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Review article

Advance supply of emergency contraception: a systematic review ☆

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Abstract

Background: Emergency contraceptive pills (ECPs) are an underutilized means to reduce unintended pregnancy. Advance provision of ECPs may increase timely use, thereby decreasing risk of unintended pregnancy.
Study Design: We searched MEDLINE and EMBASE through February 2012 for randomized, controlled trials (RCTs) pertaining to safety and efficacy of advance provision of ECP. The quality of each individual study was evaluated using the United States Preventive Services Task Force evidence grading system.
Results: The search strategy identified 714 articles. Seventeen papers reported on safety or efficacy of advance ECPs in adult or adolescent women. Any use of ECPs was two to seven times greater among women who received an advanced supply of ECP. However, a summary estimate (RR 0.90, 95% CI 0.69–1.18) of four RCTs did not demonstrate a significant reduction in unintended pregnancy over 12 months when advance provision was compared with standard provision of ECPs. Patterns of contraceptive use, pregnancy rates and incidence of sexually transmitted infections did not vary between treatment and control groups in the majority of studies among either adults or adolescents.
Conclusion: Available evidence supports the safety of advance provision of ECPs. Efficacy of advance provision compared with standard provision of ECPs in reducing unintended pregnancy rates at the population level has not been demonstrated.

Keywords: Advance supply; Emergency contraception; Post coital contraception

1. Introduction

Unintended pregnancy is a critical public health issue, carrying significant personal, social, and economic costs as well as medical risks [1,2]. Unintended pregnancy is endemic in the United States (US), where nearly half of all pregnancies are unintended [3]. Emergency contraceptive pills (ECPs) are an underutilized option to reduce unintended pregnancy [4].

ECPs offer alternatives to women who have unprotected intercourse and do not wish to become pregnant [5–7]. Several formulations of ECPs exist. The most commonly used methods consist of combined doses of estrogen and progestin, or levonorgestrel alone (LNG), or ulipristal acetate (UA). When initiated within 72 h and taken correctly, ECPs are estimated to prevent between 49% and 95% of unwanted pregnancies [8,9]. ECPs remain efficacious through 96 h following unprotected intercourse, and possibly through 120 h [9,10].

Timely access to ECPs is essential to ensuring effective use. Offering women an advance supply of ECPs, when they seek routine reproductive health care, has been proposed as a way to reduce barriers to timely use of ECPs [11,12]. Advance ECPs provision has been shown to be a cost saving measure, as well as to provide opportunities for health care providers to offer additional counseling on contraception and sexually transmitted infection (STI) prevention [4,13–15].

However, increasing access to ECPs through advanced provision remains controversial. Opponents have raised concerns that easier access to ECPs will promote promiscuity and riskier sexual behavior [14], and that women will rely on ECPs for contraception, instead of using a primary, more effective method [11,15].

☆ Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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This review summarizes the evidence available concerning safety and efficacy of advance provision of ECPs.

2. Materials and methods

We searched the MEDLINE and EMBASE databases for peer-reviewed articles concerning advance provision of emergency contraception to women of reproductive age published in any language from 1980 through February 2012. Search terms included: (Contraceptives, Postcoital [MeSH] OR Contraception, Postcoital [MeSH] OR Contraceptives, Postcoital [Pharmacological Action] OR Emergency contracept* OR Contracept* emergency OR Morning after pill OR Morning-after pill OR Postcoital contracept*) AND (Self Administration [MeSH] OR Advance* provision OR Advance* access OR Provision OR Access OR Home).

The search strategy identified a total of 714 articles. We included randomized controlled trials (RCTs) and subanalyses investigating advance supply of ECPs containing both estrogen and progestin, LNG alone or UA. Studies of other formulations, including mifepristone, or intrauterine device provision for emergency contraception were not included in this review. In addition, health care provider-based surveys, evaluations of advanced provision services without information on the impact of advanced provision, and studies describing over-the-counter provision of ECPs were excluded.

All authors participated in summarizing and systematically assessing the evidence through the use of standard data abstraction forms [16]. The quality of each individual piece of evidence was assessed using the United States Preventive Services Task Force grading system [17].

The presence of heterogeneity with respect to study designs, population characteristics, study population recruitment, extent of loss to follow-up and outcome measure definitions did not permit us to compute summary measures of association for all outcomes of included studies. A summary risk ratio was calculated for pregnancy at 12 months. Treatment effects were calculated using risk ratio estimates (RR) with 95% confidence intervals (95% CI) with the Review Manager software. A fixed effect model was applied.

