Advance provision of emergency contraception for pregnancy prevention (Review)

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[Intervention Review]

Advance provision of emergency contraception for pregnancy prevention

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ABSTRACT

Background

Emergency contraception can prevent pregnancy when taken after unprotected intercourse. Obtaining emergency contraception within the recommended time frame is difficult for many women. Advance provision could circumvent some obstacles to timely use.

Objectives

To summarize randomized controlled trials evaluating advance provision of emergency contraception to explore effects on pregnancy rates, sexually transmitted infections, and sexual and contraceptive behaviors.

Search strategy

In November 2009, we searched CENTRAL, EMBASE, POPLINE, MEDLINE via PubMed, and a specialized emergency contraception article database. We also searched reference lists and contacted experts to identify additional published or unpublished trials.

Selection criteria

We included randomized controlled trials comparing advance provision and standard access (i.e., counseling which may or may not have included information about emergency contraception, or provision of emergency contraception on request at a clinic or pharmacy).

Data collection and analysis

Two reviewers independently abstracted data and assessed study quality. We entered and analyzed data using RevMan 5.0.23.

Main results

Eleven randomized controlled trials met our criteria for inclusion, representing 7695 patients in the United States, China, India and Sweden. Advance provision did not decrease pregnancy rates (odds ratio (OR) 0.98, 95% confidence interval (CI) 0.76 to 1.25 in studies for which we included twelve-month follow-up data; OR 0.48, 95% CI 0.18 to 1.29 in a study with seven-month follow-up

data; OR 0.92, 95% CI 0.70 to 1.20 in studies for which we included six-month follow-up data; OR 0.49, 95% CI 0.09 to 2.74 in a study with three-month follow-up data), despite reported increased use (single use: OR 2.47, 95% CI 1.80 to 3.40; multiple use: OR 4.13, 95% CI 1.77 to 9.63) and faster use (weighted mean difference (WMD) -12.98 hours, 95% CI -16.66 to -9.31 hours). Advance provision did not lead to increased rates of sexually transmitted infections (OR 1.01, 95% CI 0.75 to 1.37), increased frequency of unprotected intercourse, or changes in contraceptive methods. Women who received emergency contraception in advance were equally likely to use condoms as other women.

Authors' conclusions

Advance provision of emergency contraception did not reduce pregnancy rates when compared to conventional provision. Results from primary analyses suggest that advance provision does not negatively impact sexual and reproductive health behaviors and outcomes. Women should have easy access to emergency contraception, because it can decrease the chance of pregnancy. However, the interventions tested thus far have not reduced overall pregnancy rates in the populations studied.

PLAIN LANGUAGE SUMMARY

Easier access to emergency contraception to help women prevent unwanted pregnancy

Emergency contraceptive pills can prevent unwanted pregnancy if taken soon after unprotected sex. Getting a prescription for emergency contraception can be difficult and time-consuming. Giving emergency contraception to women in advance could ensure that women have it on hand in case they need it. We searched for studies comparing women who got emergency contraception in advance to women who got it in standard ways. We examined whether these groups had different rates of pregnancy or sexually transmitted infections. We also studied how often and how quickly both groups used emergency contraception. Finally, we looked at whether advance provision of emergency contraception changed sexual behavior. Studies showed that the chance of pregnancy was similar regardless of whether or not women have emergency contraception on hand before unprotected sex. Women who had emergency contraception in advance were more likely to report use of the medication, and to use it sooner after sex. Having emergency contraception on hand did not change use of other kinds of contraception or change sexual behavior.

BACKGROUND

Emergency contraception can prevent pregnancy when taken within 120 hours of unprotected intercourse. Several types of emergency contraception regimens exist, including an estrogen-progestin combination (sometimes called "combined regimen" or "Yuzpe regimen"), levonorgestrel alone, and mifepristone. An alternate method of emergency contraception is post-coital insertion of a copper-bearing intrauterine device (IUD), but this review does not cover IUDs as emergency contraceptives.

Effectiveness and side effects vary by regimen (Cheng 2008). A meta-analysis of eight studies suggested that combined regimens reduce the risk of pregnancy by about 74% when taken within 72 hours of unprotected intercourse (Trussell 1999). A more recent analysis using potentially improved methodology suggested lower effectiveness rates, with the two largest studies showing rates of 47% and 53% (Trussell 2003). Levonorgestrel regimens are more effective than combined regimens (with estimates ranging from 59-94%), with less nausea and vomiting (Task Force 1998; Trussell 2006a).

Several barriers discourage widespread and timely use of emergency contraception, including limited knowledge among women and a lack of routine counseling by providers and/or willingness to prescribe the medication. In some countries, emergency contraception is available only after obtaining a prescription, which can be difficult and time-consuming, particularly on holidays or weekends when most clinics and physicians' offices are closed. Moreover, some women find it difficult or embarrassing to request emergency contraception from their physician, and others may not have a primary health care provider. Emergency contraception should be taken as soon as possible, and most guidelines suggest taking the medication within 72 or 120 hours of unprotected intercourse. Even under ideal circumstances, obtaining a prescription within 72 hours can be difficult (Trussell 2000); to date, no studies have investigated barriers to accessing a prescription within the 120 hour time limit. Some countries sell emergency contraception over-the-counter without a prescription, and others allow women to obtain emergency contraception directly from a phar-

macist without a doctor's prescription under collaborative practice agreements with physicians or state approved protocols.

Providing emergency contraception before it is needed in case unprotected intercourse occurs gives women rapid access to the medication. This strategy was first evaluated in a 1998 study (Glasier 1998) and has received increased attention since that time. Economic modeling indicates that advance provision of emergency contraception is a cost-effective public health strategy (Trussell 2006a). However, some worry that having emergency contraception on hand may encourage repeat or incorrect use, increase risky sexual behavior, or discourage use of ongoing or more reliable methods of contraception (particularly barrier methods), thereby increasing the risk of pregnancy or sexually transmitted infections (Gold 1997; Golden 2001; Sherman 2001).

OBJECTIVES

To summarize randomized controlled trials evaluating advance provision of emergency contraceptive pills.

METHODS

Criteria for considering studies for this review

Types of studies

This review included all randomized controlled trials in English that evaluated advance provision of emergency contraception. We excluded studies that failed to clearly report the proportion of women in each treatment arm who became pregnant (as determined by self-report and/or medical testing) during follow-up, and for which we were unable to obtain clear data by asking authors directly.

Types of participants

Women of reproductive age.

Types of interventions

Any emergency contraceptive regimen (combined, levonorgestrel, or mifepristone) provided in advance of need compared to a control group, defined as any of the following: counseling which may or may not include a discussion of emergency contraception, or provision of emergency contraception on request at a clinic or pharmacy.

Types of outcome measures

Primary outcome measures were pregnancy and sexually transmitted infection rates. Secondary outcomes were frequency of emergency contraception use, unprotected intercourse, use of more effective methods of contraception, condom use, delay in taking emergency contraception after unprotected intercourse, and knowledge about emergency contraception.

Search methods for identification of studies

See Helmerhorst 2001 for methods used in reviews of the Fertility Regulation Group.
During August 2006, we identified relevant trials from the Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library, EMBASE, POPLINE, MEDLINE via PubMed, and the website of the International Consortium for Emergency Contraception (www.cecinfo.org/database/who/index.php). Where possible, searches were restricted to human studies only. We restricted our search to English (Moher 2000; Juni 2002). We updated our literature search in November 2009.
We used the following strategy to search CENTRAL:
((postcoital or emergency) and contracept* and (advance* or self administr*))
We used the following strategy to search EMBASE:
((('emergency'/exp OR 'emergency') OR ('emergency'/exp OR 'emergency')) OR postcoit*) AND (contracept*) AND (advance AND provision OR advanced AND provision) AND [english]/lim AND [humans]/lim

We used the following strategy to search POPLINE:
(emergency contraception/contraceptive agents, postcoital/fertility control, postcoital) & (advance provision/advanced provision/self administration)
We used the following strategy to search MEDLINE via PubMed:
(emergency contracepti* OR contraception, postcoital OR contraceptives, postcoital) AND (advance OR advanced OR self administ* OR home)
We used the following strategy to search the database of scientific articles on the website of the International Consortium for Emergency Contraception (ICEC) (http://www.cecinfo.org/database/who/index.php):
"advance" or "advanced"
We also searched reference lists of included studies for information about additional trials and contacted experts in the field for information on additional published or unpublished trials.

