OBSTETRICS & GYNECOLOGY

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

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

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

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

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

Date: Feb 05, 2021
To: "C. Edward Wells" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-87

RE: Manuscript Number ONG-21-87

A Randomized Double-Blinded Placebo-Controlled Trial of Nifedipine for Acute Tocolysis of Preterm Labor

Dear Dr. Wells:

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 Feb 26, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #2: This is a randomized placebo controlled trial of nifedipine for tocolysis.

The trial was well done without methodologic concerns. It replicates findings that have been shown previously, namely that nifedipine does not prevent preterm birth. Being that this null result has been shown before, it is not surprising that the study was stopped early for futility, but it is curious that the authors expected such a dramatic reduction in the preterm birth rate when they did their power analysis.

It is also notable that 50% of the women enrolled in the study delivered at term, and 70% were able to get both doses of BMZ (and almost all that got BMZ also stayed pregnant for a week longer!). This has been shown in other studies of tocolytics and in studies regarding antenatal corticosteroids, so it is a good reminder that regardless of obstetric management strategies, it is hard to predict when preterm labor will lead to preterm birth.

Most women were multiparous without a history of prior preterm birth - it would be interesting to see if the women who had a prior preterm birth were the ones who went on to deliver preterm again - perhaps if multiparous women with no prior preterm birth have such a low rate of preterm birth (as I would expect) then the utility of nifedipine particularly in this group could be reconsidered.

It is also interesting that women in the nifedipine group and placebo group needed the 2nd dose due to continued contractions with the same frequency, showing that nifedipine did not even change the frequency of contractions within the 1st 90 minutes of administration. The frequency of stoppage for side effects was also similar, demonstrating the effectiveness of the placebo.

Thus, while this trial did not demonstrate effectiveness of nifedipine (which is not a surprise) the study does give relevant information about a contemporary cohort of women with preterm labor complaints.

Reviewer #3: A single centered RCT of Nifedipine use for acute tocolysis of PTL between 28-34 weeks in pregnancy prolongation or improving neonatal outcomes
1. Objective: lines 139-142 speak to a very broad objective. Here is your chance to state specifically. primary outcome ? and secondary
It feels a little confusing to state "treatment of preterm labor and the subsequent maternal and neonatal outcome. Our objective is to determine whether nifedipine decreases the rate of preterm birth." There are a lot of maternal and neonatal outcomes to study. Just tighten it up.
2. Overall your Materials and Methods are quite good but needs some rearrangement for the ease of the reader First paragraph of the Methods section Lines 149-155 should not lead this section but rather start with line 156. The first

paragraph should be in the Discussion or later in the Methods section
Line 161 before you start describing the actual "how the medication was administered and monitored" I would state the primary and secondary outcomes and the inclusion and exclusion criteria.
Start broad and become specific
3. line 163-164 please specify what was the Nifedipine dose every 4 hours vs a placebo
4. Randomization controlled for prior preterm birth?
5. Why did the two women withdraw?
6. Discussion: Can you talk about generalizability given that 80% were Hispanic
Table 1 prior preterm birth: Please define. Was this<37 weeks?, this is the most significant difference between the groups (although not statistically significant). Having more information about these 39 women would be helpful
8. You state that Magnesium is used for neuro prophylaxis between 24-28 weeks at UT Southwestern. Wanting to confirm that it is NOT used from 28-32 weeks?. Also did women receive another tocolytic at anytime Both of these statement would be pertinent negatives

STATISTICAL EDITOR COMMENTS:

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

Abstract: Needs to conform to our RCT template, esp re: stipulation of primary outcome and calculation of sample size. The primary outcome should be stated first in Results.

Table 1: Since the groups were randomized, there is no need for stats tests to compare characteristics. Any difference is due to random chance.

Table 2: Need to clearly separate the primary from all secondary outcomes and state the primary (% PTB < 37 wks) first.

Tables 3, 4: The study was not powered to compare maternal or neonatal outcomes, so one cannot extrapolate from these data that all NS findings could be generalized.

EDITOR COMMENTS:

1. As achieving 48 hours is important to those who use nifedipine clinically, please include data on this in your abstract.

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

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

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

5. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

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

7. 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).

8. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

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 limit for Original Research articles is 300 words. Please provide a word count.

10. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

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

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. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting

presentations, and abstracts may be included in the text but not in the reference list.

14. 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 at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

15. 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 https://wkauthorservices.editage.com/open-access/hybrid.html.

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.

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. Do not omit your responses to the Editorial Office or Editors' comments.

