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)*

**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: Aug 19, 2019
To: "Kassie Jean Bollig" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1354

RE: Manuscript Number ONG-19-1354

Challenging Current Views: A Prospective Series of Angular Pregnancies Managed Expectantly

Dear Dr. Bollig:

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).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Sep 09, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a case series looking at the outcomes of 42 angular pregnancies at a single institution that developed the sonographic criteria for diagnosis. There was a high term vaginal delivery rate and a 17% miscarriage rate. There were no catastrophic outcomes or severe maternal morbidity.

Your article is not only about angular pregnancies but also about your development of specific criteria for diagnosis. The entire article should reflect that you are proposing strict diagnostic criteria as well as presenting outcomes and your suggestions for management. For example, "we propose a new diagnostic paradigm for diagnosing angular pregnancy and if these criteria are met, pregnancies can be safely observed and managed expectantly."

Based on your findings and the history of angular pregnancies that you reference, one could argue that it is unnecessary to know if a pregnancy is angular if the patient is asymptomatic.

Throughout your abstract, you need to use a better phrase than "resolved." The pregnancy progressed to a more centric location or ultrasound normalized.

Line 86, delete the word "other" that precedes "ectopic" as you are trying to make the case that angular pregnancies are not ectopic pregnancies.

Why was consent waived? Was it considered exempt? It seems as if patients should have been consented for observation as it is a somewhat controversial management plan based on the historical definition of angular pregnancy and certainly you are doing more ultrasounds than is done on seemingly uncomplicated pregnancies.

Line 110-132, the majority of the methods section consists of arguments around why the specific diagnostic criteria were used and thus belongs in the discussion section.

Line 141, eliminate the word "of" in "initial of detection"

Another weakness of your study is the reliance on a single sonographer.

I'm not sure that Tables 2 and 4 add much to your narrative.

Reviewer #2: This is a well written, interesting and much needed article. A large study of pregnancy outcomes with observation is certainly of interest, particularly when a review of the literature shows management that ranges from expectant to excision. Clearer guidelines for diagnosis and management are clearly needed.

Methods -
- Please describe in detail how patients were identified for inclusion. It appears from your patient list that they were all identified at time of first trimester sono but this is not explicitly stated. Is a dating ultrasound standard of care in your practice?
- Were all ultrasound reports reviewed by both faculty? If so, were there any discrepancies in classification? If not, did your two ultrasound faculty review any of the same images to determine interrater reliability?
- Did any patients receive MRI to confirm the diagnosis?
- Were patients asked about symptoms or was this abstracted from the medical record?

Results
- Your data on follow up ultrasound findings and the high rate of resolution is particularly interesting.
- I would be interested to see the addition of any pregnancy outcomes that have been confirmed since time of submission

Discussion
- Your rate of preterm birth is higher than national average and this has been reported in conjunction with angular pregnancy. Please comment
- I think this an excellent discussion of how these results fit into the previous literature and agree that clear diagnostic criteria are important in discussing outcomes.

Figures and Tables
- I would be interested to see a representative image demonstrating the ultrasound criteria that you mention

Reviewer #3: Bollig et al report the prospective outcome of 42 "angular/corneal/interstitial" pregnancies managed expectantly at a single institution from March 2017 to February 2019 [2 years]. The "presumptive" diagnosis was made during the 1 st trimester by a "single-experienced" sonographer. The majority had no symptoms [33 patients - 78.6%], 8 [19%] had vaginal bleeding and 2 [4.8%] had pain. At the 1st follow up 23 cases [54.8%] had resolved leaving 19 cases for this study. Out of these 19 cases, 6 had a miscarriage leaving 13 cases with "angular pregnancies". Out of these 13 cases, 3 had decreased myometrial thickness [we have to assume that the remaining 10 had a "normal" endometrial thickness.

The authors went on to describe that TWENTY-SIX had a live birth [21 term deliveries and 5 preterm deliveries - 19 NSVD and 7 had Cesarean], 7 had miscarriages and 8 were continuing their pregnancies. The outcomes were favorable with no maternal death, no uterine rupture, no abnormal placentations and no hysterectomy.
The authors concluded that "most cases of "angular/corneal/interstitial" pregnancies can be managed "conservatively" "expectantly' with an overall "good and safe" outcomes.

