

Sexual and Contraceptive Behavior studies on Plan B A Literature Review

SUMMARY

The sponsor submitted five published and three unpublished studies of varying quality that assess the effects of advance provision of emergency contraception on sexual and contraceptive behaviors. When reviewing these studies as a body of evidence, the quality or applicability of each study must be considered. While most of the studies state that they were randomized, only one study (Ellertson) used a random number generator as the method of randomization. The other studies used systems such as date of clinic visit or other less desirable systems. The two unpublished studies would not have received peer review (although Gold et. al was recently accepted for publication by the Journal Of Pediatric and Adolescent Gynecology). Three of the studies were performed in foreign countries and may have limited generalizability to the United States. The overall summary of eight behavioral studies is presented below and in Table 1 followed by the individual reviews.

STUDY DESIGN

1. **Study Location:** Five studies were conducted in the USA and one each was conducted in the UK, Africa and India.
2. **Subjects:** All subjects in the eight studies were recruited from family planning clinics (the purposes for visiting the clinics were EC consultation, post-abortion follow-up and postpartum evaluation). The age range was 15-45 years with most enrollees being around 20 years old.
3. **Study Groups:** Subjects were randomly (in most studies) assigned to the following 2 or 3 groups. All subjects received education regarding emergency contraception use (this is in contradistinction to the actual use study submitted by the sponsor where education was not given to the subjects enrolled in the study, thereby more closely mimicking an OTC environment).

Advance EC Group: Subjects received in advance one course of EC pills in six studies and three courses of EC pills in two studies (one in US and one on India);

Control Group: Subjects received EC education only (including advice on where to get and how to use EC) except for one study where EC education was not given in the control group;

Pharmacy EC Access Group: Subjects received EC when needed from pharmacy in one US study (in California).

4. **Sample Size:** Number of subjects ranged from 160 to 1020 in the five US studies and 210-1083 in three studies outside US.

5. ***Follow-up Period:*** Subjects were followed from 8 weeks up to 1 year after admission to the studies.

RESULTS

1. ***EC Use:*** All studies suggest that the advance EC provision increase EC use. This supported the hypothesis of the studies that easier access would translate into increased use.
2. ***Unprotected Sex:*** In these studies, unprotected sex was defined as lack of use of a contraceptive. All studies demonstrated that compared to baseline, the advance EC group and control group had decreased frequency of unprotected sex. In some studies, the decrease in unprotected sex was greater in the control group.
3. ***Condom Use:*** One US study (sponsored by Women’s Capital Corporation) suggests that the advance, pharmacy and standard EC access groups plus EC education had an increase in more effective methods of contraception with a corresponding decrease in condom use. The other 6 studies either demonstrated no significant decrease in condom use with advance EC provision or in education alone (control groups) or demonstrated that “used condoms every time” increased in treatment and control groups when compared to baseline.
4. ***Consistent Use of Regular Contraception:*** Most of the studies demonstrate that women in both the treatment and control groups increase their use of a regular contraception compared to baseline. One US study suggest that women with advance EC access are more likely to use less-effective contraception (although they had less unprotected sex compared to baseline and increased “condom use every time” from 12% at baseline to 47% at study completion), and another US study showed higher frequency of missing oral contraceptive pills in subjects provided with advance EC than those in control.

COMMENTS

1. These studies were not conducted in a simulated OTC setting. However, several of the studies would have recruited a similar subject population as that used in the actual use study. The main difference in design would be that subjects in the literature review would have received education compared to the subjects in the actual use study and would have received an advanced provision of EC.
2. Subjects were recruited exclusively from clinic sites and received EC education during enrollment (except one study in which control subjects did not receive EC education), which can not be generalizable to the OTC population.
3. Study population in each study was a subset of general population and was heterogeneous among all these studies. This diversity is desirable reflecting many

subgroups and capturing the many aspects of an OTC population. The similarity of results is also reassuring in that the different subsets tend to exhibit the same behavioral trends.

4. Most studies provided only one course of advance EC. In those studies, after the one course of EC pills were used, subjects in the advance EC group would have the same accessibility to EC as the control group.
5. Subjects recruited and studies conducted outside US may not be extrapolated to US population.
6. There were limitations of design and/or methodology of the studies and conclusions should be considered in that context.

CONCLUSION

1. The literature review studies suggests that the advance access of emergency contraception did not increase the likelihood of unprotected sex in women populations who visited family planning clinics. The study duration's ranged from 4-12 months in follow-up. The results may provide certain supportive evidence to resolve some issues raised from the actual use study (such as whether consistent use of routine contraception persist greater than the one month of observation in the actual use study data submitted by the sponsors).
2. The studies did not simulate an OTC setting although some of the studies have recruited similar subject populations as those enrolled in the actual use study.
3. Most of the studies demonstrate that women in both the treatment and control groups increase their use of a routine contraception (less unprotected sex) compared to baseline.
4. Most of the studies either demonstrated no significant decrease in condom use with advance EC provision and control groups or demonstrated that "used condoms every time" increased in treatment and control groups when compared to baseline

Table 1. Effects of Emergency Contraception under Advance Provision on Sexual and Contraceptive Behavior

Author & Publication	Study Design	Study Location	Subjects	Follow-up Periods	Advance EC Access caused changes in	
					Sexual Behavior	Contraceptive Behavior
Raine et al: <i>Obstet Gynecol</i> 2000 Literature #1	Non-randomized 2 groups: Advance EC (one EC course) & Control (EC education)	USA, Family planning clinics	263 women age 16-24 (64% adolescents); 32% Latina & 29% AA; Excluded subjects presenting for EC	4 months	Decrease in unprotected sex in both groups vs. baseline (Control>Tx)	More likely to use less effective contraception (increased condom use) Increased EC use;
Raine et al: UCSF Study (NDA: vol 13, p134) Unpublished Literature #2	Randomized 3 groups: Advance EC Provision (3 EC courses), Pharmacy EC Access; Standard EC Access	USA, Family planning clinics	1020 women age 15-24 years (20±3 yrs); 20% Latina & 17% AA Excluded subjects presenting for EC	6 months	Decrease in unprotected sex in all 3 groups vs. baseline (SA>PA>AP(p<0.05 in PA & SA groups) No increase in incidence of STDs compared to Std EC Access	Increase in OC use in all 3 groups with an offset decrease in condom use in all 3 groups Decrease in condom use greatest in AP & PA groups
Jackson et al, <i>Obstet Gynecol</i> 2003 Literature #3	Randomized 2 groups by date of hospital admin: Advance EC (one EC course) & Control (<i>but no EC education</i>)	USA, Inner-city hospital	370 Postpartum women age 26±6 yrs 72% Latina; 43% Married	6 months & 12 months	Increased consistent use of contraception and more effective method in both groups. No increase in report of unprotected sex	No change in routine contraception and condom use; Increase in EC use.
Belzer et al: <i>J Adol Health</i> (Abstract), 2003 Literature #4	Randomized 2 groups: Advance EC (one EC course) & Control	USA, Inner-city (unknown site)	160 adolescent mothers age 14-20 yrs; 83% Latina & 16% AA	6 months	No increase in unprotected sex (but limited data available)	No decrease in condom use and primary contraception between groups. No data provided on within group changes; (limited data available) Increase in EC use
Gold: Unpublished Manuscript Literature #5	Randomized 2 groups: Advance EC (one EC course) & Control	USA, an urban hospital-based adolescent clinic	301 adolescent women age 15-20 (17±2); 58% AA	8 months	No increase in unprotected intercourse No increase in STDs compared to control	No decrease in condom use; Other info not available

Glazier & Baird: <i>New Eng J Med</i> 1998 Literature #6	Randomized 2 groups by birth date: Advance EC (one EC course) & Control (EC education)	UK , Family planning clinics	1083 women age 16-44 (23% age 16-20), 20% >30 y/o Post EC or Therapeutic abortion	1-year	Decrease in unprotected sex in both groups vs. baseline.	Increase in OC use in both groups with decrease in condom use similar changes between 2 groups. Increase EC use.
Lovvorn et al: <i>Contraception</i> 2000 Literature #7	Non-randomized 2 groups: Advance EC (one EC course) & Control (EC education)	Africa , Family planning clinics	211 women (spermicide users) age 18-45 yrs	8 weeks	Decrease in unprotected sex compared to baseline in both groups (Control>AEC) Significant limitations in study design.	Increase EC use; Other info not reported. Significant flaws in study design.
Ellertson et al: <i>Obetet Gynecol</i> 2001 Literature #8	Randomized 2 group: Advance EC (3 EC course) & Control	India , family planning clinics	411 women (condom users); age 25±4 yrs (83% 20-29 yr); Barrier method users	12 months (38% 12-month; 90% 3-month); pts off study if switched to more reliable method (23%)	Similar proportion having unprotected sex vs. the control	Increase EC use.

Information in the table is extracted and summarized from the individual literature reviews as attached in the following pages.

The Advance EC (AEC) or the Advance EC Provision (AP) or Treatment(Tx) group : Subjects received EC pills in advance plus EC education at the enrollment.

The Control or Standard EC access (SA) group: Subjects received only EC education (except the Jackson's study, Literature #3) and were advised to request EC pills from the clinics (the same sites as the advance group) by prescription when needed.