Data collection and analysis

All studies that met our inclusion criteria were independently evaluated by two reviewers. We assessed the methodological quality

of each study using the guidelines described in the Cochrane Reviewers' Handbook (Alderson 2004). We designed a data abstraction form, and the two reviewers abstracted the data separately. Discrepancies about the inclusion of studies or about abstracted data were resolved by discussion. When necessary, we contacted researchers to obtain additional information about study methods or outcome measures. We entered and analyzed the data using Review Manager 5.

We calculated odds ratios (OR) with 95% confidence intervals for dichotomous variables and weighted mean averages (WMA) for continuous variables for which means and standard deviations were reported. We tested the outcome data for heterogeneity using the I^2 statistic, and in cases where I^2 exceeded 50%, we employed a DerSimonian and Laird random-effects model to provide a more conservative estimate of significance (DerSimonian 1986; Higgins 2003). Finally, we conducted sensitivity analyses based on rates of loss to follow-up (Schulz 2006), in which studies that had rates of loss to follow-up over 20% were excluded.

One study (Belzer 2005) collected 12-month follow-up information, but due to the presentation of results, we were only able to include 6-month follow-up information. In cases where data were available, we calculated statistics using an intent-to-treat analysis if the author failed to do so (Belzer 2005, see also Trussell 2006b). To explore whether intervention effect waned over time, we contacted authors of studies with 12 months of follow-up to obtain pregnancy outcomes at six months, and pooled these outcomes with studies which had a total follow-up time of six months. Six-month pregnancy outcomes for Schreiber 2009 were not available. To explore whether pregnancy outcomes differed according to type of regimen, we performed subgroup analyses of studies using levonorgestrel, Yuzpe regimen, levonorgestrel or Yuzpe, and mifepristone.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Eleven randomized controlled trials (Hazari 2000; Jackson 2003; Gold 2004; Lo 2004; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008; Schreiber 2009) met our inclusion criteria. The total number of randomized participants was 7695, with sample sizes ranging from 50 to 2000. Raine 2005 enrolled 2117 total participants, but this review used only two treatment groups of that study. Seven studies were conducted in the United States (Jackson 2003; Gold 2004; Belzer 2005; Raine 2005; Raymond 2006; Schwartz 2008; Schreiber 2009), with five in California and the rest in Nevada, North Carolina, or Pennsylvania. One study was conducted in Hong Kong (Lo 2004) and one in mainland China (Hu 2005). One study was conducted in India (Hazari 2000) and one was conducted in Sweden (Ekstrand 2008). Six studies (Gold 2004; Belzer 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schreiber 2009) focused specifically on younger populations, and two of those (Belzer 2005; Schreiber 2009) focused on adolescent mothers. Two studies primarily enrolled post-partum women (Jackson 2003; Hu 2005). Three studies recruited women from family planning clinics (Lo 2004; Raine 2005; Raymond 2006), two recruited from other clinics (Ekstrand 2008; Schwartz 2008), four recruited from hospitals (Jackson 2003; Gold 2004; Hu 2005; Schreiber 2009), and one recruited adolescent mothers receiving case management services (Belzer 2005). The recruitment site was unclear in one study (Hazari 2000).

Exclusion criteria for baseline contraceptive use varied greatly between the studies. The most restrictive criteria excluded women using or planning to use any hormonal method or an IUD (Lo 2004; Hu 2005). Raymond 2006 excluded women for using some hormonal methods or sterilization, and Raine 2005 excluded women for using some hormonal methods. Schwartz 2008 excluded IUD users, women who had tubal sterilization or had partners who had undergone a vasectomy, lesbians, and women who had a hysterectomy. Gold 2004 excluded women using long acting contraceptive methods (IUD, implants and injectables), and Belzer 2005 excluded only IUD and implant users. Jackson 2003 excluded women who were sterilized or had a sterilized partner. Three studies had minimal exclusion criteria: Hazari 2000 excluded only women who were determined at baseline to be pregnant, Schreiber 2009 excluded women who desired a pregnancy in the next year, and Ekstrand 2008 did not specify exclusion criteria based on contraceptive use. Although several studies included post-partum women, only one study specified excluding women who were currently breastfeeding (Raymond 2006).

Control groups also differed considerably. Three studies did not necessarily provide any information about emergency contraception to the control group (Jackson 2003; Schwartz 2008; Schreiber 2009) Two studies (Belzer 2005; Hu 2005) specifically provided information about emergency contraception to the control group, but did not facilitate access to the medication in any other way. Control participants in six studies (Hazari 2000; Gold 2004; Lo 2004; Raine 2005; Raymond 2006; Schreiber 2009) were able to obtain emergency contraception on request at the clinic, although not necessarily through study staff. One study provided the control group with a dose of emergency contraception (Ekstrand 2008). Two studies reported providing all participants with condoms (Hazari 2000; Hu 2005), while Ekstrand 2008 provided condoms only to the intervention group.

The number of courses of emergency contraception provided in advance ranged from one to three. Seven studies provided only one course of emergency contraception in advance (Hazari 2000; Jackson 2003; Gold 2004; Belzer 2005; Ekstrand 2008; Schwartz 2008; Schreiber 2009). Gold 2004 offered two additional courses

on request at the study office, Belzer 2005 and Schreiber 2009 offered replacement packs through the study, and Jackson 2003 provided instructions on obtaining additional emergency contraceptive pills (but did not specify if that was through the study office or by prescription). One study (Raymond 2006) provided two courses in advance and made particular effort to ensure that all women in the advance provision group had two courses available at all times. Finally, three studies provided three courses of emergency contraception in advance (Lo 2004; Hu 2005; Raine 2005), and one (Lo 2004) specifically noted that women using all three packs were instructed to return for contraceptive counseling and, if appropriate, given three additional packets.

Most trials administered levonorgestrel pills. Seven studies used the same formulation of pills (two tablets of 0.75 mg levonorgestrel) (Lo 2004; Belzer 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008; Schreiber 2009). In addition, Gold 2004 replaced a Yuzpe regimen (200 µg ethinyl estradiol and 2 mg norgestrel) with levonorgestrel when it became the standard of care mid-way through their study. Two earlier studies used a combined regimen (Hazari 2000; Jackson 2003), and one study based in China provided 10 mg mifepristone (Hu 2005).

Follow-up ranged from three to 12 months. Six studies aimed to follow all participants for one year (Jackson 2003; Lo 2004; Belzer 2005; Hu 2005; Raymond 2006; Schreiber 2009). However, we report only on six-month follow-up data for most outcomes (except pregnancy) in Jackson 2003 and all outcomes in Belzer 2005, since these studies provided six-month data and six- to 12-month data, but not cumulative 12-month data. Three studies followed all participants for six months (Gold 2004; Raine 2005; Ekstrand 2008), one study followed participants for seven months (Schwartz 2008) and one study followed participants for three months (Hazari 2000).

All studies attempted to measure pregnancy, whereas only four studies measured sexually transmitted infections (Gold 2004; Raine 2005; Raymond 2006;Ekstrand 2008). Seven studies solely relied on self-reported pregnancy data (Jackson 2003; Gold 2004; Belzer 2005; Hu 2005; Ekstrand 2008; Schwartz 2008; Schreiber 2009), whereas four studies used more objective pregnancy detection methods, comprised of some combination of self-report, testing at follow-up, or medical chart review (Hazari 2000; Lo 2004; Raine 2005; Raymond 2006). Among the studies which measured sexually transmitted infections, two used self-reported data (Gold 2004; Ekstrand 2008) and two used combinations of more objective methods including testing at follow-up and medical chart review (Raine 2005; Raymond 2006).

Risk of bias in included studies

Eight studies used computer-generated randomization sequences (Hazari 2000; Lo 2004; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Schwartz 2008; Schreiber 2009). One study randomized in blocks of four using a table of random digits (Ekstrand 2008). One study had participants select a colored condom from a covered bucket to determine allocation (Gold 2004), and another used cluster randomization by date of discharge in order to avoid accidental crossover (Jackson 2003).

Seven studies had adequate allocation concealment methods. Four used either sequentially numbered, opaque, sealed envelopes or identical treatment boxes (Lo 2004; Hu 2005; Raine 2005; Raymond 2006) while three (Gold 2004; Hazari 2000; Schwartz 2008) used schemes undecipherable to clinic staff. Three studies had unclear allocation concealment (Belzer 2005; Ekstrand 2008; Schreiber 2009). One study had inadequate concealment methods that allowed for assignment prediction (Jackson 2003).