3. Results

The search yielded 714 articles. Seventeen articles from 14 studies met inclusion criteria (characteristics of included studies are presented in Tables 1 and 2). All but three studies investigated the use of LNG and the remainder used the combined estrogen/progestin (Yuzpe) regimen. No studies were identified of advance provision of UA.

A summary risk ratio of risk of pregnancy was calculated for four RCTs that assessed this outcome at 12 months by advanced or standard provision of ECPs (Fig. 1) [1,19,26,32]. These studies were selected, as they were the only four that reported pregnancy rates at 12 months with ECPs used in the US. The four trials included data from adults and adolescents. Advance provision of ECPs did not result in a statistically significant reduction in pregnancy at 12 months when compared with standard provision (RR 0.97, 95% CI 0.77–1.22).

3.1. Adults

Twelve papers from nine RCTs were identified that examined safety and efficacy of advance provision of ECPs to an adult population. An adult population was considered as any study that was not confined to women under age 20 years. The first RCT enrolled 446 women at risk of pregnancy who sought care at two urgent care clinics to assess the impact of advance supply of ECPs [21]. Women assigned to the intervention group received one package of ECPs and a 15 minute computerized educational session on the correct use of ECPs, the use of contraception and pregnancy risk. Controls received a similarly styled session about periconception folic acid use only. Participants were surveyed by phone approximately 6 months after enrolment. Rates of ECPs use were not significantly different between the two groups (Intervention=10%, Control=4%; p=.06). However, after adjusting for baseline characteristics (age, race, income, education, site of enrollment), women in the intervention group were more likely to use ECPs if needed (OR=7.17, 95% CI 1.38–37.21). This difference persisted despite large losses to follow-up in both groups. Use of condoms, hormonal contraception and incidence of sexual intercourse without a condom were similar in both groups.

Raymond et al. sought to determine how advance ECPs provision would affect rates of pregnancy and STIs [19]. A total of 1490 women were randomized to intervention and control groups. Both groups received education about ECPs; however, the intervention group also received two packs of ECPs and unlimited, free refills for 1 year. Participants underwent clinical follow-up, which included pregnancy and STI testing, at 6 and 12 months, and telephone survey follow-up of contraceptive and sexual practices, at 2, 4, 8 and 10 months post randomization. Overall study completion was 93%. The intervention group used ECPs more frequently (median use: 2 vs. 0; p<.01) and more promptly (12 vs. 36 h; p<.01) than did the control group. Pregnancy rates, rates of STIs, contraceptive use and sexual activity unprotected by contraceptives did not differ between the two groups at any of the follow-up points.

Three secondary analyses were subsequently performed on this data [20,22,33]. One reanalysis examined the timing of ECPs use, coital patterns and use of other contraceptive methods during menstrual cycles ending in pregnancy in the original RCT [22]. The objective was to determine if the pregnancies that occurred were due to ECPs failure or an increased use of ECPs (in lieu of other contraceptives) during high-risk cycles. Cycles were defined as fully or partially