Comments:
1) The reported incidence of "angular/corneal/interstitial" is estimated to be 1/2500 to 1/5,000 live birth. By the mere fact that these authors are reporting 42 cases of "angular/corneal/interstitial" pregnancies in a two years period is putting this reported incidence in question as that institution would have had to see/do 105,000 to 210,000 births during that time period.

2) If we assume that the reported incidence is "correct" and that that institution did not see/do that many deliveries, we have that to question the "diagnosis" of "angular/corneal/interstitial".

3) They mentioned that the Ultrasound technics have significantly improved and as such my 1st question is to described how many of these had a transvaginal 3-D imaging to confirm the diagnosis. Did any had a Laparoscopy to confirm the diagnosis as a "True" "angular/corneal/interstitial" has a significant risk of rupture, bleed leading to a significant maternal morbidity and even maternal mortality.

4) The numbers were also difficult to follow. If the "math" is correct, they started with 42 patients; 23 had resolved at the follow-up [putting the initial diagnosis in question], 6 had SAB's and 13 were still "viable and continuing". Yet they described TWENTY SIX deliveries [19 vaginal deliveries and 7 by cesarean]. Which 26 patients are they describing? The "true" number was 13 with 3 of these with a myometrial thinning. We have no information on the 3 patients who had the myometrial thinning?

5) Did any of these patients had a LAPAROSCOPIC assessment to prove or confirm the "angular/corneal/interstitial" diagnosis.

STATISTICAL EDITOR COMMENTS:

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

Methods: Need to cite which stats software was used to calculate means, SD and CIs.

Table 1, lines 37, 92, 148: Need units for age. The Table cites n = 41, but elsewhere the total = 42, including the denominator used to calculate proportions in Table 3. Need to clarify. Since the total is 42, cannot report precision of proportions to 0.1%, should round to nearest integer %. For age and BMI, the data are reported as mean±SD, followed by a range in (). Assuming that represents the 95% CIs for the mean value, then why does the last line of the Table reference median(range)?

Table 3: Again, should round the proportions to nearest whole number and since a comparison with the prevalence in the general population of women is implied, should include CIs for the % of cases, which will demonstrate that most ranges include the referent, and the limited sample of angular pregnancies limits power to discern all but numerical differences.

lines 188-194: Should include CIs with the proportions. Again those proportions and CIs should be rounded to nearest whole number. Should include the estimates of 0 instances with CIs, as well. A sample of 42 with 0 events has an upper bound for 95% of ~ 8.8%, so one cannot conclude from this series that uterine rupture, maternal death abnormal placentation or hysterectomy would never occur, nor could one reject that the hypothesis of one or more adverse events occurring had a < 5% probability.

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the other feedback and consistent with it, with revision please add the outcomes of the other pregnancies which were ongoing at time of initial submission. That will give you a significant stronger paper. As well, your discussion should include some comment that your sonographic findings may be too inclusive, such that you identified a large number of patients (See reviewer 3) who really are not "angular" pregnancies.

In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.

- what was interval between 1st scan an initial follow up?

- do you mean decreased relative to their initial scan? Does this mean, the others had stable or increased myometrial thickness? Line 43: what was EGA at final follow up? was there a difference in outcomes for those that persisted with thinning myometrium vs others?

- almost 20% prematurity rate needs to be mentioned. Also, as noted by reviewers, please update your paper to include the outcomes of all of the patients in your series. Given the rarity of bad outcomes, even missing a few would alter your conclusions. .

- what do you mean by "retention"? Is this at the time of delivery, there is a retained placenta?

- The Jansen and Elliot criteria seem pretty specific. What do you mean here by "vague diagnostic criteria"? IT seems to me that one of the issues is that these criteria do not include any sort of sonographic findings so that guidance for management at the time of sonographic diagnosis isn't helped by these J&E criteria.

- You also apparently developed your own criteria for making this diagnosis. Were these mostly patients who achieved pregnancy as a result of infertility treatments, including IUI, ART? That may be an explanation for the very high rate of this finding in your population.

- please describe and show images of what the uterotubal junction looks like. What sonographic markers define this portion of the anatomy?

- The myometrium wouldn't "surround" the gestational sac as you are not describing an interestitial pregnancy.

The pregnancy, as you are defining it, is intracavitary. Please explain further. This is further confused by criterium 4.

- please make it clear that you defined these criteria. Were they defined prior to collecting your patients for this study? Have they been validated by others?

- But it also potentially increased the bias towards better outcomes.

- show an image of an interestitial line. Please provide images of what you are calling an angular pregnancy with the findings above illustrated.

