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

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

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

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

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-20-622

Mifepristone Combination Therapy versus Misoprostol Monotherapy for the Management of Early Pregnancy Loss: A Cost Analysis

Dear Dr. Berkley:

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

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

***Due to the COVID-19 pandemic, your paper will be maintained in active status for 30 days from the date of this letter. If we have not heard from you by May 10, 2020, we will assume you wish to withdraw the manuscript from further consideration.***

REVIEWER COMMENTS:

Reviewer #1: This is a study designed to model the estimated costs of treatment for early pregnancy loss using mifepristone/misoprostol combination therapy versus misoprostol alone. Decision tree analyses were constructed with scenarios varying by patient income, medical versus surgical uterine evacuation and provider practice characteristics.

Human subjects: Exempt.

Abstract:
1. Line 36: Consider not using the term "finally".

Introduction:
2. The purpose is presented and the background is briefly reviewed.

Methods
3. The methods are well described and sufficient detail is provided.

Results:
4. The data answer the study question.

Discussion:
5. There is a very recent paper (Nagendra et al.) that estimates cost of treatment for early non-viable pregnancies that might be of interest (reference is listed below).

References:
6. The recent prospective cost analysis paper:
Cost-effectiveness of Mifepristone Pretreatment for the Medical Management of Nonviable Early Pregnancy: Secondary Analysis of a Randomized Clinical Trial.
Nagendra D, Koelper N, Loza-Avalos SE, Sonalkar S, Chen M, Atrio J, Schreiber CA, Harvie HS.

7. A few of the references may need to have their format completed (e.g. add 123(3) to reference 1, add practice bulletin number to reference 2, correct author information for reference 5 - Machlin SR, Adams SA)

Tables/Figures:
8. Consider defining MVA somewhere in the figures and the table.

Reviewer #2: "Mifepristone Combination Therapy versus Misoprostol Monotherapy for the Management of Early Pregnancy Loss: A Cost Analysis" is a cost analysis with a primary objective of determining if mifepristone pretreatment adversely affects cost of medical management of early pregnancy loss.

I have the following comments and queries:
1. Page 3, Line 38: One perceived barrier to the provision of mifepristone is cost. Could you elaborate on this more? Where has this been discussed in the literature?
2. Page 9, Line 170: The benefit to the patient is an incredibly important point and I would go as far as saying it does outweigh the difference in cost seen in the scenario with minimum wages and only MVA available.

Reviewer #3: This is an interesting paper on a timely topic. It provides cost insight to inform policies and practices around medication management of early pregnancy failure. The paper would nonetheless be strengthened if the authors addressed the following points:

1. Throughout: Would the authors consider generating models that speak to cost effectiveness based on a priori preference for medical vs surgical management? That is to say, the choice for medical management doesn't exist in a vacuum, but as an alternative to surgical management. Would the authors consider investigating whether the rate of choice for surgical management at the first visit affects cost effectiveness of a mifepristone- vs. monotherapy-based regimen?

2. Lines 146-150: Can the authors restate this? I think they're saying that the much lower completion rate of monotherapy drives the cost difference, and that it is unreasonable to believe based on available data that the completion difference could be low enough to make up this cost difference.

3. Figure 1 and following: Shouldn't all 1,000 patients have the cost factored in for the follow up visit, since that will be required to confirm completion? Or are the authors assuming all patients only have US confirmation of completion, with the second visit only for those who have incomplete first-line management? In short, could the authors be more explicit about the assumptions about patient flow through the model, and about those costs that are assumed to be the same across both populations? If this paper is to guide practice, the specific patient flow must be clear, to ensure that providers can strictly follow the flow studied in this paper.

4. Figure 1 and following: Would the authors consider including sensitivity analyses for various completion rates? While their data in Table 1 are useful, it may help readers contextualize the findings to see how much of a cost difference the completion rate makes.

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

General: Need to provide a table of all variables, their estimated value, their plausible range and references for each of justification for the range cited. For example, from reference #4, the proportion 67.1% had 95% CI, 59.0 % to 74.6%, while the proportion 83.8% had 95% CI, 76.8 to 89.3%). That is, they were not exact estimates to nearest 0.1%. The variability in estimates should then be used to perform sensitivity analyses to determine which factors could make one therapy more cost-effective than the other. Repeating the cost analysis multiple times and then showing results in terms of probability of one therapy being more cost effective than another would then be demonstrated more effectively than
assuming static values for the variables.