Table 1
Evidence for advanced provision of emergency contraception pills: adults

Author Year	Study Design	Population	Results	Strengths	Weaknesses	Grade
Weaver et al. 2009 [18]	Secondary data analysis of RCT [19] Evaluated Substitution of EC for contraception between groups	1490 sexually active women	Substituted EC for other contraception: 6 months Advance supply 0.52 substitutions Standard access 0.14 substitutions p<.001 12 months Advance supply .59 substitutions Standard access .18 substitutions p<.001		Non validated psychosocial framework.	
Baecher et al. 2009 [20]	Secondary data analysis of RCT [19] Used predictive modeling to estimate pregnancy risk factors and patterns of EC use	1490 sexually active women	Low risk for pregnancy: Mean EC uses: Advance supply 2.31 mean EC uses Standard access .28 mean EC uses RR 10.0 with advance supply High risk for pregnancy: mean EC uses: Advance supply 3.08 mean EC uses Standard access .48 mean EC uses RR 5.5 with advance supply		20% loss to follow-up	
Schwarz et al. 2008 [21]	RCT USA 2 urgent care clinics 6-month follow-up	446 women (18–45 years) Excluded women unlikely to become pregnant, planned to relocate, or did not have phone Intervention (n=219): ECPs computer education module and 1 pkg of LNG tablets Control (n=227): folic acid computer education	Self-reported use of ECPs: Intervention group 10%, control group 4%, p=.06 OR=7.17 (95% CI 1.38–37.21)	Intention to treat analysis	High loss to follow-up: 42% in intervention, 39% in control Inadequate power given loss to follow-up Self-report of ECP use and pregnancy data	I, Poor, Direct
Raymond et al. 2006 [19]	RCT USA 6 and 12 month clinic follow-up; 2, 4, 8 and 10 month survey follow-up	1490 sexually active women (14–24 years) Excluded used or planned use of longer term methods, pregnant within 6 weeks or breastfeeding. Intervention: given 2 packs of LNG tablets, with unlimited free refill, and ECP education Control: ECP education and told how to access ECP	Median ECP Use Intervention=2, control=0 (p<.01) Time to ECP Use (median) Intervention=12 h, control=36 h, p<.01 Pregnancy Hazard ratio 0.95, 95% CI 0.68–1.33, log-rank p=.78 STIs Hazard ratio 0.91, 95% CI 0.66–1.26 Use of other contraceptives (any method) Intervention=96%, control=94% (5–7-month follow-up) Intervention=91%, control=93% (12–14 months of follow-up) Sex without condom at least once	High study completion rate (93%) Objective pregnancy and STI testing at baseline and follow-up	Higher proportion of women with STIs at baseline in AEC group (8% vs. 5%) Self reported use of ECP and contraception	I, Good, Direct

			Intervention=65%, control=61% (5–7-month follow-up) Intervention=57%, control=61% (12–14-month follow-up) Sex without contraceptive at least once Intervention=18%, control=15% (5–7-month follow-up) Intervention=15%, control=17% (12–14-month follow-up)			
Raymond et al. 2008 [22]	Secondary data analysis of RCT [19] USA	19 menstrual cycles where pregnancy occurred Inclusion/exclusion criteria same as for RCT	Pregnancies resulting from EC failure Probable failure: intervention 29%, control 0%, Fisher's p=.058 Possible failure: intervention 41%, control 50%, no p given Probable+possible failure: intervention 12 (71%), control 1(50%), p=.012 Protection from pregnancy during cycles resulting in pregnancy Fully protected, partially protected, entirely unprotected not significantly different between groups. "More than one entirely unprotected coital act": Intervention 34%, control 16%, p=.017		Very small n Self-reported ECP use and some pregnancy data Potential for large measurement error in determining ovulation	III, Poor, Indirect
Walsh et al. 2006 [23]	RCT USA 31 community clinics in California 3–9 month survey follow-up	1090 women aged 15–45 with oversampling of certain age and ethnic groups Excluded pregnant women and women seeking pregnancy Intervention: given 1 pack LNG tables and info Control: ECP information	ECP use Intervention=19%, control=12% (p=.0009) Use within 12 h Intervention=43%, control=28% (p≤0.06) Pregnancy Intervention=5%, control=4% (not significant) Hormonal contraceptive use Intervention=65%, control=69% (not significant) Barrier contraceptive use Intervention=27%, control=23% (not significant) Unprotected intercourse/risk events Condom failure: Intervention=10%, control=10% Withdrawal: Intervention=33%, control=32% Incorrect hormonal use: Intervention=16%, control=17% Unprotected intercourse: Intervention=19%, control=22% (none significant)	Large N, community based	Self-report of outcomes 15% of control likely received advance ECPs due to protocol deviations Response bias Selection bias	I, Poor, Direct

(*continued on next page*)

Table 1 (*continued*)

