OBSTETRICS & GYNECOLOGY

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

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Date: May 13, 2022
To: "Mitchell D. Creinin" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-576

RE: Manuscript Number ONG-22-576

Long-Acting Reversible Contraception

Dear Dr. Creinin:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, STATISTICAL EDITOR COMMENTS (if applicable), and EDITORIAL OFFICE COMMENTS below. Your manuscript will be returned to you if a point-by-point response to each of these sections is not included.

The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your submission will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jun 03, 2022, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

I read with great interest the review on long-acting reversible contraception. This is a difficult topic to cover completing and thus 1 must consider what is important to our readers. I thought some sections were strong and others were either unnecessary or not of interest to our readers. Our readers are more interested in complications, bleeding patterns, acceptance/removal reasons, contraindications, etc.
Introduction: The many aspects of this introduction are not necessary and are well known to our readers.
1. Line 30-35 is unnecessary.
2. Line 27-29: Is this an opinion or is there evidence to support this statement?
3. Line 36 to 43 is confusing and I do not know what the authors are trying to convey. This this pertain to the social issues/physical issues of obtaining an IUD?
Specification and Mechanism of actions
1. this section needs to be considerably bolstered or eliminated. A very brief and incomplete description of mechanism is included, and if this is the point of this section a more complete description is needed, especially when it comes to explaining the implant.
Efficacy:
1. Needs to be more complete or eliminated
2. Line 74-75: Not important and well known to our readers
3. Line 87, stating that the implant had no risk of pregnancy secondary to clinical trials is not appropriate, description of the efficacy in real world is needed, such as described in PMID 31601619
4. In 94: The information on obesity as a risk factor for contraceptive efficacy is important and needs to be better summarize. What are the true indications what is the true evidence based data, if not please say so.
5. Ln 112-113: This is a another section extremely important to our readers in needs to be more developed. What is the data on uterine abnormalities and contraindication for IUDs. Is it a certain size, leiomyoma, congenital anomalies,

etc.. If there is no concrete data please explain so.
6. Ln 117-119: What is the data on counseling adolescent (PMID:34686301)? What is the acceptance rate what is the removal rate etc. it is my understanding that this may be a factor in recommending IUDs/implants. If no data please state so.
Placement timing, important concept for our clinicians and to counsel are patients. This section is well described and referenced.
1. Although not mention some studies have shown timing of LARC placement in the menstrual cycle may affect irregular bleeding PMID: 30831104
2. LN 131: "Trial show conflicting evidence", please attempt to summarize for our readership
Placement complications: This is another extremely important section for our readers, and thus needs to be better developed.
1. As far as implant is concern I refer the authors to an excellent recent real world review of over 7500 cases; PMID 30980825. This provides a grade summary of the complications associated with Implanon/Nexplanon.
2. Ln 196-199: Is dated material and not germane to the subject. The authors should mention when implants became radio opaque.
3. A more detailed updated protocol for removal/ nonpalpable should be included. Are serum levels for specific progestin still appropriate? What about the more unusual cases, such as implant located in pulmonary vascular system? Needed or not?
4. On a personal note, I am always confused on how/why/who to recommend a 13.5/19.5 mg IUDs. Was pain that significantly different in the randomized control trials to say that smaller is may be better tolerated? Our readers would like a more developed opinion.
5. Ln 242: Signs and symptoms and recognizing perforation is important to our clinicians. I feel a brief description of what is a high index of suspicion is needed, i.e. pain, loss of strings, vagal response, etc.
6. Abdominal or vaginal ultrasound which is better to confirm placement? Data?
7. Ln 246: Is there any data based on the 2 to force 6 weeks uterine healing?
Removal Challenges another important section for our readers. Overall I thought this section was well done however listed below are some comments
1. Ln 274: Non pop palpable implant removal a brief description on methods of diagnosis and techniques of localization should be included, rather than just a do not attempt.
2. Once again, good/interesting data is in the above mentioned review: PMID: 31601619
3. Ln 311; what about an IUD hook and its efficacy? Have any of these methods been investigated/compared? If no evidence please state.
4. Ln 320: What is the experience on those individuals that have left IUD in place, even if they were misplaced/embedded broken off?
5. Ln 321: Is there is summer to have data on pregnancies where an IUD was left in placed? How should these patients be followed? What perinatal complications are noted?
6. Ln 337: Is their data on menopausal placement? Is it more difficult to be placed in the menopause/expulsion rates?
Levonorgestrel IUD may increase breast cancer risk, PMID: 31990981> is this worth mentioning or not?
IUDs as emergency contraception: This is well known to our clinicians, including the well known recent study on progestin containing IUDs and emergency contraception, of think this is really necessary section.
Bleeding patterns: By far this section would be of most interest to our readers, and needs to be developed more. I think it is well referenced however a more detailed description is required of alternative treatment and their success rate; such as timing of placement in menstrual cycle, the success rate of various methods(NSAIDs, OCPs, progestin receptor antagonist, antibiotics, etc) symptoms listing them is not enough. A brief discussion of the pathophysiology of irregular bleeding caused by these LARCs would also be appropriate.
1. Ln 413-414; this is an important section in should be better developed as to the efficacy(EIN,e endometriosis, adenomyosis, leiomyoma,etc) not just mentioning they are used in the situation. What is the recommendation rate for progestin containing IUDs in individuals with hypercoagulable states? Please include references
Evidence based duration of use. This could be summarized in a paragraph. Much of the information included here is not necessary known to our readers.
Tables I thought were unnecessary. Figures are appendix that include protocols for removal or localization of missing IUD/implants may be helpful.

Reviewer #2:

Thank you for this submission for the Clinical Expert Series. This update on long-acting reversible contraceptives is comprehensive, well-referenced and a timely topic for readers of the journal.
Few minor suggestions from this reviewer:
- Abstract line 11 mentions "newly marketed products" which made me excited thinking I was going to learn about a product that I haven't been using. Not sure what the most reasonable definition of "newly marketed" is but most of us providing LARC have been using these products for a while.

-lines 148-151 seem out of place as the second sentence in the paragraph focused on expulsion
-consider clarifying lines 208-210 which state that if the implant cannot be palpated after placement it should be immediately removed as this seems to contradict lines 274-275
-lines 305-306 recommending continued surveillance. Consider defining what you might mean by this clinically to be more clear on guidance to clinicians
-lines 350-353 on lack of effectiveness of oral EC in women with BMI greater than 35, perhaps authors might expand on this as I think this might be a surprise to many clinicians. And that the referenced study was published in 2011. Should we even offer ulipristal or levonorgestrel to these patients and with the number of patients who call an office for a prescription after unprotected intercourse, have we done enough to properly educate these patients on efficacy?

