ORIGINAL ARTICLE

Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception

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ABSTRACT

BACKGROUND

In the United States, more intrauterine device (IUD) users select levonorgestrel IUDs than copper IUDs for long-term contraception. Currently, clinicians offer only copper IUDs for emergency contraception because data are lacking on the efficacy of the levonorgestrel IUD for this purpose.

METHODS

This randomized noninferiority trial, in which participants were unaware of the group assignments, was conducted at six clinics in Utah and included women who sought emergency contraception after at least one episode of unprotected intercourse within 5 days before presentation and agreed to placement of an IUD. We randomly assigned participants in a 1:1 ratio to receive a levonorgestrel 52-mg IUD or a copper T380A IUD. The primary outcome was a positive urine pregnancy test 1 month after IUD insertion. When a 1-month urine pregnancy test was unavailable, we used survey and health record data to determine pregnancy status. The prespecified noninferiority margin was 2.5 percentage points.

RESULTS

Among the 355 participants randomly assigned to receive levonorgestrel IUDs and 356 assigned to receive copper IUDs, 317 and 321, respectively, received the interventions and provided 1-month outcome data. Of these, 290 in the levonorgestrel group and 300 in the copper IUD group had a 1-month urine pregnancy test. In the modified intention-to-treat and per-protocol analyses, pregnancy rates were 1 in 317 (0.3%; 95% confidence interval [CI], 0.01 to 1.7) in the levonorgestrel group and 0 in 321 (0%; 95% CI, 0 to 1.1) in the copper IUD group; the between-group absolute difference in both analyses was 0.3 percentage points (95% CI, −0.9 to 1.8), consistent with the noninferiority of the levonorgestrel IUD to the copper IUD. Adverse events resulting in participants seeking medical care in the first month after IUD placement occurred in 5.2% of participants in the levonorgestrel IUD group and 4.9% of those in the copper IUD group.

CONCLUSIONS

The levonorgestrel IUD was noninferior to the copper IUD for emergency contraception. (Supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and others; ClinicalTrials.gov number, NCT02175030.)

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Worldwide, a variety of methods of emergency contraception are used to decrease the risk of pregnancy after unprotected sexual intercourse. In the United States, the Food and Drug Administration (FDA) has approved only two methods of emergency contraception: oral levonorgestrel and oral ulipristal acetate. Although the copper intrauterine device (IUD) is not approved by the FDA for emergency contraception, substantial observational evidence supports that it is highly effective, failing to prevent pregnancy in less than 0.1% of cases,[1] an order of magnitude lower than the incidence of failure with oral methods.[2,3] However, persons selecting an IUD for long-term contraception have shown a strong preference for the levonorgestrel IUD over the copper IUD, probably because the levonorgestrel IUD reduces menstrual bleeding and discomfort.[4-6]

The availability of a greater number of contraceptive options is associated with increased satisfaction with and continuation of the use of the method and decreased unintended pregnancy.[7] In addition, best practices for delivery of family planning services recommend quick-start contraception, with provision and initiation of the desired method at the point of care.[7] Although patients can quick-start contraception with the levonorgestrel IUD,[8] women obtaining a levonorgestrel IUD who report recent unprotected sexual intercourse are currently advised to take concomitant oral emergency contraception.[9]

A preliminary, prospective cohort study that offered persons seeking emergency contraception the levonorgestrel 52-mg IUD with concomitant oral levonorgestrel or the copper IUD showed user preference for the levonorgestrel IUD. Despite a high risk of emergency contraception failure among persons who chose the levonorgestrel IUD and oral levonorgestrel, with 40% of the participants in that group reporting multiple episodes of unprotected sexual intercourse and 61% having a body-mass index (the weight in kilograms divided by the square of the height in meters) of 25 or higher, there were no pregnancies resulting from failure of emergency contraception among the 121 persons who selected the levonorgestrel regimen.[10] This, along with evidence of the effectiveness of inert IUDs,[11,12] has suggested that the levonorgestrel IUD could be effective for emergency contraception. Moreover, laboratory data support the potential for levonorgestrel to directly interfere with sperm transport, sperm capacitation, the acrosome reaction, and oviduct transport.[13-16] We designed the Randomized Controlled Trial Assessing Pregnancy for IUDs as Emergency Contraception (RAPID EC) trial to assess the 1-month pregnancy risk with the levonorgestrel 52-mg IUD as compared with the copper IUD for emergency contraception. We selected a noninferiority trial design because, given the preference for the levonorgestrel IUD shown by participants in earlier trials, establishing its noninferiority to the copper IUD for emergency contraception could increase emergency contraception options for patients.