Three studies (Hu 2005; Raine 2005; Raymond 2006) provided sample size calculations based on detecting a decrease in pregnancy rates. However, Hu 2005 was underpowered due to unexpectedly low pregnancy rates in their study population. The other eight studies primarily investigated behavior change and were not powered to measure pregnancy. Of these, four (Jackson 2003; Gold 2004; Lo 2004; Ekstrand 2008; Schwartz 2008) calculated sample sizes in accordance with anticipated differences in emergency contraceptive use or timing of use between groups, two (Hazari 2000; Belzer 2005) did not provide sample-size calculations, and one feasibility trial used a sample size of convenience (Schreiber 2009).

Five studies had loss to follow-up under 20% (Hazari 2000; Lo 2004; Hu 2005; Raine 2005; Raymond 2006). Six studies had larger losses (Jackson 2003; Gold 2004; Belzer 2005; Ekstrand 2008; Schwartz 2008; Schreiber 2009), ranging up to 41% of participants lost to follow-up (Schwartz 2008). In addition, Gold 2004 showed differential loss to follow-up.

Effects of interventions

None of the studies found significant differences in pregnancy rates (Hazari 2000; Jackson 2003; Gold 2004; Lo 2004; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008; Schreiber 2009), including the two studies that were adequately powered to detect a difference (Raine 2005; Raymond 2006). Furthermore, results from the pooled analyses showed no significant difference in pregnancy rates between advance provision and control groups. The combined OR for pregnancy comparing women receiving emergency contraception in advance to women in the control group was 0.98 (95% CI 0.76 to 1.25) in studies with 12-month follow-up, 0.48 (95% CI 0.18 to 1.29) in a study with seven-month follow-up information, 0.92 (95% CI 0.70 to 1.20) in studies for which we included six-month follow-up information, and 0.49 (95% CI: 0.09 to 2.74) for one study with three-month follow-up data. Restricting this comparison in a sensitivity analysis to include only studies with a loss to follow-up rate under 20% did not substantially change the results (twelve-month follow-up: OR 1.0; 95% CI 0.76 to 1.31; six-month follow-up: OR 1.00; 95% CI 0.73 to 1.37; three-month follow-up:

OR 0.49; 95% CI 0.09 to 2.74). None of the analyses pooled by regimen type demonstrated a reduction in pregnancy rates (levonorgestrel only: OR 0.82, 95% CI: 0.64 to 1.05; Yuzpe only: OR 0.90, 95% CI: 0.47 to 1.74; levonorgestrel or Yuzpe: OR 0.83, 95% CI: 0.67 to 1.03; and mifepristone: OR 1.20, 95% CI: 0.74 to 1.93).

None of the four studies that measured sexually transmitted infection rates found significant differences between groups (Gold 2004; Raine 2005; Raymond 2006; Ekstrand 2008). The combined OR for sexually transmitted infections was 1.01 (95% CI 0.75 to 1.37). Restricting this analysis to only studies with a loss to follow-up rate under 20% did not substantially change the results (OR 0.96; 95% CI 0.69 to 1.33).

Reported emergency contraceptive use was significantly higher in the advance provision group in six studies (Jackson 2003; Lo 2004; Hu 2005; Raine 2005; Raymond 2006; Ekstrand 2008), and in four studies (Hazari 2000;Gold 2004; Schwartz 2008; Schreiber 2009), emergency contraceptive use was higher but the difference did not reach statistical significance. Belzer 2005 reported emergency contraceptive use only for a subgroup of participants and we did not include those results in this analysis. The combined OR for emergency contraception use for all studies was 2.47 (95% CI 1.80 to 3.40). The sensitivity analysis including only studies with a loss to follow-up rate under 20% yielded similar results (OR 2.55; 95% CI 1.64 to 3.97). A secondary analysis which used predictive modeling to estimate the baseline risk of pregnancy suggested that women at low baseline risk of pregnancy may have been more likely to use EC repeatedly than high risk women (Baecher 2009). Three studies (Hu 2005; Raine 2005; Raymond 2006) also showed that women in the advance provision group were significantly more likely to use emergency contraception two or more times (OR: 4.13; 95% CI 1.77 to 9.63); no sensitivity analysis was conducted for this outcome since all studies in the original analysis had loss to follow-up under 20%.

The percentage of women who did not use emergency contraception after unprotected intercourse ranged widely and was reported in different ways. Four studies (Jackson 2003; Lo 2004; Hu 2005; Raymond 2006) reported non-use of emergency contraception among women who became pregnant. Three studies reported non-use among women who had unprotected intercourse (Gold 2004; Raine 2005; Ekstrand 2008). In all studies reporting on non-use, non-use was lower among participants in the advance provision group compared to controls. Belzer 2005 reported use of emergency contraception among a subgroup of participants (data not reported).

Hu 2005 reported non-use of emergency contraception among women who became pregnant during one year of follow-up (n= 70); 79% in the advance provision group and 100% in the control group did not use emergency contraception during the cycle in which they conceived. Among women who became pregnant in Jackson 2003 (n=27), 64% in the advance provision group and 100% in the control group did not use emergency contraception. Among women who became pregnant in Lo 2004 (n=16), 71% in the advance provision group and 100% in the control group did not report using emergency contraception during the cycle in which the pregnancy occurred. Raymond 2006 reported that for the 148 menstrual cycles in which women experienced pregnancy, 77% of women in the advance provision group and 97% of women in the control group did not use emergency contraception during those cycles.

Gold 2004 reported that at six-month follow-up, 26% of participants in both arms had unprotected intercourse in the past month, but 92% of women in the advance provision group and 94% in the control group did not report use of emergency contraception. In Raine 2005, among women who reported ever having unprotected sex, 6% of women in the advance provision group and 49% of women in the control group did not report using emergency contraception during the study period. Ekstrand 2008 reported that half of adolescent girls reporting unprotected intercourse during the previous six months used ECP afterwards, with significantly more in intervention group using emergency contraceptive pills (58%) than in the control group (37%) (p=0.02).

In addition, emergency contraception was sometimes used incorrectly. Lo 2004 reported that although all participants took the first dose within 72 hours of intercourse, 17% of women in the advance provision group took the second dose of levonorgestrel incorrectly. No women in the control group reported taking the second dose incorrectly. Jackson 2003 reported incorrect use only among women who became pregnant and who reported using emergency contraception in the cycle in which they conceived (n= 4). Two of these four women used emergency contraception incorrectly. Hu 2005 reported that all women in the advance provision group took emergency contraception within the recommended 120 hours, but did not report on correct use by control participants. Eight studies (Hazari 2000; Gold 2004; Belzer 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008; Schreiber 2009) did not report on incorrect use.

Five studies collected information on reported time intervals between unprotected intercourse and use of emergency contraception. In general, this interval was shorter for women receiving emergency contraception in advance. Two studies provided mean time and standard deviation (Lo 2004; Ekstrand 2008). Women with advance provision took emergency contraception a mean of 12.98 hours earlier than women with standard provision (WMD -13.98, 95% CI -16.66 to -9.31 hours). Two other studies reached similar conclusions, the first with a comparison of median times of 11.4 hours for advance provision vs. 21.8 hrs for control (p=0.005) (Gold 2004), the second with imputed median midpoints of 12 hours for advance provision vs. 36 hours for control (p<0.010) (Raymond 2006). Raine 2005 also found a shorter delay for the advance provision group (p=0.008). One study suggested no difference in timing (eight hours for both groups), but this study was conducted in China, where levonorgestrel was available over-the-counter at the time of the study (Hu 2005). A small number of

women (n=2) in this study did report purchasing levonorgestrel over the counter.

Eight studies compared the reported frequency of unprotected intercourse using different time frames (Hazari 2000; Jackson 2003; Gold 2004; Belzer 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008). None showed any difference between comparison groups (unprotected intercourse in past two weeks: OR 0.84 (95% CI 0.66 to 1.06); unprotected intercourse in past month: OR 0.95 (95% CI 0.46 to 1.94); unprotected intercourse in past three months: OR 1.28 (95% CI: 0.73 to 2.24); unprotected intercourse in past six months: OR 0.96 (95% CI 0.79 to 1.16)).

