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Can Emergency Contraception Play a Pivotal Role in Preventing Unintended Pregnancy and Abortion?

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Abstract

Aim: On the background of ongoing efforts to reduce the number of abortions, the aim of the present study is to enhance these efforts by recommending prevention in the form of contraception. Data on Emergency Contraception are analysed, and shortcomings in presently available studies are highlighted.

Method: The study gathers information on Emergency Contraception provided by the most authoritative scholarly studies. It critically analyses this information and assesses the accuracy of data. Flawed data are brought to light and rectifications are suggested on the basis of international research.

Results: Presently, women do not obtain adequate information on the advantages of Emergency Contraception. The risk of abortion due to unintended pregnancy could be prevented if information on all reliable contraceptive methods, including non-hormonal methods, would be as comprehensive as stipulated by the principle of informed consent.

Conclusion: Women must be enabled to access comprehensive, complete, and reliable information on all available methods of contraception, especially on the efficacy and safety of all methods, including Emergency Contraception (EC). They should also receive support from their counselors in efforts to avoid abortion owing to failure to implement contraceptive measures.

Précis: The present investigation commences with an introduction into abortion and unintended pregnancy. In a subsequent step, it investigates the salient features of Emergency Contraception (EC) by highlighting from an international perspective mechanism of action, side effects, and safety of Emergency Contraception (EC). In this context it focuses on the validity of the claim that Emergency Contraception should be used only in extreme cases and not as a regular form of contraception. In conclusion, open questions regarding rankings of contraceptive methods are underscored, and the need for intensified research on the parameter safety is emphasized.

Introduction

The interlacing of contraception, unintended pregnancy, and abortion has been frequently underscored, especially in studies on health statistics. [1]

It is also common knowledge that abortion is not only a medical and ethical topic but also a legal issue and a sociocultural phenomenon. It is most succinctly defined as a "spontaneous or artificially induced expulsion of an embryo or fetus before it is viable."[2] Numerous publications highlight noteworthy aspects of abortion, such as methods and legal regulations. Different surgical methods for termination of pregnancy have evolved over the years: dilatation and curettage, power operated vacuum aspiration (VA), manual vacuum aspiration (MVA) or hysterotomy. For all these methods it is customary to use local or general anaesthesia. Pre-abortion medical or mechanical cervical preparation may reduce the incidence of cervical or uterine injuries. At times, the methods available are classified as mechanical procedures such as curettage or vacuum curettage; pharmacological methods, such as prostaglandins; and surgical procedures, such as sectio parva abdominalis.[3, p.1516]

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The legal regulations of abortion differ from one country to the other. For the European Union (EU), the German regulation has paradigmatic character. According to penal code (Strafgesetzbuch) §218 abortion is liable to prosecution, but according to §218a it is permissible under certain conditions, especially in case of consent on the part of the pregnant woman or in order to avoid danger for her life or to preclude a serious threat to her physical and mental health.[3,p.1516]

The ethical dimension of abortion has been recognized also by various medical associations, and the American Medical Association (AMA) underscores the criterion of good medical practice and lawfulness by specifying: "The Principles of Medical Ethics of the AMA do not prohibit a physician from performing an abortion in accordance with good medical practice and under circumstances that do not violate the law." [4, p.2, section 2.01] A particularly relevant area for the ethical ramifications of abortion is genetic counseling, where the dilemma faced by some physicians due to technological developments comes to the forefront. "Technological developments in the accuracy of predicting and detecting genetic disorders have created a dilemma for the physician who for personal reasons opposes contraception, sterilization or abortion." [4,p.9, section 2.12]

The interweaving of unintended pregnancy and abortion is a focal point in investigations on health statistics where the causal relationship between unintended pregnancy and abortion is emphasized. "Eighty-five million pregnancies, representing 40 percent of all pregnancies, were unintended in 2012. Of these, 50 percent ended in abortion, 13 percent ended in miscarriage, and 38 percent resulted in an unplanned birth."[5, p. 301]

One of the crucial topics of contemporary investigations in the area of health statistics is the status of the global abortion rate and the distinction between safe and unsafe abortions. A study from 2012 on the global

abortion rate between 1995 and 2008 draws attention to the incidence of unsafe abortions: "The substantial decline in the abortion rate observed earlier has stalled, and the proportion of all abortions that are unsafe has increased. Restrictive abortion laws are not associated with lower abortion rates."[6,p.625] Among the measures proposed to reduce the incidence of unintended pregnancy and unsafe abortion, investments in family planning services and safe abortion care should have highest priority, according to proponents of family planning who consider the implementation of these measures as "crucial steps toward achieving the Millennium Development Goals."[6,p.631]

In view of data provided by the above mentioned studies it seems obvious that a considerable number of abortions could be avoided if appropriate measures were implemented on several levels of health care systems. Above all, the interlacing between abortion and unintended pregnancies should receive heightened attention, and the possibilities of preventing unintended pregnancy should be explored further.

Preventing pregnancy is nowadays a relatively promising undertaking given the wide array of contraceptive possibilities. In view of these possibilities the question arises as to why the occurrence of unintended pregnancies is still high in several countries, including the United States (U.S.) which continues to be the world leader with a rate of 45%. "However, the most recent U.S. data still indicate that 45% of all pregnancies in the United States are unintended, as compared with 34% in Western Europe."[7,p.461]

It is imperative, therefore, to seek solutions for this problem, and the following discussion does so by arguing that the crux of the matter is not only restricted access to contraception or unattainability, but also deficient information available for women. Presently, women inquiring into questions of family planning, birth control, and contraception are frequently confronted with incomplete, inaccurate, and at times even misleading information. Rectification of such information is the primary target of the following discussion with focus on the salient features of Emergency Contraception (EC). This form of contraception, although well-known in the clinical practice for a considerable amount of time, is frequently ill-described especially with respect to mechanism of action and safety.