Methods

Trial Design

Beginning in August 2016, trial staff recruited patients at three Utah family planning clinics for trial participation. We added three additional sites in March 2017 and concluded enrollment in December 2019. The institutional review board at the University of Utah approved the trial protocol, available with the full text of this article at NEJM.org. The last author, who was not directly involved with analysis, generated the randomization sequence using balanced blocks of four, stratified by site, and uploaded the blinded sequence to Research Electronic Data Capture (REDCap),[17] a secure Web-based application system. We performed the trial in accordance with the principles of the Declaration of Helsinki. Trial sites purchased the study drugs, levonorgestrel 52-mg IUD (Liletta, Medicines360) and copper T380A IUD (ParaGard, Teva Women's Health), from the distributors. These companies had no role in any aspect of conduct of the trial. The first, second, and fifth authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The statistical analysis plan is provided with the protocol at NEJM.org.

Participants

Eligible participants were women 18 to 35 years of age who were fluent in English or Spanish and were requesting emergency contraception after unprotected sexual intercourse within the previous 5 days (120 hours). Other inclusion criteria were a desire to initiate use of an IUD, a

desire to prevent pregnancy for at least 1 year, a negative urine pregnancy test, a history of regular menstrual cycles (21 to 35 days), and known date of the last menstrual period (±3 days). On the basis of the menstrual history, we calculated the menstrual cycle day of unprotected sexual intercourse and IUD insertion and, if needed, an estimated date of pregnancy. Key exclusion criteria were breast-feeding, vaginal bleeding of unknown cause, current use of a highly effective method of contraception (sterilization, IUD, or contraceptive implant), intrauterine infection in the previous 3 months, untreated *Neisseria gonorrhea* or *Chlamydia trachomatis* infection in the previous 30 days, allergy to copper, use of oral emergency contraception in the preceding 5 days, and known uterine cavity anomalies. We did not exclude persons who reported having unprotected sexual intercourse more than 5 days before IUD placement.

TRIAL PROCEDURES

All women at participating sites who presented for emergency contraception received printed information describing trial participation, randomization, concealment of group assignment, and the two types of IUD in the trial. Participants who received an IUD could have it removed at any time and could switch to another contraceptive method, including another type of IUD.

All participants had a negative urine pregnancy test (Osom card pregnancy test, Genzyme Diagnostics) before IUD placement. After the participants completed screening and provided written informed consent, REDCap randomly assigned them, in a 1:1 ratio, to placement of a levonorgestrel 52-mg IUD or a copper T380A IUD. We concealed the IUD package so that participants would be unaware of their assigned intervention, but the different appearance of the IUDs and differences in insertion methods meant that the providers were aware of the IUD type that was inserted. Nurse practitioners and certified nurse midwives with experience in IUD placement performed all insertions. Health centers provided the trial interventions and devices without cost to participants and billed health insurance companies when appropriate.

Before participants left the clinic, staff scheduled a 1-month follow-up visit (28 to 30 days after insertion) and provided a home urine pregnancy test for the participant to use the morning before the follow-up appointment. There were three opportunities for participants to report urine pregnancy test results. First, research staff sent a text message to participants 27 days after enrollment instructing them to conduct the home urine pregnancy test. This text included a link to use to submit results online and an option to upload a photo of the test results. The next day, participants received a link to complete their 1-month follow-up survey through REDCap, which also prompted the participants to enter the results of their urine pregnancy tests. Finally, at the 1-month office visit, a member of the clinical research staff performed a urine pregnancy test, informed the participant which IUD she had received, and had the participant complete the follow-up survey if she had not already done so. This task sequence was not standardized; thus, some participants were notified of the IUD type they received before they had completed the survey.