Author Year	Study Design	Population	Results	Strengths	Weaknesses	Grade
Raine et al. 2005 [24]	RCT USA 4 Family planning clinics 6 months of follow-up	2117 women (15–24 years) Not seeking ECP, using long-term hormonal contraception, or desiring pregnancy 1) Provision of 3 packs LNG ECP (Adv, *n*=826) 2) Pharmacy ECP access (*n*=814) 3) Control (*n*=310)	ECP use Adv=37%, pharmacy=24%, control=21% (p<.001) Condom use at last intercourse Adv=47%, pharmacy=49%, control=54% Adv vs. control: OR=0.79 (95 % CI 0.60–1.04) STIs Adv=11%, pharmacy=12.5%, control=12% Adv vs. control: OR=0.94 (95% CI 0.62–1.44) Pregnancy Adv=8%, pharmacy=7%, control=9% Adv vs. control: OR=1.10 (95 % CI 0.66–1.84)	Adequate randomization Self-reported behavior linked to STI biomarkers (CT, HSV-2), thorough multivariable analysis	Did not follow intent-to-treat analysis completely, possible cross over of controls to pharmacy group	I, Fair, Direct
Lo et al. 2004 [25]	Randomized controlled trial Hong Kong Recruited from youth health center and birth control clinic 12 months of follow-up	1030 women (18–49 years) using less effective methods Intervention: 3 courses LNG ECP (*n*=515), Control (*n*=515)	Mean no. of ECP courses Overall: intervention=0.56±1.21 SD, control=0.20±0.59 SD (p<.001) <26 years: Intervention=0.99±1.74 SD, Control=0.32±0.79 SD ≥ 26 years: Intervention=0.39±0.88 SD, Control=0.15±0.48 SD Time to ECP use (mean) Intervention=13.9 h±14.4 h SD, Control=28.5±19.8 h SD (p<.001) Contraceptive behavior Similar between groups, unchanged during and after study Pregnancy Intervention=8 pregnancies, 5 did not take ECP, Control=9 pregnancies, none used ECP	Randomized study with appropriate allocation Follow-up every 3 months Intent to treat analysis Large sample Developing world location	Population selection from two different clinic settings	I, Good, Direct
Jackson et al. 2003 [26]	Randomized controlled trial USA Public hospital 12 months of follow-up	370 post partum women (Mean age=26.6) Intervention: 1 pack LNG ECPs Control: routine contraceptive counseling	ECP use Intervention=17% Control=4% RR 4.0, 95% CI 1.8–9.0). ECP use after unprotected sex Intervention=25%, control=4%, RR=5.8 (95% CI 2.1–16.4) Sexual behavior No difference in unprotected sex	Randomized trial Multivariable analysis	No blinding of treatment group Adjusted for only cluster design only	I, Good, Direct

Ellertson et al. 2001 [11]	Randomized controlled trial Pune, India Family planning clinic clients 12 months of follow-up	411 condom users (Mean age=25.1) Intervention: 3 courses Yuzpe Control: Information	ECP use after unprotected sex Intervention=79%, control=44% Unprotected sex Intervention=7.6%, control=5.7% 98% of intervention group reported that advanced supply did not make them take chances with condoms No pregnancies reported	Randomized controlled trial in developing country Adjusted for time in study	Loss to follow-up=19% Nature of unprotected sex not known No adjustment for other confounders	I, Fair, Direct
Hazari et al. 2000 [27]	RCT Mumbai, India Clinic population 3-month follow-up	198 women not pregnant, using condoms 1) Intervention: one pack of pills in Yuzpe method 2) Control: told to come to clinic for ECP	Use of ECP Intervention=32%; control=29% OR=1.15 (95% CI 0.63–2.11) Unprotected coital acts Intervention=47%; control=41% OR=1.28, 95% CI=0.73–2.24	High rate of study completion	Little explanation of methodology and data analysis Poor reporting of participant demographics	I, Fair, Direct
Glasier et al. 1998 [28]	RCT Scotland Hospital and family planning clinic clients 12 months of follow-up	1083 women (16–44 years) Intervention: 1 pack LNG ECP Control: information only	EC use (intervention, control) ECP once 36%, 45% ECP ×2 7%, 10% ECP ×3 3%, 2% ECP 4+1%<1% No contraceptive use Baseline: intervention=10%, control=. 10% 12 months: intervention=6%, control=4% Pregnancy Intervention=28, control=33 Abortions Intervention=3%, control=4%	Prospective study with comparative group, random assignment	High loss to follow-up, no control for confounding variables, no blinding	I, Fair, Direct

Table 2
Evidence for advanced provision of emergency contraception pills — adolescents