Table 1: Ranking based on Contraceptive Technology CTFailure Table (2011)[8]

Method	Perfect/ typical use
Implanon	0.05/0.05
Male sterilization	0.10/0.15
Mirena (LNg)	0.2/0.2
Depo-Provera	0.2/6
NuvaRing	0.3/9
Evra Patch	0.3/9
Combined pill and Progestin-only pill	0.3/9
Symptothermal method	0.4/24
Female sterilisation	0.5/0.5
Para Gard (copper T)	0.6/0.8
Male condom	2/18
Ovulation method	3/24
TwoDay method	4/24
Withdrawal	4/22
Standard Days method	5/24
Femal condom	5/21
Diaphragm	6/12
Sponge – nulliparous women	9/12
Spermicides	18/28
Sponge- parous women	20/24
Emergency Contraception	1/? (WHO, 2017) 12.5/15 (FDA, 2013)
No method	85/85

In discussing contraception, birth control and family planning it is useful to keep in mind a synoptic view of all methods presently available and their efficacy. The following table (Table 1), which is based on one of the most widely acknowledged assessments of contraceptive methods developed by Contraceptive Technology,[8] will prove conducive to identifying each one of the methods in a comparative fashion. Due to its high degree of reliability, the Contraceptive Failure Table (CTFailure Table) has been used as a source not only by the Food and Drug Administration (FDA) [9] but also by the World Health Organization (WHO).[10]

Using this table as a standard reference, the following discussion focuses first on the efficacy of Emergency Contraception (EC) and its mechanism of action. This is followed by an inquiry into side effects and the parameter safety. As a result of the analyses performed, the study propounds ways for improving presently available information, especially for those women who are at risk of abortion due to a failure to use a contraceptive method, and for women with intolerance to hormones.

Discussion

Salient features of Emergency Contraception

This author claims that Emergency Contraception (EC) can be considered as one of the most convenient forms of birth control to prevent pregnancy and preclude abortion because it requires administration of pills only twice within 12 hours and thus avoids the burden of daily administration. In addition, it does not require the intervention by a health care provider. Concerning efficacy, antiprogestin ulipristal acetate (30 mg in a single dose) is considered to be the the most effective pill for EC in the United States and Europe, "with reported estimates of effectiveness ranging from 62% to 85%." [11,p.4] If intrauterine devices are employed for EC, the efficacy is even higher, ie, 0.2 (perfect and typical use) for Mirena (levonorgestrel); 0.6 (perfect uses) and 0.8 (typical use) for ParaGard (copper T).[8]

Some authors consider EC essential also for facilitating the transition into an ongoing form of contraception. "Emergency contraception is especially important for outreach to the 4.5 million women at risk of pregnancy but not using a regular method by providing a bridge to use of an ongoing contraceptive method."[11,p.2] In contradiction to this claim, it should be emphasized that the use of EC as a transitory measure leading to an ongoing form of contraception is not a stringent necessity because recent studies do not provide evidence for any harm in case of moderately repeated use of EC. As a consequence, EC could be implemented at certain intervals without any need for venturing into ongoing forms of contraception, as for example oral contraceptives, implants, or intrauterine devices (IUD).

EC has been described as "a last chance to prevent unintended pregnancy."[11,p.1] It would be equally fitting to define this method as "ultima ratio contraception" because it is presently the only ultimate possibility to avoid pregnancy. Also suitable would be the designation "a posteriori" contraception because measures are taken subsequent to sexual intercourse in contrast to other methods of contraception which are applied previously to coitus.

One of the most comprehensive studies on EC appeared in 2017 and concluded: "Emergency contraception provides women with a last chance to prevent pregnancy after unprotected sex."[11,p.18] Concerning the question of reducing the rate of unintended pregnancy by means of EC, the authors enumerate three reasons that might interfere with such a reduction, namely a high incidence of unprotected intercourse, a merely moderate efficacy of the pills used for EC, and rare use of EC pills (ECPs). "But it is unlikely that expanding access will have a major impact on reducing the rate of unintended pregnancy, primarily because the incidence of unprotected intercourse is so high, ECPs are only moderately effective, and ECPs are not used often enough."[11,p.18]

In challenging this statement, one might argue that the incidence of unprotected intercourse could be reduced through improved educational strategies, and the moderate efficacy of Emergency Contraceptive Pills (ECPs) could be remedied through the additional use of an augmentative measure, such as periodic abstinence (fertility awareness-based) methods. In fact, especially women whose sexual activity is on the decline could easily avoid the daily administration of a pill or the risks of an intrauterine device and rely on a periodic abstinence method, given that a failure of the method could be quite effectively remedied by EC. This hypothesis finds support by one of the most important findings of contemporary studies on EC, namely the efficacy of ulipristal acetate: "The antiprogestin ulipristal acetate (30 mg in a single dose) is the most effective ECP option in the United States and Europe, with reported estimates of effectiveness ranging from 62% to 85%."[11,p.4]

Besides ulipristal acetate as one of the most recently advocated options for EC, there are of course other pills available, and they can be divided into three types, namely combined ECPs containing both estrogen and progestin; progestin-only ECPs; and ECPs which contain an antiprogestin (either ulipristal acetate or mifepristone). Presently, progestin-only ECPs have replaced the older combined ECPs "because they are more effective and cause fewer side effects."[11,p.2]

Concerning these comments on efficacy, attention must be drawn to the WHO table of 2017 which indicates an estimate of 99% efficacy by stating "If all 100 women used progestin-only emergency contraception, one would likely become pregnant."[10] Along the same line, German research argued as early as 2000 that the efficacy of Emergency Contraception by means of "interceptive pills" in case of perfect use is as effective as 99% [12,p.82] The latter research, which ranks contraceptive methods according to the Pearl Index (PI), explains that the morning-after-pill interrupts the synchronisation between blastocyst development and endometrial preparedness for nidation. According to this research, the 4 pills used for interception (50 µg ethinyl estradiol and 0.25 mg levonorgestrel) are taken within 60 hours: 2 are taken within 48 hours of unprotected cohabitation and the remaining 2 are taken after an interval of 12 hours.

Interestingly enough, this claim made in 2000 and the WHO estimate of 2017 do not harmonize with the estimate presented by the Food and Drug Adminstration (FDA) in a survey of contraceptive methods.[9] This survey, which appeared in 2013, indicates 85% efficacy in case of perfect use and 87.5% efficacy in case of typical use – which is described as "7 out of 8 women would not get pregnant after using Emergency Contraceptives." Paradoxically, according to this FDA survey, typical use (87.5%) would be more effective than perfect use (85%).