Regarding costs, they should all be adjusted to a common index year, or indexed for inflation if not known for the common year. For instance, fuel economy and hourly wages were cited for 2019, while office visit expenses were for 2013. Costs should also be formatted in table format with references for each.

EDITOR’S COMMENTS:

We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues ad other relevant topics. Adherence to these requirements with your revision will avoid delays during the revision process by avoiding re-revisions on your part in order to comply with formatting.

Numbers below refer to line numbers.

20: Did you compare Miso + Mife to Miso only or did you do other comparisons? If only the 2, you should say Miso + Mife is more cost-effective than Miso only since you didn’t compare the universe of options.

33: The objective of the abstract should be a simple “To” statement without background information.

44: Please provide the cut point for surgical costs rather saying just ‘were higher”.

46: Not sure what you mean by “minimum Federal wages”. Sounds like you are excluding all government employees. Why would that make a difference? After reading the manuscript, I think this might be clearer if you say “...patient population earned Federal minimum wage”

Abstract-Results and Results: P Values vs Effect Size and Confidence Intervals

While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, 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.

This is true for the abstract as well as the manuscript, tables and figures.

Please provide absolute values for variables, in addition to assessment of statistical significance.

We ask that you provide crude OR’s followed by adjusted OR’s for all relevant variables.

Please always list your comparisons in the same order. On line 44, you give combined therapy costs vs monotherapy costs; on line 47, you give monotherapy vs combined therapy. To assist the reader, please be consistent.

102: I’m unclear why patient salary was taken into account. Is this because of a sliding scale payment that you are assuming for lower wage earners?

117: Please name your IRB.

123: Spell out EPL throughout your paper.

120: Throughout your results section, rather than just present the numeric differences between the different strategies, please provide supporting statistical data to demonstrate their difference.

136: change again to Federal minimum wage

EDITORIAL OFFICE COMMENTS:

1. 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
2. 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.

3. 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.

4. 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.

5. 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.

6. 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).

7. 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.

8. 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.

9. 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.

10. 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").

11. 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://edmrg.ovid.com/ong/accounts/table_checklist.pdf.

12. 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.

13. Figures 1-12: The manuscript references 12 figures; however, there are only 6 included. Since two flowcharts as a single figure will likely not fit well on a printed page, please split each figure into 2 separate figures. Also, please upload the figures as figure files on Editorial Manager.

The journal usually limits in-print figures to 6 total. Would you please move 6 of the figures to Supplemental Digital Content (online-only)? You can pick which ones you want to keep for print.

14. 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://edmrg.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.

15. 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://edmrg.ovid.com/ong/accounts/authors.pdf), and
   * A point-by-point response to each of the received comments in this letter.

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

***Again, your paper will be maintained in active status for 30 days from the date of this letter. If we have not heard from you by May 10, 2020, we will assume you wish to withdraw the manuscript from further consideration.***

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.
Dear Dr. Chescheir:

I am pleased to submit revisions for our original research article entitled “Mifepristone Combination Therapy versus Misoprostol Monotherapy for the Management of Miscarriage: A Cost Analysis” by Drs. Holly Berkley, Howard Greene, and Michael Wittenberger for publication in Obstetrics & Gynecology. Please note that the title has been altered from “early pregnancy loss” to “miscarriage” to align with reVITALize terminology and that Dr. Howard Greene has been added as the second author due to significant analysis contributions during the revision process that are in alignment with the stated criteria for authorship.

Strong data from multiple randomized controlled trials published over the past three years supports the use of mifepristone in early pregnancy loss. ACOG recognized this data by updating the Practice Bulletin on Early Pregnancy Loss in 2018 with recommendation for mifepristone when available. In our manuscript, we address a major barrier to adherence to this recommendation: cost.

In this manuscript, we show that in every scenario analyzed a combination regimen with mifepristone is more cost effective than monotherapy.

We believe that this manuscript is appropriate for publication by Obstetrics & Gynecology because it aims to promote excellence in the clinical practice of obstetrics by addressing a specific barrier to the improvement of management of miscarriage—a condition managed by all obstetricians and gynecologists at all levels of trainings and in all types of practices. This manuscript supports a change in practice that would directly benefit patients.

