Direct Access to Emergency Contraception Through Pharmacies and Effect on Unintended Pregnancy and STIs

A Randomized Controlled Trial

Tina R. Raine, MD, MPH
Cynthia C. Harper, PhD
Corinne H. Rocca, MPH
Richard Fischer, MD
Nancy Padian, PhD
Jeffrey D. Klausner, MD, MPH
Philip D. Darney, MD, MSc

Context It is estimated that half of unintended pregnancies could be averted if emergency contraception (EC) were easily accessible and used.

Objective To evaluate the effect of direct access to EC through pharmacies and advance provision on reproductive health outcomes.

Design, Setting, and Participants A randomized, single-blind, controlled trial (July 2001-June 2003) of 2117 women, ages 15 to 24 years, attending 4 California clinics providing family planning services, who were not desiring pregnancy, using long-term hormonal contraception or requesting EC.

Intervention Participants were assigned to 1 of the following groups: (1) pharmacy access to EC; (2) advance provision of 3 packs of levonorgestrel EC; or (3) clinic access (control).

Main Outcome Measures Primary outcomes were use of EC, pregnancies, and sexually transmitted infections (STIs) assessed at 6 months; secondary outcomes were changes in contraceptive and condom use and sexual behavior.

Results Women in the pharmacy access group were no more likely to use EC (24.2%) than controls (21.0%) ($P=.25$). Women in the advance provision group (37.4%) were almost twice as likely to use EC than controls (21.0%) ($P<.001$) even though the frequency of unprotected intercourse was similar (39.8% vs 41.0%, respectively, $P=.46$). Only half (46.7%) of study participants who had unprotected intercourse used EC over the study period. Eight percent of participants became pregnant and 12% acquired an STI; compared with controls, women in the pharmacy access and advance provision groups did not experience a significant reduction in pregnancy rate (pharmacy access group: adjusted odds ratio [OR], 0.98; 95% confidence interval [CI], 0.58-1.64; $P=.93$; advance provision group: OR, 1.10; 95% CI, 0.66-1.84, $P=.71$) or increase in STIs (pharmacy access group: adjusted OR, 1.08, 95% CI, 0.71-1.63, $P=.73$; advance provision group: OR, 0.94, 95% CI, 0.62-1.44, $P=.79$). There were no differences in patterns of contraceptive or condom use or sexual behaviors by study group.

Conclusions While removing the requirement to go through pharmacists or clinics to obtain EC increases use, the public health impact may be negligible because of high rates of unprotected intercourse and relative underutilization of the method. Given that there is clear evidence that neither pharmacy access nor advance provision compromises contraceptive or sexual behavior, it seems unreasonable to restrict access to EC to clinics.

JAMA. 2005;293:54-62 www.jama.com

IT IS ESTIMATED THAT HALF OF THE 3.5 million unintended pregnancies that occur each year in the United States could be averted if emergency contraception (EC) were easily accessible and used.[1] This figure has been extrapolated from efficacy trials that demonstrate that the risk of pregnancy after a single act of unprotected intercourse is reduced by 75% with use of combined EC (the "Yuzpe" regimen).[2]

In efforts to increase access to EC, to date 6 states (Alaska, California, Hawaii, Maine, New Mexico, and Washington) have implemented pharmacy access legislation whereby women can obtain EC directly from pharmacists without having to see a clinician or obtain a prescription first. Although women in Washington State have had increased access to EC through direct pharmacy access since 1997, an outcome evaluation is not available, and it is not clear if reductions in pregnancy and abortion rates in Washington State over the same time period can be attributed to this increased access.[3]

For editorial comment see p 98.

Author Affiliations: Center for Reproductive Health Research and Policy, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco (Drs Raine, Harper, Padian, and Darney and Ms Rocca); Planned Parenthood Mar Monte, San Jose, Calif (Dr Fischer); and San Francisco Department of Public Health, San Francisco, Calif (Dr Klausner).
Corresponding Author: Tina R. Raine, MD, MPH, Department of Obstetrics, Gynecology, and Reproductive Sciences, San Francisco General Hospital—6D, 1001 Potrero Ave, San Francisco, CA 94110 (rainet@obgyn.ucsf.edu).

While several investigators have demonstrated that women who receive EC before they need to use it ("advance provision") are more likely to use it if unprotected intercourse occurs, there have been no trials in the United States evaluating the impact of pharmacy access on key reproductive health outcomes.[4-6] Glasier and Baird demonstrated that Scottish women who had an advance supply of EC on hand were almost twice as likely to use the medication if needed; however, the sample size was small and the difference in pregnancy rates between access groups was not statistically significant, making it difficult to draw conclusions about the effect of advance provision on unintended pregnancy rates.[7]

An important element in policy debates over making EC more widely available is a concern that it will increase risk taking. There is a concern that women who have easy access to a postcoital form of contraception may in fact have more unprotected intercourse and abandon more effective forms of regular contraception. Studies have also shown that clinicians—as well as pharmacists—and users are concerned about the impact of increased access to EC on sexual risk-taking behaviors and sexually transmitted infections (STIs).[8-10] Recent research in the field of STI and human immunodeficiency virus (HIV) prevention has shown that sexual risk-taking behaviors and unprotected intercourse in men have increased after the introduction of highly active antiretroviral therapy.[11,12] No study has yet tested whether increased access to EC might increase STI risk by affecting sexual behavior, including frequency of intercourse and number of partners. While we do have data from several small studies showing that advance provision of EC is not associated with increases in unprotected intercourse or decreases in condom use, these self-report data have not been correlated with outcome data, particularly biological markers.[4-6,13,14]

We conducted a randomized controlled trial to evaluate the effect of access to EC through pharmacies on pregnancy and STIs. A secondary objective was to test the null hypothesis that level of access does not have an effect on contraceptive and sexual behavior. Since few states have direct pharmacy access and small numbers of providers give women advance provisions, we considered access through clinics the standard of care. We also evaluated EC use and reproductive health outcomes with advance provision relative to clinic access. Since pharmacies have more flexible hours, including evenings and weekends, and do not require appointments, we hypothesized that women with direct access through pharmacies (and women with advance provision) would use EC more than women with standard access through clinics and that women with increased access to EC would experience lower unintended pregnancy rates. We also hypothesized that access affects EC use, not risk behavior, and thus STI rates would not increase.