In addition to pills, intrauterine devices are suitable for EC. As of 2017 Emergency Contraceptives available in the United States (U.S.) included not only emergency contraceptive pills (ECPs) but also intrauterine devices (IUD), namely a Copper T intrauterine contraceptive (IUC), and a levonorgestrel-releasing IUD. The copper-containing IUC (ParaGard) is a non-hormonal device and contains 380 mm2 of copper around the arms and stem. "The copper-containing IUD releases copper ions that are toxic to sperm."[7,p.462] The levonorgestrel-releasing (non-copper) intrauterine system (sold as Mirena in the U.S.) has been described comprehensively by the manufacturer in a consumer leaflet. The device consists of a T-shaped frame (T-body) made out of polyethylene and a steroid reservoir (hormone elastomer core) around the vertical stem. "The reservoir consists of a white or almost white cylinder, made of a mixture of levonorgestrel and silicone (polydimethylsiloxane), containing a total of 52 mg levonorgestrel. The reservoir is covered by a semi-opaque silicone (polydimethylsiloxane) membrane. The T-body is 32 mm in both the horizontal and vertical directions. The polyethylene of the T-body is compounded with barium sulfate, which makes it radiopaque. A monofilament brown polyethylene removal thread is attached to a loop at the end of the vertical stem of the T-body."[13,p.1]

Pills used for EC:

Originally, pills for EC have been known also under the designation "morning-after-pill."[12,p.82] This label, despite its world-wide use, is inappropriate since ECPs may be initiated earlier than the morning after, ie, immediately after unprotected intercourse -- the sooner the better, but within 120 hours.

Combined ECPs contain the hormones estrogen and progestin. The estrogen ethinyl estradiol and the progestin levonorgestrel or norgestrel (which contains two isomers, only one of them being bioactive, ie, levonorgestrel) have been studied extensively in clinical trials, according to some authors.[11,p.1] With respect to these hormones it should be noted that products dedicated as EC, ie, specially packaged for use as EC, are not the only ones that can be used. In fact, certain ordinary birth control pills in specified combinations are also effective as emergency contraception. The regimen is one dose followed by a second dose 12 hours later, where each dose consists of 4, 5, or 6 pills, depending on the brand. Currently, 26 brands of combined oral contraceptives are approved in the United States for use as emergency contraception. It has been claimed that the safety and efficacy of such an alternative regimen containing ethinyl estradiol and the progestin norethindrone has been demonstrated by research. "Research has demonstrated the safety and efficacy of an alternative regimen containing ethinyl estradiol and the progestin norethindrone; . . . this result suggests that oral contraceptive pills containing progestins other than levonorgestrel may also be used for emergency contraception."[11,p.1]

Concerning progestin-only ECPs, which do not contain estrogen, the progestin levonorgestrel is the only hormone that has been studied for free-standing use as an emergency contraceptive. "The original treatment schedule was one 0.75 mg dose within 72 hours after unprotected intercourse, and a second 0.75 mg dose 12 hours after the first dose."[11,p.1]

What transpired in these studies is the possibility of administering a single dose, which proved to be equally effective. "However, studies have shown that a single dose of 1.5 mg is as effective as two 0.75 mg doses 12 hours apart."[11,p.1] One of these studies showed no difference between the two regimens regarding adverse events, "while the other found greater levels of headache and breast tenderness (but not other side effects) among study participants taking 1.5 mg of levonorgestrel at once."[11,p.1]

Concerning marketing, it should be noted that levonorgestrel is marketed internationally increasingly in a one-dose formulation (one 1.5 mg pill) rather than the two-dose formulation (two 0.75 mg tablets, taken 12 hours apart). "The progestin-only products available in the United States include are /sic!/ Plan B One-Step (1.5 mg), approved by the FDA in July 2009 . . . and several generic forms of Plan B One-Step."[11,p.2]

Antiprogestins (Ulipristal acetate, mifepristone, COX2-inhibitor):

Ulipristal acetate (30 mg in a single dose) is a second-generation antiprogestin and entails, according to some authors, no noteworthy discomfort. "The second-generation antiprogestin ulipristal acetate (30 mg in a single dose) has been studied for use as emergency contraception and has been found to be highly effective and well-tolerated."[11,p.2] It has been marketed for use as emergency contraception in Europe since October 2009; the FDA approved it in August 2010. It is marketed under the brand name ella. In the U.S. it was available for sale by prescription only, but in Europe without prescription as ellaOne.[11,p.2] This easy access to ella has been emphasized in a study which underscores the role of the European Medicines Agency (EMA) for harmonizing the legal status of a drug: "An EMA recommendation can strongly contribute to the harmonization of a drug's legal status in the EU. In most European countries, ulipristal acetate and/or levonorgestrel are now freely available."[14]

Mifepristone:

Another antiprogestin, mifepristone, has also been studied for use as an emergency contraceptive pill.[11,p.2] Mifepristone is a first-generation progesterone receptor modulator that is approved in several countries for early first-trimester medication abortion. Mifepristone has been shown to be highly effective as emergency contraception, with only a few adverse events, such as delayed menstruation following administration. "Mifepristone has been shown to be highly effective for use as emergency contraception, with few side effects (delayed menstruation following the administration of mifepristone is one notable side effect.)"[11,p 2] Despite these advantages, authors hold that the use of mifepristone as an abortion pill will undermine a widespread acceptability for use as ECP. As of 2017, its availability was limited to Armenia, Moldova, Ukraine, China, Russia, and Vietnam.

Regarding mifepristone and its abortogenicity, it should be noted that this problem has been addressed already during the last century. As early as 1995 research in physiology described the mechanism of action by drawing attention to the progesterone receptor and by specifying that the effects of progesterone, similar to those of other steroids, are brought about by an action on DNA to initiate synthesis of new mRNA.[15] The progesterone receptor is bound to a heat shock protein in the absence of the steroid. Binding of progesterone releases the heat shock protein exposing the DNA-binding domain of the receptor. "The synthetic steroid mifepristone (RU-486) binds to the receptor but does not release the heat shock protein, and it blocks the binding of progesterone. Since the maintenance of early pregnancy depends on the stimulatory effect of progesterone on endometrial growth and its inhibition of uterine contractility, mifepristone causes abortion. In some countries, mifepristone combined with a prostaglandin is used to produce elective abortion."[15,p. 409]

COX-2 inhibitor:

The COX-2 inhibitor Meloxicam is considered an effective emergency contraceptive measure if 30 mg are administered for five consecutive days during the late follicular phase and has no bearing on the endocrine status.

"This regimen does not alter the endocrine profile of the cycle and causes no menstrual disturbance."[11,p.2] On the other hand, the COX-2 inhibitor celecoxib does not seem to have a potential for emergency contraception.

As can be seen from the above survey of pills for EC, ongoing studies lead to new insights on their dosage and administration. The most important insights are the absence of harm in case of repeated use of ECPs and the possibility of administering one larger dose once in lieu of two smaller doses twice. In addition to the pills described above, emergency contraception can be implemented also by means of intrauterine devices.