We have no conflicts of interest to disclose. This work has been deemed not under purview of the Naval Medical Center San Diego Institutional Review Board (IRB) by an Appointed IRB Exemption Determination Officer as the analysis uses publicly available information akin to a review article. We have followed the CHEERS checklist. This manuscript has not been published, is not under consideration for publication elsewhere, and is being submitted solely to Obstetrics & Gynecology. It was presented in September 2019 at the Armed Forces District Meeting of ACOG in San Diego, CA at which it was awarded 1 of 3 Resident Awards for Oral Presentation. It was accepted for poster presentation at the 2020 ACOG Annual Clinical Meeting in Seattle, WA (meeting cancelled due to COVID-19); abstract was printed in the supplement Obstetrics & Gynecology. 135:65S, May 2020.

I, Holly Berkley, as the lead author, affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. I confirm that I have read the Instructions for Authors. Our point-by-point response to each of the received comments are included below. Of note, a revised manuscript with track changes was uploaded per instructions as well as a clean copy for easier review in case it is helpful due to significant text changes after statistical analysis was incorporated into the study.

Thank you for your consideration!

Very respectfully,

Holly H. Berkley, MD
LT, MC, USN
Obstetrics & Gynecology Resident
Naval Medical Center San Diego
Response to Reviewers’ Requested Changes

Responses in bold & italics

Reviewer #1:

1. Remove “finally” from line 36 in the abstract. **Done**
2. The purpose is presented and the background is briefly reviewed.
3. The methods are well described and sufficient detail is provided.
4. There is a very recent paper (Nagendra et al.) that estimates cost of treatment for early non-viable pregnancies that might be of interest (reference is listed below).
5. Check out Nagendra et al, *JAMA 2020* reference for a cost-analysis of early non-viable pregnancies. **Thank you for this suggestion. It is now referenced in this manuscript.**
6. The recent prospective cost analysis paper reference
7. Fix references 1, 2 and 5. **Done**
8. Define MVA in figures and table. **Done**

Reviewer #2:

1. Support the assertion “One perceived barrier to the provision of mifepristone is cost”. (Page 3, line 38)

   **Response:** The verbiage has been altered to better express that it is our opinion that the difference in mean price of medication may cause physicians to hesitate from transitioning from misoprostol alone to mifepristone plus misoprostol. Review of the literature does not reveal any studies formally investigating this as a barrier.

2. The benefit to the patient is an incredibly important point and I would go as far as saying it does outweigh the difference in cost seen in the scenario with minimum wages and only MVA available. **We agree and have added emphasize of this point in our conclusions.**

Reviewer #3:

1. Would the authors consider generating models that speak to cost effectiveness based on a priori preference for medical versus surgical management? That is to say, the choice for medical management does not exist in a vacuum, but as an alternative to surgical management. Would the authors consider investigating whether the rate of choice for surgical management at the first visit affects cost effectiveness of a mifepristone- vs. monotherapy-based regimen?

   **This is an interesting suggestion, but we feel it is beyond the proposed scope of this paper and may be better addressed in another cost-analysis. For the purposes of this paper, we are only trying to determine the costs after the initial decision to proceed with medical management has been made.**
2. Can the authors restate lines 146-150. I think they're saying that the much lower completion rate of monotherapy drives the cost difference, and that it is unreasonable to believe based on available data that the completion difference could be low enough to make up this cost difference.

Indeed, the much lower completion rate of monotherapy does drive the cost difference and based on the current randomized controlled trials it is unlikely that the (real world) completion rate difference between these two approaches to medical management would be low enough to make up this cost difference. This point was rephrased in the results and discussion.