METHODS

Study Participants

The study was conducted from July 2001 to June 2003 at 4 clinics located in San Francisco and Daly City, Calif, that provide family planning services and supplies to young women. One site, a college health center, also provides primary preventive health services. Enrollment was initiated at 2 of the sites (New Generation Health Center/University of California-San Francisco [UCSF] and Planned Parenthood, San Francisco) in July 2001 and the other 2 sites (City College of San Francisco Student Health Center and Planned Parenthood, Daly City) in October 2001. The study protocol, informed consent, and questionnaires were reviewed and approved by the Committee on Human Research at UCSF, and the Planned Parenthood Federation of America.

We included women who were 15 to 24 years old, spoke English or Spanish, and had had sexual intercourse in the previous 6 months. Women who were pregnant or wished to become pregnant in the next 6 months and women who were using the contraceptive transdermal patch and vaginal ring (not approved by the Food and Drug Administration [FDA] in July 2001) or longer-acting methods (injectables, the intrauterine device, or implants) were excluded from participation. Women using other methods (oral contraceptives, condoms, other spermicides or barriers, and none) were included. Women who had had unprotected intercourse in the previous 3 days, or who were requesting EC at the time of their visit, were excluded. Participants were required to live in the San Francisco Bay Area and be available for a follow-up visit 6 months after enrollment.

Randomization

We used a computer-generated randomization sequence to assign participants to 1 of 3 treatment groups: pharmacy access, advance provision, or clinic access (control). The sequence at each site was restricted so that each consecutive block of 9 boxes randomized 3 participants to each group. Allocation concealment was implemented using sealed, sequentially numbered boxes that were identical in appearance for the 3 treatment groups. The Department of Epidemiology and Biostatistics at UCSF, which was not involved in any other study procedures or analyses, created the randomization sequence and filled and labeled the study boxes.

In January 2002, California implemented pharmacy access legislation allowing women to obtain EC from pharmacies without consulting a physician. To minimize contamination of the control group and avoid the possibility of placing women in the control group at a disadvantage relative to other treatment groups, we eliminated the clinic access group after December 2001. At the end of December 2001, the Department of Epidemiology and Biostatistics generated a new randomization sequence with 2 study groups (using randomization blocks of size 8 within location) and relabeled the remaining unused study boxes.

Procedures

Research assistants administered an eligibility-screening questionnaire to all

women attending the clinic sites who met the age criteria. Eligible participants provided a urine specimen to test for pregnancy (Clearview One Step, Unipath Diagnostics, Waltham, Mass, or equivalent) and chlamydia (BD ProbeTec, Becton Dickinson & Co, Sparks, Md). Research assistants obtained a fingerstick sample of whole blood to test for antibodies to herpes simplex virus type 2 (HSV-2) (POCkit HSV-2 Rapid Test, Diagnology Inc, Dublin, Ireland). All women who tested positive for chlamydia at enrollment were referred to the clinic site for treatment and partner management per clinic protocol. Women testing positive for HSV-2 antibodies were informed, and counseled on HSV-2 antibody results if requested. Participants provided consent to allow study staff to verify that all positive chlamydia cases were treated through the clinic sites.

All participants were given information about EC, including its effectiveness compared with regular methods, how to use it, and the need to use condoms to prevent STIs. Research assistants interviewed each subject using a questionnaire on demographics, including self-reported race/ethnicity, sexual activity, EC use, current contraceptive method and patterns of use, condom use, and unprotected intercourse. We collected information on race/ethnicity to describe the study population and because previous studies indicate contraceptive behavior may vary by race/ethnicity.

Research assistants then assigned each subject to one of the study groups by giving her a sequentially numbered treatment box labeled with a study identification number. Participants were instructed to open their box after leaving the clinic to ensure blinding of research staff. Participants randomized to the pharmacy access group received a box containing a card with instructions for obtaining levonorgestrel (Plan B EC, Women's Capital Corp, Washington, DC) directly from a pharmacist without a prescription. The cards were in English and Spanish and listed 13 Walgreens pharmacies (including two 24-hour stores) that were located in close proximity to the clinic sites, from which participants could obtain EC at no cost. Thirty-eight pharmacists from the 13 stores participated in a 3-hour training session conducted by the principal investigators (T.R.R, C.C.H.) on counseling women about EC, contraceptive options, and prevention of STIs. To simulate Washington pharmacy access programs, EC was dispensed to women requesting EC who verbally identified themselves as study participants, and pharmacists provided handouts on contraception and STIs with the EC.

Participants randomized to the advance provision group received a box that contained 3 packets of EC. The regimen contains two 0.75-mg levonorgestrel pills to be taken in 2 doses, 12 hours apart, within 72 hours of unprotected intercourse. Participants randomized to the clinic access group received a box that contained a card with instructions to return to the clinic for EC, if needed. Women who returned to the clinics for EC were treated according to standard clinic protocol, ie, appointments or triage per availability and EC at no cost for the vast majority of women. At the 2 Planned Parenthood sites, a small proportion of women (10% at the San Francisco site and 5% at the Daly City site) are not eligible for coverage under Medical or the State Family Planning Insurance Program (SOFP) and receive services on a sliding payment scale based on income. Therefore, some study participants may have had to pay all or some of the cost of obtaining EC at the clinic per standard clinic protocol. All women from the 2 remaining sites receive SOFP coverage and did not have to pay for EC at the clinics.