Intrauterine devices (IUD):

Two forms of IUDs have been described, ie, copper-bearing IUDs and levonorgestrel-containing IUDs, the latter with an estimated efficacy of 0.2% for both typical and perfect use, and the copper-bearing with an estimated efficacy of 0.8% (typical use) and 0.6% (perfect use).[8]

Levonorgestrel IUDs have been studied extensively for use as emergency contraception. The active ingredient in Mirena has been indicated by the manufacturer as "levonorgestrel USP, (-)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one."[13,p.2] It has a molecular weight of 312.4 and the molecular formula $C_{21}H_{28}O_2$. Concerning the use and administration of this IUD, it has been emphasized that the release rate decreases from 20 μg/day to 10 μg/day in the course of 5 years. "Mirena contains 52 mg of levonorgestrel. Initially, levonorgestrel is released at a rate of approximately 20 μg/day. This rate decreases progressively to half that value after 5 years."[13,p.14]

Copper IUDs can be inserted up to 5 days after ovulation to prevent pregnancy, because implantation occurs 6-12 days following ovulation. "Thus, if a woman had unprotected intercourse three days before ovulation occurred in that cycle, the IUD could prevent pregnancy if inserted up to 8 days after intercourse."[11,p.2]

As it is difficult, however, to determine with precision the day of ovulation, many protocols recommend insertion up to only 5 days after unprotected intercourse. The latest World Health Organization (WHO) guidelines have been interpreted as recommending IUDs "to be inserted up to day 12 of the cycle with no restrictions and at any other time in the cycle if it is reasonably certain that she is not pregnant."[11,p.2]

Theoretically, a copper IUD can be left in situ to provide effective continuing contraception for up to 12 years, but not all women are eligible for this device, according to a study on Long Acting Reversible Contraception (LARC) of 2016.[7] Women with active sexually transmitted infections (STIs) should avoid it, since insertion of the IUD in these women can lead to pelvic infection, which can cause infertility if not treated. For patients not exposed to STIs it is claimed that there is only a minor risk of pelvic infection following IUD insertion. In addition, it has been stated that the use of a copper IUD is not associated with an increased risk of tubal infertility among nulligravid women, although infection with chlamydia does in fact increase this risk. "Women not exposed to STIs have little risk of pelvic infection following IUD insertion, . . . and use of a copper IUD is not associated with an increased risk of tubal infertility among nulligravid women (whereas infection with chlamydia is)."[11,p.2]

Regarding comparisons of IUDs, one study compared copper IUDs and oral levonorgestrel EC pills with concomitant placement of a levonorgestrel IUD. "More women in this study chose oral LNG EC plus LNG IUD (121 women) over the copper IUD (67 women) at the time of their visit. There were no pregnancies in the copper IUD group, and one pregnancy in the LNG group, which was determined to be an existing luteal phase pregnancy rather than a failure."[11,p.3]

Concerning safety of IUDs, it should be noted that a 2016 study on Long Acting Reversible Contraception (LARC) claims that "Almost all women can safely use IUDs."[7,p.462] However, the list of exceptions deserves attention because it includes a considerable number of conditions such as "women who have hypersensitivity to copper, which would preclude the use of the copper-containing IUD, or hypersensitivity to other components of either type of IUD; women with a current pelvic infection or a sexually

transmitted disease (STD); women with gynecologic cancers; and women with certain other serious medical conditions. Women who have current purulent cervicitis or known chlamydial infection or gonococcal infection should not undergo insertion of an IUD."[7,p.462]

In contrast to this claim of a 2016 study to the effect that almost all woman can safely use IUDs, German research has drawn attention as early as 2000 to one of the most serious complications, namely perforation, especially immediately post partum. Given this risk, German authors recommended insertion only 6 weeks post partum at the earliest. Moreover, they drew attention to additional complications, namely expulsion and ascending infections.[12,p.83]

More recently, a clinical guide of the West Australian government highlights more specific side effects and complications, above all the risk of miscarriage, ectopic pregnancy, and premature birth in case of pregnancy with an IUD in situ.[16] Additional complications have been described as pelvic infection, expulsion (5% average risk), perforation (0.23 %), bleeding irregularities and dysmenorrhea (increased with copper IUDs), vasovagal response to insertion procedure, increased vaginal discharge, and partner dyspareunia due to IUD strings.

An even more detailed list of side effects is provided by the manufacturer of Mirena in a patient information leaflet of 2008 where a dichotomy is established between "serious but uncommon side effects" and "common side effects."[13]

The serious but uncommon side effects include pelvic inflammatory disease (PID), life-threatening infection, embedment (the device adheres to the uterine wall) and perforation. "Common side effects" include discomfort, expulsion, missed menstrual period, changes in bleeding, and cysts on the ovary. Concerning PID, life-threatening complications are admitted: "PID is usually treated with antibiotics. More serious cases of PID may require surgery. A hysterectomy (removal of the uterus) is sometimes needed. In rare cases, infections that start as PID can even cause death."[13,p.32]

Regarding perforation, the loss of efficacy and the serious consequences of dislocation are specified: "If your uterus is perforated, Mirena may no longer prevent pregnancy. It may move outside the uterus and can cause internal scarring, infection, or damage to other organs, and you may need surgery to have Mirena removed."[13,p.32]

Already during placement, discomfort such as "dizziness, faintness, bleeding or cramping may occur," and these are considered common. [13,p.32] Subsequent to placement, expulsion may occur which entails the risk of pregnancy. To prevent this risk, a backup birth control, such as condom is recommended.

Concerning missed menstrual periods, 20% of women seem to be affected. "About 2 out of 10 women stop having periods after 1 year of Mirena use. The periods come back when Mirena is removed."[13,p.32] Regarding bleeding and spotting between menstrual periods, the first 3 to 6 months seem to be the most critical. "Sometimes the bleeding is heavier than usual at first. However, the bleeding usually becomes lighter than usual and may be irregular."[13,p.32] Cysts on the ovary occur in approximately 12% of women using Mirena. "These cysts usually disappear on their own in a month or two. However, cysts can cause pain and sometimes cysts will need surgery."[13, p.33]

Despite the comprehensive enumeration of side effects in the leaflet, the manufacturer takes care to note that this is not a complete list of possible side effects. Furthermore, women are advised to seek medical care in the cases of assumed pregnancy; pelvic pain, or pain during coitus; unusual vaginal discharge or genital sores; or unexplained fever.