If participants had not yet provided urine pregnancy test results by their scheduled 1-month visit and did not attend the visit, trial staff called and sent text and email messages (up to three times by each means of contact) over the next week. If needed, trial staff attempted to reach alternative contacts who had been provided by the participants at enrollment. We continued to follow participants through 3-month and 6-month surveys and reviewed clinic electronic health record notes to assess IUD use and pregnancy status. Participant reimbursement included a $10 gift card for completing each follow-up survey and $30 for attending the 1-month clinic visit.

OUTCOMES AND ADVERSE EVENTS

The primary outcome was pregnancy, defined by our initial protocol as a positive urine pregnancy test conducted at home or in the clinic 1 month after IUD placement. After data collection was completed and data were unblinded, we observed that data for the primary outcome were missing for 48 participants. The protocol was then amended to consider participants who did not report pregnancy test results within 40 days after IUD placement as not pregnant if follow-up surveys up to 6 months, review of clinic notes, and review of medical records for any visits reported at other sites revealed no positive pregnancy test results. Participants who reported a pregnancy in the first 6 months of IUD use un-

derwent pregnancy dating by means of ultrasonography to determine whether the pregnancy resulted from unprotected sexual intercourse within 5 days before placement of the trial IUD. Using responses from the 1-month survey, we assessed incidents of IUD discontinuation (including date and reason), participant satisfaction, and IUD-related pain and bleeding outcomes (see the Supplementary Appendix, available at NEJM.org, for details). The 1-month participant survey included a query regarding receipt of any medical care in any setting to assess adverse events. A data and safety monitoring committee evaluated the main safety outcome of emergency contraception failure in the levonorgestrel IUD group annually. Our prespecified plan required enrollment cessation if the annual evaluation revealed that the lower bound of the 95% confidence interval for the percent difference between pregnancy rates in the two groups exceeded 2.5 percentage points, per protocol, with the use of the planned final sample sizes of the two groups as denominators.

STATISTICAL ANALYSIS

We based our sample-size calculation for the primary outcome on the established pregnancy incidence of 0.1% among copper T380A IUD emergency contraception users.[1] Because data were lacking on pregnancy risk with the use of the levonorgestrel IUD alone for emergency contraception, we conservatively estimated a 1% incidence of pregnancy among participants using levonorgestrel 52-mg IUDs, on the basis of a trial of the levonorgestrel IUD administered with oral levonorgestrel for emergency contraception.[10] To achieve 80% power to detect a two-sided 95% confidence interval around an absolute difference in the incidence of pregnancy after emergency contraception (1% with levonorgestrel minus 0.1% with copper) that would not cross the noninferiority margin of 2.5 percentage points, we required 335 participants per trial group (for a total of 670). We planned to recruit an additional 5% of that total to accommodate loss to follow-up (for a total of 706 participants).

An intention-to-treat analysis was initially specified in the protocol, but the analysis plan was changed after trial completion to a modified intention-to-treat analysis in which we excluded participants assigned to each group who did not receive an IUD (since those who received an IUD were considered the relevant trial population) and included only those for whom we had 1-month outcome data (pregnancy test results or subsequent survey or clinical data indicating no evidence of pregnancy). We also performed a per-protocol analysis limited to participants still using their IUDs at 1 month and a sensitivity analysis that included only those who reported 1-month urine pregnancy test results. (See the Supplementary Appendix for details of the analyses.)