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 Feb 26, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

March 26, 2021

Nancy C. Chescheir, MD
Editor-in-Chief
Obstetrics & Gynecology

Dear Dr. Chescheir:

Thank you for this opportunity to respond to reviewer and editor queries on our manuscript entitled "**A Randomized Double-Blinded Placebo-Controlled Trial of Nifedipine for Acute Tocolysis of Preterm Labor**". We appreciate that the editors acknowledge the paucity of published tocolytic trials and hope our responses satisfy the Journal for eventual publication. The responses to each query or comment are listed below in order:

Reviewer #2

1. The trial was well done without methodologic concerns. It replicates findings that have been shown previously, namely that nifedipine does not prevent preterm birth. Being that this null result has been shown before, it is not surprising that the study was stopped early for futility, but it is curious that the authors expected such a dramatic reduction in the preterm birth rate when they did their power analysis.

   We thank the reviewer for the feedback. As noted in the manuscript, the power was calculated using 2 prior randomized controlled trials at Parkland Hospital to establish expected rate of births < 37 weeks' gestation and was based on a 1/3rd reduction in that rate.

2. It is also notable that 50% of the women enrolled in the study delivered at term, and 70% were able to get both doses of BMZ (and almost all that got BMZ also stayed pregnant for a week longer!). This has been shown in other studies of tocolytics and in studies regarding antenatal corticosteroids, so it is a good reminder that regardless of obstetric management strategies, it is hard to predict when preterm labor will lead to preterm birth.

   Thank you. We agree.

3. Most women were multiparous without a history of prior preterm birth - it would be interesting to see if the women who had a prior preterm birth were the ones who went on to deliver preterm again - perhaps if multiparous women with no prior preterm birth have

such a low rate of preterm birth (as I would expect) then the utility of nifedipine particularly in this group could be reconsidered.

We have inserted a paragraph into the manuscript at line 235 of the original submitted version, stating:

As prior preterm delivery is a potent influencer of future outcome of preterm delivery, we performed a stratified analysis of the association between preterm delivery (<37weeks) and the randomization assignment stratified by the presence or absence of prior preterm delivery. After this adjustment the significance of the association is not altered nor the effect size as relative risks (data not shown).

With respect to the statistics for this analysis, under Methods, we added the following:

The analysis of the association between preterm delivery (<37 weeks) and the randomization assignment stratified by the presence or absence of prior preterm delivery was done using the Cochran-Mantel-Haenszel test and the Breslow-Day test.

4. It is also interesting that women in the nifedipine group and placebo group needed the 2nd dose due to continued contractions with the same frequency, showing that nifedipine did not even change the frequency of contractions within the 1st 90 minutes of administration. The frequency of stoppage for side effects was also similar, demonstrating the effectiveness of the placebo. Thus, while this trial did not demonstrate effectiveness of nifedipine (which is not a surprise) the study does give relevant information about a contemporary cohort of women with preterm labor complaints.

Thank you. We agree.

Reviewer # 3

1. Objective: lines 139-142 speak to a very broad objective. Here is your chance to state specifically. primary outcome ? and secondary
It feels a little confusing to state "treatment of preterm labor and the subsequent maternal and neonatal outcome. Our objective is to determine whether nifedipine decreases the rate of preterm birth." There are a lot of maternal and neonatal outcomes to study. Just tighten it up.

Done. We have changed the original text beginning on Line 139 of the submitted paper to read:

"This study was undertaken to evaluate the acute tocolytic effect of nifedipine compared with placebo in the treatment of preterm labor and the subsequent maternal and neonatal outcome. Our **primary objective** was to determine whether nifedipine decreases the rate of preterm birth less than 37 weeks."

The secondary objectives are as listed in the Methods section.

2. Overall your Materials and Methods are quite good but needs some rearrangement for the ease of the reader First paragraph of the Methods section Lines 149-155 should not lead this section but rather start with line 156. The first paragraph should be in the Discussion or later in the Methods section. Line 161: before you start describing the actual "how the medication was administered and monitored" I would state the primary and secondary outcomes and the inclusion and exclusion criteria.
Start broad and become specific

   Done. We have rearranged the Methods section as suggested.

3. line 163-164 please specify what was the Nifedipine dose every 4 hours vs a placebo

   Done. We have changed the sentence on lines 163-164 to read:
   "This was followed by repeat study drug dosing **(placebo or nifedipine 20 mg)** every 4 hours for a total of 48 hours."

4. Randomization controlled for prior preterm birth?

   It was not. See response #3 to Reviewer #2.

5. Why did the two women withdraw?

   We have added a comment describing the reasons to the Results section. In the first paragraph of the results trial, we have modified it as follows:

   Two women withdrew from the trial **after changing their minds about participation. One woman declined to take the study drug after consent and ultimately delivered at an outside hospital; when contacted for permission to obtain these records she declined to provide this consent. The second woman declined the 90 minute dose and withdrew further consent to participate.**

6. Discussion: Can you talk about generalizability given that 80% were Hispanic

   We are unaware of data to suggest that Hispanic women are different in their response to nifedipine.

   As noted in response to comments by the Editor, race/ethnicity information has been removed to avoid drawing inappropriate conclusions.

