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Feasibility of recruitment for an efficacy trial of emergency contraceptive pills☆

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Abstract

Background: The efficacy of emergency contraceptive pills (ECPs) is currently uncertain. The best way to obtain a robust efficacy estimate would be to conduct a placebo-controlled randomized trial. We aimed to assess the feasibility of identifying women eligible for such a trial.
Study Design: We conducted a survey of women aged 18–35 years in five sexually transmitted disease clinics and urgent care centers in Kenya and the United States in 2006.
Results: Of 177 women surveyed, only 10 (6%) reported no reasons for exclusion from a potential efficacy trial. Of the rest, 149 (83%) had not recently had sex that conferred a substantial risk of pregnancy. At all sites combined, the rate of identification of potentially eligible women was 0.6 per day of interviewing.
Conclusion: A placebo-controlled efficacy trial of ECPs would likely require several thousand participants. Recruitment for such a trial in these types of sites would be prolonged.

Keywords: Recruitment; Efficacy trial; Emergency contraceptive pill

1. Introduction

A robust estimate of the efficacy of emergency contraceptive pills (ECPs) is not currently available. The package label for the levonorgestrel product approved by the United States Food and Drug Administration indicates that the regimen reduces the expected pregnancy risk by about 88% after a single coital act. Although this figure is based on high-quality data from about 1000 women, key assumptions used in the calculation are probably false, rendering the validity of the figure uncertain. Other sources that used different data but a similar analytic approach cite a wide range of efficacy estimates, ranging from 50% to 100% [1]. The most credible estimate comes from a reanalysis using different methodology of data from two studies, which found that the levonorgestrel emergency contraceptive regimen prevents at least 49% of expected pregnancies (95% confidence limits 17–69%) [2]. This result provides strong evidence that the regimen is more effective than no treatment, but the confidence interval is wide.

The best way to measure the absolute efficacy of any treatment is with a placebo-controlled randomized trial. In an efficacy trial of ECPs, women who had recently had unprotected intercourse would be assigned to take either the active drug or a placebo, and the proportion of women subsequently becoming pregnant in the two groups would be compared.

Recruitment criteria for such a trial would be rigorous. Each participant would be required to have a moderate to high risk for pregnancy from a recent coital act — that is, an act that occurred on a fertile menstrual cycle day and that was not protected by contraceptives. For ethical reasons, women who were intent on using an emergency contraceptive could not be enrolled. Participants could not be pregnant or have a substantial risk of pregnancy from a coital act that preceded the time window within which the emergency contraceptive

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regimen is expected to exert any effect. Women with conditions that would pose a special danger in pregnancy would be excluded because offering placebos to these women would be inappropriate.

The purpose of our survey was to assess the feasibility of locating women who would meet these key eligibility criteria for a placebo-controlled trial of the efficacy of ECPs.

2. Methods

We surveyed women presenting to five health facilities between February and July 2006. Three were sexually transmitted infection clinics (two in North Carolina, one in Kenya) and two were urgent care clinics in California where an earlier study had found a substantial proportion of women reported recently having had unprotected sex [3].

Women 18–35 years old attending each facility were invited to participate in an anonymous survey designed to assess the site's suitability for an unspecified future contraception study. Interviewers then collected data by administering questionnaires designed to assess key exclusion criteria for an emergency contraceptive efficacy trial. The criteria evaluated did not include willingness to participate in a hypothetical trial. At some sites, questionnaires instructed interviewers to stop the interview as soon as one exclusion criterion was met.

Following approximately the order of questions on the questionnaires, we used a defined hierarchy of exclusion criteria (Table 1) to assign a single ineligibility reason to each ineligible woman. Because of the stopping rules on the questionnaires, we were unable to assess multiple reasons for ineligibility; therefore, the number of women assigned to most reasons represents the minimum number actually ineligible for that reason.

The project was determined to be exempt from review by the Institutional Review Board (IRB) at Family Health International, whose staff conducted the interviews at sites in North Carolina and Kenya. It was approved by the Health Department of the Nairobi City Council before initiation in Kenya. It was reviewed by the IRB at University of North Carolina at Chapel Hill before initiation at one North Carolina site and by the IRB at the University of California at San Francisco before initiation at the California sites.

3. Results

We interviewed a total of 177 women aged 18–35 years at all sites combined. Of these, only 10 (6%) reported no information that would have made them ineligible for an emergency contraceptive efficacy trial (Table 1). Each of the rest met at least one exclusion criterion. Most (n=149) were not facing a substantial risk of pregnancy: either they were using a contraceptive, they were abstinent or their last unprotected coital act occurred more than 5 days ago or on a relatively infertile menstrual cycle day. A few women were already pregnant, desired pregnancy or had a medical condition that would seriously complicate pregnancy. Information from 5 women was insufficient to allow an assessment of whether or not they met any of the ineligibility criteria. The pattern of reasons for ineligibility was similar across sites.

None of the women were considered to be ineligible because of a potential undetected early pregnancy from a sex act that occurred more than 5 days before the interview or because of plans to use emergency contraception in the future. However, ascertainment of these characteristics may have been precluded by the hierarchy of assignment of reasons for exclusion.

The 177 interviews were conducted on a total of 18 days at all sites combined (2–7 days at each of the five locations). Thus, an average of 10 screenings of women of the designated age were conducted per day, and an average of 0.6 potentially eligible women were identified per day. These figures were lowest in the California clinics (five to six

Table 1
Minimum numbers of women with specified reasons for ineligibility

Reason, in hierarchical order	CA (n=33)		NC (n=32)		Kenya (n=112)		Total (N=177)	
	n	%	n	%	N	%	n	%
Pregnant	1	3	1	3	7	6	9	5
Using highly effective contraceptive[a]	4	12	4	13	16	14	24	14
Had no sex in past 5 days	9	27	9	28	44	39	62	35
Had no unprotected sex in past 5 days	13	39	11	34	15	13	39	22
Unprotected act not on cycle days 8–20	3	9	1	3	10	9	14	8
Interviewed outside cycle days 8–25[b]	0	0	0	0	4	4	4	2
Desires pregnancy	1	3	1	3	1	1	3	2
Has condition dangerous in pregnancy	0	0	1	3	0	0	1	1
Used hormonal method in past month	0	0	1	3	5	4	6	3
Unevaluable	1	3	0	0	4	4	5	3
None (potentially eligible)	1	3	3	9	6	5	10	6

[a] Including intrauterine device, sterilization, injectable or breastfeeding.
[b] These women stopped the interview before providing information about unprotected sex. However, they could not have had an unprotected coital act that occurred both in the prior 5 days and on Cycle days 8–20.