In light of presently known adverse events, it should be noted, for historical completeness, that physiology research emphasized succinctly as early as 1995 the drawbacks of IUDs: "Their usefuleness is limited by their tendency to cause intrauterine infections."[15,p.411] Postcoital insertions of copper-bearing IUDs have been reported in the literature since the practice was introduced in 1976, and with only 10 known failures, a pregnancy rate of 0.1% has been claimed.[11,p.5] This pregnancy rate is frequently compared to the pregnancy rate of the non-copper IUD containing levonorgestrel, and there seems to be a higher efficacy of the levonorgestrel-containing IUD over the copper-containing. "Less than 1% of women become pregnant during the first year of IUD use, with pregnancy rates with the LNG-IUD (0.1 to 0.2%) generally reported as lower than the rates with the copper-containing IUD (0.5 to 0.8%)." [7,p.462] These percentages differ significantly from the figures indicated in terms of the Pearl Index, in which levonorgestrel IUDs are considered 0.14 effective, while copper containing IUDs are considered only 0.5-2 effective.[12,p.83]. The fact that such discrepancies in estimates still exist is a major obstacle for women desiring comprehensive information according to the principle of informed consent in oder "to enable an intelligent choice."[4,p.38]

Efficacy of Emergency Contraception:

As mentioned above, the efficacy of ulipristal acetate[11,p.4] has been particularly underscored as the highest among ECPs , and numerous publications reiterate this claim. However, the reliability of this claim is by no means resolved. Statistical reflections draw attention to the problem of measuring a preventive therapy. Such a therapy, it is hypothesized, is best evaluated by comparing the probability that the condition will occur if the therapy is implemented to the probability that it will occur without such implementation. For a number of preventive therapies, eg, vaccines, these probabilities are frequently determined in a randomized clinical trial comparing treatment to a placebo. "In the case of emergency contraception, however, efficacy was demonstrated initially in noncomparative observational studies, and, thereafter, use of a placebo was felt to be unethical. Therefore, the chance that pregnancy would occur in the absence of emergency contraception is estimated indirectly using published data on the probability of pregnancy on each day of the menstrual cycle. This estimate is compared to the actual number of pregnancies observed after treatment in observational treatment trials. Effectiveness is calculated as 1-O/E, where O and E are the observed and expected number of pregnancies, respectively. Calculation of effectiveness, and particularly the denominator of the fraction, involves many assumptions that are difficult to validate."[11,p.3]

Despite such reflections on the problematic assumptions made in statistical studies, data on the effectiveness of EC pills continue to be cited in the literature. Numerous studies have yielded a considerable number of non-congruent estimates by using methodologies of differing qualities.[11,pp.20-21] Also, factors impacting on effectiveness have been identified, such as treatment delay and body mass index. Concerning treatment delay, it is still assumed that efficacy is increased when pills are taken as soon as possible. "However, a pooled analysis of four WHO trials of the levonorgestrel regimen shows no decline in efficacy until day 5, when it may offer no protection at all."[11,p.5] The recommendation to administer ECPs within 120 hours after unprotected cohabitation is still considered valid simply because there are no data disproving it. "No data are available establishing efficacy if ECPs are taken more than 120 hours after intercourse."[11,p.5]

Concerning body mass index (BMI) attention has been drawn to a recent study, where the serum concentration of LNG 1.5 mg was found to be about 50% lower in obese women than in women with a normal BMI. This small pharmacokinetic study also found that doubling the dose of LNG EC, ie, 3.0 mg instead of 1.5 mg, apparently resulted in serum

concentration levels that were similar to those in normal weight women who had taken the regular 1.5 mg dose. Although this study did not measure endpoints more directly related to effectiveness (ovulation or pregnancy), "it suggests that obesity does affect the bioavailability of LNG EC and that doubling the dose of LNG EC for obese women may be a reasonable approach."[11,p.5]

This approach to the question of body mass index advocated by the 2017 study is not supported by other authorities. Thus, the European Medicines Agency (EMA) stated in a press release of 24/07/2014 that the levonorgestrel and ulipristal acetate remain suitable emergency contraceptives for all women, regardless of bodyweight:

"The European Medicines Agency has concluded its review of emergency contraceptives containing levonorgestrel or ulipristal acetate to assess whether increased bodyweight affects the effectiveness of these medicines in preventing unintended pregnancy following unprotected sexual intercourse or contraceptive failure. The Agency's Committee for Medicinal Products for Human Use (CHMP) recommends that these emergency contraceptives can continue to be used in women of all weights as the benefits are considered to outweigh the risks."[17]

Mechanism of action:

Closely related to the question of efficacy is the topic of mechanism of action which has been the focal point of innumerable studies. The results of all these studies are difficult to survey, but one of the essential findings is the insight that combined ECPs containing the estrogen ethinyl estradiol and the progestin levonorgestrel can inhibit or delay ovulation. "This mechanism of action may explain ECP effectiveness when used during the first half of the menstrual cycle, before ovulation has occurred."[11,p.6] As there are studies showing histologic or biochemical alterations in the endometrium after treatment with the regimen, it has been concluded that combined ECPs may impair endometrial receptivity so that implantation of a fertilized egg is antagonized. These effects on the endometrium, however, have not been confirmed by other studies.

Among other possible mechanisms are "interference with corpus luteum function; thickening of the cervical mucus resulting in trapping of sperm; alterations in the tubal transport of sperm, egg, or embryo; and direct inhibition of fertilization."[11,p.6] An additional mechanism could be the intrauterine concentrations of glycodelin, according to a study where levonorgestrel was administered previously to the Luteinizing Hormone (LH) surge and increased the intrauterine concentrations of glycodelin at the time of ovulation. ". . . since glycodelin inhibits fertilization, this result may indicate an additional mechanism of action when ovulation is not inhibited."[11,pp.6-7]

On the basis of several studies the important claim has been made that there is no abortogenicitiy associated with levonorgestrel. "Levonorgestrel does not impair the attachment of human embryos to an in vitro endometrial construct and has no effect on the expression of endometrial receptivity markers."[11,p.7] The claim made in favor of levonorgestrel is also made for ECPs in general, but its validity depends on the definition of pregnancy. Such a definition is provided by some authoritative institutions, including the FDA. "ECPs do not interrupt an established pregnancy, defined by medical authorities such as the United States Food and Drug Administration/National Institutes of Health and the American College of Obstetricians and Gynecologists as beginning with implantation. Therefore, ECPs are not abortifacient."[11,p.8]

As can be seen, the crucial question is the definition of the beginning of pregnancy. However, if implantation is defined as the beginning of pregnancy the ethical question is by no means resolved. In contrast to those U.S. institutions which define implantation as the beginning of pregnancy, German legislation defines the beginning of pregnancy as the completion of implantation, taking into account that implantation is not a punctual event.[3,p.1516] At a higher level of the ethical discussion it is of course not sufficient to determine the beginning of pregnancy in a legalistic fashion; the central question of ethical disputes is the beginning of life. From the perspective of physiology it is clear that the crucial process is the penetration of the sperm though the zona pellucida – facilitated by the trypsinlike protease acrosin. The fusion of a sperm to the membrane of the ovum provides the signal that initiates development. Through furrowing of the zygote, blastomeres emerge. As they divide without growth they diminish in size with each cell division, and the plasma/nucleus relation shifts towards the nucleus. "The developing embryo, now called balstocyst, moves down the tube into the uterus. Once in contact with the endometrium, the blastocyst becomes surrounded by an outer layer of syncytiotrophoblast . . . and an inner layer of cytotrophoblast. . . The syncytiotrophoblast erodes the endometrium, and the blastocyst burrows into it (implantation). The implantation site is usually on the dorsal wall of the uterus. A placenta then develops, and the trophoblast remains associated with it."[15,p.413] This description of implantation in terms of physiology justifies claims that life starts with fertilization because at this moment two essential processes start, namely cell-division and metabolism.