- How were patients counseled about this finding?

- The diagnosis of a placenta previa and an angular pregnancy seems really odd and calls the diagnosis into question. That's a very big placenta to both angular and previa!

- do you have images of the the same pregnancy in which it was present at 7 weeks but gone at 9 weeks?

- see comments in abstract section on this data

- this will need to be highlighted.

- please provide EGA ranges of preterm births.

- I would temper this. You are only describing 42 cases. "Should" seems a bit strong and the safety aspect was under very close follow up, which needs to be emphasized. You also need, in my opinion, to mention the high rate of premature births.

- emphasize that these were all prior to US diagnosis

- Did Rankin reanalyze the original 39 and include with her 46? How did you get 85 from 39+45?

- This is all speculative and the statistics would be very shaky here. I would omit lines 273-275.

- how often do you recommend follow up?

2. 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.

3. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. 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.

4. 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.

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 and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 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.

7. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

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. The most common deficiency in revised manuscripts involves the abstract. Be 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 paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

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. In your Abstract, manuscript Results sections, and tables, 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%").

13. Line 209-210: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

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. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the

editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

16. Figure 1 may be resubmitted with the revision.

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.

18. 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 21 days from the date of this letter. If we have not heard from you by Sep 09, 2019, 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

_____

[redacted]

September 8, 2019

Dear Editor,

Enclosed, please find our manuscript entitled, “Challenging current views: A prospective series of angular pregnancies managed expectantly”. This paper is being submitted for possible publication in *Obstetrics and Gynecology*. The paper describes the largest published series (42 patients) to date of expectantly-managed angular pregnancies. It challenges the extant literature by indicating that angular pregnancies are commonly diagnosed in asymptomatic patients in early pregnancy and that their clinical outcomes differ little, if at all, from those in the general population. This starkly contrasts literature indicating these are highly risky pregnancies and that termination should be considered after diagnosis.

We believe the manuscript will be of general interest to your readers who are certainly seeing these pregnancies in their clinics. It reviews commonly confused terminology for cornual, interstitial and angular gestations. More importantly, it will add to the existing sparse literature on this topic and may help to change clinical practice.

We greatly appreciate your consideration. If you need further information, please do not hesitate to contact my office.

The authors confirm that the Instructions for Authors have been reviewed. Below, please find our point-by-point response to each of the received comments.

Reviewer #1: This is a case series looking at the outcomes of 42 angular pregnancies at a single institution that developed the sonographic criteria for diagnosis. There was a high term vaginal delivery rate and a 17% miscarriage rate. There were no catastrophic outcomes or severe maternal morbidity.

Your article is not only about angular pregnancies but also about your development of specific criteria for diagnosis. The entire article should reflect that you are proposing strict diagnostic criteria as well as presenting outcomes and your suggestions for management. For example, "we propose a new diagnostic paradigm for diagnosing angular pregnancy and if these criteria are met, pregnancies can be safely observed and managed expectantly."

This is stated in our Précis statement.
Our last sentence of the introduction (lines 124-126) states the purpose of proposing new diagnostic criteria.
In our discussion:

- Lines 333-34, state that angular pregnancies can be safely conservatively managed. The following sentences given evidence for safe conservative management.

In our conclusion (lines 486-492) we make a statement of proposing new diagnostic criteria, and state that every effort should be made to expectantly manage these types of gestation.

Based on your findings and the history of angular pregnancies that you reference, one could argue that it is unnecessary to know if a pregnancy is angular if the patient is asymptomatic.

Agree. In lines 486-92 we go so far as to suggest to abandon the term angular pregnancy completely as these entities behaved similarly to non-eccentric IUPs. Based on our data, it did not matter if the patient had symptoms or not- neither were predictive of outcomes.

Throughout your abstract, you need to use a better phrase than "resolved." The pregnancy progressed to a more centric location or ultrasound normalized.

All phrases of “resolved” in regards to the US findings of angular pregnancy have been modified. See Tracked Changes.

Line 86, delete the word "other" that precedes "ectopic" as you are trying to make the case that angular pregnancies are not ectopic pregnancies.

Completed.

Why was consent waived? Was it considered exempt? It seems as if patients should have been consented for observation as it is a somewhat controversial management plan based on the historical definition of angular pregnancy and certainly you are doing more ultrasounds than is done on seemingly uncomplicated pregnancies.