Reviewer #3:

This Clinical Expert Series submission is very thorough and can accomplish many goals. First, it will bring to the forefront that ABOG has recognized CFP as a new subspecialty of OB/GYN with approved fellowships. It also does well highlighting the new information on not only how to differentiate LARCs, but to consider medical management of side effects (rather than removal) and their extended usage. I would have expanded the section on non-contraceptive benefits and potential use as endometrial protection for menopausal women on estrogen therapy but I realize that may not be in the scope of the manuscript. 127 references seems excessive at face value but may be necessary to cover the wide-ranging topics. The wording is occasionally awkward and I have included a list of suggestions.
ABSTRACT
Line 8 - "reversible contraceptives…are reversible." You do not need the second "reversible."
Line 15 - Awkward phrasing. Should be "how to mitigate side effects."
Line 15 - obstetrician/gynecologist usually not capitalized.
Line 16 - I would insert comment about CFP being recently recognized as a subspecialty by ABOG.
INTRODUCTION
Line 20 - See comment from abstract
Lines 27-29 - Very important point
SPECIFICATIONS
Line 48 - Good to point out that etonogestrel is 3-ketodesogestrel, not desogestrel.
Line 56 -Reference to "Tatum-T" is not necessary. The true "T" shape is explained in the subsequent part of that sentence. Same regarding "Nova-T."
Line 60 - No need to capitalize "Copper."
Line 64 - Copper ions effect sperm motility and viability (negatively or positively?).
Line 70 - Adding the word "may" to "not be the primary contraceptive mechanism of action" could be more neutral. Also, if there is a primary mechanism of action, there must be a secondary mechanism of action.
EFFICACY
Line 86 - What is approximately 1%? Unclear if you are referring to the LARC failures or the "if pregnancy occurs"
Line 90 - When referencing a scientific study, the term "tens of thousands" is too generic.
INITIATION
Lines 112-115 - Awkward wording.
TIMING
Line 130 - "Implant placement immediately after early pregnancy uterine aspiration…" not "Implant placement in early pregnancy…"
Line 171 - having Medicaid "coverage" would be more accurate.
COMPLICATIONS
Line 201 - … but not from the side.
Line 227 - Implies there is evidence that the smaller IUD frames will cause less discomfort even though the rest of the sections states there is not evidence.
REMOVAL
Line 264 - Isn't a scalpel an instrument?
Line 307 - Consider adding a statement to recognize that there are non-US IUDs without tail strings.
Line 316 - the "T-shaped" IUD frames…
Line 324 - Wondering why a particular IUD failed is not relevant to this section and if it was, it requires a discussion.
Line 339 - "frequent" not "frequency"
DURATION
Line 428 - This might be the place to insert the information about the ABOG recognition of this new subspecialty rather than leave for the conclusion. However, it still should be mentioned in the conclusion (in case that is all the reader chooses to see).
TABLES
On one of the tables, a column for tail string color needs to be added.

EDITORIAL OFFICE COMMENTS:

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

4. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "Patients with obesity" instead of "obese patients," "Women with disabilities" instead of "disabled women," "women with HIV" instead of "HIV-positive women," "women who are blind" instead of "blind women."

5. 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.

6. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Clinical Expert Series: 6250 words

7. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

* 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 or indicate whether the meeting was held virtually).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."
* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

8. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

In addition, the abstract length should follow journal guidelines. Please provide a word count.

Clinical Expert Series: 250 words

9. 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.

10. The journal does not use the virgule symbol (/) in sentences with words, except with ratios. 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.

11. ACOG avoids using "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.

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

13. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

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Please make sure your references are numbered in order of appearance in the text.

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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 as a Microsoft Word document. Your revision's cover letter should include a point-by-point response to each of the received comments in this letter. Do not omit your responses to the EDITOR COMMENTS (if applicable), the REVIEWER COMMENTS, the STATISTICAL EDITOR COMMENTS (if applicable), or the EDITORIAL OFFICE COMMENTS.

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

Again, your manuscript will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jun 03, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
John O. Schorge, MD
Deputy Editor, Gynecology

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

UCDAVIS HEALTH
Department of Obstetrics and Gynecology

[redacted]

June 10, 2022

Editor
Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

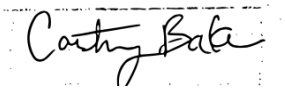
Re: Manuscript# ONG-22-576

To the Editor,

We are pleased to submit a revision of our manuscript to *Obstetrics & Gynecology* for your consideration. Please note that all line numbers are in reference to the clean version of the manuscript, and a version with tracked changes has also been provided.

We appreciate your consideration of this manuscript and look forward to your response.

Sincerely,



Courtney C. Baker, MD, MPH
Clinical Fellow, Complex Family Planning

Mitchell D. Creinin, MD
Professor and Director of Family Planning
Director, Complex Family Planning Fellowship

REVIEWER COMMENTS:

Reviewer #1:

1. Introduction: The many aspects of this introduction are not necessary and are well known to our readers.

RESPONSE: We appreciate the reviewer's comment but given that this is a broad review aimed at a general OB-GYN audience, we feel it is important to briefly state the definition of LARC, U.S. LARC products, the epidemiology of unintended pregnancy and LARC, nomenclature to be used in the review, and the statement on patient autonomy.

2. Line 30-35 is unnecessary.

RESPONSE: We respectfully disagree. Nomenclature for LARC varies, and while we endorse the Society of Family Planning nomenclature discussed here compared to others, the most important thing we want to do is set consistent and clear terminology for the reader for the remainder of the review.

3. Line 27-29: Is this an opinion or is there evidence to support this statement?

RESPONSE: We have added two references to support this statement based on outcomes from the CHOICE project in St. Louis and the Colorado Family Planning Initiative.

Lines 26-28
Old text: While multiple factors contribute to unintended pregnancy rates, there is evidence to suggest that increasing LARC use may be contributing to the decline.
New text: While multiple factors contribute to unintended pregnancy rates, increasing LARC use correlates with declining rates and are likely a contributing factor.[4,5]

4. Line 36 to 43 is confusing and I do not know what the authors are trying to convey. This this pertain to the social issues/physical issues of obtaining an IUD?

RESPONSE: We included this statement to address the "LARC first" mentality that was pervasive in the past. As this is a review about LARC, we want to express all the benefits of it, but we want to be clear that the benefits don't make it "the best". Furthermore, LARCs require a clinician for initiation and discontinuation and are thus their provision is uniquely susceptible to disparities in care. We have added a statement to improve clarity but have otherwise retained this paragraph related to disparities and reproductive justice as we feel it is important to frame the remainder of the review.

Lines 38-40
Old text: As a community reflecting on our efforts to provide tools for reproductive health goals, it is vital that we approach contraception within the framework of our patient's preferences and goals.
New text: As a community reflecting on our efforts to provide tools for reproductive health goals,

it is vital that we approach contraception, especially methods that require a clinician for initiation and discontinuation, within the framework of our patient's preferences and goals.