This process described in terms of physiology makes it difficult to uphold the claim that ECPs are not abortifacient. In fact, competent authors do admit that the possibility of implantation of a fertilized egg in the endometrium cannot be ruled out. Concerning this possibility it must be borne in mind that not only ECPs but all regular hormonal contraceptives including oral contraceptive pills, implants, the vaginal NuvaRing, the Evra patch, the injectable Depo-Provera, and even breastfeeding "prevent pregnancy primarily by delaying or inhibiting ovulation and inhibiting fertilization, but it is not scientifically possible to definitively rule out that any of these methods, including breastfeeding, may inhibit implantation of a fertilized egg in the endometrium."[11,p.8] Especially for levonorgestrel and ulipristal acetate it is emphasized that the mechanisms of action "do not involve interference with post-fertilization events."[11,p.8]. This claim, however, cannot be made for EC by means of insertion of a copper IUD where pregnancy can be prevented subsequent to fertilization. "Its very high effectiveness implies that emergency insertion of a copper IUD must be able to prevent pregnancy after fertilization."[11,p.8]

Side effects:

The problem of adverse events, highly important for each women opting for EC, is rarely discussed with the precision that seems appropriate for such a critical issue. Frequently, widely known effects are described without presenting data to support the claims made, and no evidence is provided that side effects resolve in fact as rapidly as claimed. "Side effects include nausea and vomiting, abdominal pain, breast tenderness, headache, dizziness, and fatigue. These usually do not occur for more than a few days after treatment, and they generally resolve within 24 hours."[11,p.9]

Concerning treatment of adverse events, meclizine, a non-prescription anti-nausea medicine allegedly reduces nausea significantly, but increases the risk of drowsiness. Every second woman taking combined ECPs experiences nausea and every fifth vomits. If vomiting occurs within 2 hours after taking a dose, repeating this dose is recommended by some health care providers. The non-prescription anti-nausea medicine meclizine allegedly reduces the risk of nausea by 27% and vomiting by 64% "when two 25 mg tablets are taken 1 hour before combined ECPs, but the risk of drowsiness was doubled (to about 30%)."[11,p.9]

One of the most important claims made with respect to side effects is the superiority of levonorgestrel over the combined regimen. In the

latter, about 50% of the women taking ECPs experience nausea and 20% vomit. "According to a randomized controlled trial conducted by WHO, progestin-only ECPs are associated with an incidence of nausea 50% lower and an incidence of vomiting 70% lower than that for combined ECPs."[11,p.9]

Concerning bleeding several studies found that the length of the menstrual cycle can be reduced if treatment with levonorgestrel is implemented early in the cycle. "Three studies have been specifically designed to assess the effects of ECPs consisting /sic!/ levonorgestrel on bleeding patterns. All three found that the length of the menstrual cycle can be shortened when treatment occurs early in the cycle."[11,p.9]

The first of these studies found "that when taken in the first three weeks of the menstrual cycle, 1.5 mg levonorgestrel in a single dose significantly shortened that cycle as compared both to the usual cycle length and to the cycle length in a comparison group of similar women who had not taken ECPs."[11,p.9] Intermenstrual bleeding was more common after ECP use, than among women who had not taken ECPs.

The second of these studies "compared the baseline cycle with the treatment and post-treatment cycles when 1.5 mg levonorgestrel was administered in a single dose. Cycle length was significantly shortened by one day when ECPs were taken in the preovulatory phase of the cycle. "[11,p.9] Intermenstrual bleeding during the treatment cycle occurred in 15% of the women and "this was significantly more common when ECPs were taken in the preovulatory phase."[11,p.9]

The third study investigated the effects of two 0.75 mg levonorgestrel pills taken 12 hours apart. When ECPs were taken in the follicular phase, they significantly shortened the cycle in comparison with usual cycle length; "no effect on cycle length was found when ECPs were taken in the periovulatory or luteal phase. The post-treatment cycle length was the same as the usual cycle length."[11,p.10] Concerning effects on pregnancy, it has been claimed that no teratogenic effects could be found and that there is no reason for concerns about birth defects.

"Combined data from postmarketing surveillance and clinical trials of UPA found no teratogenic effects among 232 pregnancies with a known outcome in which the woman and conceptus were exposed to ulipristal. Moreover, two observations provide reassurance for any concern about birth defects."[11,p.10]

Regarding breast feeding, it has been underscored that there is hardly any risk of pregnancy during the first 6 weeks for women who are fully breastfeeding and amenorrheic. In a study on the levonorgestrel pharmacokinetics in plasma and milk of lactating women who took 1.5 mg for emergency contraception the authors recommend avoiding infant exposure to the period of maximum LNG excretion in milk. "Mothers should discontinue nursing for at least 8 hours, but not more than 24 hours, after taking ECPs."[11,p.10] Other recommendations have been formulated in various guidelines. "European guidelines have been updated to reflect that ellaOne is not contraindicated for breastfeeding women, but that breastmilk should not be given to a baby for a week after a woman has taken the product."[11,p.11] These guidelines are not generally accepted, and in the U.S. different recommendations have been formulated. "However, the US Medical Eligibility Criteria for Contraceptive Use recommends that breastfeeding women refrain from breastfeeding and discard pumped milk for 24 hours."[11,p.11]

Drug interactions:

The comprehensive study on EC of 2017[11] does not present any data on interactions and asserts that "no specific data are available about the interactions of ECPs with other drugs"[11,p.11] Instead of gathering data, it is assumed that drug interactions are similar to those with regular oral contraceptive pills. The classification of these interactions has been attempted as early as 2000 by German authors.[12,p.72] According to this classification some of the most important interactions are: inhibition of cytochrom-P450 through oral contraceptives in case of coumarins, benzodiazepines, cyclosporine, tricyclic antidepressant drugs (eg, imipramine and amitriptyline), and pethidine (meperidine, an analgesic drug used as the hydrochloric salt); the induction of hepatic enzymes through oral contraceptive pills in case of non-steroidal anti-inflammatory drugs; cytochrom P450 induction through barbiturates, carbamazepine, rifampicin, and phenytoin.