Missing data for the secondary outcomes were imputed with multivariate imputation by chained equations, which averaged regression coefficients across five imputed data sets, with standard errors computed with the use of Rubin's rules.[18] Multiple imputation was not used for the primary outcome, because one group had no pregnancy outcomes and the model would not converge. Continuous secondary outcomes are reported as mean differences with two-sided 95% confidence intervals. Secondary categorical outcomes are reported as absolute risk differences expressed as percentage points with two-sided 95% confidence intervals. Confidence intervals for the secondary outcomes have not been adjusted for multiplicity and should not be used to infer definitive treatment effects. Data analysts were unaware of the treatment assignments. We conducted data analysis with Stata software, version 16 (StataCorp).

RESULTS

PARTICIPANTS

We assessed for eligibility 10,317 women who were seeking emergency contraception from August 2016 through mid-December 2019, until the prespecified sample size was met. Of the persons who were assessed, 805 were younger than 18 years of age, 547 did not meet inclusion criteria, and 8247 declined to participate, primarily because they desired only oral emergency contraception. Details of enrollment and trial participation are shown in Figure 1. A total of 718 participants were enrolled, of whom 711 underwent randomization; 355 participants were assigned to receive the levonorgestrel IUD and 356 to receive the copper IUD. Of these, 317 and 321 participants, respectively, received the assigned intervention and provided 1-month outcome data (and thus were included in the modi-

