should be given to vaginal administration of the medication.

Possible complications of the post-coital copper IUD include pelvic pain, abnormal bleeding, pelvic infection, uterine perforation, and expulsion.[61]

RETURN OF MENSES

Most women will have their next menses within 3 weeks of taking EC. In the 1998 WHO study,[1] the onset of next menses was similar for women taking the Yuzpe regimen and those taking the 2-dose levonorgestrel regimen, with 15% of women having an early onset of menses, 57% having menses return within 3 days of the expected day, and 28% experiencing a delay of more than 3 days. In other trials,[38,39] a number of women tended to have an early onset of menses. The time to resumption of menses may be affected by the timing of EC in relation to the date of ovulation.[24,39]

ACCESS

From a public health perspective, the promotion of EC can be seen as primary prevention of unintended pregnancy. To maximize the potential for EC to reduce the number of unintended pregnancies, women at risk of pregnancy and their partners need to be knowledgeable about EC before they require it and able to access it quickly.

Possible barriers to the appropriate use of EC include lack of knowledge, negative attitude, fear of side effects, judgemental attitudes from providers, overstating of associated health risks, impractical business hours of medical clinics and pharmacies, and unavailability of the product in some pharmacies. The cost of emergency contraception is relatively high compared with other methods and may be a barrier to access. Provincial and territorial public health sectors should make removal of cost barriers a priority. Making EC available without a prescription improves access to EC.[67]

One randomized controlled trial[68] and 2 controlled trials[69,70] have shown that, compared with women given information only, women provided with hormonal EC in advance of need were more likely to use it and to use it appropriately and were not more likely to abandon regular methods of contraception.[68–70] However, a recent review of 8 randomized trials by the Cochrane Collaboration did not demonstrate a reduction in pregnancy rates with advance provision of EC compared with conventional provision.[71] During visits to her health care provider for periodic health examinations or reproductive health concerns, any woman in the reproductive age group who has not been sterilized may be counselled about EC in advance with detailed information about how and when to use it. There is no evidence that EC use or advanced provision of EC is associated with future risky sexual behaviour, or sexually transmitted infection.[71,72]

CONCLUSION

Emergency contraception has the potential to safely and effectively reduce the number of unintended pregnancies. The effective use of EC is dependent on increasing both public and professional awareness and improving access to this important therapeutic intervention. Health care providers can encourage the appropriate use of EC by discussing it with their patients. Professionals involved in the promotion of women's health must become advocates for EC, both locally and nationally.

Summary Statements

1. Hormonal emergency contraception may be effective if used up to 5 days after unprotected intercourse. (II-2)
2. The earlier hormonal emergency contraception is used, the more effective it is. (II-2)
3. A copper IUD can be effective emergency contraception if used within 7 days after intercourse. (II-2)
4. Levonorgestrel emergency contraception regimens are more effective and cause fewer side effects than the Yuzpe regimen. (I)
5. Levonorgestrel emergency contraception single dose (1.5 mg) and the 2-dose levonorgestrel regimen (0.75 mg 12 hours apart) have similar efficacy with no difference in side effects. (I)
6. Of the hormonal emergency contraception regimens available in Canada, levonorgestrel-only is the drug of choice. (I)
7. A pregnancy that results from failure of emergency contraception need not be terminated (I)

Recommendations

1. Emergency contraception should be used as soon as possible after unprotected sexual intercourse. (II-2A)
2. Emergency contraception should be offered to women if unprotected intercourse has occurred within the time it is known to be effective (5 days for hormonal methods and up to 7 days for a copper IUD). (II-2B)
3. Women should be evaluated for pregnancy if menses have not begun within 21 days following emergency contraception treatment. (III-A)
4. During physician visits for periodic health examinations or reproductive health concerns, any woman in the reproductive age group who has not been sterilized may be counselled about emergency contraception in advance with detailed information about how and when to use it. (III-C)