Author Year	Study Design	Population	Results	Strengths	Weaknesses	Grade
Schreiber et al. 2010 [1]	RCT USA	50 postpartum teens Intervention: Advance ECPs Control: Routine postpartum care	Pregnancy Intervention 3/28, control 8/30 OR 0.57 (95% CI 0.20–1.60, p=.23)	High retention rate (78% at one year)	Not powered for statistical significance	I, Fair, Direct
Ekstrand et al. 2008 [29]	RCT Sweden Swedish youth clinic in university town 3 week return appointment for pregnancy test/3 month and 6 month telephone interview	420 teenage girls (15–19 years) requesting ECPs Intervention: immediate pack of ECPs, second pack of ECPs, condoms, and ECP information (n=214) Control: immediate pack of ECPs (n=206)	ECP Use 3 months: Intervention=24%, control=13% (p=.02) 6 months: Intervention=31%, control=19% (p=.01 Time to ECP Use (mean) 3 months: Intervention=13.61 h, control=25.47 (p=.007) 6 months: Intervention=15.57 h, control=26.38 (p=.006) Contraceptive use and sexual risk taking not significantly different between groups	Adequate sample size (80% power, 5% significance level)	Loss to follow-up of 22% Differential loss: non-Nordic girls 36.4%, Nordic girls 19.6% (p<.01); smokers 38.4%, non-smokers 20.5% (p<.01) Self report of ECP use and contraceptive use Recall bias	I, Fair, Direct
Belzer et al. 2005 [30]	RCT USA Adolescent parent case management program locations or events 12 months of follow-up (telephone interview)	160 adolescent mothers (13–20 years, mean 17.2 years) Excluded IUD and Norplant users and girls attempting pregnancy Intervention: 1 pkg of LNG ECPs (n=82) Control: information only (n=78)	ECP use 6 months: Intervention=83%, control=11% (p<.01) 12 months: Intervention=64%, control=17% (p<.01) Frequency of ECP use no significant difference between groups at 6 or 12 months Unprotected intercourse within past 6 months Baseline: Intervention=60%, control=60% 6 months: Intervention=68%, control=54% 12 months: Intervention=69%, control=45% (p=.02) No contraceptive method Baseline: Intervention=26%, control=9% 6 months: Intervention=17%, control=14% 12 months: Intervention=35%, control=18% Self reported pregnancy: 6 months: Intervention=4, control=10 control 12 months: no difference	Adolescent population at risk of pregnancy 12-month follow-up	High rate of loss to follow-up: Intervention=48%, control=38% at 12 months Limited frequency of follow-up Limited analysis of data Self report of pregnancy data Rate of unprotected intercourse not quantified Unable to determine if ECP used after unprotected intercourse Recall bias	I, Poor, Direct

Harper et al. 2005 [24]	Age-stratified analysis of RCT by Raine et al.[28] USA 4 Family planning clinics 6 months of follow-up	2117 women (20–24 year=1153, 18–19 years=481, 16–17 years=393, <16 years=90, <20 years=694) Not seeking ECP, using long-term hormonal contraception, or desiring pregnancy 1) Provision of 3 packs LNG ECP (Adv, *n*=826) 2) Pharmacy ECP access (*n*=814) 3) Control (*n*=310)	ECP use Teens: Adv=44% pharmacy=33%, Control=29% (p<.001) Overall: Teens=36%, adults=24% (p=NS) Multiple sexual partners No variation by age group, or ECP access Condom use <16=67%, 16–17=54%, 18–19=48%, adult=39% (p=NS) STIs No difference by ECP access or age Pregnancy <16=14%, 16–17=12%, 18–19=8% No difference among teens by study arm Overall: Teens=10%, adults=6% (p<.01)	Detailed analysis of adolescents vs. adults High power (86%) to detect differences between intervention and control groups Low loss to follow-up (7%), no differential loss Multiple packs of ECP given	Selected study population from health clinics Fewer very young adolescents	I, Good, Direct
Gold et al. 2004 [31]	RCT USA Hospital-based adolescent clinic 6 months of follow-up	301 women (15–20 years) Not using long acting contraceptive methods; COC users included Intervention: 1 pack Yuzpe or LNG ECP(*n*=150) Controls (*n*=151)	ECP use 1 month: Intervention=15%, control=8% (p=.05) 6 months: Intervention=8%, control=6% (p=.54) Time to ECP use (median) Intervention=11.4 h, control=21.8 (p=.005) Unprotected intercourse, past month 1 month: Intervention=28%, control=32% 6 months: Intervention=26%, control=. 26% Condom use, past month 1 month: Intervention=68%, control=70% (p=.73) 6 months: Intervention=77%, control=62% (p=.02) Hormonal contraception use, past month 1 month: Intervention=39%, control=42% 6 months: Intervention=44%, control=53% No significant differences in contraceptive use or unprotected intercourse at 1 month or 6 months of follow-up	Random assignment Monthly phone follow-up Adolescent population	High loss to follow-up (>20%) Differential loss to follow-up One course ECP offered	I, Fair, Direct