Six studies examined change in contraceptive use using a variety of measurements (Jackson 2003; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Ekstrand 2008). Belzer 2005 described this information only for a subgroup (data not reported). Jackson 2003 found no differences between treatment arms in consistency of contraceptive use or type of method use during six months of follow-up, and among women who only used condoms, there was no decrease in condom use among the group with advance provision of emergency contraception. Similarly, Hu 2005, Raine 2005 and Ekstrand 2008 reported no differences between treatment arms in patterns of contraceptive use or method change. Finally, Raymond 2006 reported that use of contraception (other than emergency contraception) as reported at follow-up did not differ significantly by group. In this study, the proportion of sexually active women who did not use any form of contraception decreased slightly in both groups during follow-up. Secondary analyses of this study suggested that advance provision may have caused an increase in unprotected or underprotected sex (Raymond 2008), and that advance provision may have caused women to substitute EC for other methods (Weaver 2009), but these findings should be considered hypothesis-generating and do not influence our overall conclusions.

Eight studies looked at condom use; none found significant differences between groups (Lo 2004; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Gold 2004; Ekstrand 2008; Schwartz 2008). The OR for condom use at 12 months was 1.01 (95% CI 0.87 to 1.16); at six months: OR 0.94 (95% CI 0.66 to 1.34), at three months: OR 0.77 (95% CI 0.48 to 1.25), in last month: OR 1.54 (95% CI 0.94 to 2.53), and at last sex: OR 1.18 (95% CI 0.71 to 1.94).

None of the studies reported adverse events (Hazari 2000; Jackson 2003; Gold 2004; Lo 2004; Belzer 2005; Hu 2005; Raine 2005; Raymond 2006; Ekstrand 2008; Schwartz 2008; Schreiber 2009).

DISCUSSION

Advance provision of emergency contraception did not reduce unplanned pregnancies when compared to standard access. None of the adequately powered trials found a decrease in pregnancy rates with advance provision of emergency contraception (Raine 2005; Raymond 2006). Pooled estimates also showed no difference in pregnancy rates, indicating that based on available data, advance provision of emergency contraception does not lead to reduced rates of unintended pregnancy. Analyses by length of follow-up and by type of regimen did not change results.

This conclusion conflicts with earlier optimistic projections of the potential public health impact of improved access (Trussell 1992). Emergency contraception is more effective than placebo in preventing unwanted pregnancy (Raymond 2004), and advance provision increases use and shortens time between unprotected intercourse and emergency contraceptive use. Since evidence now supports ia single dose of levonorgestrel 1.5 mg, and several countries now market levonorgestrel emergency contraception in a single dose, incorrect use will likely be less of a problem in the future (Arowojolu 2002; von Hertzen 2002). Nevertheless, women may not perceive themselves to be at risk of pregnancy and may fail to use the method after unprotected sex has occurred, despite ready availability. Research suggests that unperceived pregnancy risk, concerns about side effects, and inconvenience are some of the reasons why women may not use emergency contraception when needed (Sorensen 2000; Moreau 2005; Rocca 2007; Goulard 2006). A secondary analysis of data from Raymond 2006 suggested that women at the lowest baseline risk of pregnancy may have been more likely to use EC repeatedly than high risk women, which may help to explain why no effect on pregnancy was found (Baecher 2009).

As with other contraceptive methods, the disparity between theoretical and actual effectiveness can be large (Steiner 1996). More precise estimates of efficacy may help to shed light on advance provision's lack of impact on unintended pregnancy.

These trials share a common weakness. Reported information on use of emergency contraception, frequency of unprotected intercourse, and changes in contraceptive patterns was of unknown validity. Since these self reports lacked objective verification, this information should be viewed with caution (Stuart 2009). Objective evidence indicates that self reports on use of contraceptives (Lawson 1998; Macaluso 2003; Walsh 2003; Galvao 2005) and other medications (Landry 2006) are inaccurate, and that self-report of unprotected intercourse is inferior to other ascertainment methods (Rogers 2005). Some degree of underreporting of pregnancies may have occurred in both the advance provision and control groups in these trials, particularly those trials using only self-reported data. Induced abortions are routinely underreported (Fu 1998). However, results from the trials relying on pregnancy testing were consistent with results from the trials using self-reports of pregnancy.

Advance provision of emergency contraception consistently increased its reported use and usually shortened the reported interval

between unprotected intercourse and drug administration. However, changes in these measures did not correlate with changes in pregnancy rates.

The quality of these randomized controlled trials varied widely. While many had good methods of randomization and allocation concealment, follow-up rates differed greatly. One trial planned not to follow most participants after randomization (Walsh 2006), so we excluded it. In the view of Sackett and others, when losses exceed 20% of participants randomized, the credibility of a trial is suspect (Schulz 2006). Trials with high losses to follow-up resemble cohort studies in their potential for bias. For the sake of completeness, we included trials with poor follow-up and performed a sensitivity analysis with and without these reports; the results were similar.

AUTHORS' CONCLUSIONS

Implications for practice

Providing women with emergency contraception in advance of need does not reduce unintended pregnancy on a population level. Advance provision did not have any harmful effects in primary analyses: it did not increase rates of sexually transmitted infections, decrease condom use, encourage adoption of less reliable contraceptive methods, or otherwise negatively impact sexual and reproductive behavior. While derivative studies suggested theoretical concerns regarding increases in unprotected or underprotected sex, or potential substitution of EC for more effective methods, these findings should be considered tentative. Advance provision did increase use of emergency contraception and decrease the length of time between unprotected intercourse and use of emergency contraception. Conclusions about population level effects should not impede efforts to ensure all women have access to emergency contraception when they need it. Women should be given information about and easy access to emergency contraception because individual women can decrease their chances of pregnancy by using the method. However, current data on advance provision of emergency contraception indicate that tested interventions will not reduce overall unintended pregnancy rates.

Implications for research

Future research should address the behavioral issues surrounding the failure to use emergency contraception when needed, even when it is readily available.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Belzer 2005

Methods	RCT. Computer generated randomization number table. Sealed envelopes (unclear whether opaque or sequentially numbered). 12 mo follow-up, data reported in six mo intervals. We utilize only the six mo data.
Participants	160 adolescent mothers, 13-20 yrs, mostly Hispanic, receiving case management services in a large metropolitan area. Excluded if attempting to get pregnant or using implant or an IUD.
Interventions	Intervention group received 1 course levonorgestrel-only regimen (two tabs 0.75 mg levonorgestrel), to be taken in two doses 12 h apart. Replacement pack provided if package used or lost. Control group received EC info only.
Outcomes	Pregnancy rates, frequency of unprotected intercourse, condom use.
Notes	Large loss to follow-up (31% at six months). Original statistical analysis not intent-to-treat. All self-reported data. No sample size calculation. Controls significantly more likely to report condom use and sexual activity at baseline; differences not controlled for in analysis.

Ekstrand 2008

Methods	RCT. Randomization in blocks of four using a table of random digits. Sequentially labeled envelopes (unclear whether opaque or sealed). Six mo follow-up, data reported at three and six months.
Participants	420 Swedish teens, 15-19 yrs, requesting EC in a local youth clinic in medium-sized university town in Sweden. Excluded if had a language barrier.
Interventions	Intervention group received requested dose plus extra dose (1.5 mg levonorgestrel taken as a single dose), plus 10 condoms and a leaflet on EC and condom use. Control group received requested dose of EC.
Outcomes	Pregnancy rates, STI rates (unspecified), use of EC, interval between unprotected sex and EC use, frequency of unprotected sex, condom use
Notes	All self-reported data. Large loss to follow-up (22% at six months). Not powered to detect differences in pregnancy or STI rates.

Gold 2004

Methods	RCT (by colored condom chosen from age-stratified bucket). Correspondence with primary author indicated that participants could not see inside bucket before choosing and were unaware of the color assignments. Two colors, distributed 50:50, inside each bucket. Most clinic staff unlikely to have been able to decipher the color code, method unlikely to have affected randomization. Six mo follow-up.
Participants	301 sexually-active adolescents, aged 15-20 yrs, in Southwestern Pennsylvania, primarily minority and low-income. Excluded if using IUD, implant, injectable, if living in foster care or group home, or if had other characteristics which could threaten follow-up.