The Pharmacy EC Access (PA) group: Subjects received EC pills from pharmacy without prescription.

OC: Oral Birth Control Pills; AA: Africa American; EC: Emergency Contraception; STDs: sexually transmitted diseases;

Table 1 (Cont). Effects of Emergency Contraception under Advance Provision on Sexual and Contraceptive Behavior

Literature #1 (vol. 13, page 068)

Emergency Contraception: Advance Provision in a Young, High-Risk Clinic Population

Author: Tina Raine, Cynthia Harper, Kathleen Leon, and Philip Darney

Affiliate: Department of Obstetrics, Gynecology, and Reproductive Sciences
Center for Reproductive Health Research and Policy
University of California, San Francisco, California.

Sponsor: Compton Foundation, Menlo Park, California
Fred Gellert Family Foundation, San Francisco, California.

Study Location: *USA*, Family Planning Clinics, San Francisco, California
From June to November 1998

Publication: *Obstet Gynecol* 96:1–7, 2000

Design: Single-center, *non-randomized*, clinical trial;
4-month follow-up
Single course of Advance EC Provision

METHODS

Subject

A total of 263 female subjects were recruited and enrolled from a family planning clinic of San Francisco General Hospital between June and November 1998.

Inclusion criteria:

- Women age 16–24 years
- Able to speak English or Spanish
- Available for follow-up in 4 months.

Exclusion criteria:

- Pregnancy
- Using contraceptive implants
- Using intrauterine devices
- Presentation for emergency contraception
- Contraindications to oral contraceptive (OC) pills.

The subjects were assigned on an *alternating basis* into the following 2 groups:

Treatment groups: 130 subjects received EC education and one course of EC pills (comprised 8 OC pills; each contained 0.15 mg of levonorgestrel and 30 ug of ethinyl estradiol).

Control group: 133 subjects received EC education alone.

Data Collection

Research assistants interviewed subjects at enrollment and at follow-up (at 4 month by telephone or clinic visit) using a questionnaire to obtain demographic information and to measure outcomes, including contraceptive methods and patterns of use.

Data Analysis

All analyses were conducted using the intent-to-treat population, with all study subjects analyzed according to their initial group assignment. Differences between Treatment and Control were analyzed with a Chi-square test for categorical variables and t tests for continuous variables. A multiple logistic regression analysis was used to determine the effect of advance provision of emergency contraception on use at follow-up.

RESULTS

Subject Demographics

Only age and race/ethnicity were reported in the article, as summarized in Table 1. The mean age was 19 years (64% adolescents). Most subjects were minorities. The demographic distribution between 2 groups was similar.

Table 1. Demographics of Subjects
(% of enrolled subjects)

Demographic	Treatment n=130	Control n=133	Total n=263
Mean age (years)	19.2	18.8	19.0
Race or ethnicity			
Hispanic	33.1	30.1	31.6
Black	26.2	31.6	28.9
White	16.9	12.8	14.8
Asian	14.6	16.5	15.6
Other (biracial)	9.2	9.0	9.1
Primary language Spanish	16.2	14.3	15.2

Data were extracted from the author's Table 1.

Baseline Characteristics

At enrollment the sexual activity, contraception, pregnancy history and reasons for clinic visit were comparable between treatment and control groups (Table 2), except that the history of unprotected sex was lower in the treatment group than in control group (15% vs. 24%). The most common contraception method used by the study population was condoms, and a higher proportion of subjects in the treatment arm reported at baseline that they used condoms for contraception than in the control arm (47% vs. 39%). At baseline a higher proportion of the subjects in the control arm reported that their use of either condoms or oral contraceptives was consistent (used condoms every time, never missed pills) than subjects in the treatment arm. Consistent condom use was reported in 24% of control subjects who used condoms compared to 12% on the treatment arm. Consistent use of oral contraceptives was reported in 42% of the control subjects who used oral contraceptives, compared to 25% on the treatment arm.

The table below demonstrates that the subjects in the treatment arm reported higher frequency of sexual acts, higher proportion of condom use as a method of contraception, lower rate of unprotected sex, higher proportion with a history of elective abortion, higher proportion with a history of pregnancy and more births. More subjects in the treatment arm presented to the clinic visit for an “infection check”.

Table 2. Baseline Traits of Subjects at enrollment
(% of enrolled subjects)

Baseline Characteristics	Treatment n=130	Control n=133	Total n=263
<i>Reason for clinic visit*</i>			
Papanicolaou smear or check-up	16.2	19.5	17.9
Contraception	39.2	32.3	35.8
Follow-up abortion	7.7	6.8	7.2
Pregnancy test	37.7	44.4	41.4
Infection check	20.8	13.6	17.1
<i>First visit to clinic</i>	38.8	40.6	39.7
<i>Pregnancy History</i>			
Ever pregnant	56.2	47.4	51.7
Ever gave birth	20.8	16.5	18.6
Ever had an elective abortion	40.8	34.6	37.6
<i>History of sexually transmitted disease</i>	18.6	18.0	18.3
<i>Sexual Acts in past 4 months</i>			
None	3.8	5.3	4.6
Sporadic [†]	33.9	39.8	36.9
Once a week	25.4	27.8	26.6
More than once a week	36.9	27.1	31.9
New sexual partner	23.1	21.0	22.0
<i>Current contraception[‡]</i>			
Condoms	46.9	39.1	43.0
Oral contraceptive	27.7	24.8	26.2
Depot medroxyprogesterone acetate	10.0	11.3	10.6
Other	0.7	0.8	0.8
None (unprotected sex?)	14.6	24.1	19.4
Dual use (hormonal with condoms)	16.9	17.3	17.1

* Participant might have had more than one reason for clinic visit.

† Sporadic: once or twice in past 4 months or once to twice a month.

‡ Current contraception: most effective method reported if more than one used.

Changes in Sexual and Contraceptive Behavior (Table 5)

EC Use:

- Women in the treatment group were significantly more likely to use emergency contraceptives than those in control groups (20% vs. 7%, $p=0.006$). This difference between treatment arms remained statistically significant in multiple logistic regression analyses that evaluated the impact of contraceptive method, pattern of contraceptive use at enrollment and frequency of unprotected sex reported at enrollment.
- Overall EC use increased from enrollment to follow-up (4% vs. 14%) in both groups, with more increase in the treatment group.

Routine Contraception:

- Women in the treatment group were more likely to have switched to a less-effective contraception method than those in the control groups at the time of follow-up (28% vs. 17%, $p=0.05$). (Level of effectiveness was ordered from most effective to least effective for this analysis as follows: depot, oral contraceptive, barrier, none.) The proportion that didn't change method or continued to use no method at all was similar between arms at the time of follow-up.
- Women in the treatment group tended to be less likely to use more effective contraception than those in the control groups (20% vs. 29%, $p=0.1$).
- The proportion of women in the treatment group who reported consistent oral contraceptive (OC) use was less than in the control group at baseline (25% vs. 42%, $p=0.08$). Although the proportion reporting consistent oral contraceptive use remained lower on the treatment arm relative to the control arm at the time of follow-up (32% vs. 58%, $p=0.03$), the proportion of subjects who reported consistent use increased in both groups at the time of follow-up.

Unprotected Sex:

- Overall "never had unprotected sex" (had protected sex) increased at the follow-up as compared to that at the enrollment (33% vs. 56%). As compared to the baseline, increase in protected sex was 18% (from 32% to 50%) in the treatment group and 28% (from 34% to 62%) in the control group (no statistical tests were available).

Condom Use:

- Condom use increased in both groups at follow-up as compared to at enrollment (Treatment group: 12% vs. 47.4%, Control group: 24.3% vs 50%).

- There were no significant difference at the time of follow-up between treatment and control groups in the proportion of condom use.
- Since there was less condom use at baseline in the treatment group than in control group, the proportionate increase in condom use in the treatment group was greater than in control group (4x increase vs. 2x increase).

Table 5. Contraceptive Behavior during the Study Period Compared to Baseline Between Treatment and Control Groups
(% of enrolled subjects)

Contraceptive Behavior	Treatment % (n)	Control % (n)	Total % (n)	P
Initial (at Enrollment)				
Never had unprotected sex	32.3 (42)	33.8 (45)	33.1 (87)	0.92
Used condoms every time	12.0 (10)	24.3 (18)	17.8 (28)	0.08
OC users who never missed pills	25.0 (11)	42.2 (19)	33.7 (30)	0.08
Used emergency contraception	4.6 (6)	3.0 (4)	3.8 (10)	0.75
Follow-up				
Never had unprotected sex	50.4 (56)	61.8 (63)	55.9 (119)	0.42
Used condoms every time	47.4 (18)	50.0 (19)	48.7 (37)	0.71
OC users who never missed pills	31.7 (13)	57.8 (26)	45.4 (39)	0.03
Used emergency contraception	19.8 (22)	6.9 (7)	13.6 (29)	0.006
More effective method [†]	19.8 (22)	29.4 (30)	24.4 (52)	0.10
Less effective method [‡]	27.9 (31)	16.7 (17)	22.5 (48)	0.05
No method at enrollment and follow-up	7.2 (8)	6.9 (7)	7.0 (15)	0.92
Same method at enrollment and follow-up	45.0 (50)	47.1 (48)	46.0 (98)	0.77

Data are extracted from the author's Tables 2, 4 and 5.

