OBSTETRICS & GYNECOLOGY

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

Personal or nonessential information may be redacted at the editor's discretion.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

Date: Jun 26, 2020
To: "Christy Marie Boraas" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-1220

RE: Manuscript Number ONG-20-1220

Levonorgestrel-releasing intrauterine system prevents pregnancy 6-14 days after unprotected sex

Dear Dr. Boraas:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Due to the COVID-19 pandemic, your paper will be maintained in active status for 30 days from the date of this letter. If we have not heard from you by Jul 26, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

SUMMARY:
This is a prospective cohort of 187 individuals undergoing LNG IUD insertion with recent unprotected intercourse in the 6-14 days prior to insertion across several institutions and using multiple procedural protocols for insertion and most notably, follow-up. The objective was to identify the risk of pregnancy for this quick start LNG IUD process when the UPT was negative but luteal pregnancy could not yet be definitely ruled out.

COMMENTS:
LINE 104: Please clarify why the cut off day of 6 was chosen as the soonest possible reported unprotected intercourse.

LINE 125: This is initially confusing as stated- why were there four different protocols employed (was the intention to gather the same data but carried out differently due to differing IRBs? Were these separate protocols from already existing and separate data sets?)

LINE 156: reasonable proxy given no incentive to lie and follow-up at 3 and 6 months would have flushed out any ambiguity.

LINE 195: The discussion in general needs beefing up to further articulate the significance of a "quick start" LNG IUD. The context with Plan B and Ella is great, but the glaring difference here is that people are more willing to accept an oral EC exposure in a luteal phase pregnancy that turns out to be desired, than they are an IUD whose mechanical presence itself may increase the risk of SAB (however illogical it may seem to providers). So while these two options cannot be directly compared (especially given access issues to LARC vs OTC EC) it's a first step in this discussion.

The other thing the discussion is missing is an explanation of why the pregnancy risk may be so low or at least lower than expected fecundity for these presumably highly fertile and at-risk people.

Reviewer #2: This is a multi-institutional single arm prospective cohort study to report rate of contraception failure for the use of LNG-IUS as an emergency contraception!

Main issues:
1- This might be a good paper for a "research report" study type as the amount of data presented is based on a limited amount of data and data analysis!

2- How the results in this study differ and add to the literature beyond the study by Castano and colleagues published in the Gray Journal in 2020 or the study by Turok and colleagues published in Contraception in 2016.

3- Is there any overlap between the data in this current report and the study published in 2016 by Turok in 2016 and that is ongoing at the University of Utah as well expected to be done by the end of 2020!

Specific issues:
1- Disclosure and funding: Can funding for research be from an "anonymous foundation"!

2- Introduction: well written!

3- Methods:
a. Did the authors have plan to optimize recruitment and plan to optimize follow up for those included, please include!
b. Given that utilization of other medication was allowed in the study, how can the authors assume that the observed results are related only to LNG-IUS use?

4- Results:
a. Please include a flow chart with the number of patients included from each of the 3 sites?

5- Discussion:
a. What is the explanation of slow recruitment for this indication? Is it the emergency need or the presence of other more effective treatments?

Reviewer #3: Thank you for submitting your article on Levonorgestrel-Releasing Intrauterine System Prevents Pregnancy 6 - 14 Days After Unprotected Sex. The time and effort you dedicated to this article is evident in your work. Your submission addresses a critical question regarding emergency contraception. You do an excellent job of discussing pre-existing literature on the use of levonorgestrel IUDs being used as emergency contraception, in addition to showing how your submission meaningfully expands upon that literature. While the study could have been improved with each site using the same protocol, the study provides valuable data as is. Your inclusion and exclusion criteria were appropriate for the study, and the methodology is appropriate when considering the difficulties of conducting a randomized controlled trial for this type of research. This submission will hopefully open the door to a robust RCT that can provide more conclusive evidence for the use of levonorgestrel IUDs as emergency contraception.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

line 135: Some women did not have UPT results and those with UPT results were done by 4 weeks. Is there other follow-up data available to corroborate the absence of pregnancy among the 186 women?

lines 196-197, 202: As the Authors note, this report is based on only 1 reported pregnancy. Therefore the point estimates are imprecise and it would be prudent to cite the upper bound of the estimates, rather than citing risks < 1% or of 1.4%. It would require a much larger series with more adverse events to have a more precise estimate.