Gold 2004 (*Continued*)

Interventions	From study start until April 2000, intervention group received one course Yuzpe regimen 200 mcg ethinyl estradiol plus 2 mg norgestrel, plus an extra dose in case of vomiting, in addition to diphenhydramine. After April 2000, when levonorgestrel only regimens became standard of care, a levonorgestrel-only regimen was used (two tabs of levonorgestrel 0.75 mg). Participants could obtain two additional courses over six mo period by request, regardless of whether unprotected intercourse had occurred. Participants also received counseling and EC info. Control group received EC on request at the clinic and EC info.
Outcomes	Pregnancy and STI rates (specific STIs not specified), use of EC, interval between unprotected intercourse and EC use, frequency of unprotected intercourse, condom use.
Notes	Large loss to follow-up (26% at six mo - for reasons other than pregnancy), and loss to follow-up differential by treatment group (33% in advance provision group, 19% in control group). Not powered to detect differences in pregnancy or STI rates.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Hazari 2000

Methods	RCT. Coded randomization slips prepared off-site. Three mo follow-up.
Participants	200 condom-using women in Mumbai, India, generally low SES and mostly between the ages of 25-34 yrs. Excluded if pregnant at baseline as determined by history of last menstrual period and recent unprotected intercourse, vaginal exam, or if required, urine pregnancy test and ultrasonography.
Interventions	Intervention group received one course Yuzpe regimen (50 µg ethinyl estradiol and 0.25 mg levonorgestrel) to be taken in two doses 12 h apart. Replacement pills were provided on request at the clinic. Control group received EC on request at the clinic. Both groups were provided with condoms.
Outcomes	Pregnancy rates, EC use, frequency of unprotected sex.
Notes	Small loss to follow-up (1%). One pregnancy was missed at baseline, excluded from this review. Article poorly described methodology, participants, and outcomes. Unclear whether differences between groups at baseline. No discussion of sample size.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	

Hu 2005

Methods	RCT. Computer generated simple randomization list. Sequentially numbered, opaque, sealed envelopes. 12 mo follow-up.
Participants	2000 post-partum women in Shanghai hospital. Excluded if planning on using an IUD or hormonal contraception.
Interventions	Intervention group received three courses of mifepristone (10 mg). Control group received only informatin on EC (but levonorgestrel available in China OTC). All participants received ten condoms.
Outcomes	Pregnancy rates, use of EC, interval between unprotected intercourse and EC use, change in contraceptive methods, condom use.
Notes	Reasonable loss to follow-up (17%). Originally powered to detect a difference in pregnancy rates, but pregnancy rates much lower than expected, reducing statistical power. Failure to perform intent-to-treat analysis (inappropriately excluded those who chose IUD and sterilization). High potential for crossover due to OTC levonorgestrel.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Jackson 2003

Methods	RCT. Cluster randomization by date of discharge from postpartum care, done with random number generator by separate researcher so clinic staff could not predict day's assignment. Data analyzed by individual, re-evaluated accounting for cluster sampling, no substantial differences. Researchers conducting baseline interviews not masked to group assignment, blinded personnel conducted follow-up, data entry, and analysis. 12 mo follow-up.
Participants	370 post-partum, low income, racially diverse English- or Spanish-speaking women at public inner-city hospital in San Francisco. Excluded if major contraindications to estrogen use, post-partum tubal ligation or partner with vasectomy, employees of Labor and Delivery at the hospital, enrolled in another study, or difficult to reach for follow-up (lack of a phone, psychiatric disorder, untreated substance abuse, plans for relocation).
Interventions	Intervention group received one course of Yuzpe regimen (eight tabs 0.15 mg levonorgestrel plus 30 µg ethinyl estradiol), educational session, verbal and written instructions. Additional pills available on request. Control group received routine counseling, which may or may not have included a discussion of EC.
Outcomes	Pregnancy rates, use of EC, frequency of unprotected intercourse, change in contraceptive methods, EC knowledge. Except for pregnancy rates, most outcomes can only be included for six-month follow-up data, as they were reported separately for the six months prior to the six and twelve-month follow-up visits.
Notes	Large loss to follow-up (31% at 12 months). All self-reported data. Powered to detect difference in EC use.

Jackson 2003 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	No	

Lo 2004

Methods	RCT. Computer generated randomization list, blocks of 10. Sequentially numbered opaque, labeled, sealed envelopes. 12 mo follow-up.
Participants	1030 women, 18-45 yrs, attending two Hong Kong clinics using "less effective contraceptive methods" (condoms, spermicide, fertility awareness based methods, withdrawal, or nothing).
Interventions	Intervention group received three courses (two tabs 0.75 mg levonorgestrel), to be taken in two doses 12 h apart, and up to three more courses if needed. Control group received EC on request at clinic.
Outcomes	Pregnancy rates, use of EC, interval between unprotected intercourse and EC use, condom use.
Notes	Small loss to follow-up (4%). Pregnancy confirmed by pregnancy test. Powered to detect a 10% difference in EC use, not powered to detect a difference in pregnancy rates.

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	

Raine 2005

Methods	RCT. Computer generated randomization sequence assigned participants to one of three groups before December 2001, to one of two groups after December 2001 (clinic access group eliminated because pharmacy access instated in CA). We include only data from intervention and clinic access groups (pre 12/2001). Sequentially numbered treatment boxes with labeled study ID, opened after leaving the clinic. Six mo follow-up.
Participants	1228 English or Spanish speaking women, 15-24 yrs, sexually active in past six mo, largely uninsured and low-income, at moderately high risk for negative reproductive health outcomes, living in the San Francisco Bay area, attending four California family planning clinics, available for six mo follow-up. Excluded if pregnant or desiring pregnancy, using hormonal contraception or IUD, or if had unprotected intercourse during the past three days or were requesting EC at enrollment.
Interventions	Intervention group received three courses (two tabs 0.75 mg levonorgestrel), to be taken in two doses 12 h apart, within 72 hours of intercourse. Control group received EC on demand at a clinic. Although EC is generally available at no cost through the clinic, some study participants ineligible for insurance coverage may have had to pay all or some of the cost of EC at two of the four study sites.

Raine 2005 (*Continued*)

Outcomes	Pregnancy rates, STI rates (only information on Chlamydia and HSV2 included because these STIs were confirmed by testing at follow-up) use of EC, frequency of unprotected intercourse, change in contraceptive methods, condom use.
Notes	Small loss to follow-up (7% at six months). Some crossover reported. This review excludes information from pharmacy access group as we are interested in comparing advance provision and standard access (before statewide pharmacy access was implemented). Participants differed at baseline by enrollment site, race/ethnicity was linked to enrollment site. Differences controlled for, adjustment did not substantially change results. Powered to detect a difference in pregnancy rates.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Raymond 2006

Methods	RCT. Computer generated randomization scheme in blocks of four, six, and eight. Sequentially numbered, opaque, sealed envelopes. 12 mo follow-up.
Participants	1490 sexually active women, 14-24 yrs, who did not desire pregnancy and were attending clinics in Nevada and North Carolina. Excluded if using or planning on using sterilization, IUD, hormonal contraception, or if pregnant or breastfeeding in past 6 wks.
Interventions	Intervention group received two courses (two tabs of 0.75 mg levonorgestrel) to be taken together in one dose. More courses provided, attempt to ensure two packages on hand at all times. Control group received EC on request at a clinic.
Outcomes	Pregnancy rates, STI rates (gonorrhea, Chlamydia, trichomoniasis), use of EC, interval between unprotected intercourse and EC use, frequency of unprotected intercourse, change in contraceptive methods, condom use.
Notes	Small loss to follow-up (6%). Pregnancy and STIs outcomes based primarily on medical chart review plus testing at follow-up, some women self-tested at home, sent vaginal samples for confirmation. Powered to detect a difference in pregnancy rates. More intervention participants had STIs at baseline; differences controlled for, adjustment did not substantially change results.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Schreiber 2009

Methods	RCT. Randomization generated in permutated blocks in research unit by computer before recruitment phase. Assignments placed in sealed envelopes in consecutive order. Not clear if envelopes were opaque. 12-month follow-up.
Participants	50 young (14-19 yrs), English-speaking women recruited from a hospital post-partum unit who had delivered a live infant and were planning to parent, who desired to delay pregnancy for at least one year, and who were in good general health. Excluded if had allergy to levonorgestrel, current substance abuse, or plans to relocate outside of Philadelphia.
Interventions	Intervention group received one package of emergency contraceptive pills (Plan B) with routine instructions about EC as well as the chosen primary contraceptive method, a prescription for chosen primary method when applicable, or the first dose of injectable contraception (if injectable contraception was the chosen method). The intervention group had access to additional packages of Plan B upon request. Control group participants were discharged with instructions about their chosen primary contraceptive method and a prescription or first dose for that method.
Outcomes	Pregnancy rates, EC use.
Notes	Large loss to follow-up (24% at 12 months). All outcomes self-reported.