The study was considered exempt. In the state of Missouri, pregnancies cannot be terminated unless there is an immediate threat to maternal life. In all of our cases, there was not an immediate threat. Therefore, particularly in light of the existing literature, the safest mode of management was to continue to follow these pregnancies closely and monitor for concerning signs or symptoms. We choose to do this with serial ultrasound exams and patient follow up. Since observation was the only type of management that could be offered to these patients under the laws of our state, this plan of care did not differ from care that would have been provided if the patient was not part of this study. Therefore, consent was waived. Furthermore, in all prior studies to date (to our knowledge), no cases were detected in the first trimester and therefore, all reported cases to date could be presumed to be managed by observation throughout the first and even second trimesters.

This point has been added to the Materials and Methods section in lines 131-133.

Line 110-132, the majority of the methods section consists of arguments around why the specific diagnostic criteria were used and thus belongs in the discussion section.

Change made.

Line 141, eliminate the word "of" in "initial of detection"

Completed.

Another weakness of your study is the reliance on a single sonographer.

This has now been stated in the discussion.

I'm not sure that Tables 2 and 4 add much to your narrative.

The idea of presenting the information in Table 2 was to account for any maternal of fetal factors that would contribute to the measured study outcomes. For example, the history of prior CS is a risk factor for uterine rupture, a reported adverse event of angular pregnancies. In the same vein, we wanted to note any genetic

abnormalities that could have contributed to outcomes such as miscarriage or preterm delivery for fetal indications.

The thought behind presenting the information in Table 4 was to be able to see the relationships of various factors with pregnancy outcomes. For example, were patients with vaginal bleeding more likely to have miscarriages, early deliveries, etc? Did women with pain more often have thinner myometrial thickness measurements? Was a combination of pain and myometrial thickness predictive of an early delivery? Answers to these questions address some of the historical associations and diagnostic criteria and place our report in better context.

Reviewer #2: This is a well written, interesting and much needed article. A large study of pregnancy outcomes with observation is certainly of interest, particularly when a review of the literature shows management that ranges from expectant to excision. Clearer guidelines for diagnosis and management are clearly needed.

Methods -
- Please describe in detail how patients were identified for inclusion. It appears from your patient list that they were all identified at time of first trimester sono but this is not explicitly stated. Is a dating ultrasound standard of care in your practice?

Any patient at our institution that had a first trimester US for any reason was included in the study if they met our diagnostic criteria. A dating US is offered to all patients, but by no means mandated. This is now clarified in the manuscript (see Tracked Changes in Methods section, lines 143-145).

- Were all ultrasound reports reviewed by both faculty? If so, were there any discrepancies in classification? If not, did your two ultrasound faculty review any of the same images to determine interrater reliability?

All ultrasound reports were not reviewed by both faculty. Each patient presenting for 1st trimester scan and her report was initially reviewed by only one faculty member to select cases but then reviewed by the other faculty member again for final inclusion in the study. There were no patients selected initially for inclusion that were then excluded on secondary review.

- Did any patients receive MRI to confirm the diagnosis?

We did not use MRI in our study. We wanted to use diagnostic criteria that would be financially feasible for all patients and reflective of common modalities used across all centers. We furthermore did not see any strong evidence in the literature showing improvement in the accuracy of diagnosis of angular pregnancy when MRI was added to the workup. Therefore, we limited our imaging to US.

- Were patients asked about symptoms or was this abstracted from the medical record?

This was abstracted from the medical record by the listed indication for the first trimester ultrasound.

Results
- Your data on follow up ultrasound findings and the high rate of resolution is particularly interesting.
- I would be interested to see the addition of any pregnancy outcomes that have been confirmed since time of submission

All pregnancy outcomes have now been updated.

Discussion
- Your rate of preterm birth is higher than national average and this has been reported in conjunction with angular pregnancy. Please comment

3rd Paragraph of Discussion: Four of our five preterm deliveries were medically indicated due to diagnosis of PPROM (2), severe preeclampsia (1), and HELLP syndrome (1). We do not believe that the diagnosis of angular pregnancy creates any risks or predisposition for these diagnoses. As an academic medical center, our patient population is enriched for these and other adverse pregnancy outcomes. Given the overall small number of patients in our study, this fraction of patients creates a high rate of preterm birth. If the study were larger, we believe this rate would more closely resemble the rate of preterm birth in academic practices across the nation as a whole.