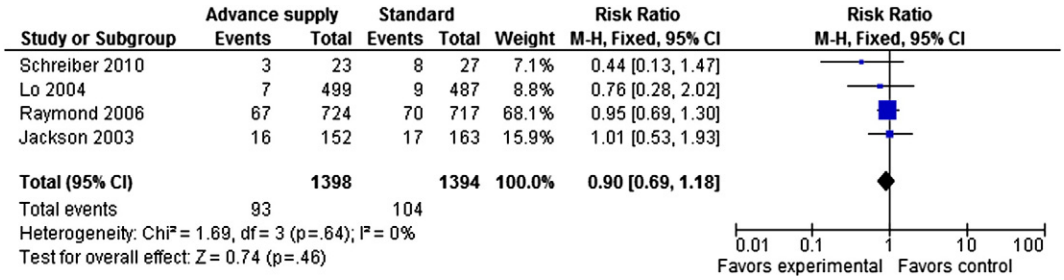

Fig. 1. Risk of pregnancy.

protected, or entirely unprotected depending on whether intercourse occurred and consistency of contraceptive use. Ovulation dates were estimated for menstrual cycles. Pregnancies were categorized as "probably," "possibly" or "unlikely" ECP failures based on timing of ECP use to ovulation. In the intervention group, 17 pregnancies occurred during cycles where ECPs were used. In the control group, two pregnancies occurred in cycles in which ECPs were used. While the number of probable ECP failures was not different between the two groups, the numbers of possible ECP failures were significantly higher in the intervention group (12 vs. 1, p=.012).

A second re-analysis of the same RCT looked at the impact that advanced ECP access had on use of other contraceptive methods [33]. Women were asked whether they had ever used EC because they did not want to use an alternate contraceptive. Responses were categorized as never, once, a few times and many times. At both 6- and 12-month follow-up, women in the increased access arm were significantly more likely to report a greater frequency of substituting ECPs for alternate contraception (p<.001).

A third sub-analysis of this RCT looked at the baseline level of risk for pregnancy among women using ECP [18]. Women were characterized as being at either high or low baseline pregnancy risk. Twenty variables likely to be predictors of unintended pregnancy were used to create a predictive logistic regression model of risk for pregnancy. Women were subsequently stratified into high or low risk for pregnancy. The association between randomization group and ECP use was examined by pregnancy risk, to see if baseline pregnancy risk modified the association. Baseline pregnancy risk did not affect the association between increased access to ECP and ever using the method. However, repeated use of ECP varied by baseline pregnancy risk. Women at high risk of pregnancy and increased access were 2.6 times more likely to repeatedly use ECP than women at high risk with standard access. Among women at low risk, repeated use of ECP was 10 times as high among women with increased access to ECP compared with standard access (RR 10.0, 95% CI 6.5–15.4 and RR 5.5 95% CI 3.8–7.9).

Walsh and Frezieres conducted a trial in 31 community clinics to evaluate the impact of advance ECP provision [23]. More than 9,000 family planning clients were randomized to receive ECP information only, or information and a pack of ECPs. Follow-up telephone surveys were conducted 3–9 months after randomization. ECP use was higher in the intervention group (19% vs. 12%, p=.0009), and subsequent use was more likely to be within 12 h of unprotected intercourse (43% vs. 28%, p<.06). Incidence of pregnancy, hormonal contraceptive use, barrier contraceptive use and pregnancy risk events did not vary significantly between the two groups.

In one RCT, women relying on condoms for contraception were randomized to receive one packet of ECP in advance of need, or were instructed to seek ECP from their clinic if needed [27]. Neither rates of use of ECPs (OR 1.15, 95% CI 0.63–2.11) nor unprotected coital acts (OR 1.28, 95% CI 0.13–2.24) differed between the two groups at 3 months of follow-up.