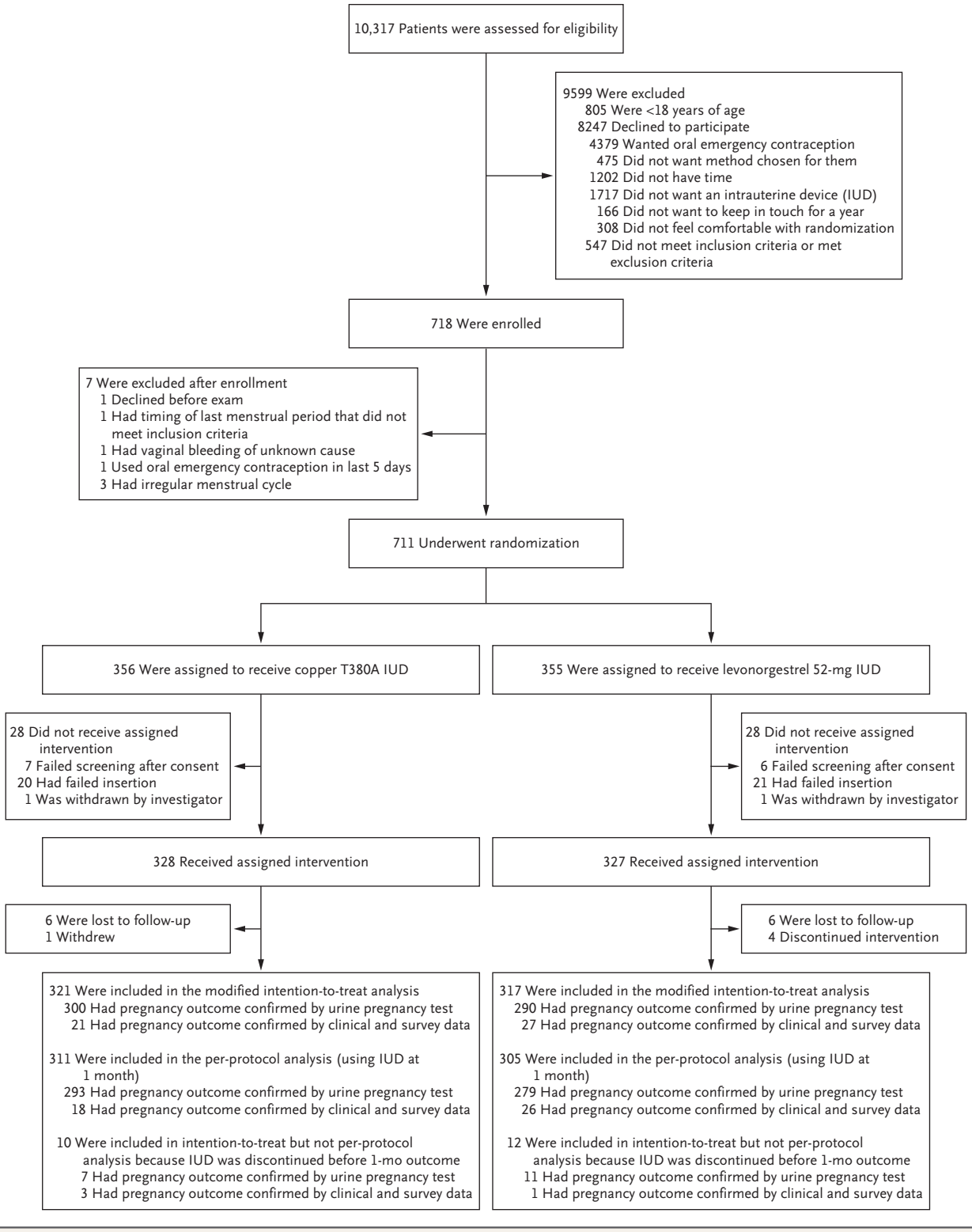

Figure 1. Enrollment, Randomization, Follow-up, and Analysis.

Table 1. Characteristics of the Participants at Enrollment.*

Characteristic	Levonorgestrel IUD (N=327)	Copper IUD (N=328)
Age — yr	24.0±4.9	23.9±4.6
Body-mass index — no. (%)†		
<25	168 (51.4)	155 (47.3)
25 to 29.9	70 (21.4)	85 (25.9)
≥30	89 (27.2)	88 (26.8)
Education — no./total no. (%)		
High school or less	169/326 (51.8)	168/326 (51.5)
Attending college	123/326 (37.7)	120/326 (36.8)
College degree or higher	34/326 (10.4)	38/326 (11.7)
Annual income — no./total no. (%)		
<$12,000	133/326 (40.8)	141/326 (43.3)
$12,000 to $35,999	151/326 (46.3)	152/326 (46.6)
≥$36,000	42/326 (12.9)	33/326 (10.1)
Race or ethnic group — no. (%)‡		
White	179 (54.7)	190 (57.9)
Hispanic or Latinx	108 (33.0)	98 (29.9)
Black or African American	12 (3.7)	12 (3.7)
Other	28 (8.6)	28 (8.5)
Relationship status — no./total no. (%)		
Married	16/326 (4.9)	21/326 (6.4)
Living together or in committed relationship	112/326 (34.4)	107/326 (32.8)
Single or actively dating	169/326 (51.8)	171/326 (52.5)
Divorced or separated	17/326 (5.2)	18/326 (5.5)
Other or did not answer	12/326 (3.7)	9/326 (2.8)
Reason for seeking emergency contraception — no./total no. (%)		
Did not use any method at last sexual intercourse	132/324 (40.7)	165/327 (50.5)
Incorrect use of rhythm or withdrawal method	61/324 (18.8)	68/327 (20.8)
Condom broke	61/324 (18.8)	41/327 (12.5)
Ran out of contraception or missed dose	15/324 (4.6)	8/327 (2.4)
Did not plan or was forced to have sexual intercourse	40/324 (12.3)	28/327 (8.6)
Other	15/324 (4.6)	17/327 (5.2)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. IUD denotes intrauterine device.
† Body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race and ethnic group were reported by participants.

fied intention-to-treat analysis), and 290 and 300 participants, respectively, provided a urine pregnancy test result at the 1-month follow-up.

Baseline characteristics were similar in the two groups except for imbalances in reasons for seeking emergency contraception (Table 1). Participants reported an average of 2.1 episodes of unprotected sexual intercourse in the 5 days preceding IUD placement. At the 1-month follow-up, urine pregnancy test results for participants who received an IUD were obtained by home report for 172 participants (27.0%), by clinic report for 66 (10.3%), and by both reports for 352 (55.2%). Information on pregnancy was