3. Shouldn’t all 1,000 patients have the cost factored in for the follow up visit, since that will be required to confirm completion? We agree and have re-organized our patient flow diagram to more explicitly present the included costs at each step of treatment for each group (See Figure 1)

4. Would the authors consider including sensitivity analyses for various completion rates? (While the data in Table 1 are useful, it may help readers contextualize the findings to see how much of a cost difference the completion rate makes). Yes. The confidence intervals for the completion rates have now been incorporated into the statistical analysis. Using the Monte Carlo simulation, the full range of completion rates (utilizing the confidence interval of the completion rates reported by Schreiber et al. 2018) were analyzed in a run of 30,000 iterations for each scenario. We generated mean costs of treatment per patient with 99% confidence intervals that demonstrated that the mean costs of combination therapy and monotherapy in every scenario are statistically different. Additionally, we performed a sensitivity analysis by re-running the Monte Carlo analyses with incrementally increased completion rates of monotherapy to determine what completion rate monotherapy would have to perform at in order for the cost of combination and monotherapy to be equal (see Results).

Statistical Editor:

5. Need to provide a table of all variables, their estimated value, their plausible range and references for each of justification for the range cited. (Examples given for completion rates). The variability in estimates should then be used to perform sensitivity analyses to determine which factors could make one therapy more cost-effective than the other. Repeating the cost analysis multiple times and then showing results in terms of probability of one therapy being more cost effective than another would then be demonstrated more effectively than assuming static values for the variables.

See table 1 for cost of all variable with plausible ranges and references. We utilized Monte Carlo simulation analysis to repeat the analysis with 30,000 iteration for each scenario. This was then repeated 10 times for each scenario in each wage category to generate 99% confidence intervals. The probability of one therapy being more cost effective than another is then shown by the resulting mean costs per patient for each treatment and confidence intervals which are statistically different.

6. Regarding costs, they should all be adjusted to a common index year, or indexed for inflation if not known for the common year. Cost should also be formatted in table format with references for each.
We have adjusted all costs to a common index year (2019) and presented this in now Table 1 with references included.

Editor:

1. Need to be formatted to the Green Journal format. Done
2. Need to change line 20 to say, “Mifepristone + Misoprostol is more cost-effective than Misoprostol only. Done
3. Remove background from the abstract objective section. It should simple state, “To determine if mifepristone pretreatment adversely affects cost of medical management of early pregnancy loss (EPL).” Done
4. Please provide the cut point for surgical costs rather than saying just “were higher”. (line 44) This has been reworded. In our updated statistical analysis, combination therapy is more cost-effective than monotherapy in scenarios estimating surgical cost to be lower due to utilization of in-office manual vacuum aspiration and in scenarios estimating surgical cost to be higher due to utilization of in-operating room dilation and curettage. See Table 1 for specific cost ranges.
5. Clarify “minimum Federal wages” on line 46. Might be clearer if you say, “patient population earned Federal minimum wage”. Done
6. On both the Abstract Results and Results section, consider changing the effect size from a p value to the preferred citation 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. Do this for tables and figures as well. The mean difference with confidence interval is now presented.
7. Please provide absolute values for variables, in addition to assessment of statistical significance. The mean difference with confidence interval is now presented.
8. We ask that you provide crude OR’s followed by adjusted OR’s for all relevant variables. We elected to not use odds ratios to describe the results of this study, but rather means with confidence intervals.
9. Please always list your comparisons in the same order. On line 44, you give combined therapy costs vs monotherapy costs; on line 47, it is reversed. To assist the reader, please be consistent. Done
10. Unclear why patient salary was taken into account. Since time away from work is lost income for the patient, we were attempting to capture this “cost” by adjusting the salary of our hypothetical patients. This is significant because the lower completion rate of monotherapy leads to more appointments and treatment which results in an increase in lost wages.
11. Please name your IRB. (line 117) Naval Medical Center San Diego IRB was added to text.
12. Spell out EPL throughout your paper. (line 123) Done—early pregnancy loss changed to miscarriage to align with revitalize terminology.
13. Throughout your results section, rather than just present the numeric differences between the different strategies, please provide supporting statistical data to demonstrate their difference. The mean difference with confidence interval is now presented.
14. On line 136, change again to Federal minimum wage. Done
1. 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:
   **Response: OPT-IN: Yes, please publish my point-by-point response letter.**

2. 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.

3. 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.
   **Response: Included in cover letter**

4. 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](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.

   **Response: All terms are in alignment with the revitalize initiative. Specifically, “early pregnancy loss” has been changed to “miscarriage.”**
5. 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. Adherent.

6. 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). Included in cover letter and on title page.

7. 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.

8. 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. Completed.

9. 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. Completed.

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