[†] More effective methods: Depot medroxyprogesterone acetate and OC; and [‡] less effective methods: spermicides, diaphragms, and withdrawal.

COMMENTS

1. The subjects were not randomly assigned. This created an imbalance at baseline (unprotected sex, condom use, missed OC pills and EC use) and could have introduced bias into the study. This is a major flaw and limits conclusions.
2. Only a single course of EC was provided to the treatment group (advance provision), so the study observation may not truly reflect changes in sexual and contraceptive behaviors that may occur in the OTC setting.
3. Information on education, literacy level, and income of subjects were not provided. Given the non-randomized design there are no assurances of an even distribution of these demographics.
4. Sample size was small (n=130 in the Advance group and n=133 in the Control group).
5. Subjects were recruited from clinical sites and were high risk, which may not be generalizable to OTC population.

CONCLUSION

This study demonstrated the following: Compared to their baseline, women age 16-24 with advance EC provision are::

- Less likely to have unprotected sex
- More likely to use condoms (every time)
- More likely to use EC pills
- More consistent with their use of OC pills
- Compared to the control group, the women provided with Advance EC were more likely to switch to a less effective routine contraception method and have a higher proportional increase in condom use

When compared to the treatment group, the control group was more likely to have a greater absolute change in “Never had unprotected sex” and “Never missed pills”. However, it should also be noted that at baseline, the treatment group appeared to potentially be a higher risk group compared to the control group, with a greater percentage of subjects that were presenting to the clinic for contraception, infection checks, had been pregnant, had given birth, had an elective abortion, had a new sexual partner in the past 4 months and had an elective abortion. Because of these imbalances at baseline, between group comparisons should be made with caution.

Literature #2: UCSF Study #H9738-18501-02
(Vol. 32/p134; EDR dated 2003-09-08)

Provision of Emergency Contraception to Women enrolled in the study prior to December 31, 2001: Pharmacy Access and Advance Distribution Evaluation

Investigator: UCSF (by Tina Raine, et al)

Sponsor: Women's Capital Corporation

Study Location: USA, Family Planning clinics four clinical (San Francisco)
July 9, 2001 to December 31, 2001

Report Date: January 30, 2003 (prepared by Pinney Associates)

Published: Not

Study Design: Randomized 3-arm clinical trial
6-12-month follow-up
3 courses of advance EC.

Primary objectives:

To compare the rates of unintended pregnancy and sexually transmitted disease (STD) among three different distributions (*advance provision, pharmacy access and standard access*) for emergency contraception.

Secondary objectives:

To assess the effects of the three different emergency contraception distribution methods on *sexual and contraceptive behaviors*, such as the frequency of unprotected sex, and use of condoms, oral contraceptives, and emergency contraception use.

METHODS

Subjects

Subjects were recruited from four family planning clinic sites (Table 1) in the San Francisco bay area (CA) with the following inclusion and exclusion criteria.

Inclusion Criteria

- Women age 15-24 at high risk for unintended pregnancies
- Speak either Spanish or English
- Be available in 6 months for a follow-up visit.

Exclusion Criteria

- Women were currently pregnant;
- Actively trying to get pregnant;
- Sterilized; using Depo-Provera, IUD, Norplant or Lunelle;
- Reported having had unprotected sexual intercourse in the past 3 days.
- Women who presented to the clinic specifically requesting emergency contraception (*the rationale was not specified*)

Table 1. Enrolled subjects and follow-up compliance from 4 clinical sites

Clinical Sites (San Francisco, CA)	Pharmacy Access (N = 343)	Advance Provision (N = 340)	Standard Access (N = 337)	Total (N = 1020)
City College	30 (96.8)	29 (90.6)	31 (96.9)	90 (94.7)
Planned Parenthood: Dale City	44 (97.8)	42 (95.5)	40 (88.9)	126 (94.0)
New Generations	136 (91.9)	141 (95.9)	128 (90.8)	405 (92.9)
Planned Parenthood: San Francisco	104 (87.4)	104 (88.9)	107 (89.9)	315 (88.7)

Data were adapted from the author's Table 4 (p6).

Subject Disposition

Of 2012 screened women, 1,020 were enrolled (see below) and randomly assigned into 3 groups.

Total approached women:	2,012	(100%)
Total screened women:	1,804	(89.7%)
Ineligible women:	992	(49.3%)
Eligible women:	1,024	(56.7%)
Enrolled subjects:	1,020	(56.4%)

Pharmacy Access (PA): Subjects in this group obtained Plan B at the local pharmacy without a prescription through a collaborative agreement between clinics and pharmacies;

Advance Provision (AP): Subjects were given Plan B (3 complete packages) to take home and use as needed;

Standard Access (SA): Subjects returned to the clinic to obtain supplies.

All subjects received information and counseling on emergency contraception, and were reimbursed \$10 (during the visit). They were also reimbursed \$20 for completing the follow-up visit procedure.

Data Collection

Baseline data: urine tests (for pregnancy, Chlamydia and gonorrhea) and blood test (for HSV-2 antibody) and interview (for demographics, sexual history, knowledge of emergency contraception).

Follow-up visit: occurred 6 months or more (up to 1 year) after enrollment. Data were collected on sexual history, use of emergency contraception, urine test (for pregnancy, Chlamydia, and gonorrhea), and blood test (for HSV-2 antibody).

Data Analysis

One-way analysis of variance, contingency table analyses, and a Chi-square test were used for different variables. In cases of small numbers, when cells had fewer than 5 observations, the Fisher's exact test was conducted. All analyses were evaluated at the two-tailed probability level of $p < 0.05$ and no adjustments were made for the number of analyses or pair-wise comparison.

RESULTS

Subject Demographics

Demographic characteristics of the enrolled subjects are summarized in Table 2. Overall they were comparable among the 3 study groups. Races (white, black, Latina, and Asian) were evenly distributed among 3 groups. The following were the major characteristics:

Mean age:	20±2.6 (15-24) years
Marital status:	86% single
Active sex (within 6 months):	100%
Unprotected intercourse (within 6 months):	50%
Currently using condoms:	67%
Currently using oral contraceptives:	41%
Previous emergency contraception:	35%
Education and literacy level:	unknown (not reported).

A third of participants reported having been pregnant previously, with 9% reporting ever given birth.

Follow-up Compliance

Approximately 92% of subjects (936 of 1,020) in each group completed follow-up assessment within one year (211±39 days) (Table 3).

Table 2. Demographics of subjects

Demographics	Pharmacy Access (N = 314)	Advance Provision (N = 316)	Standard Access (N = 306)	Total (N = 936)
<i>Age (years)</i>				
Mean ± SD	19.7 ± 2.6	19.7 ± 2.6	19.9 ± 2.6	19.7 ± 2.6
<i>Race</i>				
Latina	66 (21.0)	64 (20.3)	60 (19.6)	190 (20.3)
Black	53 (16.9)	54 (17.1)	52 (17.0)	159 (17.0)
White	79 (25.2)	100 (31.7)	83 (27.1)	262 (28.0)
Asian/Pacific Islander	57 (18.2)	62 (19.6)	69 (22.6)	188 (20.1)
Multiracial	48 (15.3)	29 (9.2)	35 (11.4)	122 (12.0)
Other	11 (3.5)	7 (2.2)	7 (2.3)	25 (2.7)
<i>Marital Status</i>				
Single	263 (83.8)	273 (86.4)	271 (88.6)	807 (86.2)
Cohabiting	42 (13.4)	31 (9.8)	28 (9.2)	101 (10.8)
Married	7 (2.2)	10 (3.2)	6 (2.0)	23 (2.5)
Married, but separated	2 (0.6)	-	-	2 (0.2)
Divorced	-	2 (0.6)	1 (0.3)	3 (0.3)
Widowed	-	-	-	-

Data were extracted from the author's Table 5 (p7) and presented as "No. (%)."

Table 3. Subject Disposition at Follow-up

Disposition	Pharmacy Access No. (%)	Advance Provision No. (%)	Standard Access No. (%)	Total No. (%)
Enrolled Subjects	343	340	337	1020
Lost to Follow-up	23 (6.7)	23 (6.8)	27 (8.0)	73 (7.2)
Refused Follow-up	6 (1.8)	1 (0.3)	4 (1.2)	11 (1.1)
Completed Follow-up*	314 (91.6)	316 (92.9)	306 (90.8)	936 (91.8)

* Mean follow-up days (post-baseline) was 211±39 days, median follow-up days: 195 days. There were no statistical differences in demographics of subjects between Lost-to-Follow-up and Completed-Follow-up.

Sexual and Contraceptive Behavior

Pregnancy:

The overall pregnancy rate (Table 4) in the 936 subjects who completed the follow-up interview was 8%. There were no differences in pregnancy rate among 3 groups including when analysis was controlled for baseline history of pregnancy ($p < 0.89$, Chi-square test).

Sexually Transmitted Diseases (STDs):

Subjects were considered to have acquired an STD during the follow-up period if they were positive for herpes (new diagnosis), chlamydia, gonorrhea (self-reported *or* by laboratory tests), trichomonas, PID (self-reported). There were no differences in STD acquisition among 3 groups when controlling for baseline history of STDs ($p < 0.427$, Chi-square test).