What is true about EC in general is also true for the levonorgestrel-containing IUD. The patient information leaflet states specifically that the influence of drugs on the contraceptive efficacy of Mirena has not been studied, but an increased drug-metabolism is assumed whenever liver enzymes are induced by a drug. "The metabolism of progestogens may be increased by concomitant use of substances known to induce drug-metabolizing liver enzymes, specifically cytochrome P450 enzymes."[13,p.12]

The reduction of efficacy of EC is one of the most relevant interactions, and women taking drugs are advised that rifampicin, certain anticonvulsant drugs, Saint John's wort and certain antiretroviral agents may reduce the efficacy of ECPs. "Consideration may be given to increasing the amount of hormone administered in the ECPs, either by increasing the amount of hormone in one or both doses, or by giving an extra dose."[11,p.11]

An important question in this context is the transition from EC into a regular form of contraception, and implications have been indicated for immediately starting progestin-containing hormonal contraceptives after taking ulipristal acetate, which, it must be remembered, is an antiprogestin. One study found no difference in the time, ie, 14 days, necessary to achieve ovarian quiescence when the placebo group was compared to the group who took combined oral contraceptives for 14 days. According to some authors, this finding implies that women should abstain or use a condom for 14 days when quick-starting combined hormonal contraceptives.[18]

Another pharmacodynamic study examined women who quick-started a desogestrel progestin-only oral contraceptive (75 µg desogestrel, which is not available in the US) after taking UPA or a placebo.[19] "No significant differences were found in time to ovarian quiescence or cervical mucus penetrability."[11,p.11]

On the basis of such studies, the FDA advises women who wish to use hormonal contraception after using ella, to do so no sooner than 5 days after the intake of ella and to use a reliable barrier method until the next menstrual period. The European Medicines Agency (EMA) did not decide to modify its clinical recommendations for ella concerning quick-starting a progestin-only oral contraceptive which might reduce the efficacy of UPA.

The American Society for Emergency Contraception offers a patient-centered protocol for the implementation of ongoing contraception subsequent to EC by taking into consideration the specific method chosen by the woman. Crucial parameters are the necessity of placement by a healthcare provider, the woman's willingness to return for a follow-up contraception visit (if she choses a provider-dependent method), "and whether she is at greater risk of pregnancy from the previous act of intercourse or future acts of intercourse."[11,p.11]

As the foregoing analysis of drug interactions and side effects shows, numerous adverse events are associated with the use of EC. The question therefore arises as to whether side effects, risks, and complications can have a serious impact on a woman's health and her quality of life,[20] a topic that is most properly discussed under the heading "safety."

Safety of EC:

In a discussion of the concept of "safety" one must assume that most women will understand safe as not harmful in the sense of the ethical principle "nil nocere" (no harm). Of course, "safe" can be interpreted also as meaning effective in preventing pregnancy or suitable for avoiding sexually transmitted infections (STI). In addition, the meaning of "safe period" should be borne in mind which in the past (1979) has been defined as "the nonovulatory phase of the menstrual cycle, when conception cannot occur. Since the time of ovulation is variable in different women, the safe period is also variable."[2,p.719]

The comprehensive 2017 study on EC defines safety with referenc to death or serious complications: "No deaths or serious complications have been causally linked to emergency contraception. According to the U.S. Medical Eligibility Criteria for Contraceptive Use (US MEC), there are no situations in which the risks of using combined, progestin-only or ulipristal acetate ECPs outweigh the benefits."[11,p.8]

With reference to the United States Medical Eligibility Criteria for Contraceptive Use (US MEC) it is assumed that ECPs can be used also by women with previous ectopic pregnancy, cardiovascular disease, migraines, and liver disease and women who are breastfeeding. "Given the very short duration of exposure and low total hormone content, combined ECP treatment can be considered safe for women who would ordinarily be cautioned against use of combined oral contraceptives for ongoing contraception."[11,p.8]

As to the danger of thrombosis reference is made to a rather outdated study of 1993 [21], and based on this study it is asserted that no alteration of clotting factors has been detected subsequent to combined ECP treatment. However, in cases where a woman has a history of stroke or blood clots in the lung or legs "ulipristal acetate or progestin-only ECPs or insertion of a copper IUD may be preferable to use of combined ECPs."[11,p.8] The most pertinent conditions for safety cautions, ie, pregnancy, migraine, or history of thromboembolism, are identified through medical history screening so that there is no need for a woman desiring combined ECPs to undergo pelvic exam or laboratory tests.[11,p.8]

One of the crucial questions is safety in case of ECP use over a longer period of time, especially in view of the frequently encountered warning that EC should not be used as a regular form of contraception.[12,p.82] Although no data are available on the safety of current regimens of ECPs if used frequently over a long period of time, there is experience with similar regimens.[22] "However, a pharmacodynamic study of repeated use of UPA EC (every 7 days for 8 weeks) showed no safety concerns, indicating that UPA can be safely used more than once per cycle."[11,p.9] In the same vein, review by the Centers for Disease Control (CDC) and the WHO did not give rise to any safety concerns. "In addition, recent comprehensive review by CDC/WHO did not suggest any special safety concerns for the use of any type of ECPs among women with particular medical conditions or personal characteristics, such as pregnancy, lactation or frequent ECP use."[11,p.9]

Such studies indicating that UPA can be used safely more than once per cycle and studies suggesting no special safety concerns for the use of ECPs by women with particular medical conditions or personal characteristics support the claim made by this author: EC can truly be considered as one of the most convenient contraceptive measures presently available, suitable to prevent unintended pregnancy and abortion. This holds true also for such indications as unprotected intercourse, failure of the contraceptive method used, or sexual assault. Moreover, its potential for reducing the numer of unintended pregnancies and abortions is of socio-economic importance and should be the target of future research. What should be clarified too is the accessibility of EC, ie, the question of prescription and availability for special populations, such as teenagers.

Non-hormonal methods

Despite undeniable advantages of Emergency Contraception, adverse events, risks and complications can be serious, and some women might be willing to embark on birth control only under the condition that risks can be precluded. Prevention of harm seems possible owing to the existence of non-hormonal methods. Some of these methods are being investigated according to principles of evidence-based medicine. In particular, the so-called "fertility awareness-based" methods (FAB) – also designated as periodic abstinence or natural family planning - receive increasingly attention, especially in Western Europe where the first investigations took place.[12,pp.61-64] Van de Velde from the Netherlands described the Basal Body Temperature method als early as 1927. The Japanese Ogino (1932) and the Austrian Knaus (1933) were instrumental in developing the Calendar method (also designated as "rhythm"), and in 1964 the

Table 2: Safety – Efficacy – Convenience – Cost Ranking (SECCR), 2018.