Six months after enrollment, research assistants conducted follow-up visits with participants at one of the clinic sites or the home of the participant. A follow-up questionnaire assessing behaviors and study outcomes including self-report of EC use, pregnancies, and STIs (chlamydia, gonorrhea, HSV-2, genital warts, *Trichomonas vaginalis*, and pelvic inflammatory disease) was administered. A urine specimen for pregnancy and chlamydia testing and fingerstick blood for HSV-2 testing was collected. Participants who were not available for a follow-up visit completed the questionnaire by telephone. Bilingual research assistants conducted study procedures with Spanish-speaking participants using translated questionnaires. Subjects received $10 for completing enrollment procedures and $20 for the follow-up visit. We also obtained consent from study participants to review their medical charts at the study sites for positive test results indicating interim pregnancies or chlamydial, gonococcal, or HSV-2 infections.

Outcome Measures

Pregnancies and Contraceptive Use. The study questionnaire was developed using previously tested questions and was pretested on a small sample of women from the study sites to assess clarity of the questions and time required to administer the questionnaire.[4,15] The primary outcome measure was pregnancy, determined by positive urine pregnancy test at follow-up, self-report over the study period, or positive test on medical chart review. Pregnancies documented by more than 1 measure were counted only once. Information was collected on the number of times EC was used over the study period as well as why it was used and how it was obtained at last use. Unprotected intercourse was categorized by reported frequency of intercourse without contraception or condoms as never, some of the time, most of the time, or every time a participant had intercourse. Among women using oral contraceptive pills, we assessed the reported number of pills missed per pack over the study period. We created a variable to assess changes in contraceptive method at enrollment compared with follow-up. Participants who used no method at enrollment and adopted any method were categorized as adopting contraception; those who changed from any method to no method were categorized as abandoning contraception. Subjects who changed methods were categorized as either women who changed from oral contraceptive pills to condoms or other nonhormonal methods,

or as women who changed from condoms or other nonhormonal methods to any hormonal method (oral contraceptives, injectables, or the contraceptive transdermal patch or vaginal ring, which became available to women in 2002).

STIs, Risk Behavior, and Condom Use. Sexually transmitted infection measures included the following: (1) chlamydia, based on positive test at follow-up; (2) new HSV-2 infections based on positive test at follow-up after a negative test at enrollment; (3) self-report of STIs (chlamydia, gonorrhea, HSV-2, genital warts, *T vaginalis*, and pelvic inflammatory disease) during the follow-up period; and (4) medical chart review for positive chlamydia, gonorrhea, or HSV-2 tests during the follow-up period. The variable "any STI" was defined as a positive chlamydia or HSV-2 test at follow-up or any additional infection identified by self-report or medical chart review; more than 1 type of STI in a participant was counted only once. To examine risk behavior, we measured frequency of intercourse (>once per week, once per week, 1-3 times per month, <once per month), number of sex partners, and length of time with main partner for women who reported having a main partner. We examined frequency of condom use (every time, most of the time, sometimes, never) and condom use at last intercourse (yes, no). Consistent condom use was defined as women who reported using condoms every time they had intercourse both at enrollment and at follow-up.

Sample Size

Our study was powered to detect significant differences in pregnancy rates in comparisons between the control group, clinic access, and either of the 2 treatment groups. A final sample size of 620 women per treatment group would allow us to reject a null hypothesis that there is no difference in pregnancy rates in (1) women with direct pharmacy access compared with women with clinic access to EC and (2) women with advance provision compared with women with clinic access to EC with 90% power in a 2-sided test with an α of .05 if the true reduction was 50% or greater. Our effect size was based on prior estimates that use of combined EC has the potential to reduce unintended pregnancy rates in half.[1] Based on prior research, we assumed a 6-month pregnancy rate of 10% in the clinic access group, and thus a 5% pregnancy rate in the pharmacy access and advance provision groups.[4]

Statistical Analysis

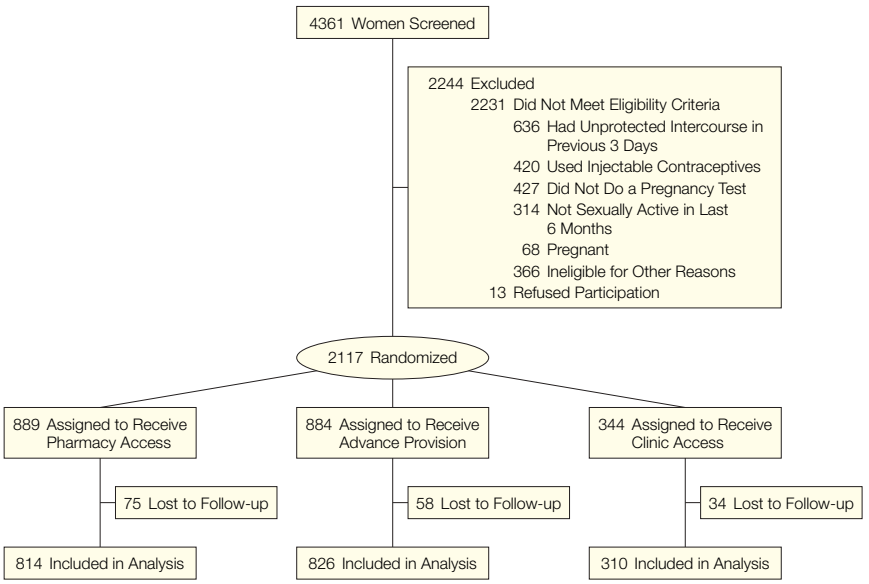
We used a "modified" intent-to-treat analysis: all participants who completed follow-up were analyzed as a part of the group to which they were randomized. Contingency tables and χ^2 statistics were used for significance tests with categorical variables and *t* tests for continuous variables. We compared the pharmacy access group with the clinic access group and the advance provision group with the clinic access group; we present *P* values for both comparisons. The number and percentage of pregnancies that occurred in each study group over the follow-up period are presented. Since women who report unprotected intercourse, women who experience method failures, and women who use less effective contraceptive methods represent different risk groups, pregnancy rates are also presented by frequency of unprotected intercourse and contraceptive method.