Table 4. Pregnancy and STD during study

Outcome		Pharmacy Access (N = 314)	Advance Provision (N = 316)	Standard Access (N = 306)	Total (N = 936)
Pregnancy	Previous	108 (34.4)	97 (30.7)	99 (32.5)	304 (32.5)
	Follow-up	24 (7.6)	26 (8.2)	25 (8.2)	75 (8.0)
STDs*	History	62 (19.8)	69 (21.8)	77 (25.4)	208 (22.3)
	Acquired during Study	58 (18.5)	47 (14.9)	51 (16.7)	156 (16.7)

Data were extracted from author's Tables 6, 7 & 8 (p8-9) and presented as "No. (%)."

* STDs at follow-up were newly acquired (not included baseline).

Emergency Contraception (Table 5):

Overall 29% (269 of 936) of subjects used emergency contraception during the study period.

1. Subjects were more likely to use emergency contraception in the Advance Provision group (39.2%) than in the Pharmacy Access group (26.5%) or in the Standard Access group (20.3%); they were also more likely to report convenience of emergency contraception compared to those in the Pharmacy Access group or the Standard Access group (96%, 87% and 87%, respectively).
2. There were no differences in the time to take the first pill among the 3 groups or in overall proper use of emergency contraception ($p > 0.05$). Subjects in the Standard Access group tended to have higher correct use than other 2 groups, 97% (SA), 92% (AP) and 90% (PA), and were more likely (100%) to take the second pill than the Advance Provision group (93%) and the Pharmacy Access group (90%). It should be

noted that the time interval for use of the second pill was not defined in this study as it was in the actual use study (12 hours after first pill).

- The proportion of repeat use was highest in the Advance Provision group. The baseline EC use was 35% for the entire study population.

Table 5. Emergency Contraception Usage during Study

EC Use	Pharmacy Access (N = 314)	Advance Provision (N = 316)	Standard Access (N = 306)	All Subjects (N = 936)
Total*	83 (26.5)	124 (39.2)	62 (20.3)	269 (28.8)
Never	230 (73.5)	192 (60.8)	244 (79.7)	666 (71.2)
One time	52 (16.6)	75 (23.7)	45 (14.7)	172 (18.4)
Two times	20 (6.4)	28 (8.9)	13 (4.3)	61 (6.5)
> 3 times	11 (3.5)	21 (6.7)	4 (1.3)	36 (3.8)

Data were extracted from the author's Table 10 (p13) and presented as "No. (%)".

*Pair-wise comparisons: AP vs. PA (p<0.001), AP vs. SA (p<0.001), and PA vs. SA (p<0.067).

Sexual behavior (Table 6):

Overall 96.6% (903 of 936) were sexually active during the study period.

- There were no statistically significant differences in the rates of unprotected sex among the 3 groups. Subjects in the Advance Provision group tended to have higher frequency of unprotected intercourse (47% in AP, 41% in PA and SA).
- As compared to the baseline, the frequency of unprotected sex decreased in all three groups. This change was statistically significant in the SA and PA groups but not in the AP group (Decrease from 50% to 41% in PA, and from 53% to 41% in SA, p<0.01 by McNemar's test; but from 49% to 47% in AP, p=NS).

Table 6. Sexual and Contraceptive Behaviors

Behavior	Pharmacy Access N=314	Advance Provision N=316	Standard Access N=306	Total N=936
Unprotected Intercourse				
<i>At Baseline (past 6 month)</i>				
Total	156 (49.7)	153 (48.6)	162 (52.9)	471 (50.4)
Every time	12 (3.8)	13 (4.1)	12 (3.9)	37 (4.0)
Most of the time	18 (5.7)	32 (10.2)	25 (8.2)	75 (8.0)
Some of the time	126 (40.1)	108 (34.3)	125 (40.9)	359 (38.4)
Never	158 (50.3)	162 (51.4)	144 (47.1)	464 (49.6)
At last sex	26 (8.3)	32 (10.1)	35 (11.4)	93 (9.9)
<i>At Follow-up(= 6 month)</i>				
Total	127 (40.6)	147 (46.7)	124 (40.5)	398 (42.6)
Every time	9 (2.9)	11 (3.5)	7 (2.3)	27 (2.9)
Most of the time	16 (5.1)	24 (7.6)	22 (7.2)	62 (6.6)
Some of the time	102 (32.6)	112 (35.6)	95 (31.1)	309 (33.1)
Never	186 (59.4)	168 (53.3)	182 (59.5)	536 (57.4)
At last sex	30 (9.6)	37 (11.8)	24 (7.9)	91 (9.7)
Condom Use				
<i>At Baseline (past 6 month)</i>				
Total	257 (81.8)	254 (80.4)	248 (81.3)	759 (81.2)
Every time	87 (27.7)	83 (26.3)	75 (24.6)	245 (26.2)
Most of the time	86 (27.4)	83 (26.3)	86 (28.2)	255 (27.3)
Some of the time	84 (26.8)	88 (27.9)	87 (28.5)	259 (27.7)
Never	57 (18.2)	62 (19.6)	57 (18.7)	176 (18.8)
Use at last sex	190 (60.5)	184 (58.2)	174 (56.9)	548 (58.6)
Currently using	219 (69.8)	214 (67.7)	192 (62.8)	625 (66.8)
<i>At Follow-up(= 6 month)</i>				
Total	226 (72.7)	232 (74.4)	224 (73.4)	682 (73.5)
Every time	84 (27.0)	68 (21.8)	78 (25.6)	230 (24.8)
Most of the time	77 (24.8)	82 (26.3)	75 (24.6)	234 (25.2)
Some of the time	65 (20.9)	82 (26.3)	71 (23.3)	218 (23.5)
Never	85 (27.3)	80 (25.6)	81 (26.6)	246 (26.5)
Use at last sex	159 (50.6)	154 (48.9)	170 (55.7)	483 (51.7)
Currently using	178 (56.7)	179 (56.7)	186 (60.8)	543 (58.0)
Oral Contraceptive Use				
<i>At Baseline (past 6 month)</i>				
Missing pill (per pack)	243 (63.6)	74 (58.3)	90 (68.7)	79 (63.7)
Use at last sex	117 (37.3)	125 (39.6)	115 (37.6)	357 (38.1)
Currently using	129 (41.1)	132 (41.8)	125 (40.9)	386 (41.2)
<i>At Follow-up(= 6 month)</i>				
Missing pill (per pack)	276 (68.0)	96 (65.7)	97 (70.3)	83 (68.0)
Use at last sex	159 (50.6)	150 (47.8)	141 (46.2)	450 (48.2)
Currently using	159 (50.6)	150 (47.5)	139 (45.4)	448 (47.9)

Data were extracted and summarized from author's Table 6 (p8) and Table 9 (p11), presented as "No. (%)"

Contraception Methods (Table 6):

There were no statistically significant differences in condom and OC uses among the 3 groups during the study period.

1. Overall condom use decreased in all 3 groups as compared with the baseline; condom use “at last sex” significantly decreased in the Advance Provision and the Pharmacy Access groups ($P < 0.01$), but remained relatively stable in the Standard Access group ($p < 0.65$).
2. During the same period that condom use decreased, there were increase in “currently using” OC in all groups compared to the baseline. The “Use at last sex” increased in all groups (PA change=37% to 51%, AP change=40% to 48% and SA change=38% to 46%).

Age difference:

There were no significant differences in observed parameters (pregnancy, condom use, unprotected sex, routine OC use) between adolescents (15-17 years old) and adults (18-24 years old).

COMMENTS

1. The proportion of 15-17 year olds and the literacy level of subjects were not provided.
2. “Baseline” STDs were reported, but the exposure period over which an infection was acquired was not captured. However, STDs acquired during the study among the 3 groups were comparable and were lower than the “baseline” history.
3. Overall unprotected intercourse decreased in all three groups compared to baseline. This change was statistically significant in the SA and PA groups but not in the AP group (from 50% to 41% in PA, and from 53% to 41% in SA, $p < 0.01$ by McNemar’s test; but from 49% to 47% in PA, $p = \text{NS}$).

SUMMARY

1. Advance Provision did not increase STDs as compared with the Pharmacy Access and the Standard Access to EC.
2. Subjects in the Advance Provision group were more likely to use EC pills as compared to the Standard and Pharmacy Accesses.
3. All three groups had less unprotected intercourse during the follow-up as compared to baseline. When compared to baseline, the PA and SA groups decreased more ($P < 0.01$) than the advance EC provision group ($p = \text{NS}$).
4. All three EC accesses were associated with a decrease in condom use, with statistically significant decreased differences in “use at last use” among the Advance Provision and the Pharmacy Access groups. However, the decrease in condom use was offset with increased oral contraceptive use.
5. Although there was greater OC use at study end compared to baseline for “use at last sex” and “currently using” in all 3 groups the proportion in all three groups who reported “missing OC pills” at study end compared to baseline increased.

CONCLUSION

Advance Provision of emergency contraception was not found to be associated with a difference in pregnancy rates or acquired STDs compared to Pharmacy Access or Standard Access. Advance Provision decreased unprotected intercourse compared to baseline, but to less of an extent than the Pharmacy Access or Standard Access groups. All three groups had increased OC use and decreased condom use. All three groups had increased “missing oral contraceptive pills” compared to baseline at study end. The highest rate of unprotected sex was in the AP group (49% vs. 41% in the PA & SA groups).