REFERENCES

1. Task Force on Postovulatory Methods of Fertility Regulation. Randomized controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. Lancet 1998;352:428–33.
2. Trussell J, Rodriguez G, Ellertson C. Updated estimates of the effectiveness of the Yuzpe regimen of emergency contraception. Contraception1999;59:147–208.
3. Ho PC, Kwan MSW. A prospective randomized comparison of levonorgestrel with the Yuzpe regimen in post-coital contraception. Hum Reprod 1993;8:389–92.
4. Fisher W, Boroditsky R, Morris B. The 2002 Canadian Contraception Study: Part I. J Obstet Gynaecol Can 2004;26:580–90.
5. The Alan Guttmacher Institute. Sharing responsibility: women, society and abortion worldwide. New York: AGI; 1999.
6. Henshaw SK. Unintended pregnancy in the United States. Fam Plann Perspect 1998;30:24–9,46.
7. Statistics Canada. Induced abortions in hospitals and clinics, by area of report and type of facility performing the abortion, Canada, provinces and territories, 2006. Available at: http://www5.statcan.gc.ca/cansim/a05?lang=eng&id=1069005. Accessed June 27, 2012.
8. Bayer Inc. Bayer expands women's health portfolio to include a new emergency contraceptive option: NorLevo® is now available in pharmacies across Canada without a doctor's prescription. Toronto: Bayer Inc.; May 26, 2009. Available at: http://www.bayer.ca/files/Norlevo%20press%20release_English_FINAL.pdf. http://www.bayer.ca/?q=en/node/1458. Accessed December 22, 2010.
9. United States Food and Drug Administration. Prescription drug products; certain combined oral contraceptives for use as post-coital emergency contraception. Federal Register 1997;62:8610–2.
10. Glasier A, Thong KJ, Dewar M, Mackie M, Baird D. Mifepristone (RU486) compared with high-dose estrogen and progestogen for emergency post-coital contraception. N Engl J Med 1992;327:1041–4.
11. Ashok PW, Stalder C, Wagaarachchi PT, Flett GM, Melvin L, Templeton A. A randomized study comparing a low dose of mifepristone and the Yuzpe regimen for emergency contraception. Br J Obstet Gynaecol 2002;109:553–60.
12. Task Force on Postovulatory Methods of Fertility Regulation. Comparison of three single doses of mifepristone as emergency contraception: a randomised trial. Lancet 1999;353:697–702.
13. Ashok PW, Wagaarachchi PT, Flett GM, Templeton A. Mifepristone as a late post-coital contraceptive. Hum Reprod 2001;16(1):72–5.
14. Xiao BL, von Hertzen H, Ahao H, Piaggio G. A randomized double blind comparison of two single doses of mifepristone for emergency contraception. Hum Reprod 2002;17(12):3084–9.
15. Glasier AF, Cameron ST, Fine PM, Logan SJ, Casale W, Van Horn J, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: randomized non-inferiority trial and meta-analysis. Lancet 2010;375(9714)555–62.
16. Hitt E. FDA panel gives ulipristal acetate unanimous positive vote for emergency contraception indication. Medscape News [Internet site]. Available at: http://www.medscape.com/viewarticle/723822. Accessed June 27, 2012.
17. Lippes J, Malik T, Tatum HJ. The postcoital copper-T. Adv Plan Parent1976;11:24–9.
18. Zhou LY, Ziao BL. Emergency contraception with multiload Cu-375SL IUK: a multicenter clinical trial. Contraception 2001;64:107–12.

19. Wu S, Godfrey EM, Wojdyla D, Dong J, Cong J, Wang C, et al. Copper T380A intrauterine device for emergency contraception: a prospective, multicentre, cohort clinical trial. BJOG 2010;117(10):1205–10.

20. Fasoli M, Parazzini F, Cecchetti G, La Vecchia C. Post-coital contraception: an overview of published studies. Contraception 1989;39:459–68.

21. American College of Obstetricians and Gynecologists. Emergency contraception. ACOG Practice Bulletin No. 112, May 2010. Obstet Gynecol 2010;115:1100–9.

22. Croxatto HB, Devoto L, Durant M, Ezcurra E, Larrea F, Nagle C, et al. Mechanism of action of hormonal preparations used for emergency contraception: a review of the literature. Contraception 2001;63:111–21.

23. Durand M, del Carmen Cravioto M, Raymond EG, Durán-Sánchez O, De la Luz Cruz-Hinojosa M, Castell-Rodríguez A, et al. On the mechanisms of action of short-term levonorgestrel administration in emergency contraception. Contraception 2001;64:227–34.

24. Hapangama D, Glaxier AF, Baird DT. The effects of peri-ovulatory administration of levonorgestrel on the menstrual cycle. Contraception 2001;63:123–9.

25. Croxatto HB, Fuentealba B, Brache V, Salvatierra AM, Alvarez F, Massai R, et al. Effects of the Yuzpe regimen, given during the follicular phase, on ovarian function. Contraception 2002;65:121–8.