Multiple logistic regression analysis was used to estimate the odds of pregnancy during the study by treatment arm (odds ratios [ORs] are presented with 95% confidence intervals). Variables known to influence pregnancy risk from previous research were included in the model.[16,17] The final model included the following baseline variables: clinic site, age (measured continuously), race/ethnicity (Latina, black, white, Asian, multiracial/other), pregnancy history, attitude about pregnancy in the next year (very happy, somewhat happy, don't know, somewhat unhappy, very unhappy), frequency of unprotected intercourse, and contraceptive method (oral contraceptive pills, condoms, other, none). After analyzing main effects, we assessed interactions between various predictor variables and treatment group. For example, we tested whether there were interactions between contraceptive method at baseline and either of the treatment groups. None of the interactions tested were significant; therefore, we present a main effects model. The number and percentage of participants who were positive for any STIs by study group are presented, and we also used multiple logistic regression to estimate the odds of acquiring an STI during the study. There were no significant interactions between treatment group and predictor variables; the final STI model included main effects only, including the following baseline variables: clinic site, age, race/ethnicity, history of STIs (ever), number of sex partners in past 6 months (1, 2, or ≥3), and frequency of condom use.

Since we found baseline differences in race/ethnicity and clinic site by treatment group, we also conducted multivariate analyses to control for these variables on outcomes including EC use, unprotected intercourse, contraceptive method change, frequency of condom use, and condom use at last intercourse. We constructed separate models with each of these outcomes as the dependent variable and assessed whether treatment arm was a significant predictor after controlling for race/ethnicity and clinic site. All analyses were also performed using Bonferroni corrections; we present results from analyses in which no corrections were made for multiple comparisons since the findings were consistent. Data were analyzed using Stata 8.0 (Stata Corporation, College Station, Tex).

An interim analysis of the 1020 participants recruited through December 2001 was conducted in July 2002 by an outside consultant. The investigators and research staff were not informed of the results of the analysis until after the completion of the study. The investigators would have been notified of the results prior to completion of the study only if a difference in pregnancy rates or STI rates with a critical *P* value of less than or equal to .001 was observed between either the pharmacy access group

Figure. Study Participant Flow



or the advance provision group compared with the clinic access group. As a result of this interim analysis, we reduced the *P* value in our current analysis of the data from .050 to .049, as determined by the sequential design criteria of Fleming et al.[18] After the completion of the study, we also performed an analysis of the subsample, women who were enrolled prior to January 2002, to verify that these results were consistent with the full study sample. In addition, to assess whether there was an independent study effect on pregnancy rates by time period of recruitment into the study (before and after December 31, 2001), we included a time period variable in the multiple logistic regression analysis of the full study sample and found no effect.

RESULTS

We screened 4361 women and enrolled and randomized 2117 at the 4 study sites (FIGURE). Of 2244 women excluded, 2231 did not meet eligibility criteria. In total, 167 women were lost to follow-up, and 1950 (92%) women were included in the follow-up analyses. Only 3.7% of participants who completed follow-up were not available for a visit and completed the questionnaire by telephone and thus did not complete chlamydia or HSV-2 infection testing at follow-up. Our final group sizes were 814, 826, and 310 in the pharmacy access, advance provision, and clinic access groups, respectively. The medical charts of 1613 study participants (1562 who completed follow-up and 51 who were lost to follow-up) were available for review.

Equal proportions of women were lost to follow-up from the 3 treatment groups and the 4 study sites. The mean age of participants who were lost to follow-up was 20.0 years compared with 19.9 years for those who completed follow-up. An analysis of study attrition showed no significant differences in other baseline demographic traits, history of pregnancy or STIs, or contraceptive method.

Baseline characteristics of the study sample are shown in TABLE 1. Since enrollment was initiated earlier at 2 of the sites and elimination of the clinic access group occurred simultaneously at all 4 sites, there was a smaller proportion of participants assigned to the clinic access group at the 2 sites that initiated recruitment later ($P<.001$). There was also a slightly higher proportion of blacks in the clinic access group ($P=.045$). Half of study participants were adolescents: 483 (25%) were 15 to 17 years old and 481 (25%) were 18 to 19 years old. About half of the sample used oral contraceptives, with or without condoms, and the other half of the sample relied on condoms as their contraceptive method; however, only 27% of women reported condom use at every intercourse. The study sample was moderately high-risk for negative reproductive health outcomes in that 27% of these young women had had an abortion, and 11% tested positive for chlamydia or HSV-2 antibodies at baseline.

The mean follow-up time was 6.9 months (SD, 1.3 months). Overall, 29% of women used EC during the study, and there were significant differences by study group (TABLE 2). Women in the pharmacy access group were no more likely to use EC than women in the clinic access group ($P=.25$). As expected, women in the advance provision group (37%) were significantly more likely than women in the clinic access group to report having used EC 1 or more times ($P<.001$). Only 6.8% of women used EC 2 times, and 4.1% used it 3 or more times over the study period. Women in the advance provision group (15.1%) were significantly more likely than the clinic access group (5.8%) to use EC 2 or more times ($P<.001$); however, women in the pharmacy access group (8.5%) were not more likely than women in the clinic access group to use EC 2 or more times ($P=.29$).