Literature #3 (sNDA 21-045, Serial No. 105, p5162)

Advance Supply of Emergency Contraception: Effect on Use and Usual Contraception—A Randomized Trial

Author: Rebecca A. Jackson, Eleanor Bimla Schwarz, Lori Freedman, and Philip Darney

Affiliate: Center for Reproductive Health Research and Policy and Department of Obstetrics, Gynecology, and Reproductive Sciences, and Division of General Internal Medicine Department of Medicine, UCSF, and San Francisco General Hospital, San Francisco, California.

Sponsor: Partially funded by an unrestricted grant from the Packard Foundation. The Packard Foundation is a nonprofit organization. They provided funds for supplies and oral contraceptive pills.

Study Location: *USA*, a public inner-city hospital in San Francisco
From September 1998 through March 1999

Publication: *Obetec Gynecol* 102: 8-16, 2003

Design: Randomized (by date of discharge) controlled clinical trial
1 year observation
Single course of advance EC provision

METHODS

Subject: A total of 370 *postpartum women* were enrolled from a public inner-city hospital (San Francisco, CA) from September 1998 through March 1999, with the following eligibility criteria:

- Age: (*was not specified in the Method*)
- Postpartum women (had a live birth)
- Spoke English or Spanish
- Available for follow-up in 1 year
- Had not undergone a postpartum tubal ligation

Subjects were randomly assigned to the following 2 groups:

Advance Provision Group: 184 subjects received one course of EC pills and EC education. The one course EC contained 8 oral contraceptive pills containing 0.15 mg of levonorgestrel and 30 ug of ethinyl estradiol. The educational session was a 5-minute

intervention and included instructions for obtaining additional emergency contraception pills if needed.

Control group: 186 subjects received only routine contraceptive counseling, and this *did not* usually include EC education.

To prevent interference of the difference education's that provided to each group, the investigators enrolled all women on a given day to the same group.

Data Collection: A Kaiser Family Foundation Questionnaire (survey) was the data collection instrument. The questionnaire was administered in person at enrollment and by phone at 6 and 12 months. The primary outcome was self-reported use of emergency contraception. Secondary outcomes included change in use of other contraceptive methods and knowledge about emergency contraception. Contraceptive and sexual behaviors were assessed by asking about types of contraception used and consistency of use.

Data Analysis: The individual subject was used as the unit of analysis. Differences between groups and differences within each group over time were analyzed using the Fisher exact test, Student *t* test, or the McNemar test.

RESULTS

Subject Demographics

Of 721 screened subjects, 370 were enrolled and randomized to the Advance EC group (184) and Control group (186). The demographics and baseline characteristics of the enrolled subjects are summarized in Table 1; there were no statistically significant differences between the two groups. Approximately 18% were teens; 72% were Latina; 43% married. About half had a high school education.

Follow-up Compliance

At 6 months after enrollment, follow-up was available for 78% and at 1 year, 69%. Overall, 85% were available for at least one follow-up session. There were no differences between groups in the proportion lost to follow-up; nor were there differences in baseline traits between those lost to follow-up and those who completed the study (Table 1).

Table 1. Demographics and Baseline characteristics of enrolled subjects
(% of enrolled subjects)

Characteristic	Advance EC	Control
	(n = 184)	(n = 186)
<i>Age</i> (mean \pm SD), <i>years</i>	26 \pm 6	26 \pm 6
<i>Ethnicity</i>		
Hispanic	69	74
Non-Hispanic black	11	11
Asian/Pacific islander	10	11
Non-Hispanic white	9	3
<i>Education</i>		
High school graduate	47	48
<i>Employed</i>	62	53
<i>Income > \$20,000</i>	11	11
<i>Private insurance</i>	4	2
<i>Married</i>	42	45
<i>Pregnancy history</i>		
Multiparous	49	48
Prior elective abortion(s)	16	18
Index pregnancy unplanned	65	64
Prior unwanted pregnancy	39	38
<i>Lost to Follow-up</i>		
At 6 months	25	20
At 12 months	30	31
Both 6 and 12 months	17	12

Data were extracted from author's Table 1 and Figure 1.

Sexual and Contraceptive Behavior

Sexual and contraceptive behaviors of subjects during 6 month period before and after enrollment in both groups were summarized in Tables 2 and 3.

Unprotected sex:

- Half the women in both groups reported at least one episode of unprotected intercourse during the 1-year follow-up period with no significant differences between groups, although the proportion was somewhat lower on the EC arm.

EC use:

- Women in the Advance EC provision group were significantly more likely to use ECPs during the study (13% vs 2% at one year).
- Subjects in both groups became more knowledgeable about emergency contraception during study periods; the Advance group demonstrated the greatest increase in knowledge.
- Five subjects used multiple doses of EC over the one year period, and three of them were in the Advance EC group.
- Approximately 25% of the study subjects could state the correct timing for using EC pills, which was consistent with results (18% correct use) from another study (Endres et al: *Experience with self-administered emergency contraception in a low-income, inner-city family planning program. J Reprod Med 2000;45:827–30*).

Condom use:

Among exclusive condom users, there was an increase in the use routine (“use mostly or always”) of condoms in both groups as compared to the baseline. The proportion of routine condom use was similar between groups at follow-up although the proportional increased from baseline was greatest in the control group.

Primary contraception:

As compared to baseline, there was a significant improvement in contraceptive use (more effective methods and consistency) in both groups during the 12-month follow-up, similar between groups.

COMMENTS

1. The study population, postpartum women from an inner-city hospital, is not completely generalizable to the spectrum of sexually active women expected in an OTC setting.
2. Only a single course of EC was provided to the Advance provision group, and few requested additional EC pills during the study.
3. There were not observed differences between the Advance EC group compared to the control group regarding unprotected intercourse rates at 6 month and 12 months..
4. Randomization procedure was by date of discharge was not ideal and the sample size was small (n=370). The majority of the study population was Latina postpartum women.

CONCLUSION

Advance EC access in the *postpartum women* during the 1-year observation:

1. Increases EC use
2. Did not adversely change routine contraception, including condom use. The advance EC group maintained similar contraception use as the control group. Routine contraception use increased in Advance EC and Control groups.
3. Did not increase the frequency of unprotected intercourse as compared to control subjects and over time.

Table 2. Use and knowledge of Emergency Contraception
(% of subjects who provided data)

Outcome	Baseline		At 6 months			At 12 months		
	Advance EC N=184	Control N=186	Advance EC N=138	Control N=149	RR (95% CI)	Advance EC N=128	Control N=128	RR (95% CI)
<i>Use of EC in prior 6 months</i>								
Use at least once	3	3	10	3	3.56 (1.19, 10.7)	13	2	5.21 (1.55, 17.5)
New users of EC			8	1	6.03 (1.36, 26.7)	10	2	4.17 (1.21, 14.4)
In those with any unprotected intercourse			22	3	7.74 (1.81, 33.2)	16	3	5.14 (1.14, 23.1)
<i>General EC knowledge†</i>								
Has heard of “EC” or “MAP”	34	38	90	47	1.91 (1.59, 2.29)	91	70	1.31 (1.16, 1.49)
Salient knowledge about EC	18	20	70	32	2.14 (1.66, 2.77)	71	52	1.38 (1.13, 1.69)

Data were extracted from author’s Table 2.

† “Heard of EC” indicates familiarity with the name “emergency contraception” or “morning-after pill.” “Salient knowledge” indicates the subject was able to correctly name or describe EC pills.

Table 3. Changes in contraceptive behavior
(% of subjects who provided data)

Outcome	Baseline		At 6 months			At 12 months		
	Advance EC N=184	Control N=186	Advance EC N=136	Control N=149	RR (95% CI)	Advance EC N=120	Control N=125	RR (95% CI)
Consistency of contraceptive use								
Routine use of contraception	35	37	85	83	1.02 (0.92, 1.12)	83	81	1.02 (0.91, 1.15)
Less consistent use compared with prior 6 mo			8	13	0.60 (0.30, 1.21)	18	25	0.74 (0.45, 1.20)
Any unprotected intercourse	?*	?*	47	52	0.91 (0.71, 1.17)	47	54	0.87 (0.67, 1.13)
Routine use of condoms in exclusive condom users [‡]	43	28	76	75	1.02 (0.79, 1.31)	87	92	0.94 (0.80, 1.12)
Effectiveness of contraceptive method[§]								
Very (< 5% failure)	56	57	71	70	1.01 (0.87, 1.18)	70	67	1.04 (0.88, 1.23)
Poor (> 10% failure)	44	43	29	30	0.97 (0.68, 1.38)	30	33	0.92 (0.63, 1.33)
Less effective method compared with prior 6 mo			18	22	0.79 (0.50, 1.27)	21	20	1.02 (0.62, 1.67)

[§] Very effective methods: sterilization, intrauterine device, depot medroxyprogesterone acetate, levonorgestrel implants, and oral contraceptives.

Poorly effective methods: barrier, withdrawal, rhythm, and none.

[‡] Condom use mostly or always in those who use only condoms. Numbers in EC and control at baseline, respectively: n = 54, 53; at 6 months: n = 38, 40; at 12 months: n = 31, 36; however, calculation of the percentages on this event in the Table was not specified in the report.