- I think this an excellent discussion of how these results fit into the previous literature and agree that clear diagnostic criteria are important in discussing outcomes.

Figures and Tables
- I would be interested to see a representative image demonstrating the ultrasound criteria that you mention

The manuscript has now been updated with corresponding figures of our diagnostic criteria: implantation medial to the uterotubal junction (Figure 1); myometrial thickness (Figure 2); surrounding endometrium (Figure 3, Figure 4 3D representation). Each of these figures has been uploaded as separate attachments and other formats of these images can be provided if needed. If helpful, we can show several representative images. Since we did not have any patients with an interstitial pregnancy, we would need to request permission for a representative image from the study referenced. At this time, I have included this image as an attachment for your reference labeled, “Interstitial line image example.”

Reviewer #3: Bollig et al report the prospective outcome of 42 "angular/corneal/interstitial" pregnancies managed expectantly at a single institution from March 2017 to February 2019 [2 years]. The "presumptive" diagnosis was made during the 1 st trimester by a "single-experienced" sonographer. The majority had no symptoms [33 patients - 78.6%], 8 [19%] had vaginal bleeding and 2 [4.8%] had pain. At the 1st follow up 23 cases [54.8%] had resolved leaving 19 cases for this study. Out of these 19 cases, 6 had a miscarriage leaving 13 cases with "angular pregnancies". Out of these 13 cases, 3 had decreased myometrial thickness [we have to assume that the remaining 10 had a "normal" endometrial thickness.

The authors went on to describe that TWENTY-SIX had a live birth [21 term deliveries and 5 preterm deliveries - 19 NSVD and 7 had Cesarean], 7 had miscarriages and 8 were continuing their pregnancies. The outcomes were favorable with no maternal death, no uterine rupture, no abnormal placentations and no hysterectomy.
The authors concluded that "most cases of "angular/corneal/interstitial" pregnancies can be managed "conservatively" "expectantly' with an overall "good and safe" outcomes.

Comments:
1) The reported incidence of "angular/corneal/interstitial" is estimated to be 1/2500 to 1/5,000 live birth. By the mere fact that these authors are reporting 42 cases of "angular/corneal/interstitial" pregnancies in a two years period is putting this reported incidence in question as that institution would have had to see/do 105,000 to 210,000 births during that time period.

One purpose of our study was to determine the true incidence of angular pregnancies, particularly when first trimester scans are included. The current reported incidences of this type of pregnancy are largely based on case reports and reviews that identified only cases in the late second and third trimesters—due to severe clinical presentations. By developing diagnostic criteria that could be used in the first trimester, we hoped to provide insight into the true incidence of this type of pregnancy. Furthermore, such early detection allowed us to appreciate that most cases of angular pregnancies resolve, or move to a more centric location, with time. Therefore, by the second or third trimester, these pregnancies appear to be “normal” intrauterine gestations. As sonographic imaging improves and use of first trimester sonography expands, more and more of these early non-centric pregnancies will be detected and there is currently little guidance on their management. Further, some of the available guidance suggests overly aggressive management according to our study.

We have added some clarification of this argument in the last paragraph of the introduction as well as the first paragraph of the discussion.

2) If we assume that the reported incidence is "correct" and that that institution did not see/do that many deliveries, we have that to question the "diagnosis" of "angular/corneal/interstitial".

Another purpose of our study **was to question** the diagnosis of angular, cornual, and interstitial pregnancies represented in the literature. In fact, during the creation of our study plan, we found that many past publications used any combination of angular, interstitial, and cornual as synonymous terms when this in fact is not the case. After repeatedly finding these contradicting definitions in past studies (thus adding further confusion to the true incidence of each type of pregnancy), we sought to clearly define each term as its own entity (paragraph 2 in the introduction), and then propose the best way to define angular pregnancy in the first trimester using current technology and clinical practice patterns.

3) They mentioned that the Ultrasound technics have significantly improved and as such my 1st question is to described how many of these had a transvaginal 3-D imaging to confirm the diagnosis. Did any had a Laparoscopy to confirm the diagnosis as a "True" "angular/corneal/interstitial" has a significant risk of rupture, bleed leading to a significant maternal morbidity and even maternal mortality.