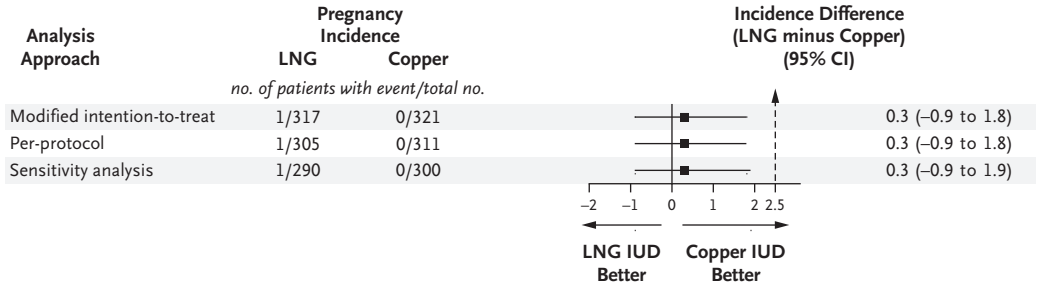

Figure 2. One-Month Pregnancy Outcomes with the Levonorgestrel 52-mg IUD versus the Copper T380A IUD, According to Type of Analysis.

The primary outcome, a positive urine pregnancy test 1 month after IUD insertion, was designed to test the efficacy of the levonorgestrel (LNG) 52-mg IUD and copper T380 IUD for emergency contraception. Forty-eight participants did not provide urine pregnancy tests and had their pregnancy outcomes reported by survey and health record data. The modified intention-to-treat analysis includes all participants receiving an IUD who reported the 1-month pregnancy outcome by any method. The per-protocol analysis includes only participants who were still using the IUD to which they were randomly assigned when the 1-month pregnancy outcome was reported. The sensitivity analysis includes only participants with the 1-month pregnancy outcome confirmed by a urine pregnancy test. The Miettinen–Nurminen method was used to compute the two-sided 95% confidence interval around the proportion difference to test noninferiority.

available for 45 of the remaining 48 participants on the basis of their returning at least one of the three follow-up surveys (at 1 month, 3 months, and 6 months). A review of data from electronic health record data confirmed the outcome for 17 participants, including 3 who did not complete any surveys.

OUTCOMES

Pregnancy 1 month after IUD placement occurred in a single participant in the levonorgestrel IUD group (0.3%; 95% confidence interval [CI], 0.01 to 1.7), and in no participants in the copper IUD group (0%; 95% CI, 0 to 1.1). The between-group absolute difference was 0.3 percentage points (95% CI, −0.9 to 1.8) in both the modified intention-to-treat and per-protocol analyses (Fig. 2).

The lone pregnancy occurred in a participant who reported a single episode of unprotected sexual intercourse 48 hours before IUD placement. Pregnancy dating by an ultrasound examination at 10 weeks was consistent with conception occurring as a result of an emergency contraception failure. The pregnancy ended in a spontaneous abortion at 10 weeks with the IUD still in place.

Table 2 shows results for secondary outcomes, both unadjusted and adjusted post hoc for the reason participants provided for seeking emergency contraception, given the baseline imbalance. One participant in the copper IUD group had an expulsion of her IUD and same-day reinsertion on day 11, and one participant in the levonorgestrel IUD group switched to a copper IUD on day 28. Among levonorgestrel IUD users, 5.2% sought medical care for adverse events in the first month after IUD placement as compared with 4.9% of copper IUD users (Table 3).

DISCUSSION

This randomized trial showed that the levonorgestrel 52-mg IUD was noninferior to the copper T380 IUD for use as emergency contraception after unprotected sexual intercourse in the previous 5 days. Pregnancy at the 1-month follow-up was reported in 0.3% of participants in the levonorgestrel IUD group and in no participants in the copper IUD group, in both the modified intention-to-treat and per-protocol analyses, with confidence intervals around the difference excluding the noninferiority margin of 2.5 percentage points. These data can also support provision of quick-start contraception with the levonorgestrel 52-mg IUD after recent unprotected sexual intercourse and a negative pregnancy test.