* The frequency of unprotected intercourse at baseline was not reported.

Literature #4 (vol. 13, page 007; Abstract)

Advanced supply of emergency contraception for adolescent mothers increased utilization without reducing condom or primary contraction use

Author: Marvin Belzer, Elizabeth Yoshida, Talar Tejirian, Diane Tucker, Katie Chung, Kathleen Sanchez

Affiliate: Children's Hospital Los Angeles, Los Angeles, California

Sponsor: Unknown

Study Location: USA, a large urban city (LA, California)
(Unknown site)

Publication: *J Adolescent Health* 32 (2): 5086 (Abstract only), 2003

Design: Randomized, 2-arm, single center trial
6-month follow-up
Single course of advance EC provision

METHODS

Subject

Adolescent mothers were recruited and enrolled from a large urban city (location and sites were not specified), age 14–20 years and not desiring pregnancy. Exclusion criteria were not reported. The subjects were randomized into the following 2 groups:

Treatment groups: subjects received *an advance supply* of levonorgestrel-only EC;

Control group: subjects received education on emergency contraception alone.

Data Collection

Subjects were contacted by phone at 6 months to collect the following data with a questionnaire: hormonal contraception use, condom use, sexual activity, unprotected sex, EC use, reasons for not using EC and pregnancy.

Data Analysis

Chi-square tests were conducted to assess differences between groups. Odds ratio and 95% CI were calculated to determine the association between contraceptive use and group assignment at baseline and follow-up.

RESULTS

Subject Demographics and Follow-up compliance

A total of 160 *adolescent mothers* were enrolled (number of screened subjects was not provided); their compliance with follow-up contacts at 6th and 12th month after enrollment is summarized in Table 1.

Table 1. Subject enrollment and follow-up compliance

Subject	Treatment	Control	Total
Enrollment	82	78	160
6 th month follow-up	57	54	110 (69%)*
12 th month follow-up	42	46	88 (55%)*

* % of enrolled subjects.

Demographics:

Mean age:	14-20 years
Hispanic:	83%
African American:	16%
Education:	unknown

Changes in Contraceptive Behavior

There were limited data available in the abstract about sexual and contraceptive behavior at baseline and follow-up (6th and 12th month) from both groups. Table 2 was extracted from text of the abstract.

Unprotected sex: The author stated that there were no increases in unprotected sex in the treatment group; but no data were provided.

EC use: Subjects in the treatment group were more likely to use EC.

Condom use: The author stated that there were no changes in condom use at 6th month between treatment and control groups, but no data were provided.

Primary contraception: The author stated that there were no changes in primary contraception at 6th month between 2 groups, but no data were provided.

Table 2. Sexual and contraceptive behavior

	Treatment One package EC N=57	Control Education only N=54	Total N=111
<i>Sexually active</i>			
Baseline	ND	ND	59%
At 6 th month	62%	57%	
<i>Unprotected sex</i>			
Baseline			7%
At 6 th month	ND	ND	No change
<i>EC Use*</i>			
At 6 th month	85%	19%	
At 12 th month	79%	21%	
Pregnancies at 6 th month	4 (7%)	10 (18%)	
Change in primary contraception	OR = 0.77 Between group comparison (95% CI: 0.47-1.25)		
Change in condom use	OR = 0.71 Between group comparison (95% CI: 0.32-1.57)		

ND: no data were reported in the abstract.

* % of subjects who had unprotected sex.

COMMENTS

1. There were limited data provided on primary parameters to evaluate changes of interest, particularly condom use and unprotected sex.
2. Subjects were adolescent mothers and may have limited generalizability to the OTC setting.
3. Only a single course of EC was provided to the advance provision group, which did not reflect access in an OTC setting.
4. Small study size may have led to lack of observed statistically significant differences.

CONCLUSION

Advance EC provision was reported not to decrease condom use and primary contraception during the 6-month follow-up.

Literature #5 (vol 13, page 023)

The Effects of Advance Provision of Emergency Contraception on Adolescent Women's Sexual and Contraceptive Behaviors

Author: Melanie A. Gold

Affiliate: University of Pittsburgh School of Medicine
Children's Hospital of Pittsburgh, Division of Adolescent Medicine

Sponsor: Laurel Foundation (unknown location) for financial support.
Woman's Capital Corporation provided Plan B.

Study Location: USA, an urban hospital-based adolescent clinic
Pittsburgh, PA from June 1997 to June 2002.

Publication: Unpublished Manuscript

Design: Single-center, randomized clinical trial
8 months follow-up
Single course of advance EC provision

METHODS

Subject

Sexually active female adolescents were recruited from the waiting room of an urban hospital-based adolescent clinic in a Children's Hospital in southwestern Pennsylvania between June 1997 and October 2001, with the following criteria:

Inclusion criteria:

Age 15–20 years
Available for monthly follow-up by phone.

Exclusion criteria:

Live in a foster-care or group home setting
Using long-acting contraception (such as IUD, Norplant, Depo-Provera)
OC users were not excluded.

Of 779 screened adolescent women, 301 (39%) were enrolled and randomly assigned to the following 2 groups:

Advance EC group: 150 subjects received EC education information and one course of EC pills, and were informed that they could obtain up to 2 additional EC courses during 6 months. Yuzpe (Jun 1997 – March 2000) and Plan B (after March 2000) were used.

Control group: 151 subjects received EC education information and were told how to request EC from the adolescent clinic (the same regimen as the Advance EC) if/when needed.

Data Collection

Self-reported sexual, contraceptive behavior, pregnancy, STDs and EC use for the past month and at last episode of intercourse were collected monthly by telephone interview for 6 months after enrollment. At least 5 attempts were made to reach each subject for monthly interview. EC knowledge was assessed at month 1 and 6 interviews only.

RESULTS

Subject Demographics

The following are major demographic characteristics. They were comparable between the 2 groups.

Mean age:	17.1 ± 1.7 years.
Race:	57% African-American (45% used public Medical Assistance for health care insurance coverage); 30% white.
Pregnancy history:	20%
STD history:	30%
Education:	59% high school (<i>not specified "in" or "completed"</i>) 28% college/trade school.
Contraception:	73% condom use; 69% aware of EC.

Compliance of follow-up

Approximately 85% of enrolled subjects at month 1 and 65% at month 6 were interviewed. The median length of follow-up was 252 ± 32 days from enrollment. The follow-up compliance between the 2 groups was comparable.

Changes in Sexual and Contraceptive Behaviors

Sexual and contraceptive behaviors of subjects from the Advance EC and control groups at the 1st and 6th month after enrollment are summarized in Table 1. In the original Table, the author did not indicate how the percentages were calculated. Therefore, this reviewer compiled the data from the original table using the number of subjects who completed interview as a denominator (Table 1). The trends of the results are similar to the original presentation. At study entry 20% of subjects had a history of pregnancy, 30% had a history of STD, and 69% reported awareness of EC. Twenty-five percent reported their last intercourse was unprotected, 73% reported condom use and 38% reported OC use.

Table 1. Sexual and contraceptive Behaviors
 [No. (% of subjects who completed interview)]

Behavior	First Month Follow-up		Sixth Month Follow-up	
	Advance EC	Control	Advance EC	Control
<i>Enrolled Subjects</i> †	150	151	150	151
<i>Completed Interview</i> †	123 (82)	131 (87)	91 (61)	105 (70)
<i>EC Use</i> ‡	(15)	(8)	(8)	(6)
<i>STDs</i> ‡			12 (13)	12 (11)
<i>In past month</i>				
Unprotected intercourse	24 (20)	28 (21)	16 (18)	19 (18)
Used condom	73 (59)	85 (65)	70 (77)	65 (62)
Used OC pills	42 (34)	51 (39)	33 (36)	50 (48)
Used any hormonal contraception	42 (34)	51 (39)	40 (44)	56 (53)
<i>At last intercourse</i>				
Unprotected	21 (17)	25 (19)	10 (11)	19 (18)
Used condom	70 (57)	80 (61)	67 (74)	66 (63)
Used OC pills	35 (28)	41 (31)	34 (37)	46 (44)
Used any hormonal contraception	35 (28)	41 (31)	39 (43)	50 (48)

Data were extracted from the author's Table 2, or Figure A (†) or text (‡).

The denominators used for percentage calculation was not defined in original Table, nor indicated in the report. The percentages in this table were recalculated using number of subjects who completed interview as a denominator.

EC Use:

At the first month, Advance EC group used EC more than control group (15% vs. 8%, $p=0.05$); there was no difference between the 2 groups at the 6th month. In multivariate analysis the only independent variable that predicted EC use was past pregnancy.

During the entire study, 22 subjects (15%) in the Advance EC group returned to request extra course of EC (17 returned once, 4 twice, and one 3 times). The Advance EC group reported more rapid first dose administration compared to the control group- 11 hours vrs 22 hours ($p<0.005$).

Unprotected Sex:

At both the first and sixth month, there were not differences in unprotected intercourse recorded for “in past month” or “at last intercourse” between Advance EC and control

groups. The proportion for both arms at month 1 and 6 were slightly lower than the baseline rate of unprotected intercourse, 25% on the Advanced EC arm and 24% on the control arm.