25 of these pregnancies also had 3D ultrasonography as stated in paragraph 4 of the Results section. We did not want to use 3D US as a way to “confirm” the diagnosis because routine 3D ultrasonagraphy is not available at every center, requires specific training, and possibly longer examination time. An aim of this diagnostic criterion was to be applicable for use at a variety of care centers to help standardize future detection of this entity. Furthermore, a relative diminishment in contrast in 3D images (compared to 2D) was thought to potentially lead to inaccurate measurements of myometrial thickness, which was part of our diagnostic criterion.

In regards to using laparoscopy, we did not confirm cases using this modality. We specifically chose to not make this part of our diagnostic criterion for reasons similar to those previously mentioned. As discussed in an earlier reply to another reviewer’s comment, due to the legal restrictions in our state, we cannot offer pregnancy termination unless there is an *immediate* threat to maternal life. Therefore, even if we would have performed laparoscopy in every case to “confirm” the diagnosis, we could not offer any management other than expectant unless we discovered an unexpected imminent threat to maternal life. We did not envision any additional advantage in offering and then subjecting every patient to a surgical procedure and its inherent risks. Additionally, one of our aims was to challenge the concept of “significant risks” with this type of pregnancy that is currently based on poor and limited data.

4) The numbers were also difficult to follow. If the "math" is correct, they started with 42 patients; 23 had resolved at the follow-up [putting the initial diagnosis in question], 6 had SAB's and 13 were still "viable and continuing". Yet they described TWENTY SIX deliveries [19 vaginal deliveries and 7 by cesarean]. Which 26 patients are they describing? The "true" number was 13 with 3 of these with a myometrial thinning. We have no information on the 3 patients who had the myometrial thinning?

Paragraph 4 of results:
First follow up scan results were 23 cases resolved, 13 cases persisted as angular, and 6 were miscarriages (23 + 13 + 6 = 42). Of the 13 persistent angular pregnancies, 3 of these had thinner myometrial thickness.

At continued follow up (next scan) of the 13 persistent cases, 11 of these then resolved, 1 was a miscarriage, and 1 was lost to follow up (11 + 1 + 1 = 13).

Of these 11 cases that resolved at the continued follow up (next scan), 9 resulted in a live birth and 2 were still continuing gestations at the time of submission.

Paragraph 5 of results:
Our total of 26 deliveries describes the total number of live births whether the angular pregnancy resolved on the first scan or with continued follow up. For example, six of the 23 pregnancies that resolved on the first scan were still continuing pregnancies (not yet delivered) at the time of submission. A straight calculation from total resolved on the first scan and resolved on the second follow up scan cannot be made.

Further information ofnthe 3 patients who had thinner myometrial thicknesses on follow up US, is shown by their additional designation in Table 4 asbolded cases for emphasis. As shown in this table, one resulted in an incomplete abortion, one was a preterm CS, and the other was a term CS.

Finally, all of these totals have now been updated to include pregnancies that were continuing at the time of submission. This should simplify any confusion introduced with partial follow-up numbers.

5) Did any of these patients had a LAPAROSCOPIC assessment to prove or confirm the "angular/corneal/interstitial" diagnosis.

None of these pregnancies had a laparoscopic assessment. Please see response above to comment 3).

STATISTICAL EDITOR COMMENTS:

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

Methods: Need to cite which stats software was used to calculate means, SD and CIs.

As these were basic statistical measures, all calculation were done without the aid of specific software (ie were done “by hand”).

Table 1, lines 37, 92, 148: Need units for age. The Table cites n = 41, but elsewhere the total = 42, including the denominator used to calculate proportions in Table 3. Need to clarify. Since the total is 42, cannot report precision of proportions to 0.1%, should round to nearest integer %. For age and BMI, the data are reported as mean±SD, followed by a range in (). Assuming that represents the 95% CIs for the mean value, then why does the last line of the Table reference median(range)?

Age units have been added.

The n=41 is incorrect. It is now corrected to n= 42. Later on in the study, one patient was lost to follow up so the denominator changed to 41 when calculating the % of final pregnancy outcomes for the new total number of 41. However, we used n=42 for all study population “baseline characteristics” (tables 1 & 3) because this was our initial number of enrollees.

Proportions are now reported to nearest integer %.

The assumption of mean with SD and CI for mean value is correct for the statistics for age and BMI. The last line of the table that states “median (range)” refers to how gravidity and parity were statistically analyzed. To summarize, Age and BMI were means±standard deviations (95% CI); Race was a proportion (%); and gravidity and parity were medians (ranges).