Another RCT evaluated whether enhanced pharmacy access to ECP or advanced provision of three packages of ECP at health clinics had an impact upon ECP use, sexual behavior, use of contraception, rates of STIs and pregnancy [34]. The control group received only information on how to use ECP. After 6 months, use of ECP was significantly greater in the advanced group compared with the pharmacy access or control group (37%, 24%, and 21% respectively; p<.01); there were no differences in reports of unprotected intercourse, use of contraception, rates of STIs or pregnancy among the 3 groups.

An RCT assigned women to receive either three packs of ECPs in advance or information about how to use and where to obtain ECPs [32]. At the end of the 12-month study period, 29.9% of women in the advanced ECP group had used at least one course of ECPs compared with 12.9% in the control group. The mean number of ECP courses taken was significantly higher among women in the advanced group compared with controls (p<.001). Women in the advanced ECP group were more likely to take ECP sooner after intercourse compared with controls (mean 13.9 vs. 28.5 h; p<.001). Use of other contraceptives and pregnancy rates were similar between the intervention group and controls.

Postpartum women, who received an advance supply of ECPs, were four times as likely to use ECPs when compared with controls who received routine contraceptive counseling by 12 months of follow-up (RR 4.0, 95% CI 1.8–9.0) [26]. When the study population was restricted to women who

reported unprotected intercourse, women in the advanced group were nearly six times more likely to use ECPs (RR 5.8, 95% CI 2.1–16.4) than controls. At 12 months of follow-up, use of less effective contraceptive methods was comparable between the two groups (RR 0.92, 95% CI 0.63–1.3). Reports of inconsistent contraceptive use during the previous 6-month period were not significantly different between the two groups (RR 0.74, 95% CI 0.45–1.2). There were no differences in pregnancy rates between the two groups.

Another RCT followed barrier contraceptive users for up to one year [11]. Condom users were randomly assigned to receive either information about ECP and 3-month supply, or only information about ECP (along with where it could be obtained if needed). The proportion of women who reported unprotected sexual intercourse was low and similar between the two groups. Among women who reported unprotected intercourse, 79% of women in the advanced group used ECP compared with 44% in the control group (p=.18). Importantly, 98% of women in the treatment group said they did not take greater risks with their condoms because they had a supply of ECP. No pregnancies were reported.

A trial reported that women who received an advance supply of ECPs were significantly more likely to use ECP than controls who received information on how to use and obtain ECPs (36% vs. 14%; p<.001) [28]. Despite greater use of ECPs in the treatment group, the proportion of women who did not use any contraception, reported multiple use of ECPs, experienced an unintended pregnancy or sought an abortion during the 12-month follow-up period did not significantly differ between the groups.

3.2. Adolescents

Five RCTs report on the safety and efficacy of advance provision of ECPs to female adolescents (under age 20). An RCT evaluated efficacy of advance provision of ECPs in postpartum teens [1]. Fifty postpartum adolescents were randomized to receive an advanced supply of ECP or routine postpartum care. The retention rate in the study was 78%. At 1-year follow-up, there was a repeat pregnancy rate of 13% in the intervention arm and 30% in the control arm. The relative risk of pregnancy was lower in the intervention arm than the control arm, but this difference did not reach statistical significance (RR 0.57, 95% CI 0.20–1.60).

In another RCT, conducted in Sweden, adolescents requesting EC were randomized to intervention or control groups [29]. Both groups received a supply of ECPs at the visit. The intervention group received an additional pack of ECPs, a supply of condoms and an informational leaflet about ECPs and condom use. ECP use, time to use following unprotected intercourse, contraceptive use and sexual risk taking were queried during 3- and 6-month follow-up phone surveys. Adolescents in the intervention group were more likely to use ECPs at both 3 months (24% vs. 13%; p=.02) and 6 months (31%, vs. 19%; p=.01) post-intervention. In addition, those in the advance ECP group used ECPs approximately 12 h earlier than those in the control group (3-month: 13.6 vs. 25.5 h; p=.007; 6-month: 15.6 vs. 26.4 h; p=.006). Use of contraceptives and condoms were not significantly different between the groups at either the three or the 6-month follow-up visits. The study was limited by differential loss to follow-up of non-Nordic (36.4% loss) compared to Nordic (19.6% loss, p<.01) girls and smokers (38.4% vs. 20.5%, p<.01).