26. Marions L, Hultenby K, Lindell I, Sun X, Stabi B, Bemzell Danielsson K. Emergency contraception with mifepristone and levonorgestrel: mechanism of action. Obstet Gynecol 2002;100:65–71.

27. Raymond EG, Lovely LP, Chen-Mok M, Seppälä M, Kurman RJ, Lessey BA. Effect of Yuzpe regimen of emergency contraception on markers of endometrial receptivity. Hum Reprod 2000;15(11):2351–5.

28. Landgren BM, Johanisson E, Aedo AR, Kummar A, Shi Ye. The effect of levonorgestrel administered in large doses at different stages of the cycle on ovarian function and endometrial morphology. Contraception 1989;39:275–89.

29. Noé G, Croxatto HB, Salvatierra AM, Reyes V, Villarroel C, Muñoz C, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. Contraception 2010;81:414–20.

30. Gemzell-Danielsson K. Mechanism of action of emergency contraception. Contraception 2010;82;404–9.

31. Trussell J, Raymond EG. Statistical evidence about the mechanism of action of the Yuzpe regimen of emergency contraception. Obstet Gynecol 1999;93:872–6.

32. Kesseru E, Garmendia F, Westphal N, Parada J. The hormonal and peripheral effects of dl-norgestrel in postcoital contraception. Contraception 1974;10:411–24.

33. Trussell J, Rodriguez G, Ellertson C. New estimates of the effectiveness of the Yuzpe regimen of emergency contraception. Contraception1998;57:363–9.

34. Trussell J, Ellertson C, Stewart F. The effectiveness of the Yuzpe regimen of postcoital contraception. Fam Plann Perspect 1993;9:75–82.

35. Trussell J, Ellertson C, Dorflinger L. Effectiveness of the Yuzpe regimen of emergency contraception by cycle day of intercourse: implications for mechanism of action. Contraception 2003;67:167–71.

36. Trussell J, Ellertson C, von Hertzen H, Bigrigg A, Webb A, Evans M, et al. Estimating the effectiveness of emergency contraceptive pills. Contraception 2003;67:259–65.

37. von Hertzen H, Piaggio G, Ding J, Chen J, Song S, Bartfai G, et al. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. Lancet 2002;360:1803–10.

38. Arowojolu AO, Okewole IA, Adekunle AO. Comparative evaluation of the effectiveness and safety of two regimens of levonorgestrel for emergency contraception in Nigerians. Contraception 2002;66:269–73.

39. Ellertson C, Webb A, Blanchard K, Bigrigg A, Haskell S, Shochet T, et al. Modifying the Yuzpe regimen of emergency contraception: a multicenter randomized controlled trial. Obstet Gynecol 2003;101:1160–7.

40. Cheng L, Gulmezoglu AM, Piaggie G, Ezcurra E, Van Look PF. Interventions for emergency contraception. Cochrane Database Syst Rev 2008 Apr 16;(2)CD001324.

41. Trussell J, Ellertson C. Efficacy of emergency contraception. Fert Control Rev 1995;4:8–11.

42. Piaggio G, von Hertzen H, Grimes DA,Van Look PFA. Timing of emergency contraception with levonorgestrel and the Yuzpe regimen. Lancet 1999;353:721.

43. Ellertson C, Evans M, Ferden S, Leadbetter C, Spears A, Johnstone K, et al. Extending the time limit for starting the Yuzpe regimen of emergency contraception to 120 hours. Obstet Gynecol 2003;101:1168–71.

44. Rodrigues I, Grou F, Joly J. Effectiveness of emergency contraceptive pills between 72 and 120 hours after unprotected intercourse. Am J Obstet Gynecol 2001;184:531–7.

45. United Nations Development Programme/United Nations Population Fund/World Health Organizations/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, Task Force on Post-Ovulatory Methods for Fertility Regulation. Efficacy and side effects of immediate postcoital levonorgestrel used repeatedly for contraception. Contraception 2000;61:303–8.

46. Dunn S, Brown TE, Alldred J. Availability of emergency contraception after its deregulation from prescription-only status: a survey of Ontario pharmacies. CMAJ 2008;178(4):423–4.

47. Society of Obstetricians and Gynaecologists of Canada: sexualityandu [website]. S.O.S. Stay on schedule. Available at: http://www.sexualityandu.ca. Accessed June 28, 2012.

48. Espinos JJ, Rodriguez-Espinosa J, Senosiain R, Aura M, Vanrell C, Gispert M, et al. The role of matching menstrual data with hormonal measurements in evaluating effectiveness of postcoital contraception. Contraception 1999;60:215–20.