We did not directly compare IUD use with other emergency contraception methods. However, the incidence of pregnancy with the use of

Table 2. Clinical Outcomes among Users of Emergency Contraception in the First Month after IUD Placement.*

Outcome	Levonorgestrel IUD (N=327)	Copper IUD (N=328)	Unadjusted Mean Difference (95% CI)	Unadjusted Risk Difference % (95% CI)	Adjusted Mean Difference (95% CI)†	Adjusted Risk Difference % (95% CI)†
IUD expulsion — no. (%)	2 (0.6)	3 (0.9)		−0.3 (−1.6 to 1.0)¶		−0.3 (−1.5 to 1.0)‖
IUD removal — no. (%)	10 (3.1)	8 (2.5)		0.6 (−1.9 to 3.1)¶		1.0 (−1.5 to 3.6)‖
Participant satisfaction level — no./total no. (%)						
Very satisfied	42/308 (13.6)	50/307 (16.3)		−2.9 (−8.4 to 2.6)**		−0.28 (−8.3 to 2.8)††
Satisfied	116/308 (37.7)	119/307 (38.8)		−1.2 (−9.0 to 6.5)**		−1.5 (−9.4 to 6.4)††
Neutral	107/308 (34.7)	88/307 (28.7)		6.3 (−1.1 to 13.7)**		6.2 (−1.3 to 13.7)††
Unsatisfied	23/308 (7.5)	22/307 (7.2)		0.3 (−3.8 to 4.3)**		0.3 (−3.9 to 4.4)††
Very unsatisfied	20/308 (6.5)	28/307 (9.1)		−2.8 (−7.1 to 1.4)**		−2.6 (−6.8 to 1.7)††
Pain						
Pain associated with IUD since insertion — no./total no. (%)	210/308 (68.2)	207/306 (67.7)		1.0 (0.7 to 1.4)**		1.0 (0.7 to 1.4)††
Cramping since insertion‡	59.5±1.9	66.6±1.8	−9.9 (−15.2 to −4.6)**		−10.3 (−15.6 to −4.9)††	
Sharp pain since insertion‡	66.6±1.4	72.5±1.3	−8.6 (−12.9 to −4.4)**		−9.0 (−13.2 to −4.8)††	
Bleeding and spotting days in first month of IUD use§						
No. of bleeding days	10.8±0.5	7.2±0.3	3.5 (2.4 to 4.6)**		3.5 (2.4 to 4.6)††	
No. of spotting days	11.0±0.6	5.7±0.3	5.2 (3.7 to 6.4)**		5.4 (3.8 to 6.9)††	

* Plus–minus values are means ±SE.
† Mean difference and risk difference are adjusted for differences in reason for seeking emergency contraception by IUD type. Confidence intervals have not been adjusted for multiple comparisons, and therefore inferences drawn from these intervals may not be reproducible.
‡ Mean values for cramping and sharp pain represent the level that participants in each group had in the first month after IUD insertion, as assessed with the use of a visual analogue scale ranging from 0 to 100 (with higher scores indicating greater pain). Data on cramping were missing for 34 participants (5.1%) in the levonorgestrel IUD group and for 33 (4.1%) in the copper IUD group; data on sharp pain were missing for 28 (8.6%) in the levonorgestrel IUD group and for 28 (8.5%) in the copper IUD group.
§ Data on bleeding were missing for 51 participants (15.6%) in the levonorgestrel IUD group and for 77 (23.5%) in the copper IUD group; data on spotting were missing for 48 (14.7%) in the levonorgestrel IUD group and for 76 (23.3%) in the copper IUD group.
¶ Values are unimputed difference and confidence interval.
‖ Unimputed difference was adjusted for reason for seeking emergency contraception.
** Values are imputed difference and confidence interval; they will not always match descriptive statistical difference.
†† Imputed difference was adjusted for reason for seeking emergency contraception and will not always match descriptive statistical difference.

the levonorgestrel IUD for emergency contraception in this trial (0.3%; 95% CI, 0.01 to 1.7) appears to compare favorably with that reported with oral emergency contraception (1.4 to 2.6%).[2,3] Unlike the case with oral levonorgestrel, the efficacy of the levonorgestrel IUD for emergency contraception does not appear to be affected by higher body-mass index.[19] Since the IUD also provides ongoing contraception, it avoids the delayed initiation of ongoing contraception that is recommended when ulipristal acetate is used for emergency contraception.[9,20]