Schwartz 2008

Methods	RCT. Computerized randomization with automatic launching of counseling modules after baseline questionnaire (Research assistant remained unaware of allocation until counseling was completed). follow-up phone survey by blinded participants. Seven mo follow-up.
Participants	446 English-speaking adult women (18-45 yrs) from waiting areas of two urgent care clinics in San Francisco who had a phone and no plans to relocate. Excluded if pregnant, had a hysterectomy or tubal ligation, had an IUD, had a partner with vasectomy, or a lesbian.
Interventions	Intervention group received a single package of two 0.75 mg levonorgestrel pills and computerized conseling on EC. Control group received computerized counseling about pre-conception folate and a sample of folate.
Outcomes	Pregnancy rates, use of EC, unprotected sex in last six months, condom use.
Notes	Large loss to follow-up (41% at seven months). All outcomes self-reported. Powered to detect a difference in use of EC.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	

Characteristics of excluded studies *[ordered by study ID]*

Blanchard 2003	Not a randomized controlled trial.
Ellertson 2001	Proportion of women in each treatment arm who became pregnant during follow-up not clearly reported; raw data unavailable
Endres 2000	Not a randomized controlled trial.
Glasier 1998	Not a randomized controlled trial.
Glasier 2004	Not a randomized controlled trial.
Golden 2004	Randomized controlled trial of partner notification, not advance provision. Collected qualitative data on EC interest.
Golden 2009	Intervention was advanced prescription, not advanced provision of emergency contraception
Harper 2005	Based on same data as Raine 2005, restricted to adolescents.
Larsson 2006	Not a randomized controlled trial.
London 2006	Review of Harper 2005.
Lovvorn 2000	Not a randomized controlled trial.
Ng 2003	Did not collect pregnancy data.
Petersen 2007	Did not collect pregnancy data.
Raine 2000	Not a randomized controlled trial.
Rocca 2007	Derivative of Raine 2005, did not assess pregnancy as an outcome
Sander 2009	Derivative of Raymond 2006, used only data from control arm.
Skibiak 1999	Not a randomized controlled trial.
Stehle 1999	Appears on PubMed as a randomized controlled trial, but actually a review of Glasier 1998
Teal 2008	Not a randomized controlled trial (alternate assignment).
Walker 2006	Intervention is not advance provision of emergency contraception
Walsh 2006	Not conducted as a randomized controlled trial since no attempt was made to follow-up 70% of randomized participants.

DATA AND ANALYSES

Comparison 1. Advance provision vs. standard provision of emergency contraception

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pregnancy (at twelve-month follow-up)	5	4728	Odds Ratio (M-H, Fixed, 95% CI)	0.98 [0.76, 1.25]
2 Pregnancy (at seven-month follow-up)	1	265	Odds Ratio (M-H, Fixed, 95% CI)	0.48 [0.18, 1.29]
3 Pregnancy (at six-month follow-up)	8	6329	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.70, 1.20]
4 Pregnancy (at three-month follow-up)	1	198	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.09, 2.74]
5 Pregnancy for levonorgestrel regimens only	7	4271	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.64, 1.05]
6 Pregnancy for Yuzpe regimens only	2	513	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.47, 1.74]
7 Pregnancy for mifepristone regimens only	1	1948	Odds Ratio (M-H, Fixed, 95% CI)	1.20 [0.74, 1.93]
8 Pregnancy for levonorgestrel or Yuzpe regimens	10	5038	Odds Ratio (M-H, Fixed, 95% CI)	0.83 [0.67, 1.03]
9 Sexually transmitted infections	4	3123	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.75, 1.37]
10 Ever use of emergency contraceptives during trial	10	6971	Odds Ratio (M-H, Random, 95% CI)	2.47 [1.80, 3.40]
11 Multiple uses of emergency contraceptives during trial	3	4574	Odds Ratio (M-H, Random, 95% CI)	4.13 [1.77, 9.63]
12 Mean time interval between unprotected intercourse and use of emergency contraception	2	1315	Mean Difference (IV, Random, 95% CI)	-12.98 [-16.66, -9.31]
13 Ever unprotected intercourse in past two weeks	1	1140	Odds Ratio (M-H, Fixed, 95% CI)	0.84 [0.66, 1.06]
14 Ever unprotected intercourse in past month	1	254	Odds Ratio (M-H, Fixed, 95% CI)	0.95 [0.46, 1.94]
15 Ever unprotected intercourse in past three months	1	198	Odds Ratio (M-H, Fixed, 95% CI)	1.28 [0.73, 2.24]
16 Ever unprotected intercourse in past six months	5	2024	Odds Ratio (M-H, Fixed, 95% CI)	0.96 [0.79, 1.16]
17 Condom use at 12 months	3	3766	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.87, 1.16]
18 Condom use at 6 months	2	1247	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.66, 1.34]
19 Condom use at 3 months	1	296	Odds Ratio (M-H, Fixed, 95% CI)	0.77 [0.48, 1.25]
20 Condom use in last month	1	254	Odds Ratio (M-H, Fixed, 95% CI)	1.54 [0.94, 2.53]
21 Condom use at last sex	1	265	Odds Ratio (M-H, Fixed, 95% CI)	1.18 [0.71, 1.94]

Analysis 1.1. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 1 Pregnancy (at twelve-month follow-up).

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 1 Pregnancy (at twelve-month follow-up)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hu 2005	38/974	32/974		24.9 %	1.20 [0.74, 1.93]
Jackson 2003	16/152	17/163		11.9 %	1.01 [0.49, 2.08]
Lo 2004	7/499	9/487		7.3 %	0.76 [0.28, 2.05]
Raymond 2006	67/724	70/717		51.6 %	0.94 [0.66, 1.34]
Schreiber 2009	3/16	8/22		4.4 %	0.40 [0.09, 1.86]
Total (95% CI)	**2365**	**2363**		**100.0 %**	**0.98 [0.76, 1.25]**

Total events: 131 (Treatment), 136 (Control)

Heterogeneity: $Chi^2 = 2.27$, df = 4 (P = 0.69); $I^2 = 0.0\%$

Test for overall effect: Z = 0.19 (P = 0.85)

Analysis 1.2. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 2 Pregnancy (at seven-month follow-up).

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

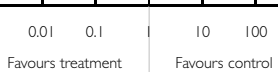
Outcome: 2 Pregnancy (at seven-month follow-up)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Schwartz 2008	6/127	13/138		100.0 %	0.48 [0.18, 1.29]
Total (95% CI)	**127**	**138**		**100.0 %**	**0.48 [0.18, 1.29]**

Total events: 6 (Treatment), 13 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 1.45 (P = 0.15)



Analysis 1.3. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 3 Pregnancy (at six-month follow-up).

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

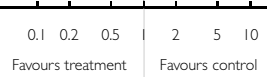
Outcome: 3 Pregnancy (at six-month follow-up)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Belzer 2005	4/57	10/54		8.5 %	0.33 [0.10, 1.13]
Ekstrand 2008	4/158	3/136		2.8 %	1.15 [0.25, 5.24]
Gold 2004	13/119	18/135		13.4 %	0.80 [0.37, 1.71]
Hu 2005	10/904	5/911		4.4 %	2.03 [0.69, 5.95]
Jackson 2003	4/138	5/149		4.2 %	0.86 [0.23, 3.27]
Lo 2004	2/507	4/503		3.6 %	0.49 [0.09, 2.71]
Raine 2005	66/826	27/310		32.2 %	0.91 [0.57, 1.45]
Raymond 2006	37/708	37/714		31.1 %	1.01 [0.63, 1.61]
Total (95% CI)	**3417**	**2912**		**100.0 %**	**0.92 [0.70, 1.20]**

Total events: 140 (Treatment), 109 (Control)

Heterogeneity: $Chi^2 = 5.61$, df = 7 (P = 0.59); $I^2 = 0.0\%$

Test for overall effect: Z = 0.65 (P = 0.52)



Analysis 1.4. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 4 Pregnancy (at three-month follow-up).