An RCT assessed the impact of providing advance ECPs or information only to adolescent mothers [30]. Those who received an advance supply of ECPs were significantly more likely to have used ECPs than the control group (83% vs. 11%; p<.001 at 6-month follow-up; 64% vs. 17%; p<.01 at 12-month follow-up). There were no differences in self-reported pregnancy rates or choice of contraceptive methods between the two groups. Although reports on unprotected intercourse were similar at 6 months of follow-up, at 12 months, more girls in the advanced ECP group reported unprotected intercourse (69% vs. 45%; p=.02). However, the trial had high rates of loss to follow-up at 6 months (31%) and 12 months (43%); at 12 months, loss to follow-up was higher in the advanced ECP group (48%) compared with controls (38%). Additionally, this analysis was flawed by violation of intention to treat principles because women reporting abstinence as contraception at time of follow-up were excluded from the analysis. Re-analysis of the data according to intention to treat principles demonstrated no significant differences in unprotected intercourse between groups [35].

To determine whether younger women behave differently when offered an advanced supply of ECPs, Harper et al. conducted an age-stratified analysis of an earlier trial [29,34]. Teens in the advanced ECP group were significantly more likely to use ECPs than teens assigned to the pharmacy access or control groups by 6 months of follow-up (44% vs. 29%; p<.001). Among teens, reports of unprotected intercourse, consistent condom use, number of sexual partners, rates of STI acquisition, or pregnancy did not differ according to study group.

An RCT compared advance ECP provision to information only among adolescents recruited at a hospital-based clinic [31]. At 1-month follow-up, women in the advanced group were more likely to have used ECPs than controls (15% vs. 8%; p<.05) and women in the advanced group initiated ECP use sooner after unprotected intercourse than the control group (11.4 vs. 21.8 h; p=.005). At 6-month follow-up, use of ECPs, reports of unprotected intercourse, use of hormonal contraception, use of contraception at last intercourse, and pregnancy rates did not differ significantly between study groups. However, women in the advanced group were more likely to use condoms during the past month compared with controls at 6 months of follow-up (p=.02).

4. Discussion

The studies in this review offer direct evidence on whether ECPs can be safely given to a woman in advance of when she might need to use them. Among adult women, nine

trials, ranging from poor to good in quality, support the safety of advance provision [11,19,21–24,26–28,32,34]. Women receiving an advance supply were more likely to take ECPs and to do so more promptly, after unprotected sex. There is no evidence that advance provision increases the likelihood of unprotected intercourse, frequent ECP use, STIs or changes in regular contraceptive use.

Evidence was similar from five trials studying use in adolescents [1,24,29–31]. Evidence among postpartum teens suggests that advance provision might reduce their use of primary contraception, but the study was not adequately powered for this outcome [1].

No studies found that advanced provision of ECPs reduced the likelihood of unintended pregnancy. A summary odds ratio of four RCTs did not demonstrate a significant reduction in pregnancy incidence at 12 months of follow-up. Several possible theories have been suggested for why advance provision of ECPs has not resulted in reduction in unintended pregnancies at a population level. Limited data suggests that women may substitute ECP for another method [19]. It could be that even though women had an advance supply of ECP, they did not always use ECP when indicated. In one trial, five of eight women who had received advance ECP and became pregnant, reported not using ECP in the cycle they conceived [25]. One study suggests that women at higher baseline risk for pregnancy may use ECP less than women who are at a lower risk of pregnancy [33].

A Cochrane Review with a meta-analysis also evaluated a total of eleven RCTs assessing effects of advance ECP provision on pregnancy rates, STIs and sexual and contraceptive behaviors [36]. One of the eleven trials included mifepristone, which is not available in the US for ECP [37]. They found that women randomized to advance ECP access were more likely to use ECP (summary OR=2.47, 95% CI 1.80–3.40), but that incidence of pregnancy, STIs, unprotected sexual intercourse and condom use did not differ significantly between advance access and control group. In addition, they found that women randomized to advance access were more likely to use ECP multiple times (summary OR=4.13, 95% CI 1.77–9.63) when compared to controls.

The quality of the evidence ranged from poor to good. Among the nine trials evaluating outcomes among adults, three were of poor, three of fair and three of good in quality. Among studies restricted to women under age 20, three were deemed fair in quality, while one was poor and one was good. Available evidence supports that advance provision of ECP to women and adolescents is safe and increases use of ECP following unprotected intercourse.

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