5. Specification and Mechanism of actions: this section needs to be considerably bolstered or eliminated. A very brief and incomplete description of mechanism is included, and if this is the point of this section a more complete description is needed, especially when it comes to explaining the implant.

RESPONSE: As this is a general review, we feel a brief understanding of mechanism of action is clinically important, but that further details are not useful for everyday practice. We agree with the reviewer that the section on the implant could be bolstered somewhat, and we have added to it as below.

Lines 49-53
Old text: When placed subdermally, etonogestrel diffuses from the implant into systemic circulation at concentrations which prevent ovulation.[6]
New text: When placed subdermally, etonogestrel diffuses from the implant into systemic circulation at concentrations which inhibit ovulation by preventing the mid-cycle luteinizing hormone surge.[8] *Ovarian activity is not fully suppressed, as evidenced by near normal levels of follicle stimulating hormone and estradiol with continued use.*

6. Efficacy: Needs to be more complete or eliminated

RESPONSE: As a LARC overview, we feel it would be incomplete if efficacy was not addressed. We have highlighted a few points we feel are especially important and less well known – efficacy over duration of use, ectopic pregnancy rates, and efficacy with obesity. We appreciate the additional comments below regarding this section, and we have incorporated many of the reviewer's comments.

7. Line 74-75: Not important and well known to our readers

RESPONSE: We agree that the terms "perfect-use" and "typical-use" are self-explanatory, even if people are not familiar with where those numbers come from. We have removed the lines felt to be extraneous by the reviewer.

Lines 75-76
Old text: Contraceptive efficacy is often reported in "perfect-use" and "typical-use" failure rates in the first year of use. "Perfect-use" rates are calculated from carefully controlled clinical trials while "typical use" rates are often estimated from population data collected by the National Survey of Family Growth. Given that LARCs are not user-dependent after placement, "perfect-use" and "typical-use" failure rates are similar.
New text: Given that LARCs are not user-dependent after placement, "perfect-use" and "typical-use" failure rates are similar.

8. Line 87, stating that the implant had no risk of pregnancy secondary to clinical trials is not appropriate, description of the efficacy in real world is needed, such as described in PMID

31601619

RESPONSE: We appreciate the reviewer bringing this article to our attention. In this section, we are only trying to discuss ectopic pregnancy. Our intent was to describe ectopic rates in the implant and IUD in clinical trials and then in population studies. The line in reference is merely meant to say that no ectopic pregnancies occurred in clinical trials, and thus there is no data. We have edited the sentence to improve clarity.

Lines 83-85
Old text: During 11 international clinical trials, no pregnancies occurred in people with the etonogestrel implant in place.[22]
New text: During 11 international clinical trials, no pregnancies occurred in people with the etonogestrel implant in place, and thus no rate of ectopic pregnancy could be determined.[24]

9. In 94: The information on obesity as a risk factor for contraceptive efficacy is important and needs to be better summarize. What are the true indications what is the true evidence based data, if not please say so.

RESPONSE: We agree with the reviewer that this is an important topic, and more information could be provided. We have added a reference from secondary analyses of the CHOICE study to support our discussion of contraceptive failure and BMI. We have elaborated further on the numbers in those studies as below. We also discuss this more in the section on extended duration of implant use.

Lines 102-109
Old text: While no studies have primarily assessed implant efficacy in overweight and obese users, secondary analyses from a population-based study provide evidence that there is no clinically significant correlation between contraceptive failure and BMI.[32] *Conversely, given that IUDs have a local mechanism of action, it follows that their efficacy should not change in relation to body weight.*
New text: No studies have primarily assessed implant efficacy in overweight and obese users; although, secondary analyses from a population-based study of 1,168 implant users of which 28% were overweight and 30% were obese provide evidence that there is no clinically significant correlation between contraceptive failure and BMI.[34] *Conversely, given that IUDs have a local mechanism of action, it follows that their efficacy should not change in relation to body weight; this is also supported by findings from 4,200 users of the copper or levonorgestrel IUD of which 27% were overweight and 35% were obese in the aforementioned cohort study.*[34]

10. Ln 112-113: This is a another section extremely important to our readers in needs to be more developed. What is the data on uterine abnormalities and contraindication for IUDs. Is it a certain size, leiomyoma, congenital anomalies, etc.. If there is no concrete data please explain so.

RESPONSE: We agree with the reviewer that further guidance can be provided here. We were unable to find strong supporting data, but we have added some statements in regard to the evidence we found.

Lines 113-127
Old text: Contraindications to IUD placement include uterine cavity anomalies, untreated cervical cancer, and active pelvic infection.[33]
New text: Uterine cavity anomalies, untreated cervical cancer, and active pelvic infection are contraindications to IUD placement.[35] *Uterine cavity anomalies, including congenital anomalies (e.g., septate and bicornuate uterus) and other structural anomalies (e.g., cavity-distorting leiomyoma, uterine synechiae), may increase the risk of complications such as expulsion and decrease contraceptive efficacy. A review of the literature assessing the safety and efficacy of IUD use in patients with Mullerian anomalies or uterine synechiae found 19 case reports or case series with reported complications of expulsion, pregnancy, bleeding, perforation, and pain; some cases did not report complications.*[36] *Regarding leiomyoma, a systematic review evaluated 8 studies that reported on hormonal IUD expulsion rates among women with uterine fibroids and concluded that expulsion rates may be higher in this group; although, no comparative studies achieved a statistically significant difference in expulsion rates between women with fibroids and those who did not have them.*[37] *Given the limited data, IUDs cannot be recommended for patients with uterine cavity distortion seeking contraception. IUDs may be considered for those seeking only non-contraceptive IUD benefits who are willing to accept the possible increased risk of expulsion or other complications.*

11. Ln 117-119: What is the data on counseling adolescent (PMID:34686301)? What is the acceptance rate what is the removal rate etc. it is my understanding that this may be a factor in recommending IUDs/implants. If no data please state so.

RESPONSE: The references cited support that adolescents and young adults accept LARC (Mestad 2011) and that it is safe and efficacious (Jataloui 2017). We appreciate the reviewer's reference regarding counseling on condom use in this population, and we feel this is standard counseling in practice for all patients at risk for STIs regardless of age. Overall, we feel the counseling for teens and young adults is not significantly different than the general population, and we edited the line to remove the notion that teens and young adults must be counseled differently.

Lines 133-134
Old text: Implants and IUDs are appropriate and recommended if desired by appropriately counseled adolescents and young people without a history of prior pelvic examination or pregnancy.[34,35]
New text: Implants and IUDs are appropriate and recommended if desired by adolescents and young people without a history of prior pelvic examination or pregnancy.[38,40]

12. Placement timing, important concept for our clinicians and to counsel are patients. This section is well described and referenced. Although not mention some studies have shown timing of LARC placement in the menstrual cycle may affect irregular bleeding PMID: 30831104

RESPONSE: We appreciate the reviewer sharing this reference. Given that it is regarding the LNG 13.5 mg IUD only and showed only short-term (30-day benefit), we would not recommend incorporating this into practice as it may impose further barriers on quick start contraception

initiation.