Although studies of conventional oral emergency contraception commonly limit participants to those who have had a single episode of unprotected sexual intercourse occurring 3 to 5 days before emergency contraception, many of this trial's participants were at higher risk for pregnancy, reporting multiple episodes of unprotected sexual intercourse in the previous 5 days and some reporting unprotected sexual intercourse 6 to 14 days before IUD placement. Despite this, we found a lower frequency of pregnancy than expected.[21] We previously reported no pregnancies at follow-up at 2 to 4 weeks or longer among a pooled cohort of 134 women who had a copper IUD placed 6 to 14 days after unprotected sexual intercourse and for whom follow-up information was available; that report included data from 27 participants in the copper IUD group in the present trial.[22] Our conclusions were unchanged in a sensitivity analysis that included only participants who provided data from urine pregnancy tests.

Although our enrollment met the sample size target (706), we overestimated the number of participants who would provide 1-month follow-up (638). However, the number of pregnancies in the levonorgestrel IUD group was lower than projected, and noninferiority was shown. We were able to obtain urine pregnancy testing, the prespecified primary outcome, for 92.5% (590) of the 638 participants who provided 1-month follow-up. We addressed missing tests by confirming no report of pregnancy in survey information and clinic records, although the timing of clinic record review after data unblinding could have potentially introduced bias. If participants who did not report 1-month urine pregnancy tests underwent abortions, it is unlikely that these would have been missed on record review, because the vast majority of abortions in Utah occur within the same health system as the clinic sites. For practical reasons, clinicians were aware of the IUD type the participants received, and some participants seen in a clinic for the 1-month follow-up visit may have been informed of their IUD type before they completed their follow-up survey. However, these situations would not be expected to affect rates of the primary outcome. Selection bias is possible, since only 7% of clinic patients seeking emergency contraception enrolled in this trial. The majority of persons who declined participation did not want an IUD. Enrollment rates were lower than in a previous trial in which we allowed participants to select their preferred IUD type for emergency contraception.[10] Because the clinics serving as trial sites are known to provide low-cost oral emergency contraception rapidly, some women may not have wanted to spend the additional time at the clinic required for trial

Table 3. Adverse Events Resulting in Request for Medical Care during the First Month of IUD Use.

Event	Levonorgestrel IUD (N=327)	Copper IUD (N=328)
	number (percent)	
Total events*	17 (5.2)	16 (4.9)
Type of event		
Bleeding	2 (0.6)	1 (0.3)
Bleeding and cramping	3 (0.9)	2 (0.6)
Bleeding and pain	0	3 (0.9)
Cramping	4 (1.2)	1 (0.3)
Pain	3 (0.9)	3 (0.9)
Vulvovaginal infection	1 (0.3)	2 (0.6)
Urinary tract infection	0	2 (0.6)
Concerns related to IUD†	3 (0.9)	1 (0.3)
Nausea	1 (0.3)	0
Headache	1 (0.3)	0
Pruritus or dermatologic condition	0	2 (0.6)
Depressed mood	1 (0.3)	0
Ovarian cyst	1 (0.3)	0
Swollen lymph nodes	1 (0.3)	0

* The unimputed absolute risk difference in total events between the groups is −0.2 (95% CI, −3.6 to 3.3). This difference was adjusted for the participant-reported reason for seeking emergency contraception.

† Concerns included confirming that the IUD was still in place, concerns that pain caused by a kidney infection might be related to the IUD, and concerns about the string length or about not being able to feel the strings (or both).

enrollment and IUD placement. The nature of the trial sites may also limit generalizability, as did our exclusion of persons outside the 18-to-35-year age range and those with irregular menstrual cycles.

In this multicenter randomized trial, the levonorgestrel 52-mg IUD was noninferior to the copper IUD for emergency contraception.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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