Table 2: Although it is mentioned in the text, should include a footnote stating that all the rates are based on the only pregnancy in the cohort of n= 187.

EDITOR COMMENTS:

1. Please be sure to update your revision's title page to name the Susan T. Buffett Foundation.

2. The Editors would like you to reformat the submission into a Research Letter. You would be permitted to have SDC, if needed, to assist in condensing the content of the submission.

The guidelines for the Research Letter article type are as follows:

The Research Letter is a concise, focused report of original research (including pre-clinical research, sub-analyses or updates of previously published research, small studies, or pilot studies). Length should not exceed 600 words (approximately 2 1/2 manuscript pages). Figures or tables are limited to two, total.

Research Letters should be organized using the following headings: Introduction, Methods, Results and Discussion.

3. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
A. OPT-IN: Yes, please publish my point-by-point response letter.
B. OPT-OUT: No, please do not publish my point-by-point response letter.

4. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

5. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

6. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 2.5 pages (600 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

9. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. ACOG is moving toward discontinuing the use of "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

13. In your submission, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

14. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

15. Figure 1 may be resubmitted as-is with the revision.

16. Each supplemental file in your manuscript should be named an "Appendix," numbered, and ordered in the way they are first cited in the text. Do not order and number supplemental tables, figures, and text separately. References cited in appendixes should be added to a separate References list in the appendixes file.

17. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 30 days from the date of this letter. If we have not heard from you by Jul 26, 2020, we will assume you wish to withdraw the manuscript from further consideration..

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

[redacted]

July 23, 2020

Re: ONG-20-1220 (resubmission with revisions)
Title: Levonorgestrel-releasing intrauterine system prevents pregnancy 6-14 days after unprotected sex
Authors: Christy Boraas, MD, MPH; Jessica N. Sanders, PhD, MSPH; E. Bimla Schwarz, MD, MS; Ivana Thompson, MD, MSCI; David K. Turok, MD, MPH

To the editors of *Obstetrics & Gynecology*:

On behalf of my co-authors, I would like to thank you and the reviewers for providing us with constructive suggestions for this manuscript. As requested, we have reformatted our Original Research manuscript into a Research Letter. Below we address each of the reviewers' comments.

I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. I would like to acknowledge there have been no interval changes in the conflicts of interest for any of the authors. None of the authors report any related conflicts of interest.

REVIEWER COMMENTS:

Reviewer #1
COMMENTS:
1- LINE 104: Please clarify why the cut off day of 6 was chosen as the soonest possible reported unprotected intercourse.

Response: Day 6 was chosen as it is the first day outside the standard window for emergency contraceptives (this window being up to 5 days following unprotected sex per the Centers for Disease Control (CDC) Selective Practice Recommendations (SPR) and the Medical Eligibility Criteria). For individuals presenting for levonorgestrel intrauterine device (IUD) placement and reporting unprotected sex up to 5 days prior, we would offer oral emergency contraceptives (typically levonorgestrel) in addition to placing the levonorgestrel IUD. We wanted to capture the risk of pregnancy for people who want an IUD placed but also report unprotected sex further than 5 days prior to placement. This clinical scenario currently falls outside of the SPR guidelines.

2- LINE 125: This is initially confusing as stated- why were there four different protocols employed (was the intention to gather the same data but carried out differently due to differing IRBs? Were these separate protocols from already existing and separate data sets?)

Response: We have clarified that we used data from four projects that were funded to address other clinical questions. For example, we identified some participants in studies evaluating the LNG-IUS for emergency contraception and additional protocols specifically identifying women reporting unprotected intercourse 6-14 days prior to presenting for care. Normally, these people would be

turned away and told to return for care during their next menses. Participation in these studies permitted them to receive the a levonorgestrel IUD (LNG-IUS) in this circumstance. These four study protocols were started independently and produced relevant data that was more informative when combined. The primary outcome for all four, however, was pregnancy within one month of IUD placement and thus, for this manuscript, we combined all four pre-existing data sets into one combined data set (n=187) which this manuscript describes.

3- LINE 156: reasonable proxy given no incentive to lie and follow-up at 3 and 6 months would have flushed out any ambiguity.

Response: Thank you.

4- LINE 195: The discussion in general needs beefing up to further articulate the significance of a "quick start" LNG-IUS. The context with Plan B and Ella is great, but the glaring difference here is that people are more willing to accept an oral EC exposure in a luteal phase pregnancy that turns out to be desired, than they are an IUD whose mechanical presence itself may increase the risk of SAB (however illogical it may seem to providers). So while these two options cannot be directly compared (especially given access issues to LARC vs OTC EC) it's a first step in this discussion.