Contraception:

There were no significant differences in condom use, OC pill use or injectable contraceptive methods between Advance EC and control groups at one month. The proportion of EC subjects who reported condom use, 59% decreased from the baseline 76%. At 6 months a higher proportion of EC subjects reported use of condoms, 77%, than the control, 62% ($p=0.02$). At 6 months the proportion of EC subjects reporting condom use had returned to the baseline level. Over the course of the study, there were 13 (9%) pregnancies reported by the advance therapy group compared to 18 (11%) pregnancies reported by the control group.

STDs

There were 12 subjects each in the Advance EC and control groups who reported a newly-diagnosed STD during the study. By using number of subjects who completed interview as a denominator, 10% of subjects in the Advance EC group acquired STDs, compared to 9%.

COMMENTS

1. Data process and analysis were not clearly presented.
2. Only one course of EC was provided. Although the subjects could obtain an additional 2 courses, few subjects returned for additional request.
3. Subjects were interviewed monthly; however, only data from months 1 and 6 were reported.
4. About 50% of eligible women declined to participate in the study due to “lack of interest”.
5. Comparisons between months 1 and 6 should be made with caution due to high attrition rate in both groups at month 6.

CONCLUSION

Advance provision of EC did not increase frequency of unprotected intercourse and did not decrease condom use during the 6-month follow-up in women ages 15-20 compared to a control group.

Literature #6 (vol 13, page 012)

The Effects of Self-Administering Emergency Contraception

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Financial Support: Chief Scientist's Office
Scottish Home and Health Department.

Study Location: UK, Family planning clinic and hospital in Edinburgh
From Jan 1994 to Dec 1996

Publication: *New Eng J Med* 339 (1): 1-4, 1998

Design: Randomized clinical trial, randomized by birthdate
1-year follow-up
Single course of advanced EC provision

METHODS

Subject

A total of 1083 women, ages 16-44, were recruited from a family-planning clinic and a large hospital in Edinburgh (Scotland, UK) between January 1994 and December 1996; 60% (650) were returning for follow-up of prior EC consultations and 40% (433) were returning for follow-up after therapeutic abortion.

Subjects were randomly assigned into the following 2 groups (on the basis of their birthday (even-numbered birthdays were assigned to the treatment group):

Treatment group: 553 women received one package of EC pills (four pills, each contained 50 µg of ethinyl estradiol and 0.25 mg of levonorgestrel), written instructions and telephone numbers to call with questions.

Control group: 530 women received EC education and informed where to get and how to use emergency contraception.

Data Collection

A questionnaire was sent to subjects *one year* after enrollment to collect information about EC use, other contraception methods, and pregnancy. If EC was used subjects

were to mail in a notification card with time of administration relative to intercourse and date of last menstrual period. They were also instructed to go to the clinic within one week after the date of expected menstrual period. At that time she was given a replacement packet.

Data Analysis

Differences between the groups were tested by chi-square tests with Yates' correction for binary factors or Mann–Whitney tests for ordinal factors.

RESULTS

Subject Demographics

Only age and education of subjects were reported (Table 1). Twenty-three percent of subjects were age < 20 years old. Comparability of the UK educational levels to the US system is unknown; but the author stated in the report, approximately 50% of subjects had gone to a university or college and <20% had left school before age 16.

Table 1. Demographics and follow-up compliance of subjects
[No. (% of enrolled subjects)]

Variable	Treatment Group	Control Group
<i>Enrolled Subjects</i>	553	530
Recruited after EC use	323 (58)	327 (62)
Recruited after abortion	230 (42)	203 (38)
Lost to Follow-up	34 (6)	44 (8)
<i>Subjects with results available for analysis</i>	549 (99)	522 (98)
<i>Age (years)</i>		
<20	132 (24)	116 (22)
20–29	314 (57)	309 (58)
>30	107 (19)	105 (20)
<i>Education</i>		
Age full-time education ended		
< 16 yr	93 (17)	92 (17)
17–18 yr	127 (23)	106 (20)
19–22 yr	116 (21)	114 (22)
= 23 yr	54 (10)	61 (12)
Still in school full time	154 (28)	145 (27)
Educational status unknown	9 (2)	12 (2)

Data were extracted from the author's Table 1.

Follow-up Compliance

Approximately 98% of subjects had data available for analysis of pregnancy at the one-year follow-up. Ascertainment methods included contacting the family doctor and the Scottish Health Department. However, only 64% the subjects in both groups (350 of 549 in the treatment group and 336 of 522 in the control group) were used for the final analyses of sexual and contraceptive behaviors because they provided the responses to the detailed questionnaire.

Changes in Contraceptive Behavior:

Sexual and contraceptive behaviors of subjects from treatment and control groups at the enrollment and one-year follow-up are summarized in Table 2.

EC Use:

Women in the advance EC group were more likely to use emergency contraceptives than those in control groups; 47% used EC at least once in the treatment group vs. 27% in the control group at the one year follow-up. The difference in single use between groups (36% vs. 14%) was statistically significant ($P < 0.01$).

The proportion of subjects in each arm who were recruited after prior use of EC was 58% in the treatment group and 62% in the control group. Comparison of multiple users was not statistically different between treatment and control groups.

Condom Use:

Condom uses similarly decreased in both arms. Condom use decreased from 74% at baseline to 31% at one year in the treatment group and from 70% at baseline to 28% at one year in the control group.

Contraception Methods

The proportion of oral contraception use increased similarly in both groups.

Unprotected Sex:

Data on unprotected sex were not provided in the report. The “None contraception” shown in Table 2, which may include unprotected sex, decreased in both group at one year follow-up.

Table 2. Contraceptive behavior of subjects at enrollment and one year later
 [No. (% of subjects who provided contraception data)]

Contraceptive Behavior	Treatment Group N=350*		Control group N=336*	
	At Enrollment	One Year Later	At Enrollment	One Year Later
Contraception Methods				
Oral contraception	45 (13)	169 (48)	46 (14)	171 (51)
Condom	258 (74)	108 (31)	235 (70)	94 (28)
Diaphragm	7 (2)	7 (2)	11 (3)	15 (4)
Combination	3 (1)	31 (9)	6 (2)	34 (10)
None	34 (10)	21 (6)	33 (10)	15 (4)
Other or no answer	3 (1)	12 (3)	5 (1)	6 (2)
EC Use†				
Did not use		199 (53)		239 (73)
Used once		135 (36)		45 (14)[#]
Used twice		27 (7)		33 (10)
Used 3 times		13 (3)		8 (2)
Used > 3 times		5 (1)		1 (<1)
Pregnancy‡				
Total Pregnancies		28 (5)		33 (6)
Unintended Pregnancies		18 (3)		25 (5)
Abortions		15 (3)		19 (4)

* The number of subjects who responded to the question regarding the method of contraception.

† Percentage was calculated based on the subjects who provided data, 379 in the Treatment group and 326 in Control group.

‡ Percentage was calculated based on the subjects who provided data, 549 in the Treatment group and 522 in the Control group.

P < 0.001

COMMENTS

1. The study population may not represent an OTC setting in US. Subjects were recruited from UK clinics (60% of them previously used emergency contraception and 40% had an abortion). Half of the subjects went to college/university.
2. Only 64% of enrolled subjects provided data for analysis.
3. A single course of EC was provided to the subjects in the advance EC provision group but they could return for further Advance Provisions after use of the single course.

CONCLUSION

1. Women with advance EC access were more likely to use EC, and had lower frequency of “none” method of contraception compared to baseline at one year. The control group had a greater decrease in “none” method of contraception at one year compared to baseline than the advance EC group.
2. Although 135 (36%) of the treatment group used the advance supply of EC, only about half returned for subsequent provisions of advanced supplies.
3. Oral contraception use increased in both groups and condom use decreased in both group compared to baseline.

Literature #7 (vol 13, page 067a)

Provision of Emergency Contraceptive Pills to Spermicide Users in Ghana

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Sponsor: Family Health International (FHI) with funds from the United States Agency for International Development (USAID).

Study Location: *Africa*, Planned Parenthood Association of Ghana
July 1998 - June 1999

Publication: *Contraception* 61: 287–293, 2000

Design: Nonrandomized clinical trial
8 weeks follow-up
Single course of advance EC provision, with opportunity to return for additional courses

METHODS

Subject

A total of 210 women *spermicide users* were recruited and enrolled from 4 Planned Parenthood clinics (Accra, Nkawkaw, Kumasi, Takoradi) in Ghana, with the following eligibility criteria:

- Age 18-45 years
- No current pregnancy.
- Spermicides as the primary contraception method and EC as a backup method during the 8-week study period
- Expected to have at least 6 coital acts per month
- No history of thromboembolic disease

Subjects were counseled on the use of spermicide and given at least 40 spermicide tablets, and then non-randomly assigned into the following 2 groups (2 clinic sites each group):

Control (On Demand Provision) Group: 100 subjects recruited from clinics in Kumasi and Takoradi received EC education and advised to return to the clinic within 3 days after unprotected intercourse to obtain EC.

Advance Provision Group: 110 subjects recruited from clinics in Accra and Nkawkaw were given one packet of EC and advised to return to the clinic for re-supply immediately if she used, lost, or gave away the ECPs. Subjects were also asked to refill the ECPs at each of 2 visits.