Table 3: Again, should round the proportions to nearest whole number and since a comparison with the prevalence in the general population of women is implied, should include CIs for the % of cases, which will demonstrate that most ranges include the referent, and the limited sample of angular pregnancies limits power to discern all but numerical differences.

These numbers are now rounded to nearest whole number. Confidence intervals are now added

lines 188-194: Should include CIs with the proportions. Again those proportions and CIs should be rounded to nearest whole number. Should include the estimates of 0 instances with CIs, as well. A sample of 42 with 0 events has an upper bound for 95% of ~ 8.8%, so one cannot conclude from this series that uterine rupture, maternal death abnormal placentation or hysterectomy would never occur, nor could one reject that the hypothesis of one or more adverse events occurring had a < 5% probability.

CI with proportions are now included for this information. All proportions throughout the manuscript are now rounded to the nearest whole number.

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the other feedback and consistent with it, with revision please add the outcomes of the other pregnancies which were ongoing at time of initial submission. That will give you a significant stronger paper. As well, your discussion should include some comment that your sonographic findings may be too inclusive, such that you identified a large number of patients (See reviewer 3) who really are not "angular" pregnancies.

All totals are now updated. Additionally, a comment on our diagnostic criteria and the possibility of over-diagnosing angular pregnancy has been added in the “weakness” portion in the second to last paragraph of our discussion

In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor’s specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.

- what was interval between 1st scan an initial follow up?

The planned interval was 2 weeks later; however, it sometimes changed to a 1 week or 3 week follow up due to patient ability to return for a scan. This information is in paragraph 3 of the Materials and Methods section in lines 155-157

- do you mean decreased relative to their initial scan? Does this mean, the others had stable or increased myometrial thickness? Line 43: what was EGA at final follow up? was there a difference in outcomes for those
that persisted with thinning myometrium vs others?

Decreased myometrial thickness on the follow up scan is in reference to the first scan. For follow up scans, the others were noted to have either a normal US (no longer met criteria for angular pregnancy), increased myometrial thickness but still angular pregnancy, or decreased myometrial thickness and still angular pregnancy.

Line 43 (prior version): Since now all pregnancies have been followed to completion, the final EGA varies on the specific pregnancy. In other words, we stopped following the pregnancy once there was a delivery, miscarriage, or other pregnancy outcome (patient moving away).

Due to our small sample size, we can probably not comment specifically whether pregnancies with thinning myometrium have significantly different outcomes. However, in table 4, we decided to emphasize these three pregnancies so that their outcomes were specifically noted. Here, one resulted in an incomplete miscarriage, one a preterm CS, and the other a term CS. A comment on this is in the 3rd paragraph of the discussion section (lines 388-390) to further highlight these findings.

- almost 20% prematurity rate needs to be mentioned. Also, as noted by reviewers, please update your paper to include the outcomes of all of the patients in your series. Given the rarity of bad outcomes, even missing a few would alter your conclusions.

The prematurity rate is mentioned in the last paragraph of the results section.
The final outcomes of all patients are now added.

- what do you mean by "retention"? Is this at the time of delivery, there is a retained placenta?

Yes, this part of the criteria was made at the time of delivery. It meant that there was a retained placenta. This clarification has been added in lines 103-104..

- The Jansen and Elliot criteria seem pretty specific. What do you mean here by "vague diagnostic criteria"? IT
seems to me that one of the issues is that these criteria do not include any sort of sonographic findings so that guidance for management at the time of sonographic diagnosis isn't helped by these J&E criteria.

The term vague has been deleted. A clarification to this sentence has been made (lines 115-117) to reflect that these criteria may be dated in that they don't include perhaps the most frequently used method to assess early pregnancy (ultrasound).

- You also apparently developed your own criteria for making this diagnosis. Were these mostly patients who
achieved pregnancy as a result of infertility treatments, including IUI, ART? That may be an explanation for the very high rate of this finding in your population.

Yes, an aim of this study was to propose criteria for diagnosis that could be used to identify angular pregnancy in the first trimester. Three patients (7%) achieved conception with the assistance of ovulation induction or ART. This is noted in lines 249-251 of the results section.

- please describe and show images of what the uterotubal junction looks like. What sonographic markers define this portion of the anatomy?

Figure 1 has been added to the manuscript (referenced in lines 147-148 and uploaded as separate attachment) to label the uterotubal junction on two of our 3D ultrasound images. As the uterotubal junction is actually a pathologic diagnosis based on a change in cell type, we did not use a specific "sonographic marker." This part of our diagnostic criteria was extracted from the original Jansen & Elliot definition. Since Jansen & Elliot also used a visual diagnosis (at the time of laparoscopy) of the uterotubal junction in their original criteria, we also utilized a visual representation of this junction using ultrasound images.