13. LN 131: "Trial show conflicting evidence", please attempt to summarize for our readership

RESPONSE: The data, as we stated, is conflicting and difficult to summarize. We have tried to clarify further and have revised the first sentence (see reviewer 2 comment 35).

Lines 145-149
Old text: Implant placement in early pregnancy immediately after uterine aspiration or at the time of medication abortion is safe, although trials show conflicting evidence of the effect on repeat pregnancy rates.[38-41] *Placing an implant at the time of initiating medication abortion with mifepristone does not change treatment outcome and should be considered based on patient preference and plan for follow-up.*[40]
New text: Implant placement at the time of medication abortion or immediately after procedural abortion is safe.[43-46] *Placing an implant at the time of initiating medication abortion with mifepristone does not change treatment outcome and should be considered based on patient preference and plan for follow-up.*[45] Two population studies reported decreased repeat pregnancy and abortion in the 2 years following immediate post-abortion implant placement.[44,46]

14. Placement complications: This is another extremely important section for our readers, and thus needs to be better developed.

RESPONSE: We agree that this is an important topic. We have incorporated some edits from comments from all reviewers as discussed under the respective comments. Please see the response to your comment 15 and 16, reviewer 2 comment 35, and reviewer 3 comment 56.

15. As far as implant is concern I refer the authors to an excellent recent real world review of over 7500 cases; PMID 30980825. This provides a grade summary of the complications associated with Implanon/Nexplanon.

RESPONSE: We appreciate the reviewer's reference, and we have incorporated it in two places as below.

Lines 130-132
Old text: Certain enzyme-inducing anticonvulsants may decrease the efficacy of an etonogestrel implant
New text: Certain enzyme-inducing anticonvulsants may decrease the efficacy of an etonogestrel implant, and drug interactions were found to account for 4% of method failures in a study of 234 reported pregnancies during implant use.[38]

Lines 215-221
Old text: Though most implants are easily removed, 14 per 1000 removals are reported by providers as difficult and 1 per 1000 implants are nonpalpable.[64,65] The etonogestrel 68 mg implant is meant to be placed in the subcutaneous tissues of the upper arm over the triceps 8 to 10 centimeters proximal to the medial epicondyle.
New text: Though most implants are easily removed, 14 per 1000 removals are reported by

providers as difficult and 1 per 1000 implants are nonpalpable.[68,69] The importance of post-placement implant palpation by the clinician and patient is highlighted by the fact that "missing implants" attributed to non-placement accounted for 26% of 463 pregnancies in implant users in a population study.[38] The etonogestrel 68 mg implant is meant to be placed in the subcutaneous tissues of the upper arm over the triceps 8 to 10 centimeters proximal to the medial epicondyle.

16. Ln 196-199: Is dated material and not germane to the subject. The authors should mention when implants became radio opaque.

RESPONSE: We agree with the reviewer that we should add a comment about when implant became radiopaque. We choose to keep the material about the inserter, as we feel limitations of the current inserter may contribute to deep implant placement.

Lines 210-211
Old text: Subsequently the one-handed inserter was introduced in 2010.
New text: Subsequently in 2010, the one-handed inserter was introduced, and barium-sulfate was added to the implant to make it radiopaque.[67]

17. Placement complications: A more detailed updated protocol for removal/ nonpalpable should be included. Are serum levels for specific progestin still appropriate? What about the more unusual cases, such as implant located in pulmonary vascular system? Needed or not?

RESPONSE: We feel that removal of nonpalpable implants should be evaluated and performed by clinicians with expertise in this area. As such, we do not feel it is appropriate for a review of LARC for the general OB-GYN. We feel the most important points regarding specialist consultation and risk factors for deep placement have been included.

18. Placement complications: On a personal note, I am always confused on how/why/who to recommend a 13.5/19.5 mg IUDs. Was pain that significantly different in the randomized control trials to say that smaller is may be better tolerated? Our readers would like a more developed opinion.

RESPONSE: The opening sentence to this paragraph has been changed per the recommendation of another reviewer. We hope it now conveys a more direct opinion. Please see reviewer 3, comment 57.

19. Ln 242: Signs and symptoms and recognizing perforation is important to our clinicians. I feel a brief description of what is a high index of suspicion is needed, i.e. pain, loss of strings, vagal response, etc.

RESPONSE: We agree with the reviewer and have added a sentence regarding possible signs of perforation.

Lines 257-262
Old text: As patients may have minimal to no symptoms at time of perforation, a high index of suspicion must be maintained as the risks of laparoscopy to remove an intra-abdominal IUD far

outweigh the risks of unnecessary removal and replacement. If perforation is suspected at time of placement, the IUD position should be confirmed by ultrasound.
New text: As patients may have minimal to no symptoms at time of perforation, a high index of suspicion must be maintained as the risks of laparoscopy to remove an intra-abdominal IUD far outweigh the risks of unnecessary removal and replacement. Signs of perforation may include a loss of resistance or greater than anticipated depth during sounding or IUD placement, unusual pain, or brisk bleeding. If perforation is suspected at time of placement, the IUD position should be confirmed by ultrasound.

20. Placement complications: Abdominal or vaginal ultrasound which is better to confirm placement? Data?

RESPONSE: To our knowledge there is no data regarding this topic. Practically, we feel a clinician should use whichever ultrasound modality is available and provides an adequate image to ensure intrauterine placement.

21. Ln 246: Is there any data based on the 2 to force 6 weeks uterine healing?

RESPONSE: We found limited data that supported rapid healing of the uterus as evidenced by cases where laparoscopy was performed shortly after perforation, summarized in the Rowlands 2019 source now added to the reference list.

Lines 263-266
Old text: Repeat placement should be delayed 2 to 6 weeks for uterine healing, and asymptomatic stable patients can often be discharged home with return precautions.
New text: Uterine healing after perforation can be rapid as evidenced by cases of laparoscopy shortly following identified perforations;[79] repeat placement should be delayed 2 to 6 weeks, and asymptomatic stable patients can often be discharged home with return precautions.

22. Ln 274: Non pop palpable implant removal a brief description on methods of diagnosis and techniques of localization should be included, rather than just a do not attempt.

RESPONSE: Please see response to your comment 17.

23. Placement complications: Once again, good/interesting data is in the above mentioned review: PMID: 31601619

RESPONSE: Please see response to your comment 15.

24. Ln 311; what about an IUD hook and its efficacy? Have any of these methods been investigated/compared? If no evidence please state.