There were no significant differences in frequency of unprotected intercourse by study group; 37.5% of study participants reported having unprotected intercourse (Table 2). Only half (46.7%) of study participants who had unprotected sex reported using EC 1 or more times over the study period; 54.9% of women who had unprotected intercourse in the advance provision group used EC. There were no significant differences in patterns of oral contraceptive use or the proportion of women switching their regular contraceptive method by study group (Table 2). Sexual risk behaviors, including frequency of intercourse or number of partners, were also the same across study groups (TABLE 3). While a significantly lower

proportion of participants in the advance provision group (47%) reported condom use at last intercourse than in the clinic access group (54%), this difference was not significant after adjusting for race/ethnicity and clinic site (OR,0.79; 95% CI, 0.60-1.04, *P*=.09). There were no differences in frequency of condom use or proportion of women who reported consistent condom use across study groups (Table 3).

Over the 6-month follow-up period, 151 (7.7%) of participants became pregnant; there were no significant differences by study group. Seventy-one pregnancies (3.6%) were identified by a positive test at follow-up, 76 pregnancies (3.9%) were identified by self-report, and 4 pregnancies (0.2%) were identified by a positive test on chart review. The pregnancy rate correlated with self-reported measures of risk; the pregnancy rate increased as the reported frequency of unprotected intercourse increased. The risk of pregnancy over the study period was also lower for women who used hormonal contraceptives (adjusted OR, 0.63; 95% CI, 0.40-1.00, *P*=.05). Twelve percent of women acquired an STI over the study period. One hundred eighteen infections (6.0%) were identified by a positive test at follow-up, 107 (5.5%) by self-report, and 9 (0.5%) by a positive test on chart review. There were no differences in positive chlamydia or HSV-2 tests across study groups (Table 3) or STI risk after adjusting for variables known to influence STI rates (TABLE 4).

Additional multivariate analyses were performed to adjust for group differences in race/ethnicity and clinic site at enrollment; there were no differences from the unadjusted results except that the difference between the study groups in condom use at last intercourse was no longer significant. Additional analyses performed using Bonferroni corrections were consistent with analyses performed without corrections for multiple comparisons.

COMMENT

To increase use of EC, 6 states have emulated the Washington State model allowing women to obtain EC directly from a pharmacist; however, in our study population, direct pharmacy access did not appear to be any more useful than access through clinics. While study participants had a choice of 13 pharmacies, they could have been reluctant to go to a pharmacy or experienced difficulty getting to a pharmacy or finding a pharmacist on duty who was trained to dispense EC. The requirement to go through pharmacists or clinics to obtain EC appears to be a barrier that limits use. Even though rates of unprotected intercourse were similar across study groups, women in the advance provision group were still almost twice as likely to use EC than women in the clinic access group. Furthermore, contrary to concerns that increased access to EC will entice women to use EC repeatedly, only a small fraction of women in the pharmacy access and advance provision groups used EC more than once over the 6-month period, even though EC was supplied at no cost. Recently, the FDA rejected an application to switch levonorgestrel EC to over-the-counter status, leaving in place many of the barriers associated with pharmacy or clinic access. These data support the previous scientific literature that indicates that

Table 1. Characteristics of Participants at Enrollment

Characteristic	Pharmacy Access, No. (%) (n = 889)	Advance Provision, No. (%) (n = 884)	Clinic Access, No. (%) (n = 344)	Total Sample (N = 2117)
Clinic site*				
City College of San Francisco	55 (6.2)	54 (6.1)	32 (9.3)	**141** (6.7)
Planned Parenthood-San Francisco	312 (35.1)	311 (35.2)	119 (34.6)	**742** (35.1)
New Generation Health Center	251 (28.2)	251 (28.4)	148 (43.0)	**650** (30.7)
Planned Parenthood-Daly City	271 (30.5)	268 (30.3)	45 (13.1)	**584** (27.6)
Age, mean (SD), y	19.9 (2.6)	19.9 (2.7)	19.8 (2.6)	19.9 (2.6)
Race/ethnicity†				
Latina	181 (20.4)	172 (19.5)	68 (19.8)	**421** (19.9)
Black	119 (13.4)	135 (15.3)	64 (18.6)	**318** (15.0)
White	268 (30.2)	284 (32.1)	96 (27.9)	**648** (30.6)
Asian	189 (21.3)	205 (23.2)	76 (22.1)	**470** (22.2)
Multiracial/other	132 (14.9)	88 (10.0)	40 (11.6)	**260** (12.3)
Current contraceptive method				
Oral contraceptive plus condoms	166 (18.8)	156 (17.7)	46 (13.5)	**368** (17.5)
Oral contraceptives	239 (27.0)	258 (29.3)	91 (26.6)	**588** (27.9)
Condoms	413 (46.7)	406 (46.1)	175 (51.2)	**994** (47.2)
Other	19 (2.2)	16 (1.8)	7 (2.1)	**42** (2.0)
None	47 (5.3)	45 (5.1)	23 (6.7)	**115** (5.5)
Contraceptive history				
Used condoms every time‡	244 (27.5)	236 (26.8)	87 (25.4)	**567** (26.8)
Never had unprotected intercourse§	481 (54.1)	492 (55.8)	161 (46.8)	**1134** (53.6)
Ever used emergency contraception	285 (32.1)	320 (36.2)	124 (36.1)	**729** (34.5)
Ever had an abortion	244 (27.5)	225 (25.5)	93 (27.0)	**562** (26.6)
Test results				
Positive for chlamydia	34 (3.9)	37 (4.3)	16 (4.8)	**87** (4.2)
Positive for herpes simplex virus type 2	81 (9.1)	66 (7.5)	23 (6.7)	**170** (8.1)

*$P<.001$.
†$P = .045$.
‡In the 6 months prior to enrollment.
§Intercourse without contraception or condoms in the 6 months prior to enrollment.