Response: We agree. However, condensing this paper to a research letter limited the discussion.

5- The other thing the discussion is missing is an explanation of why the pregnancy risk may be so low or at least lower than expected fecundity for these presumably highly fertile and at-risk people.

Response:
We appreciate that there are many factors which affect fecundability – such as cigarette smoking and a history of gonorrhea and chlamydia to name two. However, this data is not available to inform the current study and condensing this paper to a research letter limited the discussion.

Reviewer #2:
Main issues:
1- This might be a good paper for a "research report" study type as the amount of data presented is based on a limited amount of data and data analysis!

Response: Thank you. We have reformatted our originally submitted manuscript into Research Letter format.

2- How the results in this study differ and add to the literature beyond the study by Castano and colleagues published in the Gray Journal in 2020 or the study by Turok and colleagues published in Contraception in 2016.

Response:
Castaño and colleagues (PMID 31945336) reported on a retrospective cohort of 239 patients that did not meet checklist criteria to reasonably exclude pregnancy prior to IUD placement. This checklist included: is ≤7 days after spontaneous or induced abortion; has been correctly and consistently using a reliable method of contraception; is ≤7 days after the start of normal menses; has not had

intercourse since the beginning of last normal menses; is within 4 weeks postpartum; is fully or nearly fully breastfeeding, amenorrheic, and <6 months postpartum. It is not detailed why those that were included in the study didn't meet pregnancy checklist criteria. It is certainly possible that this study included participants that were similar to those in our study. However, our study only includes patients that report unprotected sex 6-14 days prior to IUD placement. The number of participants in the Castaño study who who also reported unprotected sex 6-14 days prior to IUD placement cannot be ascertained from their article directly.

The 2nd paper cited in the comment (PMID 26944863, labeled as University of Utah COLIEC protocol, n = 24 in Figure 1) is a study of participants presenting for emergency contraception offered a LNG-IUS and oral LNG or a copper T380A IUD. These participants reported unprotected sex up to 120 hours (5 days) prior to IUD placement and the study concluded a low risk of pregnancy when a levonorgestrel IUD is placed with concomittant oral levonorgestrel for emergency contraception. Twenty-four participants from this study who received the LNG combination are included in this analysis because they also reported unprotected intercourse in the last 6-14 days.

3- Is there any overlap between the data in this current report and the study published in 2016 by Turok in 2016 and that is ongoing at the University of Utah as well expected to be done by the end of 2020!

Response: Yes, there is overlap with data from the Turok 2016 publication as identified above (PMID 26944863, labeled as University of Utah COLIEC protocol, n = 24 in Figure 1 of the 110 study participants who received a LNG-IUS). In addition, data are also included from the forthcoming analysis of the ClinicalTrials.gov Identifier NCT02175030 study (labeled as University of Utah RAPID EC protocol, n = 54 in Figure 1 of the 327 study participants who received a LNG-IUS for EC).

Specific issues:

1- Disclosure and funding: Can funding for research be from an "anonymous foundation"!

Response: The previously listed "anonymous foundation" has been updated to reflect a change to name the funder, the Susan Thompson Buffett Foundation. See lines 24-25.

2- Introduction: well written!

Response: Thank you.

3- Methods:

a. Did the authors have plan to optimize recruitment and plan to optimize follow up for those included, please include!

Response: All of the four study protocols that contributed data for this manuscript attempted to optimize both recruitment and follow up. All sites and protocols had dedicated study staff involved in recruitment so that eligible participants would not be missed. Clinic staff at all sites received regular study updates and education on protocols. All participants received compensation for participation and provided multiple modalities (email, telephone, letters) and backup contact numbers (secondary contact person) to maximize follow up.

[redacted]

b. Given that utilization of other medication was allowed in the study, how can the authors assume that the observed results are related only to LNG-IUS use?

Response: Correct, this study represents the 3 combined data sets of observational prospective trials and 1 randomized clinical trial. None of the 4 protocols that contributed data to this combined data set for this study excluded participants who reported use of certain medications that may affect fertility or other contraceptive methods (withdrawal, inconsistent condom use, etc.) at enrollment as the goal was to capture the "real world" chance of pregnancy if an IUD is placed when people report unprotected sex 6-14 days prior to placement. Participants in the University of Utah COLIEC protocol (N=24) also received oral LNG for emergency contraception. However, this medication does not have any known effect to reduce pregnancy following unprotected intercourse 6-14 days prior to use.