RESPONSE: We agree that there should be mention of IUD hooks and plastic thread removers, although this is not our recommended method due to decreased success rates. We have added a sentence and 2 sources (Swenson 2014, Bounds 1992) to address this.

Lines 334-341
Old text: A paracervical block can be offered and concurrent abdominal ultrasound guidance is helpful. Long, narrow instruments with jaws that open only at the distal end, such as alligator forceps or hysterographic grasping forceps, can be utilized; if not successful, a manual vacuum aspiration device can also be used to attempt removal through suction.[85-89]
New text: A paracervical block can be offered and concurrent abdominal ultrasound guidance is helpful. An IUD thread retriever can be used and may work up to 50% of the time.[90] *While there are case reports of successful T-shaped IUD removal with an IUD hook, this instrument is designed and intended for removal of ring IUDs.*[91] *Long, narrow instruments with jaws that open only at the distal end, such as alligator forceps or hysterographic grasping forceps, can be utilized with higher rates of successful removal (83-98%); if not successful, a manual vacuum aspiration device can also be used to attempt removal through suction.*[92-96]

25. Ln 320: What is the experience on those individuals that have left IUD in place, even if they were misplaced/embedded broken off?

RESPONSE: To our knowledge, there is not published literature of this topic. We have provided our best recommendation for this clinical expert series.

26. Ln 321: Is there is summer to have data on pregnancies where an IUD was left in placed? How should these patients be followed? What perinatal complications are noted?

RESPONSE: We feel the most important point is that IUD removal should be attempted when possible. We have added information on the specific obstetric risks. However, we do not feel a full discussion of how to follow pregnant patients with an IUD in place is within the scope of this review.

Lines 355-367
Old text: If the patient wishes to continue the pregnancy, the IUD should always be removed after appropriate counseling if strings are visible or ultrasound confirms its presence within the cervix. If no strings are present and ultrasound confirms an intrauterine IUD below the level of the pregnancy, ultrasound-guided removal with forceps or hysteroscopy can be attempted after thorough counseling of the risks and benefits of attempted removal versus the increased obstetric risks of IUD retention.[92,93] *Removal should not be attempted if the IUD is superior to the gestational sac.*
New text: If the patient wishes to continue the pregnancy, the IUD should always be removed after appropriate counseling if strings are visible or ultrasound confirms its presence within the cervix. Pregnant patients with retained IUDs are at greater risk of spontaneous abortion, septic abortion, preterm delivery, and chorioamnionitis.[99] *In a comparative cohort study of 144 pregnancies with an IUD in situ, the combined risk of adverse pregnancy outcomes was significantly higher in patients who retained their IUD versus those who had it removed during the first trimester [relative risk (RR)=2.0, 95% confidence interval (CI) 1.3-3.3], especially in patients who retained an IUD in a low-lying position (RR=3.9, 95% CI 1.8-8.6); removal was only performed on patients with visible IUD strings.*[100] *If no strings are present and ultrasound confirms an intrauterine IUD below the level of the pregnancy, ultrasound-guided removal with forceps or hysteroscopy can be attempted after thorough counseling of the risks and benefits of*

attempted removal versus the increased obstetric risks of IUD retention.[101]

27. Ln 337: Is their data on menopausal placement? Is it more difficult to be placed in the menopause/expulsion rates? Levonorgestrel IUD may increase breast cancer risk, PMID: 31990981> is this worth mentioning or not?

RESPONSE: To our knowledge, there is no specific data comparing IUD insertion in pre-menopausal versus menopausal women. As none of the IUDs are currently indicated or widely used for this indication, the information is beyond the scope of this review. Regarding breast cancer risk, we feel the effects of progestins on breast cancer risk are known, but as there are no recommendations limiting hormonal IUD use in patients at-risk for breast cancer at this time, we do not feel this is worth including. We appreciate the reference, and we did note that the odds ratio was higher (1.15 versus 1.5) for women over 50, but we feel this is a different population from a contracepting population.

28. IUDs as emergency contraception: This is well known to our clinicians, including the well known recent study on progestin containing IUDs and emergency contraception, of think this is really necessary section.

RESPONSE: We feel this is not well known, and we also feel we have highlighted important points about the study's implication on same day start and back-up contraception. In addition, we feel it is important to remind clinicians to consider IUD for emergency contraception in obese patients.

29. Bleeding patterns: By far this section would be of most interest to our readers, and needs to be developed more. I think it is well referenced however a more detailed description is required of alternative treatment and their success rate; such as timing of placement in menstrual cycle, the success rate of various methods(NSAIDs, OCPs, progestin receptor antagonist, antibiotics, etc) symptoms listing them is not enough. A brief discussion of the pathophysiology of irregular bleeding caused by these LARCs would also be appropriate.

RESPONSE: We agree with the reviewer that this is an important section. We agree that a brief description of the pathophysiology of irregular implant bleeding is helpful and is added below. Regarding placement timing in the menstrual cycle, please see our response to your comment 12. Regarding success rates of methods for improving implant bleeding, we listed those that have been studied but highlighted COCs given that they are the only method consistently shown to show significant improvement. Given the breadth of this topic, we chose not to discuss the other methods further, although we provided the appropriate sources if readers would like to investigate further.

Lines 404-408
Old text: The etonogestrel implant is widely known for its typically light yet unpredictable bleeding pattern, and thus it can be difficult to counsel patients on what to expect following placement. While only 13% of subjects discontinued implant use due to bleeding complaints in U.S. phase 3 clinical trials…
New text: The etonogestrel implant is widely known for its typically light yet unpredictable

bleeding pattern, and thus it can be difficult to counsel patients on what to expect following placement. Continuous systemic progestin exposure can result in bleeding due to the atrophic endometrium with dilated, thin-walled vessels.[114] While only 13% of subjects discontinued implant use due to bleeding complaints in U.S. phase 3 clinical trials…

30. Ln 413-414; this is an important section in should be better developed as to the efficacy(EIN,e endometriosis, adenomyosis, leiomyoma,etc) not just mentioning they are used in the situation. What is the recommendation rate for progestin containing IUDs in individuals with hypercoagulable states? Please include references

RESPONSE: Please see the response to reviewer 2, comment 38.

31. Evidence based duration of use. This could be summarized in a paragraph. Much of the information included here is not necessary known to our readers.

RESPONSE: We feel that readers may know about extended duration but may not know the evidence as well as some of the nuances we have addressed, including the effects of obesity. When using a product off-label, a clinician should be well-informed of the evidence. We are hoping this section and the sources will empower clinicians to understand the evidence and make shared decisions with their patients.

32. Tables I thought were unnecessary. Figures are appendix that include protocols for removal or localization of missing IUD/implants may be helpful.

RESPONSE: Please see our response to your comment 17.

Reviewer #2:

33. Abstract line 11 mentions "newly marketed products" which made me excited thinking I was going to learn about a product that I haven't been using. Not sure what the most reasonable definition of "newly marketed" is but most of us providing LARC have been using these products for a while.