Table 2. Intervention Effect: Contraceptive Behavior

	Pharmacy Access, No. (%) (n = 814)	Advance Provision, No. (%) (n = 826)	Clinic Access, No. (%) (n = 310)	Total Sample, No. (%) (N = 1950)	*P* Value	
					Pharmacy vs Clinic	Advance vs Clinic
Used emergency contraception*	197 (24.2)	309 (37.4)	65 (21.0)	**571** (29.3)	.25	<.001
Frequency of unprotected intercourse						
Every time	26 (3.2)	25 (3.0)	7 (2.3)	**58** (3.0)		
Most of the time	39 (4.8)	50 (6.1)	23 (7.4)	**112** (5.8)		
Some of the time	209 (25.7)	253 (30.7)	97 (31.3)	**559** (28.7)	.07	.46
Never	506 (62.2)	472 (57.2)	168 (54.2)	**1146** (58.8)		
Not sexually active	34 (4.2)	25 (3.0)	15 (4.8)	**74** (3.8)		
Pill users						
Never missed a pill	146 (37.3)	137 (34.7)	39 (31.7)	**322** (35.4)		
Missed 1 or 2 pills per pack	202 (51.7)	218 (55.2)	71 (57.7)	**491** (54.0)	.48	.83
Missed >2 pills per pack	43 (11.0)	40 (10.1)	13 (10.6)	**96** (10.6)		
Contraceptive method change						
No change	523 (68.2)	545 (69.2)	206 (71.5)	**1274** (69.1)		
Adopted contraception	24 (3.1)	29 (3.7)	10 (3.5)	**63** (3.4)		
Abandoned contraception	47 (6.1)	50 (6.4)	13 (4.5)	**110** (6.0)	.74	.77
Changed from oral contraceptive pills†	56 (7.3)	51 (6.5)	21 (7.3)	**128** (7.0)		
Changed from condoms‡	117 (15.3)	113 (14.3)	38 (13.2)	**268** (14.5)		

*Used emergency contraception 1 or more times over the study period.
†Participants who changed from oral contraceptive pills at enrollment to condoms or other nonhormonal methods (ie, spermicides) at follow-up.
‡Participants who changed from condoms or other nonhormonal methods at enrollment to any hormonal method at follow-up.

Table 3. Intervention Effect: Sexual Behavior and Sexually Transmitted Infection Test Results

	Pharmacy Access, No. (%) (n = 814)	Advance Provision, No. (%) (n = 826)	Clinic Access, No. (%) (n = 310)	Total Sample, No. (%) (N = 1950)	*P* Value	
					Pharmacy vs Clinic	Advance vs Clinic
Frequency of intercourse						
Never	34 (4.2)	25 (3.0)	15 (4.8)	**74** (3.8)		
<1 time/mo	91 (11.2)	123 (14.9)	44 (14.2)	**258** (13.2)		
1-3 times/mo	243 (29.9)	218 (26.4)	84 (27.1)	**545** (28.0)	.63	.14
1 time/wk	195 (24.0)	188 (22.8)	69 (22.3)	**452** (23.2)		
>1 time/wk	250 (30.8)	272 (32.9)	98 (31.6)	**620** (31.8)		
No. of sex partners						
None	34 (4.2)	25 (3.0)	15 (4.8)	**74** (3.8)		
1	587 (72.2)	621 (75.2)	236 (76.1)	**1444** (74.1)	.18	.25
2	140 (17.2)	127 (15.4)	37 (11.9)	**304** (15.6)		
≥3	52 (6.4)	53 (6.4)	22 (7.1)	**127** (6.5)		
Frequency of condom use						
Every time	195 (24.0)	174 (21.2)	66 (21.4)	**435** (22.4)		
Most of the time	182 (22.4)	191 (23.3)	76 (24.6)	**449** (23.1)		
Some of the time	177 (21.8)	198 (24.2)	71 (23.0)	**446** (23.1)	.80	.61
Never	224 (27.6)	232 (28.3)	81 (26.2)	**537** (27.7)		
No intercourse	34 (4.2)	25 (3.0)	15 (4.8)	**74** (3.8)		
Condom use at last intercourse	383 (49.1)	373 (46.6)	158 (53.7)	**914** (48.8)	.18	.04
Consistent condom use*	110 (14.1)	99 (12.5)	39 (13.3)	**248** (13.3)	.73	.71
Sexually transmitted infection test results						
Positive for chlamydia (n = 1852)†	23 (3.0)	18 (2.3)	4 (1.4)	**45** (2.3)	.14	.35
Positive for herpes simplex virus type 2 (n = 1672)†	29 (4.2)	31 (4.4)	13 (4.8)	**73** (4.4)	.69	.78

*Women who reported using condoms every time they had intercourse both at enrollment and at follow-up.
†Tests done at follow-up.

among young sexually active women, unprotected intercourse leads to EC use, not the converse.[4,7]

We did not observe a difference in pregnancy rates in women with either pharmacy access or advance provision; the adjusted risk of pregnancy for both treatment groups was not significantly less than 1. Previous studies also failed to show significant differences in pregnancy or abortion rates among women with advance provisions of EC.[6,7,19] It is possible that the effect of increased access on pregnancy rates is truly negligible because EC is not as effective as found in the single-use clinical trials, or because women at highest risk do not use EC frequently enough or at all. Indeed, almost half of women in the advance provision group who reported having unprotected sex did not use EC. Thus, it is not surprising that the vast majority of pregnancies (73%) occurred in the women who reported having unprotected intercourse rather than in women experiencing method failures.