- The myometrium wouldn't "surround" the gestational sac as you are not describing an interestitial pregnancy.
The pregnancy, as you are defining it, is intracavitary. Please explain further. This is further confused by criterium 4.

The term "surround" in regards to criteria 3) has been modified (lines 149-150).

- please make it clear that you defined these criteria. Were they defined prior to collecting your patients for this study? Have they been validated by others?

A clarification has been made in the paragraph first describing the criteria. Additionally, this clarification has been added to the discussion section when we discuss how we chose each criteria. Criteria were defined prior to patient collection. This is the first study in which we used this specific set of criteria, so it has not

been validated by others. This is noted as a weakness (480-81).

- But it also potentially increased the bias towards better outcomes.

Agree with this point. This has been added as a potential weakness of our study in the discussions section (481-83).

- show an image of an interestitial line. Please provide images of what you are calling an angular pregnancy with the findings above illustrated.

Please seen separate attachments of figures representing aspects of our diagnostic criteria from images included in our study. As stated earlier in a reply to another reviewer, as we did not have any interstitial pregnancies, we do not have these representative images and would have to request permission from the original study that identified this ultrasound marker. However, although this image is not in our manuscript, we have attached the example from the original study for your reference. .

- How were patients counseled about this finding?

Patients were counseled that this was a potentially abnormal pregnancy and that it would be followed closely. We discussed that there is limited information on outcomes when identification is made early in the first trimester and precautions for re-presentation were discussed. This clarification has been added in lines 157-160.

- The diagnosis of a placenta previa and an angular pregnancy seems really odd and calls the diagnosis into question. That's a very big placenta to both angular and previa!

The angular pregnancy in these cases had resolved by 9-11 weeks gestation. Both previas were diagnosed on morphology scans at 20 weeks, long after the angular pregnancy had resolved.

- do you have images of the same pregnancy in which it was present at 7 weeks but gone at 9 weeks?

Yes, these images are available if needed.

- see comments in abstract section on this data

Noted and addressed.

- this will need to be highlighted.

Further elaboration on this outcome has been addressed in lines 384-387

- please provide EGA ranges of preterm births.

This has been added in the last paragraph of the results section (lines 292-293).

- I would temper this. You are only describing 42 cases. "Should" seems a bit strong and the safety aspect was under very close follow up, which needs to be emphasized. You also need, in my opinion, to mention the high rate of premature births.

This wording has now been changed to reflect the close follow up that allowed for these cases to be watched expectantly. Additionally, another comment on the rate of preterm births has been added to the discussion where we describe that four of the five preterm births were medically indicated, and very unlikely to be due to the fact that these pregnancies were initially angular pregnancies (lines 383-87).

- emphasize that these were all prior to US diagnosis

This emphasis has been added in lines 344-45.

- Did Rankin reanalyze the original 39 and include with her 46? How did you get 85 from 39+45?

Yes, Rankin added 46 cases to the 39 described by Jansen for a total of 85 cases.

- This is all speculative and the statistics would be very shaky here. I would omit lines 273-275.

This has been omitted.

- how often do you recommend follow up?

As our study is small and certainly not comprehensive given the limitations described, we would still recommend close (2 week follow up). The importance of close follow up has been added to concluding paragraph (lines 490-91).

2. 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:
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3. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. 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.

4. 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.

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 and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-

Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Noted

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 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.

Done and noted.

7. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

Done and noted

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* 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).

Done and noted

9. The most common deficiency in revised manuscripts involves the abstract. Be 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 paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

Done and noted

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

A total word count has been added to manuscript.

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.

This has been reviewed.

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.

The use of / has been deleted from sentences with words.

12. In your Abstract, manuscript Results sections, and tables, 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%").

Noted and corrections made.

13. Line 209-210: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

This claim has been removed and the phrasing modified.

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.

Reviewed.

15. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions
and Practice Bulletins) may be found via the Clinical Guidance & Publications page athttps://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

Referenced practice bulletins have been confirmed to be the most up to date documents.

16. Figure 1 may be resubmitted with the revision.

Revisions made.

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* A point-by-point response to each of the received comments in this letter.

Sincerely,

Danny Schust, MD

[redacted]