The EC pills were LoFemenal oral contraceptive pills (each pill contains 0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel).

Data Collection

Subjects returned to the clinics for follow-up visits at 4 and 8 weeks after enrollment to collect the following information: the reason for EC use or EC request, the dates and times of unprotected sex, the disposition of ECPs dispensed, side effects of ECPs, coital activity, and contraceptive use.

Data Analysis

All data were presented separately by clinics without any statistical analysis.

RESULTS

Subject Demographics and Follow-up Compliance

Of 210 enrolled subjects, 95% (200) provided any follow-up information for analyses. The duration of follow-up was 8.2-8.6 weeks per subject.

The demographics of the enrolled subjects were summarized in Table 1. Differences in the following characteristics of subjects were found among the 4 clinics: age, education, marriage and condom use (unknown statistical significance).

Table 1. Demographics of enrolled subjects
No. (% of enrolled subjects)

Characteristics	Advance clinics		Control clinics	
	Accra	Nkawkaw	Kumasi	Takoradi
Enrolled subjects	60	50	51	49
Age (years)				
18–24	20 (33)	6 (12)	13 (25)	14 (29)
25–34	26 (43)	21 (42)	14 (27)	18 (37)
= 35	14 (23)	23 (46)	24 (47)	16 (33)
Education				
None	3 (5)	6 (12)	11 (22)	3 (6)
Primary	14 (23)	9 (18)	21 (41)	1 (2)
Middle school	26 (43)	22 (44)	11 (22)	24 (49)
Higher	17 (28)	13 (26)	8 (16)	21 (43)
Marital status				
Single	8 (13)	5 (10)	6 (12)	21 (43)
Married	52 (87)	45 (90)	45 (88)	28 (57)
Contraception in Past month				
Spermicide	51 (85)	37 (74)	47 (92)	21 (43)
Oral contraceptive pills	4 (7)	10 (20)	0	1 (2)
Condom	14 (23)	2 (4)	2 (4)	11 (22)
Pregnancy History				
Pregnancies (mean)	3.6	3.9	4.5	3.2
Living children (mean)	2.3	3.2	2.9	2.0
Miscarriages/abortions (mean)	1.3	0.7	1.4	1.1

Data were extracted from the author's Table 2.

Changes in Contraceptive Behavior

Sexual and contraceptive behaviors of subjects before (one month) and after (approximately 8 weeks) enrollment were summarized in Table 2.

Table 2. Sexual and contraceptive behavior

Behavioral Variables	Advance Clinics		Control Clinics	
	Accra	Nkawkaw	Kumasi	Takoradi
<i>Analyzed subjects</i>	53	50	48	49
<i>Mean Number of sex acts†</i>				
Month before enrollment	7.1	11.4	9.4	10.9
During study	18.1	24.3	18.4	24.6
<i>Mean Unprotected sex acts‡</i>				
Month before enrollment	1.3	0.1	1.2	2.9
During study	1.2	0.1	0.2	0.1
<i>EC Use during study (8 weeks)</i>				
Total subjects	48 (91)	6 (12)	14 (29)	6 (12)
0 use	5 (9)	44 (88)	34 (71)	43 (88)
1 use	26 (49)	5 (10)	10 (21)	6 (12)
2 uses	16 (30)	0	3 (6)	0
3 uses	6 (11)	1 (2)	1 (2)	0

Data were extracted from the author's Table 3 but re-processed/re-calculated.

† mean sex acts per subjects; ‡ % of unprotected sex over total sex acts.

* % of EC use over unprotected sex.

Unprotected sex: The mean number of sex acts per participant per month increased at all clinic sites, but the proportion of acts that were unprotected declined.. This study was not randomized and there were imbalances between study sites in many factors. Comparisons between Advanced Clinics and Controlled Clinics are not valid.

EC use: Subjects in Advance Clinics group seemed more likely to use EC although this conclusion is powered by the Accra site. Repeat use was 8% in 3 clinical sites (41% in Accra site).

Condom use: Changes on condom use was not assessed during the study.

Primary contraception: Change in primary contraception (spermicide) before and after enrollment, and the differences in primary contraception between Advance and Control were not reported.

COMMENTS

1. Study has significant flaws; the assignment was not randomized and there was great variability in demographics between the 4 clinic sites.
2. Study subjects did not have access to other forms of contraception.
3. The study was conducted outside US, and is not readily generalizable to US population, particularly an OTC setting.
4. A single course of EC was provided to the advance provision group. Subjects were asked to receive refills of advanced EC. There was 41% of participants that had repeat use at one advanced provision clinic and 2% at the other. This compared to 8% at one “on demand” clinic and 0 % at the other “on demand” clinic.
5. There were 2 follow-up visits (weeks 4 and 8) during the study. However, comparisons in sexual and contraceptive behaviors of subjects between 2 visits were not reported.

CONCLUSION

1. Subjects with advance EC access were more likely to use EC.
2. Behavioral changes between groups can not be assessed due to significant deficiency in study design.

Literature #8 (vol 13, page 011a)

Emergency Contraception: Randomized Comparison of Advance Provision and Information Only

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- Sponsor:** The David and Lucile Packard Foundation (Los Altos, California) funded this study
- Study Location:** *India*, family planning clinics
From April 1997 to June 2000
- Publication:** *Obstet Gynecol* 98:570-575, 2001
- Design:** Randomized clinical trial
1-year follow-up (38% 12-month and 90% 3-month)
Three courses of advance EC provision

METHODS

Subject

A total of 411 *condom users* visiting an urban family planning clinic in Pune (India) between April 1997 and June 2000 were recruited and randomly assigned into the following 2 groups:

Control group: 198 women received EC education to obtain emergency contraception if needed.

Advance EC group: 213 women received EC education plus *three courses* of EC pills (Yuzpe regimen). Each course consisted of 8 tablets (30 mg ethinyl estradiol and 30 mg norgestrel per tablet) of combined oral contraceptive.

Data Collection

Subjects returned quarterly to the clinic for follow-up for up to 1 year to collect information about frequency of unprotected intercourse, EC use, pregnancies, and sexually transmitted infections.

RESULTS

Subject Demographics (Table 1)

The mean age was 25 years, and approximately 5% of subjects were < 20 years old. Comparability of the educational levels in India to the US was unknown; apparently, 84% of subjects completed = 9 years education.

Table 1. Demographics and Follow-up Compliance of Enrolled Subjects

Characteristics	Control (n = 198)	Advance EC (n = 213)
<i>Age (years), No. (%)</i>		
< 20	10 (5)	9 (4)
20–29	166 (84)	172 (81)
> 30	22 (11)	32 (15)
Mean ±SD	24.9 (3.7)	25.1 (3.8)
<i>Years of schooling, No. (%)</i>		
0–8	29 (15)	36 (17)
9–12	96 (48)	103 (48)
13–16	60 (30)	61 (29)
> 16	13 (7)	13 (6)
Mean ± SD	11.7 ± 3.5	11.4 ± 3.4
<i>Follow-up Compliance†, No. (%)</i>		
Lost to Follow-up	45 (33)	34 (16)
3 months	172 (87)	194 (91)
12 months	66 (33)	99 (46)

Data were adapted from the author's Table 1, otherwise from Table 2 and Figure 1 (†).

Follow-up Compliance

Approximately 87% (172 in control group) and 91% (194 in advance EC group) of subjects completed at least 3 months in study and available for analysis. Women who switched to non-barrier contraceptives left the study.

Sexual and Contraceptive Behavior (Table 2)

Unprotected sex: Women with advance EC provision did not have statistically greater frequency of unprotected sex and a similar proportion of women on the two study arms reported unprotected sex during the study, 8% in the advanced provision vs. 6% in the control group.

EC use: Women with advance EC provision were more likely to use EC pills (79% vs 44%) after unprotected intercourse (Eleven (5%) EC users were in the Advanced Provision group and four (2%) in the control group)..

Condom use: The study subjects used condom as a primary contraception method and 23% in both arms went off study because they changed to a more effective contraceptive method. Ninety-eight percent of women in the advanced supply arm stated that availability of EC did not “tempt them to talk changes with their condoms”.

STDs: one subject reported an STD. Details of the STD (nature and study group) were not provided in the report. STDs were self reported and no clinical laboratory screening was performed.

Table 2. Unprotected sex and Emergency contraceptive Use
(Excluded 24 subjects who left the study)

Unprotected Intercourse	Control	Advance EC	P value
Mean number of unprotected sex acts per month among all women followed	0.016	0.012	0.62
Median number of unprotected sex acts per month among women with at least one unprotected sex	0.250	0.292	0.97
Number of women, <i>no.</i> (%)	9/157 (5.7)	14/185 (7.6)	0.53
EC use, <i>no.</i> (%)	4/9 (44.4)	11/14 (78.6)	0.18

Data were adapted from the author’s Table 3.

COMMENTS

1. It is not clear if the rate of unprotected sex changed from baseline since baseline information (at the enrollment) was not provided.
2. The study was conducted in India, which is unlikely to be representative of US population.

CONCLUSION

Advance EC provision did not appear to increase the frequency of unprotected sex as compared to control in the population who used condom as a primary contraception method. The proportion of participants who did have unprotected sex who used EC was higher in the Advanced EC group.