We would not expect the pregnancy rate to be lower in the pharmacy access group given the similar EC use rate as the control group; however, EC use was increased in the advance provision group. An alternative explanation for the lack of observed difference in pregnancy rates is that women in the advance provision group used EC more because they were using it "unnecessarily," ie, as a backup to a regular method. We think this is unlikely since the proportion of women reporting using EC because of condom mishaps or using no birth control method the last time they used EC was similar for women in the advance provision group and the control group (94.9% vs 96.9%, $P=.74$).

Our sample size calculations were based on equally sized groups; however, with our unequal group sizes, we had an 80% power to detect a 50% difference in pregnancy rates. It is possible that with a larger sample or widespread increased public access that a smaller, yet meaningful reduction in pregnancy rates would be observed. While we set out to demonstrate a large reduction in pregnancy rates, even a 10% or 20% reduction in unintended pregnancy rates would be a significant and desirable public health achievement.

Access to EC did not have a detrimental effect on contraceptive use or sexual behavior. While women who used condoms or other less effective forms of contraception were more likely to become pregnant than women who used hormonal contraception, women with advance provision or pharmacy access were not more likely to abandon contraception or switch to less effective methods. Given this finding, it is unlikely that increased access to EC would lead to higher pregnancy rates, even though our risk estimates indicate that the true effect may also be greater than 1. Our study supports the hypothesis that behavior is not influenced by access to EC and that women who have increased access to EC do not have more unprotected intercourse. There were no significant differences in self-reported frequency of unprotected intercourse. One might argue that self-report is not an accurate measure of actual behavior, ie, there is underreporting. Pregnancy is an outcome that is less susceptible to recall bias and was assessed by several measures in our study, including biological markers. We demonstrate that baseline self-report of unprotected intercourse, as well as contraceptive method, correlated directly with pregnancy rates at follow-up, adding validity to our self-report measures.

Across all measures, we also found similar rates of sexual risk behaviors in all study groups. The finding of similar STI acquisition rates among study groups seems plausible given the lack of difference in self-reported measures of risk. Using the combined STI variable including test results, self-report, and medical chart review, we had 90% power to detect an increase in STIs from 12% to 18%. It is possible that we failed to detect a smaller yet clinically meaningful increase in STIs; however, given our increased power to detect small differences in self-reported

Table 4. Reproductive Health Outcomes

	No. (%)	Odds Ratio (95% Confidence Interval)*	*P* Value
Pregnancies			
Treatment group			
Clinic access	27 (8.7)	Reference	
Pharmacy access	58 (7.1)	0.98 (0.58-1.64)	.93
Advance provision	66 (8.0)	1.10 (0.66-1.84)	.71
Frequency of unprotected intercourse†			
Never	40 (3.8)	Reference	
Some of the time	75 (10.9)	1.98 (1.29-3.05)	.002
Most of the time	19 (14.7)	2.12 (1.10-4.06)	.02
Every time	17 (21.0)	4.96 (2.18-11.30)	<.001
Contraceptive method			
Condoms	90 (9.9)	Reference	
Oral contraceptives	35 (4.0)	0.63 (0.40-1.00)	.05
Other	6 (15.0)	1.33 (0.47-3.76)	.59
None	19 (18.1)	0.89 (0.44-1.81)	.75
Any Sexually Transmitted Infection, No. (%)‡			
Treatment group			
Clinic access	38 (12.3)	Reference	
Pharmacy access	102 (12.5)	1.08 (0.71-1.63)§	.73
Advance provision	94 (11.4)	0.94 (0.62-1.44)§	.79

*Adjusted for clinic site, age, race, prior pregnancy, pregnancy desire, frequency of unprotected intercourse, and contraceptive method at baseline.
†Intercourse without condoms or any form of contraception.
‡Positive test results for chlamydia, herpes simplex virus type 2 (HSV-2), or gonorrhea at follow-up or chart review, or self-report of chlamydia, gonorrhea, HSV-2, genital warts, *Trichomonas vaginalis,* or pelvic inflammatory disease at follow-up.
§Adjusted for clinic site, race/ethnicity, age, history of sexually transmitted infection (ever), number of partners, and frequency of condom use at baseline.

measures of risk, like number of sex partners, this seems less plausible. The FDA's decision to reject over-the-counter sale of EC was based on concerns that increased access to EC could lead to unsafe sexual practices and the spread of STIs and HIV/AIDS, a notion that is contrary to the findings of our current study and the published literature.[4-7,13,20-22]

Our study has limitations. There was cross over of treatment groups as participants could obtain EC through any of the 3 methods. The majority of participants (67%) reported obtaining EC at last use consistent with the study group to which they were assigned. Thirty percent of women in the pharmacy access group and 26% of women in the advance provision group reported obtaining EC through clinics and 12% of women in the clinic access group reported obtaining EC directly from pharmacies without speaking with a provider. This cross over may have diminished our ability to demonstrate a difference in reproductive health outcomes in treatment groups.

This was not a strict intent-to-treat analysis as some study participants were lost to follow-up. Follow-up rates were equal across study groups, but if all participants lost to follow-up in the advance provision group became pregnant or acquired an STI and no one in the clinic access group did, study results would have changed. This is an unlikely scenario, as attrition analysis showed no difference in characteristics of women lost to follow-up, and chart review of women lost to follow-up revealed that only 1 of 14 women in the advance provision group lost to follow-up tested positive for chlamydia and 1 of 10 women in the advance provision group tested positive for pregnancy.

Another limitation of the study is that EC use in the clinic access group was relatively high compared with previous studies.[4,6] High use rates in the control group may explain why we did not observe a difference compared with the pharmacy access group. Pharmacy access might be more useful for women who do not have a source of care. The study was conducted in a clinic population and all women received education on EC; results may not be generalizable to other women. While this is an urban clinic population, the women were young and mostly uninsured, low-income representing an important at-risk population.