7. Table 1 prior preterm birth: Please define. Was this<37 weeks?, this is the most significant difference between the groups (although not statistically significant). Having more information about these 39 women would be helpful

   We have added further description as a footnote in Table 1. See response #3 to Reviewer #2.

8. You state that Magnesium is used for neuro prophylaxis between 24-28 weeks at UT Southwestern. Wanting to confirm that it is NOT used from 28-32 weeks? Also did women receive another tocolytic at any time Both of these statement would be pertinent negatives

   As stated in the manuscript, magnesium was not used after 28 weeks' gestation. Other tocolytics were not given. On line 154, after the listed interventions, we add, "Tocolysis is not part of the management of preterm labor at Parkland Hospital."

Statistical Editor

1. Abstract: Needs to conform to our RCT template, esp re: stipulation of primary outcome and calculation of sample size. The primary outcome should be stated first in Results.

   Done. On Line 66 of the original abstract, we insert: "A total of 150 women were necessary to detect a 1/3 reduction in the rate of birth <37 weeks."

   Being mindful of word counts and with Editor Comment #13 in mind, we have changed the sentence beginning on Line 73 (under Results) in the original abstract to read: "There was no significant difference in the primary outcome for delivery prior to 37

weeks' gestation (24 (52%) vs 20 (48%); P=0.67, RR (95% CI) 1.1 (0.7, 1.7)), nor were there differences between nifedipine and placebo for gestational age at delivery or median days from randomization until delivery."

2. Table 1: Since the groups were randomized, there is no need for stats tests to compare characteristics. Any difference is due to random chance.

   Removed.

3. Table 2: Need to clearly separate the primary from all secondary outcomes and state the primary (% PTB < 37 wks) first.

   Done. We have rearranged some items.

4. Tables 3, 4: The study was not powered to compare maternal or neonatal outcomes, so one cannot extrapolate from these data that all NS findings could be generalized.

   We acknowledge the Statistical Editor's admonition by adding to Line 292 of the original paper, we begin the sentence with: "**Although not powered for neonatal outcomes**, our second finding regarding neonatal outcomes comports with the American College of Obstetricians and Gynecologists statement…"

EDITOR COMMENTS:

1. As achieving 48 hours is important to those who use nifedipine clinically, please include data on this in your abstract.

   Done. On Line 67 of the original abstract, we add to this sentence: 'Study drug was continued every 4 hours to complete a 48-hour regimen**, the "betamethasone window."'**

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:
OPT-IN: Yes, please publish my point-by-point response letter.
OPT-OUT: No, please do not publish my point-by-point response letter.

We choose to OPT-IN.

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

Thank you.

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

Done.

5. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Race/ethnicity has been removed to avoid drawing inappropriate conclusions.

6. Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

   Race/ethnicity has been removed to avoid drawing inappropriate conclusions.

7. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

   Done.

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

   We do not anticipate this to be a problem.

9. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

   Nifedipine for Acute Tocolysis

10. 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 limit for Original Research articles is 300 words. Please provide a word count.

    289 words

11. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

    Reviewed

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

    On Line 172, the statement “Providers and patients were blinded to the treatment allocation.” is changed to “Physicians and patients were blinded to the treatment allocation.”

13. 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.

    We have modified the abstract, relevant results and tables to better reflect this suggestion. In the discussion of statistics in the Methods section, we have added:

The Clopper-Pearson method was used to estimate the confidence intervals for relative risks, and the Hodges-Lehmann method was used to estimate the location shift and 95% confidence interval for median differences.

14. 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.

    Not applicable

15. 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%").

    Reviewed

16. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

    Reviewed

17. 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 at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

Reviewed. ACOG Practice Bulletin 171 (Management of Preterm Labor) is current.

18. 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 Feb 26, 2021, we will assume you wish to withdraw the manuscript from further consideration.

On February 19, Emily Hernandez of the Editorial Office granted an extension to the revision due date to March 26th.

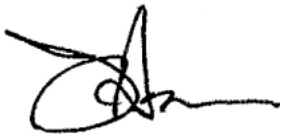
As previously noted, this study was presented at the Society of Maternal-Fetal Medicine 39th Annual Pregnancy Meeting on February 11-16, 2019 in Las Vegas, Nevada.

The manuscript has not been published elsewhere and is not currently in consideration at another journal. All authors have sufficiently participated in this study to satisfy the requirements for authorship. None of the authors have conflicts of interest. The Institutional Review Board for the University of Texas Southwestern approved this study. This study was registered at clinicaltrials.gov with trial number NCT02132533.

Please note that following the completion of this research project, one of our co-authors, Dr. Ken Leveno, passed away. His involvement was integral throughout the entirety of this project. As a result, we are requesting a posthumous inclusion of Dr. Ken Leveno as an author of this report should it be accepted for publication.

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 have been explained.

Thank you for considering our manuscript for publication.



J. Seth Hawkins, MD