(Based on WHO, 2018, FDA, 2013, and CT Failure table, 2011. Efficacy is indicated as percentage of women experiencing an unintended pregnancy within the first year of use).

Method	**Safety** (no harm in the sense of "nil nocere")	**Efficacy Perfect-Typical use**	**Convenience**	**Cost & Specifications**
Symptothermal	High	0.4-24	High	No cost. Body temperature must be measured, cervical mucus must be observed (clear texture), cervix must be palpated (soft consistency and open).
Ovulation (based on cervical mucus)	High	3-24	High	No cost. Cervical mucus must be observed ("spinnbarkeit")
TwoDay (based on cervical mucus)	High	4-24	High	No cost. Coitus must be avoided during fertile days. Fertile days determined by presence of cervical mucus (color and consistency). Coitus may be resumed after 2 consecutive dry days (or absence of secretion).

Standard Days Method (SDM) – based on calendar	High	5-24	High	No cost. Fertile period is tracked and coitus avoided (usually days 8-19 of each 26-32 day cycle).
Basal Body Temperature (BBT)	High	1-25	High	No cost. Fertile phase has passed when body temperature has risen (0.2-0.5° C) and remained such for 3 days. Conception is unlikely from 4th day following rise of temperature until next menstruation.
Calendar (rhythm) method	High	9-25	High	No cost. Menstrual cycle is monitored for at least 6 months. 18 is subtracted from shortest cycle (this is the estimated first fertile day). 11 is subtracted from the shortest cycle (this is the estimated last fertile day). Caution when drugs are used (NSAID, certain antibiotics, anxiolytics, anti-depressants, etc.).
Male condoms	Moderate	2-18 .	High	Low cost. Protects against sexually transmitted diseases (STD) including HIV.
Female condom	Moderate	5-21	Moderate	Moderate cost. Prevents contact between sperm and egg. Protects against sexually transmitted diseases (STD) including HIV (according to WHO).
Implant (Small, flexible rod or capsule placed under the skin of the upper arm; contains progestogen hormone only).	Moderate	0.05-0.05	High	High cost. Implanted by clinician. Irregular vaginal bleeding common.
Mirena (LNG) Intrauterine device (IUD) (T-shaped plastic device inserted into the uterus; releases continuously small amounts of levonorgestrel).	Moderate	0.2-0.2	Moderate	High cost. Prevents contact between sperm and egg by thickening cervical mucus. Amenorrhea.
ParaGard (copper IUD)	Moderate	0.6-0.8	Moderate	High cost. Copper component damages sperms.
Depo-Provera	Moderate	0.2-6	Moderate	High cost.
Combined oral contraceptives (COCs)= "the pill"	Moderate	0.3-9	Moderate	Moderate cost. Contains estrogen and progestogen.
Progestogen-only pill (POP) or "minipill"	Moderate	1-3 (10)	Moderate	Moderate cost. Thickens cervical mucus and prevents ovulation.

Evra patch	Moderate	0.3-9	Moderate	High cost.
NuvaRing	Moderate	0.3-9	Moderate	High cost.
Combined contraceptive patch and combined contraceptive vaginal ring (CVR)	Moderate	1-8(?) (Research on efficacy limited).	Low	High cost. Continuously releases a progestin and an estrogen directly through the skin (patch) or from the ring. Prevents ovulation, copper component damages sperms. Pharmaco-kinetic profile comparable to COCs.
Monthly injectables or combined injectable contraceptives (CIC)	Moderate	1-3	Low	High cost. Irregular vaginal bleeding. Injected monthly into muscle.
Progestogen-only injectables	Moderate	1-3	Low	High cost. Injected into the muscle or under the skin every 2 or 3 months, depending on product. Irregular vaginal bleeding; delayed return to fertility after use.
Diaphragm	Moderate	6-12	Low	High cost. Must be used for each coitus.
Emergency Contraception (EC)	Moderate - Low	1-15	High	Moderate cost. Pills (ulipristal acetate 30 mg or levonorgestrel 1.5 mg) must be taken twice to prevent pregnancy up to 5 days after coitus. Alternatively IUD (copper or levonorgestrel) to be inserted.
Lactational Amenorrhea (LAM)	High	1-2	Moderate	No cost. Effective in preventing ovulation as long as monthly bleeding has not yet returned. Requires exclusive breastfeeding day and night of infant less than 6 months old.
Male sterilization (vasectomy)	Moderate	<1 (after 3-months semen evaluation). 2-3 (without semen evaluation).	High	High cost. Surgical intervention. Permanent contraception by cutting vas deferens tubes which transport sperm from the testicles.
Female sterilization (tubal ligation)	Low	0.5-0.5	Moderate-Low	High cost. Surgical intervention. Permanent contraception by blocking or cutting the fallopian tubes.
Sponge	Moderate	20-24 - parous women 9-12-nulliparous women	Moderate	Moderate cost. To be used for each coitus.
Spermicides	Moderate	18-28	High	Moderate cost.

Australian John Billings delineated the Ovulation or Cervical Mucus method as a result of extensive research on fertility. The latter was then amalgamated with the other methods and defined as symptothermal method by the Austrian Rötzer. Extensive discussion of these methods and their assessments have been presented recently in a scholarly investigation. [23]

So far, these methods have received only sporadic attention because their main benefit, namely safety in the sense of no harm, has been considered only marginally in ratings and rankings. In order to rectify this deficit, it sems appropriate to conceive of new ways of rating and ranking contraceptive methods and include also the hitherto neglected parameter safety. In a ranking which gives priority to safety over efficacy and convenience, non-hormonal methods would be ranked highest, as can be seen from Table 2 (Safety – Efficacy - Convenience - Cost Ranking, 2018).

Conclusion and Implications

The foregoing discussion has delineated the salient features of EC and has drawn special attention to new insights, such as repeated use of ECPs, dosage to be administered, and safety concerns. Regarding the latter it is obvious that EC has its limitations and is as problematic as other hormonal methods of contraception for women with intolerance to hormones and devices. In order to meet the needs of these women, who are at a particular risk of unintended pregnancy, non-hormonal methods might be an effective alternative, although they belong to the category of a priori birth control. However, with the availability of EC as ultima ratio contraception, they might prove to be a viable option for women refraining from the use of hormones and devices.

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