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 4 Pregnancy (at three-month follow-up)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hazari 2000	2/99	4/99		100.0 %	0.49 [0.09, 2.74]
Total (95% CI)	**99**	**99**		**100.0 %**	**0.49 [0.09, 2.74]**
Total events: 2 (Treatment), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.81 (P = 0.42)					

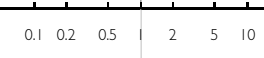
Analysis 1.5. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 5 Pregnancy for levonorgestrel regimens only.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 5 Pregnancy for levonorgestrel regimens only

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Belzer 2005	4/57	10/54		6.9 %	0.33 [0.10, 1.13]
Ekstrand 2008	4/158	3/136		2.3 %	1.15 [0.25, 5.24]
Lo 2004	7/499	9/487		6.5 %	0.76 [0.28, 2.05]
Raine 2005	66/826	27/310		26.0 %	0.91 [0.57, 1.45]
Raymond 2006	67/724	70/717		45.9 %	0.94 [0.66, 1.34]
Schreiber 2009	3/16	8/22		3.9 %	0.40 [0.09, 1.86]
Schwartz 2008	6/127	13/138		8.5 %	0.48 [0.18, 1.29]
Total (95% CI)	**2407**	**1864**		**100.0 %**	**0.82 [0.64, 1.05]**
Total events: 157 (Treatment), 140 (Control)					
Heterogeneity: Chi^2 = 5.05, df = 6 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 1.54 (P = 0.12)					



Analysis 1.6. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 6 Pregnancy for Yuzpe regimens only.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 6 Pregnancy for Yuzpe regimens only

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hazari 2000	2/99	4/99		21.1 %	0.49 [0.09, 2.74]
Jackson 2003	16/152	17/163		78.9 %	1.01 [0.49, 2.08]
Total (95% CI)	**251**	**262**		**100.0 %**	**0.90 [0.47, 1.74]**

Total events: 18 (Treatment), 21 (Control)

Heterogeneity: Chi^2 = 0.58, df = 1 (P = 0.45); I^2 =0.0%

Test for overall effect: Z = 0.31 (P = 0.76)

Analysis 1.7. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 7 Pregnancy for mifepristone regimens only.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 7 Pregnancy for mifepristone regimens only

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hu 2005	38/974	32/974		100.0 %	1.20 [0.74, 1.93]
Total (95% CI)	**974**	**974**		**100.0 %**	**1.20 [0.74, 1.93]**

Total events: 38 (Treatment), 32 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 0.73 (P = 0.47)

Analysis 1.8. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 8 Pregnancy for levonorgestrel or Yuzpe regimens.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

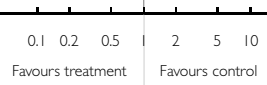
Outcome: 8 Pregnancy for levonorgestrel or Yuzpe regimens

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Belzer 2005	4/57	10/54		5.5 %	0.33 [0.10, 1.13]
Ekstrand 2008	4/158	3/136		1.8 %	1.15 [0.25, 5.24]
Gold 2004	13/119	18/135		8.7 %	0.80 [0.37, 1.71]
Hazari 2000	2/99	4/99		2.3 %	0.49 [0.09, 2.74]
Jackson 2003	16/152	17/163		8.5 %	1.01 [0.49, 2.08]
Lo 2004	7/499	9/487		5.2 %	0.76 [0.28, 2.05]
Raine 2005	66/826	27/310		20.9 %	0.91 [0.57, 1.45]
Raymond 2006	67/724	70/717		37.0 %	0.94 [0.66, 1.34]
Schreiber 2009	3/16	8/22		3.2 %	0.40 [0.09, 1.86]
Schwartz 2008	6/127	13/138		6.9 %	0.48 [0.18, 1.29]
Total (95% CI)	**2777**	**2261**		**100.0 %**	**0.83 [0.67, 1.03]**

Total events: 188 (Treatment), 179 (Control)

Heterogeneity: Chi^2 = 5.70, df = 9 (P = 0.77); I^2 =0.0%

Test for overall effect: Z = 1.66 (P = 0.097)



Analysis 1.9. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 9 Sexually transmitted infections.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 9 Sexually transmitted infections

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Ekstrand 2008	5/158	2/136		2.4 %	2.19 [0.42, 11.47]
Gold 2004	12/119	12/135		11.9 %	1.15 [0.50, 2.67]
Raine 2005	49/826	17/310		27.3 %	1.09 [0.62, 1.92]
Raymond 2006	49/725	53/714		58.4 %	0.90 [0.60, 1.35]
Total (95% CI)	**1828**	**1295**		**100.0 %**	**1.01 [0.75, 1.37]**
Total events: 115 (Treatment), 84 (Control)					
Heterogeneity: Chi^2 = 1.28, df = 3 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 0.09 (P = 0.93)					

Analysis 1.10. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 10 Ever use of emergency contraceptives during trial.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

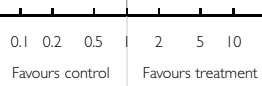
Outcome: 10 Ever use of emergency contraceptives during trial

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ekstrand 2008	54/172	29/157		10.5 %	2.02 [1.21, 3.38]
Gold 2004	26/119	20/135		9.1 %	1.61 [0.84, 3.06]
Hazari 2000	32/99	29/99		9.6 %	1.15 [0.63, 2.11]
Hu 2005	183/974	90/974		13.1 %	2.27 [1.73, 2.98]
Jackson 2003	28/152	9/163		7.7 %	3.86 [1.76, 8.49]
Lo 2004	149/499	63/487		12.6 %	2.87 [2.07, 3.97]
Raine 2005	309/826	65/310		12.8 %	2.25 [1.66, 3.06]
Raymond 2006	527/746	236/744		13.6 %	5.18 [4.15, 6.46]
Schreiber 2009	12/23	8/27		5.0 %	2.59 [0.81, 8.29]
Schwartz 2008	13/127	6/138		6.0 %	2.51 [0.92, 6.81]
Total (95% CI)	**3737**	**3234**		**100.0 %**	**2.47 [1.80, 3.40]**

Total events: 1333 (Treatment), 555 (Control)

Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 46.97$, df = 9 ($P<0.00001$); $I^2 = 81\%$

Test for overall effect: $Z = 5.55$ ($P < 0.00001$)



Analysis 1.11. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 11 Multiple uses of emergency contraceptives during trial.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

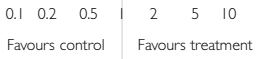
Outcome: 11 Multiple uses of emergency contraceptives during trial

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hu 2005	54/974	21/974		32.3 %	2.66 [1.60, 4.45]
Raine 2005	125/826	18/310		32.3 %	2.89 [1.73, 4.83]
Raymond 2006	381/746	81/744		35.3 %	8.54 [6.51, 11.21]
Total (95% CI)	**2546**	**2028**		**100.0 %**	**4.13 [1.77, 9.63]**

Total events: 560 (Treatment), 120 (Control)

Heterogeneity: $Tau^2 = 0.51$; $Chi^2 = 23.76$, df = 2 (P<0.00001); $I^2 = 92\%$

Test for overall effect: Z = 3.28 (P = 0.0010)



Analysis 1.12. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 12 Mean time interval between unprotected intercourse and use of emergency contraception.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 12 Mean time interval between unprotected intercourse and use of emergency contraception

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Ekstrand 2008	172	15.57 (12.69)	157	26.38 (19.34)		42.7 %	-10.81 [-14.38, -7.24]
Lo 2004	499	13.9 (14.4)	487	28.5 (19.8)		57.3 %	-14.60 [-16.77, -12.43]
Total (95% CI)	**671**		**644**			**100.0 %**	**-12.98 [-16.66, -9.31]**

Heterogeneity: $Tau^2 = 4.91$; $Chi^2 = 3.16$, df = 1 (P = 0.08); $I^2 = 68\%$

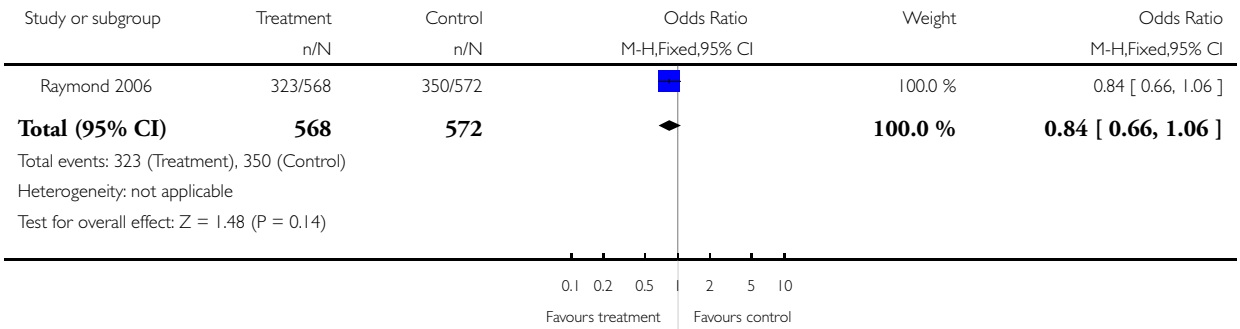
Test for overall effect: Z = 6.92 (P < 0.00001)