RESPONSE: Thank you for pointing this out. As the most recently FDA-approved product we discuss is Liletta in 2015, we agree that this is not necessarily “recent” and removed it.

Lines 10-11:
Old text: With increasing prevalence and duration of use, and with the addition of newly marketed products, our understanding of efficacy, risks, and benefits has evolved.
New text: With increasing prevalence and duration of use, our understanding of efficacy, risks, and benefits has evolved.

34. lines 148-151 seem out of place as the second sentence in the paragraph focused on expulsion

RESPONSE: Thank you for this comment. Upon further review of the cited source, 5 pregnancies occurred in people who chose post-placental IUD, and only 1 was from a recognized (not unrecognized as previously stated) expulsion. Furthermore, 15 of 17 expulsions were recognized and 15 of 17 people with expulsion (when recognized) initiated another highly effective method. Therefore, I don't think this supports our original point and should be removed entirely.

Lines 162-163
Old text: Expulsion is one significant disadvantage of immediate post-placental IUD placement. One study of 248 people receiving post-placental IUD or prior-to-discharge implant placement demonstrated higher pregnancy rates at 12 months in those who chose IUDs; most pregnancies occurred when the IUD was discontinued without initiation of alternative contraception and one occurred after unrecognized expulsion.[46] According to a systematic review and meta-analysis…
New text: Expulsion is one significant disadvantage of immediate post-placental IUD placement. According to a systematic review and meta-analysis…

35. consider clarifying lines 208-210 which state that if the implant cannot be palpated after placement it should be immediately removed as this seems to contradict lines 274-275

RESPONSE: We agree with the reviewer. We have chosen to clarify the context in both locations as below.

Lines 225-226
Old text: If the implant cannot be easily palpated following placement, it should be immediately removed and replaced through a different incision.
New text: If the implant cannot be easily palpated immediately following placement, it should be removed at that time and replaced through a different incision.

36. lines 305-306 recommending continued surveillance. Consider defining what you might mean by this clinically to be clearer on guidance to clinicians

RESPONSE: We agree with the reviewer. We have clarified that continued surveillance is for the development of related symptoms as below.

Lines 324-325
Old text: While continued surveillance in these circumstances may be warranted, removal is not necessarily indicated.
New text: While continued surveillance for the development of corresponding symptoms may be warranted in these circumstances, removal is not necessarily indicated.

37. lines 350-353 on lack of effectiveness of oral EC in women with BMI greater than 35, perhaps authors might expand on this as I think this might be a surprise to many clinicians. And that the referenced study was published in 2011. Should we even offer ulipristal or levonorgestrel to these patients and with the number of patients who call an office for a prescription after unprotected intercourse, have we done enough to properly educate these patients on efficacy?

RESPONSE: While we agree with the reviewer that the limitations of EC use in obese individuals is an important topic for the general OB-GYN, as this is a review on LARC a discussion of the limitations of oral EC is beyond the scope of this review.

Reviewer #3:

38. I would have expanded the section on non-contraceptive benefits and potential use as endometrial protection for menopausal women on estrogen therapy but I realize that may not be in the scope of the manuscript.

RESPONSE: We agree that non-contraceptive benefits are an evolving and important use of LARC. As we were asked to write a Clinical Expert Series review on "Long-Acting Reversible *Contraception*" and have a limited word count for such a broad topic, we have chosen to center the manuscript on contraceptive use of LARC while limiting our discussion of non-contraceptive uses. To reflect this choice, I have removed it from the abstract.

Lines 11-14
Old text: In addition to a brief discussion on nomenclature and LARC use within a framework of bodily autonomy and reproductive justice, this review covers clinical challenges with placement and removal, non-contraceptive benefits, evidence-based duration of use, and how to mitigate side effects.
New text: In addition to a brief discussion on nomenclature and LARC use within a framework of bodily autonomy and reproductive justice, this review covers clinical challenges with placement and removal, evidence-based duration of use, and how to mitigate side effects.

39. 127 references seems excessive at face value but may be necessary to cover the wide-ranging topics.

RESPONSE: We feel we have included references to support all the findings in such a broad topic, and we hope the sources can be used by others to explore topics further for which we had limited space to discuss.

40. Line 8 - "reversible contraceptives...are reversible." You do not need the second "reversible."

RESPONSE: We agree with the reviewer. We have removed the second instance of "reversible".

Lines 8-9
Old text: Long-acting reversible contraceptive (LARC) methods, are effective and reversible options for pregnancy prevention.
New text: Long-acting reversible contraceptive (LARC) methods are effective options for pregnancy prevention.

41. Line 15 - Awkward phrasing. Should be "how to mitigate side effects."

RESPONSE: We agree with the reviewer and have made the suggested edit.

Lines 13-14
Old text: this review covers clinical challenges with placement and removal, non-contraceptive benefits, evidence-based duration of use, and side effects and how to mitigate them.
New text: this review covers clinical challenges with placement and removal, non-contraceptive benefits, evidence-based duration of use, and how to mitigate side effects.

42. Line 15 - obstetrician/gynecologist usually not capitalized.

RESPONSE: We agree with the reviewer and have made the suggested edit here and in the conclusion.

Lines 14-15
Old text: While all Obstetrician-Gynecologists as well as primary care clinicians can safely provide LARCs,
New text: While all obstetrician-gynecologists as well as primary care clinicians can safely provide LARCs,

Lines 501-502
Old text: While all Obstetrician-Gynecologists as well as primary care clinicians can safely provide LARCs,
New text: While all obstetrician-gynecologists as well as primary care clinicians can safely provide LARCs,

43. Line 16 - I would insert comment about CFP being recently recognized as a subspecialty by ABOG.

RESPONSE: We agree with the reviewer that the recognition of CFP by ABOG is worth mentioning, and we do so in the conclusion. However, we do not feel accreditation and board-certification is necessary to be an expert for the OB-GYN community and have chosen to limit our reference to ABOG to the conclusion alone. We did alter the sentence in the conclusion to broaden the recognition from ACGME fellowship to ABOG subspeciality.

Lines 499-501
Old text: The subspeciality of Complex Family Planning (CFP) has continued to grow as it takes a step forward as a newly accredited fellowship with the Accreditation Council for Graduate Medical Education.
New text: Complex Family Planning has continued to grow as it takes a step forward as a subspeciality newly recognized by the American Board of Obstetrics and Gynecology.

44. Line 20 - See comment from abstract

RESPONSE: We agree with the reviewer and have made the suggested edit.

Lines 19-20
Old text: Long-acting reversible contraceptive (LARC) methods are effective and reversible options that can be used by most patients seeking to prevent pregnancy.
New text: Long-acting reversible contraceptive (LARC) methods are effective options that can be used by most patients seeking to prevent pregnancy.