Despite these limitations, our study has important public health implications. While removing the requirement to go through pharmacists or clinics to obtain EC increases use, the public health impact may be negligible because of high rates of unprotected intercourse and relative underutilization of the method. Given that there is clear evidence that neither pharmacy access nor advance provision compromises contraceptive or sexual behavior, it seems unreasonable to restrict access to EC through clinics.

Author Contributions: As principal investigators, Drs Raine and Harper had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Raine, Harper, Rocca, Padian, Klausner, Darney.
Acquisition of data: Raine, Harper, Rocca, Fischer, Klausner.
Analysis and interpretation of data: Raine, Harper, Rocca, Padian, Klausner, Darney.
Drafting of the manuscript: Raine, Harper, Rocca.
Critical revision of the manuscript for important intellectual content: Raine, Harper, Fischer, Padian, Klausner, Darney.
Statistical analysis: Harper, Klausner.
Obtained funding: Raine, Harper, Rocca, Klausner, Darney.
Administrative, technical, or material support: Raine, Rocca, Fischer, Padian, Klausner, Darney.
Study supervision: Raine, Harper, Rocca, Fischer, Padian, Darney.
Funding/Support: This research was supported by grants from the Compton Foundation, Inc, the Open Society Institute, the Walter Alexander Gerbode Foundation, and the William and Flora Hewlett Foundation. The Women's Capital Corporation, distributor of Plan B, donated the emergency contraception for use in the trial.
Role of the Sponsors: The funding organizations played no role in the design and conduct of the study; in the collection, management, analysis, and interpretation of the data; and in the preparation, review, or approval of the manuscript for submission.
Disclaimer: The opinions in this article do not necessarily reflect those of the funding organizations or the Planned Parenthood Federation of America, Inc.
Acknowledgment: The San Francisco Department of Public Health and Diagnology LTD donated the tests for the sexually transmitted infections. We are indebted to the staffs of the New Generation Health Center/UCSF, the Planned Parenthood Golden Gate Affiliate clinics in San Francisco and Daly City, and the City College of San Francisco Student Health Center for allowing us to conduct the studies at their sites.

REFERENCES

1. Trussell J, Stewart F, Guest F, Hatcher RA. Emergency contraceptive pills: a simple proposal to reduce unintended pregnancies. *Fam Plann Perspect*. 1992;24:269-273.
2. World Health Organization. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet*. 1998;352:428-433.
3. Gardner JS, Hutchings J, Fuller TS, Downing D. Increasing access to emergency contraception through community pharmacies: lessons from Washington State. *Fam Plann Perspect*. 2001;33:172-175.
4. Raine T, Harper C, Leon K, Darney P. Emergency contraception: advance provision in a young, high-risk clinic population. *Obstet Gynecol*. 2000;96:1-7.
5. Ellertson C, Ambardekar S, Hedley A, Coyaji K, Trussell J, Blanchard K. Emergency contraception: randomized comparison of advance provision and information only. *Obstet Gynecol*. 2001;98:570-575.
6. Jackson R, Schwarz EB, Freedman L, Darney PD. Advance supply of emergency contraception: effect on use and usual contraception—a randomized trial. *Obstet Gynecol*. 2003;102:8-16.
7. Glasier A, Baird D. The effects of self-administering emergency contraception. *N Engl J Med*. 1998;339:1-4.
8. Bissell P, Anderson C. Supplying emergency contraception via community pharmacies in the UK: reflections on the experiences of users and providers. *Soc Sci Med*. 2003;57:2367-2378.
9. Gold MA, Schein A, Coupey SM. Emergency contraception: a national survey of adolescent health experts. *Fam Plann Perspect*. 1997;29:15-19, 24.
10. Harvey SM, Beckman LJ, Sherman C, Petitti D. Women's experience and satisfaction with emergency contraception. *Fam Plann Perspect*. 1999; 31:237-240, 260.
11. Katz MH, Schwarcz SK, Kellogg TA, et al. Impact of highly active antiretroviral treatment of HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health*. 2002; 92:388-394.
12. Porco TC, Martin JN, Page-Shafer KA, et al. Decline in HIV infectivity following the introduction of highly active antiretroviral therapy. *AIDS*. 2004;18:81-88.
13. Gold MA, Wolford JE, Smith KA, Parker AM. The effects of advance provision of emergency contraception on adolescent women's sexual and contraceptive behaviors. *J Pediatr Adolesc Gynecol*. 2004;17: 87-96.
14. Roye C. Routine provision of emergency contraception to teens and subsequent condom use: a preliminary study. *J Adolesc Health*. 2001;28:165-166.
15. Mosher WD. Design and operation of the 1995 National Survey of Family Growth. *Fam Plann Perspect*. 1998;30:43-46.
16. Raine T, Harper C, Paukku M, Darney PD. Race, adolescent contraceptive choice, and pregnancy at presentation to a family planning clinic. *Obstet Gynecol*. 2002;99:241-247.
17. Paukku M, Quan J, Darney PD, Raine TR. Adolescent's contraceptive use and pregnancy history: is there a pattern? *Obstet Gynecol*. 2003;101:534-538.
18. Fleming TR, Harrington DP, O'Brien PC. Designs for group sequential tests. *Control Clin Trials*. 1984;5:348-361.
19. Glasier A, Fairhurst K, Wyke S, et al. Advance provision of emergency contraception does not reduce abortion rates. *Contraception*. 2004;69:361-366.
20. Lovvorn A, Nerquaye-Tetteh J, Glover EK, et al. Provision of emergency contraception to spermicide users in Ghana. *Contraception*. 2000;61:287-293.
21. Drazen JM, Greene MF, Wood AJJ. The FDA, politics, and Plan B. *N Engl J Med*. 2004;350:1561-1562.
22. Vastag B. Plan B for "Plan B"? FDA denies OTC sales of emergency contraceptive. *JAMA*. 2004;291: 2805-2806.