4- Results:
a. Please include a flow chart with the number of patients included from each of the 3 sites?

Response: Added information to the flow chart in Figure 1 (left hand column).

5- Discussion:
a. What is the explanation of slow recruitment for this indication? Is it the emergency need or the presence of other more effective treatments?

Response: Identifying prospective study participants obtaining a LNG-IUS and who report unprotected intercourse 6-14 days prior is challenging in part because of the number of clinics adhering to the CDC SPR guidelines that would not provide this service secondary to the lack of evidence demonstrating pregnancy risk in this situation. This was the motivation to collect these data. After collecting data for 6 years we decided it was prudent to cease data collection and report the results we had obtained to date rather than to further struggle with current guidelines which constrain our attempt to reach our initial enrollment goal.

Reviewer #3:
Thank you for submitting your article on Levonorgestrel-Releasing Intrauterine System Prevents Pregnancy 6 - 14 Days After Unprotected Sex. The time and effort you dedicated to this article is evident in your work. Your submission addresses a critical question regarding emergency contraception. You do an excellent job of discussing pre-existing literature on the use of levonorgestrel IUDs being used as emergency contraception, in addition to showing how your submission meaningfully expands upon that literature. While the study could have been improved with each site using the same protocol, the study provides valuable data as is. Your inclusion and exclusion criteria were appropriate for the study, and the methodology is appropriate when considering the difficulties of conducting a randomized controlled trial for this type of research. This submission will hopefully open the door to a robust RCT that can provide more conclusive evidence for the use of levonorgestrel IUDs as emergency contraception.

Response: Thank you.

STATISTICAL EDITOR COMMENTS:

[redacted]

The Statistical Editor makes the following points that need to be addressed:

line 135: Some women did not have UPT results and those with UPT results were done by 4 weeks. Is there other follow-up data available to corroborate the absence of pregnancy among the 186 women?

Response: All study protocols included 3 and 6 month follow up that also assessed pregnancy status. There were no reports of additional pregnancies that dated back to the cycle of exposure in which the study LNG-IUS was originally placed.

lines 196-197, 202: As the Authors note, this report is based on only 1 reported pregnancy. Therefore, the point estimates are imprecise and it would be prudent to cite the upper bound of the estimates, rather than citing risks < 1% or of 1.4%. It would require a much larger series with more adverse events to have a more precise estimate.

Response: We now only report the chance of pregnancy based on 1 pregnancy among 187 participants. This includes the point estimate and 95% CI. “Only 1 participant reported a pregnancy within four weeks of LNG-IUS placement (0.5%; 95% confidence interval 0.01%-2.9%).” We no long include sub-analyses of smaller groups such as those who reported unprotected intercourse during the fertile window in the main text of the manuscript (in Research Letter format). We have added the table of subanalyses to Appendix 1.

Table 2: Although it is mentioned in the text, should include a footnote stating that all the rates are based on the only pregnancy in the cohort of n= 187.

Response: Original Table 2 (detailing the results of the subanalyses) has been removed from the manuscript and added to Appendix 1 for supplemental digital content. A footnote to this table, now in Appendix 1, has been added as suggested.

EDITOR COMMENTS:

1. Please be sure to update your revision's title page to name the Susan T. Buffett Foundation.

Response: The previously listed “anonymous foundation” has been updated to reflect the change to the Susan Thompson Buffett Foundation. See lines 24-25.

2. The Editors would like you to reformat the submission into a Research Letter. You would be permitted to have SDC, if needed, to assist in condensing the content of the submission.

The guidelines for the Research Letter article type are as follows:

The Research Letter is a concise, focused report of original research (including pre-clinical research, sub-analyses or updates of previously published research, small studies, or pilot studies). Length should not exceed 600 words (approximately 2 1/2 manuscript pages). Figures or tables are limited to two, total.

[redacted]

Research Letters should be organized using the following headings: Introduction, Methods, Results and Discussion.

Response: Thank you for this suggestion. We reformatted our manuscript submission into a Research Letter.

3. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
A. OPT-IN: Yes, please publish my point-by-point response letter.
B. OPT-OUT: No, please do not publish my point-by-point response letter.

Response: OPT-IN. Please feel free to publish our point-by-point response letter.

4. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

Reponse: All authors confirm that the disclosures listed on the manuscript's title page are correct.

5. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

Reponse: Added this transparency declaration statement to the resubmission Cover Letter.

6. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-

[redacted]

data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Reponse: We edited our resubmission manuscript and accompanying documents to ensure use reVITALize definitions.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 2.5 pages (600 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

Reponse: Our revised manuscript is now in Research Letter format and text of the body of the manuscript (Introduction, Methods, Results and Discussion) does not exceed 2.5 pages nor 600 words.

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

Response: The previously listed “anonymous foundation” has been updated to reflect the change to the Susan Thompson Buffett Foundation in the Acknowledgements section of the Title page. See lines 24-25.

9. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

Response: The short title is: Quickstart levonorgestrel intrauterine device. See line 34.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

[redacted]

Response: We reviewed our manuscript to ensure only standard abbreviations and acronyms. All other abbreviations have been spelled out the first time they are used in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

Response: We removed the virgule symbol from the manuscript.

12. ACOG is moving toward discontinuing the use of "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

Response: Thank you for this suggestion. Recognizing that many advanced practice clinicians (nurse practitioners, physician assistants) place IUDs, we prefer the term clinician.

13. In your submission, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

Response: In the revised manuscript, we have focused on ensuring emphasis on effect size and standardized presentation P values and percentages (see Table 1).

14. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

Response: We have reviewed the Table Checklist and with submitted revisions, believe our Tables conform to journal style.

15. Figure 1 may be resubmitted as-is with the revision.

Response: Revisions made to Figure 1 with suggested edits and re-ordered the study protocols to reflect the order they are listed in the text. We also added study protocol name abbreviations to the legend.

[redacted]

16. Each supplemental file in your manuscript should be named an "Appendix," numbered, and ordered in the way they are first cited in the text. Do not order and number supplemental tables, figures, and text separately. References cited in appendixes should be added to a separate References list in the appendixes file.

Response: Each supplemental file has been named as an Appendix (only one, Appendix 1). References in the appendixes have also been added to a separate References list in the appendixes file.

17. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

Response: Thank you. We will ensure a prompt response to this future email.

Please clarify whether any of your participants were seeking IUD placement for the purposes of emergency contraception or whether all of them were women who were seeking IUD placement for general contraceptive or AUB purposes who happened to have had unprotected intercourse in the prior 6-14 days. In addition, in a general population of reproductive aged non contraception women, the per-cycle pregnancy rate with unprotected intercourse is on the order of 15-20%. Why do you think the pregnancy rate was so low in your population?

Response: The vast majority of participants presented seeking IUD placement for general contraceptive or other perceived positive side effects (for example, lighter menstrual bleeding profile) purposes and happened to have had unprotected intercourse in the prior 6-14 days. Based on their pursuit of a new contraceptive method, and for some participants emergency contraception as well, we can assume that participants did not desire pregnancy.

Fecundability (per cycle pregnancy rate with unprotected sexual intercourse) is frequently referenced in a non-contracepting population as 15-20%. We did not formally collect data about some patient characteristics that may affect fecundability - cigarette smoking, male age, history of gonorrhea and chlamydia. These factors may be contributing in some way to the lower pregnancy rate in this study.

One of the goals of this study was to help assess pregnancy risk so that health professionals would have better data to counsel patients who present for IUD placement (for any reason) and also report unprotected sex outside a traditional emergency contraception window (greater than 5 days prior to IUD placement). Thus, in all four protocols that contributed data to this combined dataset study, participants were included if they reported at least one episode of unprotected sex 6-14 days prior to enrollment. While all participants reported unprotected intercourse, some may have used a method that failed or they were uncertain about. For example, condom breakage or slippage or imperfect use

[redacted]

of withdrawal may reduce the overall risk by partial or imperfect use of a method. Not all participants reported unprotected sexual intercourse during their calculated fertile window either (just over 1/3 of participants in this study) and thus would have a lower expected pregnancy rate.

We also expect the levonorgestrel IUD (or any IUD) to have some effect on implantation that may also help explain some of the reduction in pregnancy rates in this study.

If you need additional information or if you have any questions, feel free to contact me at cboraas@gmail.com. Thank you very much for your consideration.

Sincerely,

Christy M. Boraas, MD MPH
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Department of Obstetrics, Gynecology and Women's Health
University of Minnesota Medical School
[redacted]