45. Lines 27-29 - Very important point

RESPONSE: Thank you.

46. Line 48 - Good to point out that etonogestrel is 3-ketodesogestrel, not desogestrel.

RESPONSE: Thank you.

47. Line 56 -Reference to "Tatum-T" is not necessary. The true "T" shape is explained in the subsequent part of that sentence. Same regarding "Nova-T."

RESPONSE: We respectfully disagree with the reviewer. We feel utilizing the Tatum and Nova terminology is important when describing groups of IUD frame shapes, and we think it might be a new and useful term for some general OB-GYNs.

48. Line 60 - No need to capitalize "Copper."

RESPONSE: We have made the suggested edit.

Line 62-63
Old text: The Copper 380 mm^2 IUD is 32-mm-wide by 36-mm-long with 380 mm^2 of exposed copper surface area.
New text: The copper 380 mm^2 IUD is 32-mm-wide by 36-mm-long with 380 mm^2 of exposed copper surface area.

49. Line 64 - Copper ions effect sperm motility and viability (negatively or positively?).

RESPONSE: We have added the word “adversely” to clarify the negative effect.

Line 66
Old text: The copper ions effect sperm motility and viability.[7]
New text: The copper ions adversely affect sperm motility and viability.[9]

50. Line 70 - Adding the word "may" to "not be the primary contraceptive mechanism of action" could be more neutral. Also, if there is a primary mechanism of action, there must be a secondary mechanism of action.

RESPONSE: We agree that “primary” is misleading. Cervical mucous changes are the first progestin-mediated change encountered by sperm and thus is the mechanism for pregnancy-prevention. We have edited the phrasing as below to clarify our meaning.

Lines 70-72
Old text: Although levonorgestrel IUDs cause foreign body reactions and progestin-mediated endometrial changes, the latter being the mechanism through which they decrease bleeding frequency, this is not the primary contraceptive mechanism of action.[10] *Pregnancy is prevented by thickening of cervical mucous as a barrier to sperm penetration.*[11]
New text: Although levonorgestrel IUDs cause foreign body reactions and progestin-mediated endometrial changes, the latter being the mechanism through which they decrease bleeding frequency, pregnancy is prevented by thickening of cervical mucous as a barrier to sperm penetration.[12,13]

51. Line 86 - What is approximately 1%? Unclear if you are referring to the LARC failures or the "if pregnancy occurs"

RESPONSE: We agree with the reviewer. We have changed the format of the sentence to ensure that the 1% is clearly ectopic pregnancies in the general population.

Lines 80-83
Old text: Compared to non-contraceptive users, the risk of ectopic pregnancy in LARC users is much lower because the likelihood of conception is very low; however, if pregnancy occurs, the likelihood of an extrauterine gestation is higher than the rate in the general population, which is approximately 1%.[20,21]
New text: Compared to non-contraceptive users, the risk of ectopic pregnancy in LARC users is much lower because the likelihood of conception is very low; however, if pregnancy occurs, the likelihood of an extrauterine gestation is higher than the approximately 1% rate in the general population.[22,23]

52. Line 90 - When referencing a scientific study, the term "tens of thousands" is too generic.

RESPONSE: We have provided the approximate study population numbers below.

Lines 87-89
Old text: In population-based studies including tens of thousands of participants, ectopic pregnancy rates were 20% in implant users, 15% in copper IUD users, and 27% in levonorgestrel 52 mg IUD users.[26,27]
New text: In population-based studies, ectopic pregnancy rates were 20% in a systematic review including 240,000 implant users, 15% in a cohort of about 17,000 copper IUD users, and 27% in a cohort of about 41,000 levonorgestrel 52 mg IUD users.[28,29]

53. Lines 112-115 - Awkward wording.

RESPONSE: We have tried to rearrange these sentences to improve the flow and clarity as below.

Lines 112-114
Old text: LARCs can generally be initiated at any time it is reasonably certain the person is not

pregnant. There are few other contraindications to LARC use. Contraindications to IUD placement include uterine cavity anomalies, untreated cervical cancer, and active pelvic infection.[33]
New text: If pregnancy has been reasonably excluded, LARCs can be initiated in most people. Uterine cavity anomalies, untreated cervical cancer, and active pelvic infection are contraindications to IUD placement.[35]

54. Line 130 - "Implant placement immediately after early pregnancy uterine aspiration..." not "Implant placement in early pregnancy..."

RESPONSE: We agree with the reviewer and have revised the statement as below.

Lines 145-146
Old text: Implant placement in early pregnancy immediately after uterine aspiration or at the time of medication abortion is safe
New text: Implant placement at the time of medication abortion or immediately after early pregnancy uterine aspiration is safe

55. Line 171 - having Medicaid "coverage" would be more accurate.

RESPONSE: We agree with the reviewer and have made the suggested edit.

Lines 181-182
Old text: In both clinical trials and population-based studies, postpartum follow-up rates are higher in privately-insured patients and lower in those who have Medicaid.
New text: In both clinical trials and population-based studies, postpartum follow-up rates are higher in privately insured patients and lower in those who have Medicaid coverage.

56. Line 201 - ... but not from the side.

RESPONSE: We feel the inability to see the inserter from above may contribute to deep placement. That is why we have mentioned it here. We agree with the reviewer that you can still see the inserter needle from the side, and thus we have edited the text below.

Lines 211-214
Old text: It features a depth guide designed to minimize risk of improper placement, although, with the consequence of blocking the clinicians view of the inserter needle from above.
New text: This inserter features a depth guide designed to minimize risk of improper placement, although, with the consequence of blocking the clinicians view of the inserter needle from above, requiring clinicians to attempt to view the inserter needle from the side.

57. Line 227 - Implies there is evidence that the smaller IUD frames will cause less discomfort even though the rest of the sections states there is not evidence.

RESPONSE: We agree that using “benefits” is misleading given the subsequent discussion. We have changed the introductory sentence to better reflect our conclusion.

Lines 243-244
Old text: When discussing pain with IUD placement, it is important to contextualize the benefits of smaller IUD frames and inserters within their disadvantages.
New text: Placement of IUDs with smaller frames and inserters may be presumed easier or less painful, but the available data does not favor a significant clinical difference.

58. Line 264 - Isn't a scalpel an instrument?

RESPONSE: We agree with the reviewer. We have added “following incision of the skin” to clarify that we mean use of a clamp or pop-out.

Lines 283-284
Old text: Implant removal can be accomplished with or without instruments and is best performed with techniques for which the operator feels most comfortable.
New text: Following incision of the skin, implant removal can be accomplished with or without instruments and is best performed with techniques for which the operator feels most comfortable.

59. Line 307 - Consider adding a statement to recognize that there are non-US IUDs without tail strings.

RESPONSE: We agree with the reviewer that this is worthwhile to mention as IUDs with no strings, not just missing strings, also can remain in place.