Analysis 1.13. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 13 Ever unprotected intercourse in past two weeks.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 13 Ever unprotected intercourse in past two weeks

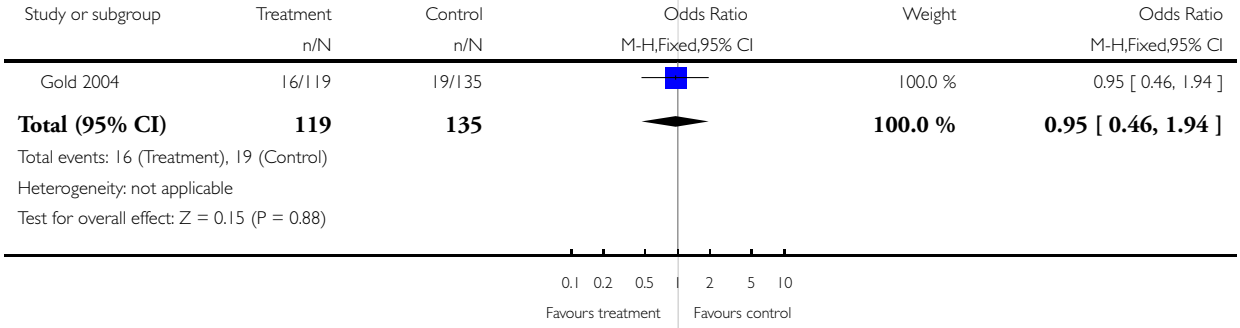


Analysis 1.14. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 14 Ever unprotected intercourse in past month.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 14 Ever unprotected intercourse in past month



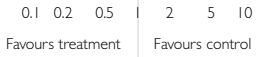
Analysis 1.15. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 15 Ever unprotected intercourse in past three months.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 15 Ever unprotected intercourse in past three months

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hazari 2000	47/99	41/99		100.0 %	1.28 [0.73, 2.24]
Total (95% CI)	**99**	**99**		**100.0 %**	**1.28 [0.73, 2.24]**
Total events: 47 (Treatment), 41 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.86 (P = 0.39)					



Analysis 1.16. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 16 Ever unprotected intercourse in past six months.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 16 Ever unprotected intercourse in past six months

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Belzer 2005	26/57	26/54		6.6 %	0.90 [0.43, 1.90]
Ekstrand 2008	54/121	45/107		12.0 %	1.11 [0.66, 1.88]
Jackson 2003	47/136	52/149		14.8 %	0.99 [0.60, 1.61]
Raine 2005	328/825	127/310		50.5 %	0.95 [0.73, 1.24]
Schwartz 2008	60/127	70/138		16.1 %	0.87 [0.54, 1.41]
Total (95% CI)	**1266**	**758**		**100.0 %**	**0.96 [0.79, 1.16]**
Total events: 515 (Treatment), 320 (Control)					
Heterogeneity: Chi^2 = 0.50, df = 4 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 0.43 (P = 0.66)					

Analysis 1.17. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 17 Condom use at 12 months.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

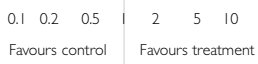
Outcome: 17 Condom use at 12 months

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hu 2005	625/822	629/817		41.0 %	0.95 [0.75, 1.19]
Lo 2004	395/499	391/487		22.4 %	0.93 [0.68, 1.27]
Raymond 2006	285/569	271/572		36.6 %	1.11 [0.88, 1.41]
Total (95% CI)	**1890**	**1876**		**100.0 %**	**1.01 [0.87, 1.16]**

Total events: 1305 (Treatment), 1291 (Control)

Heterogeneity: Chi^2 = 1.23, df = 2 (P = 0.54); I^2 =0.0%

Test for overall effect: Z = 0.08 (P = 0.94)



Analysis 1.18. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 18 Condom use at 6 months.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

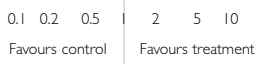
Outcome: 18 Condom use at 6 months

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Belzer 2005	21/57	21/54		21.4 %	0.92 [0.43, 1.97]
Raine 2005	99/826	39/310		78.6 %	0.95 [0.64, 1.41]
Total (95% CI)	**883**	**364**		**100.0 %**	**0.94 [0.66, 1.34]**

Total events: 120 (Treatment), 60 (Control)

Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.94); I^2 =0.0%

Test for overall effect: Z = 0.35 (P = 0.73)



Analysis 1.19. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 19 Condom use at 3 months.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 19 Condom use at 3 months

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Ekstrand 2008	48/149	56/147		100.0 %	0.77 [0.48, 1.25]
Total (95% CI)	**149**	**147**		**100.0 %**	**0.77 [0.48, 1.25]**
Total events: 48 (Treatment), 56 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.06 (P = 0.29)					

Analysis 1.20. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 20 Condom use in last month.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 20 Condom use in last month

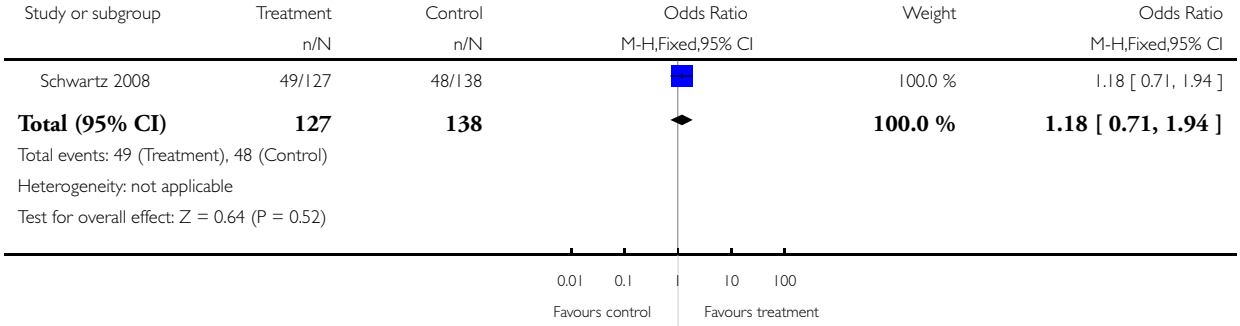
Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Gold 2004	70/119	65/135		100.0 %	1.54 [0.94, 2.53]
Total (95% CI)	**119**	**135**		**100.0 %**	**1.54 [0.94, 2.53]**
Total events: 70 (Treatment), 65 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.70 (P = 0.090)					

Analysis 1.21. Comparison 1 Advance provision vs. standard provision of emergency contraception, Outcome 21 Condom use at last sex.

Review: Advance provision of emergency contraception for pregnancy prevention

Comparison: 1 Advance provision vs. standard provision of emergency contraception

Outcome: 21 Condom use at last sex



WHAT'S NEW

Last assessed as up-to-date: 9 November 2009.

11 January 2010	New search has been performed	Added information from 3 new included studies and noted new excluded studies.

HISTORY

Protocol first published: Issue 4, 2005

Review first published: Issue 2, 2007

14 April 2009	Amended	Converted to new review format.
14 January 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Chelsea Polis and Kate Schaffer generated drafts of the protocol, and all authors provided input. Chelsea Polis drafted the data abstraction sheets and conducted the literature search with input from all authors. Chelsea Polis and David Grimes abstracted and entered the data for the original study and for the November 2009 update. All authors provided input to the analysis and writing.

DECLARATIONS OF INTEREST

Two review co-authors were also co-authors of included studies (Cynthia Harper: Raine 2005, and Anna Glasier: Lo 2004 and Hu 2005).

SOURCES OF SUPPORT

Internal sources

- Ibis Reproductive Health, USA.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Pregnancy Rate; Contraception, Postcoital [*methods; utilization]; Contraceptives, Postcoital [administration & dosage; *supply & distribution]; Randomized Controlled Trials as Topic; Sexually Transmitted Diseases [*epidemiology]

MeSH check words

Female; Humans; Pregnancy