49. Wilcox A, Dundon D, Weinberg C, Trussell J, Baird DD. Likelihood of conception with a single act of intercourse: providing benchmark rates for assessment of post-coital contraceptives. Contraception 2001;63:211–5.

50. Stirling A, Glasier A. Estimating the efficacy of emergency contraception how reliable are the data? Contraception 2002;66:19–22.

51. Shelton JD. Repeat emergency contraception: facing our fears. Contraception 2002;66:15–7.

52. F, Yu W, Cheng L. Pregnancy outcome after levonorgestrel-only emergency contraception failure: a prospective cohort study. Hum Reprod 2009;24:1605–11.

53. De Santis M, Cavaliere AF, Straface G, Carducci B, Caruso A. Failure of the emergency contraceptive levonorgestrel and the risk of adverse effects in pregnancy and on fetal development: an observational cohort study. Fertil Steril 2005;84:296–9.

54. Bracken MB. Oral contraception and congenital malformations in offspring: a review and meta-analysis of the prospective studies. Obstet Gynecol 1990;76:552–7.

55. Improving access to quality care in family planning: medical eligibility criteria for contraceptive use. 3rd ed. Geneva: WHO; 2004.

56. Glasier A. Emergency postcoital contraception. N Eng J Med1997;337:1058–64.

57. Grimes DA, Raymond EG, Scott Jones B. Emergency contraception over-the-counter: the medical and legal imperatives. Obstet Gynec012001;98:151–5.

58. Vasilakis C, Jick SS, Jick H. The risk of venous thromboembolism in users of postcoital contraceptive pills. Contraception 1999;59:79–83.

59. Webb A. How safe is the Yuzpe method of emergency contraception? Fert Control Rev 1995;4:16–8.

60. Sheffer-Mimouni G, Pauzner D, Maslovitch S, Lessing JB, Gamzu R. Ectopic pregnancies following emergency levonorgestrel contraception. Contraception 2003;67: 267–9.

61. Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Stewart F, Kowal D. Contraceptive technology. 19th ed. New York: Ardent Media Inc.; 2007.

62. Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. Ectopic pregnancy and emergency contraceptive pills: a systematic review. Obstet Gynecol 2010;115(6):1263–6.

63. Grimes DA, Schulz KF. Antibiotic prophylaxis for intrauterine contraceptive device insertion. Cochrane Database Syst Rev 2001(2): CD001327.

64. Sinei SK, Schulz KF, Lamptey PR, Grimes DA, Mati JK, Rosenthal SM, et al. Preventing IUCD-related pelvic infection: the efficacy of prophylactic doxycycline at insertion. Br J Obstet Gynaecol 1990;97:412–9.

65. The International Consortium for Emergency Contraception. Emergency contraceptive pills: medical and service delivery guidelines. 2nd ed. Washington DC: The International Consortium for Emergency Contraception; 2004.

66. Raymond EG, Creinin MD, Barnhart KT, Lovvorn AE, Wountree RW, Trussell J. Meclizine for prevention of nausea associated with use of emergency contraceptive pills: a randomized trial. Obstet Gynec012000;95:271–7.

67. Soon JA, Levine M, Osmond BL, Ensom MHH, Fielding DW. Effects of making emergency contraception available without a physician's prescription: a population-based study. CMAJ 2005;172(7):878–83.

68. Ellertson C, Ambardekar S, Hedley A, Coyaji K, Trussell J, Blanchard K. Emergency contraception: randomized comparison of advance provision and information only. Obstet Gynecol 2001;98:570–5.

69. Glasier A, Baird D. The effects of self-administering emergency contraception. N Engl J Med 1998;339:1–4.

70. Raine T, Harper C, Leon K, Darney P. Emergency contraception: advance provision in a young, high-risk clinic population. Obstet Gynecol 2000;96:1–7.

71. Polis CB, Schaffer K, Blanchard K, Glasier A, Harper CC, Grimes DA. Advance provision of emergency contraception for pregnancy prevention (full review). Cochrane Database Syst Rev 2007 Apr 18;(2):CD005497.

72. Sander PM, Raymond EG, Weaver MA. Emergency contraceptive use as a marker of future risky sex, pregnancy, and sexually transmitted infection. Am J Obstet Gynecol 2009;201:146–7.

73. Woolf SH, Battista RN, Angerson GM, Logan AG, Eel W. Canadian Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. CMAJ 2003;169:207–8.