Lines 331-333
Old text: A properly positioned IUD with missing strings can remain in situ until removal is desired or device expiration is reached.
New text: Some IUDs available outside the United States do not have strings. A properly positioned IUD with missing or no strings can remain in situ until removal is desired or device expiration is reached.

60. Line 316 - the "T-shaped" IUD frames...

RESPONSE: See response to your comment 47.

61. Line 324 - Wondering why a particular IUD failed is not relevant to this section and if it was, it requires a discussion.

RESPONSE: We are considering the context of a patient with an IUD in place who is found to have an ectopic pregnancy visualized on imaging or laparoscopy and is managed with medication or surgery. We want the reader to know why we recommend IUD removal in this case. This seems different to us than a patient with a PUL and therefore a possible IUP. We would like to give the reader a reason for why we would still remove the IUD. In our practice, we do this because we are concerned about why that particular IUD failed, such as a manufacturing error. We have added that clarification.

Lines 350-352
Old text: pregnancy with IUD in place is rare, and one must wonder what made this particular IUD fail.
New text: pregnancy with IUD in place is rare, and one must wonder what made this particular IUD fail (e.g., a manufacturing defect).

62. Line 339 - "frequent" not "frequency"

RESPONSE: Thank you for pointing out this typographical error. We have also changed "perimenopausal people" to more patient-centered language per the journal's requirements.

Lines 373-374
Old text: In addition, perimenopausal people who experience heavy or frequency bleeding…
New text: In addition, people who are perimenopausal and experience heavy or frequent bleeding…

63. Line 428 - This might be the place to insert the information about the ABOG recognition of this new subspecialty rather than leave for the conclusion. However, it still should be mentioned in the conclusion (in case that is all the reader chooses to see).

RESPONSE: Please see our response to your comment 43.

64. On one of the tables, a column for tail string color needs to be added.

RESPONSE: We agree that string color should be added to this review. We are not able to find a logical place to incorporate it into the tables given that table 1 and 2 include the implant, and table 3 does not include the copper IUD. We have chosen to incorporate it into the text as below.

Lines 326-331
Old text: IUD strings are present to increase ease of removal, but lack of strings is not an indication for intervention.
New text: IUDs available in the United States have strings which are meant to come through the external cervical os and sit in the upper vagina after placement. IUD strings are present to increase ease of removal, but lack of strings is not an indication for intervention. The copper 380 mm2 IUD has white strings, levonorgestrel 13.5 mg IUD has brown strings, levonorgestrel 19.5 mg IUD has blue strings, and levonorgestrel 52 mg IUDs have blue (Liletta) and brown (Mirena) strings.

EDITORIAL OFFICE COMMENTS:

65. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

RESPONSE: We do not choose to opt out.

66. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

RESPONSE: As this is a Clinical Expert Series, we do not have funding information, study registration numbers, IRB, etc.

67. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

RESPONSE: This has been completed by both authors.

68. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "Patients with obesity" instead of "obese patients," "Women with disabilities" instead of "disabled women," "women with HIV" instead of "HIV-positive women," "women who are blind" instead of "blind women."

RESPONSE: We have edited where applicable to change to person-first language.

69. 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://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-obstetrics-data-definitions&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=pgXEdMzLzi6EVcBru1PV3ThoCkp5WLUrsjMEOkJkx5c%3D&reserved=0 and the gynecology data definitions
at https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpr

actice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-gynecology-data-definitions&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=%2F4BZVrgxNjca23tfaGz%2F1BXdLVKx9f2RAm9walcQQWk%3D&reserved=0. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

RESPONSE: We have used the definitions provided and made edits for all terms except for "amenorrhea." Recently published recommendations stipulate use of "absence of bleeding/spotting" because amenorrhea refers to a pathologic condition and not a contraceptive-induced bleeding change (Creinin MD, Vieira CS, Westhoff CL, Mansour DJA. Recommendations for standardization of bleeding data analyses in contraceptive studies. Contraception. 2022 May 28:S0010-7824(22)00152-4. doi: 10.1016/j.contraception.2022.05.011). We have used this more updated and appropriate terminology in our manuscript. Given that the journal does not allow use of the "/" symbol, we have altered the terminology to "absence of bleeding or spotting."

70. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Clinical Expert Series: 6250 words

RESPONSE: Our word count is within the requirements. It is 6,062 words.

71. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

* 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 or indicate whether the meeting was held virtually).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to

Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."
* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

RESPONSE: We acknowledge these rules.

72. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

RESPONSE: We have ensured that our abstract is reflective of the manuscript.

73. In addition, the abstract length should follow journal guidelines. Please provide a word count.

Clinical Expert Series: 250 words

RESPONSE: The current abstract word count is 117 words.

74. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fabbreviations.pdf&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=9wpGpipWzybOBpDdbfJxyPjsBe90XRmh0UArq%2FX%2BRwU%3D&reserved=0. 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.

RESPONSE: We have used only standard abbreviations and acronyms.

75. The journal does not use the virgule symbol (/) in sentences with words, except with ratios. 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 have not used the virgule symbol.

76. ACOG avoids using "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: We have replaced all instances of the word “provider” with the preferred term.

77. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available at https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Ftable_checklist.pdf&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=TIYUDMlJ0ZBnStG%2F1iK40Oef2L0ir3iyYpwZsjdo4lM%3D&reserved=0.

RESPONSE: Our tables conform to guidelines with the exception that we have included brand names. We feel this is important to differentiating the Liletta and Mirena IUD, as they are the same hormone and dose.

78. Please review examples of our current reference style at https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fifa_suppl_refstyle.pdf&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=cd8ZYLRXMX4uylbl8W%2BJbDBhSRMLDXFPLo22hFGcOsI%3D&reserved=0. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the formal reference list. Please cite them on the line in parentheses.

If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fclinical&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=SgpBYD6PEfKwjmJPBYuxGoixvNtO%2Bg5FG57IKHrNx90%3D&reserved=0 (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Please make sure your references are numbered in order of appearance in the text.

RESPONSE: We have reviewed out references to conform to the journal style.

79. 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 https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Flinks.lww.com%2FLWW-ES%2FA48&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=zPSJQjd8QACkZTEPNoosc6O76lN3Q3E3yFtw9AfwQUE%3D&reserved=0. The cost for publishing an article as open access can be found at https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwkauthorservices.editage.com%2Fopen-access%2Fhybrid.html&data=05%7C01%7Ccobaker%40ucdavis.edu%7Cac311490a02147a77c6008da399479e6%7Ca8046f6466c04f009046c8daf92ff62b%7C0%7C1%7C637885607127624269%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=d%2FJ02LoVyDjQeo%2FS%2FA7ddJLX4rI7f%2BAik5CXNo8eikA%3D&reserved=0.

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: We understand and will look out for the email communication.