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.*

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

Date: Jan 22, 2021
To: "Marian S McDonagh"[redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-3300

RE: Manuscript Number ONG-20-3300

Cervical Ripening in the Outpatient Setting: A Systematic Review and Meta-analysis

Dear Dr. McDonagh:

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.

We understand that there is a desire to publish the full report of this systematic review and meta-analysis through AHRQ along with the submitted abbreviated report. The editors are interested in this possibility if your manuscript is ultimately accepted for publication. However, we anticipate that the proposed timeline for publishing will need to be pushed back to allow time for the authors to respond to the reviewers' and editors' comments.

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2. Consider tempering your conclusion in the abstract. It seems that with the available data, definitive statements about safety cannot be made.

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 12, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is a systematic review evaluating types of cervical ripening (inpatient versus outpatient and one type versus another) in induction of labor for any indication on obstetrics practice. I appreciate the authors' contribution to the field and undertaking a challenging systematic review, and appreciate the editors giving me the change to evaluate this interesting manuscript.

Strengths:
* This is an extremely important systematic review…on a topic where increasing focus is being placed. Outpatient cervical ripening is becoming an important trend in obstetric practice, and this systematic review highlights important findings in that sphere. The amount of evidence/study on the topic is appropriate for systematic review, with a large number of high-quality studies and a large number of participants contributing to the evidence.
* The study adheres to guidelines for systematic review methodology and appropriate screening and study identification procedures.
* The authors do an excellent job reviewing the strength/validity of the studies and highlighting to what types of populations the results of this review apply.

Limitations
* The study seems to lack a clear sense of focus. What is the main comparison that the authors sought to evaluate? Inpatient versus outpatient? Or what type of ripening is best if outpatient is done? Just doing a search for all forms of ripening is too broad, and does not make it clear to the reader what the overarching question of the review is.
* As there are a lot of things being compared here, there needs to be much clearer language around what is being

compared to what when "no differences" are found. Particularly in the abstract, the way the sentences read makes it very hard to interpret.
* It appears that the authors "meta-analyzed" (Tables 2-3) anytime there were results, and this is misleading. There should only be meta-analysis done where 3 or more different studies made the same comparison (same two interventions being compared) on the same outcome. See comments below.

Comments for authors by section:

Abstract
* Line 63-65: The first part of this sentence a bit unclear to the reader. Was there no difference in Cesarean between inpatient VERSUS outpatient dinoprostone, or dinoprostone (either inpatient or outpatient) was not different VERSUS single balloon catheters in regard to Cesarean. This sentence may need to be broken up and reworded so the reader can tell exactly what is being compared to what in which Cesarean section was not different. As this is one of the main comparisons/outcomes of the review, this is key to keep clear.
* Line 70-73: It is very hard to tell from reading this sentence what was compared to what when "no differences" were found. For neonatal infection, for example, what was dinoprostone "not different" from? For birth trauma, what was single-balloon catheter not different from? This sentence is very difficult to understand.

Introduction
* Line 86: It would be key to briefly summarize here what the ARRIVE trial studied and what the key findings were. I agree it is important to mention here, but the reader that is not as familiar with the ARRIVE trial needs to hear a short summary.
* Line 101-104: These are two very large goals, and it might be key to emphasize which was the PRIMARY aim of the study. If comparing outpatient versus inpatient ripening is the primary aim of the review, then all emphasis and comparisons should emphasize that, and then secondarily compare different types of ripening. That would also help with clarity around what is being compared to what in results.
* The introduction should include slightly more information about past systematic reviews on this topic (not just the Cochrane), and why this review is necessary at this time.

Sources
* Line 112: Define for the reader what "gray literature search" means. Not all readers will be familiar with this term. Also, gray literature is not all that is found in ClinicalTrials.gov (ClinicalTrials.gov includes literature from both traditional and non-traditional sources), so I am not sure if this is the best term to use here.
* Did you search for references that were not found within the citation lists of identified systematic reviews and studies on the topic? Be clear about how other relevant systematic reviews were utilized to identify primary papers.

Study Selection
* The PICOS ("population, intervention, comparator(s), outcomes, and study types") could be a bit clearer here, particularly in regard to whether or not the study was required to have an arm that included outpatient ripening? Or did any study that compared two types of ripening, regardless of inpatient/outpatient, get included? As it appears that the primary focus of the study is to compared inpatient to outpatient, that should have been the focus of the PICOS, with secondary plans to compare different types of ripening within inpatient or outpatient. The PICOS should clearly follow the focus of the study, and not be quite so broad.
* Did you include all women with pregnancies in the "population" part of the PICOS? In other words, did you put any clinical parameters on what populations are appropriate for induction, or say that any study with any maternal or pregnancy characteristics that compared one type of ripening to another was appropriate for this review?

Results
* Grouping by outcomes rather than interventions gets quite messy and confusing for the reader. I highly suggest grouping the parts of the results by COMPARISON between two different interventions, so a subheading would be "inpatient versus outpatient dinoprostone" rather than "Cesarean section". That way, when clinicians are choosing between two available interventions and want to know what benefits/harms there are, they can go the comparisons that have evidence to support them rather than sorting through a large paragraph on "Cesarean section" that has many different comparisons embedded in the text.
* Line 171-172: This is really a point about Methods, but I would recommend only performing meta-analysis when 3 or more studies make the same comparison on the same outcome. This is pretty standard practice in systematic review, as reporting the results of only one or two studies as "meta-analysis" violates some assumptions.
* Line 171-172: There is very limited reporting of meta-analysis in the results; I would like to see more OR and numbers from relevant meta-analysis where this is sufficient evidence highlighted in the text.
* Line 235-236: It would be helpful in this sentence to list what interventions had evidence around infection, so we know what interventions were being compared here and found "no difference". This sentence does not help the reader evaluate, when choosing between interventions, which ones have evidence of non-different infection rates. This also furthers my case for grouping by intervention in the results, rather than by outcome and saying "no difference was found", which does not help the reader.
* Line 246-247: This sentence does not make clear which intervention (outpatient or inpatient) was favored (better) for avoiding shoulder dystocia, only that there was a different that was moderate. In all statements of a different in results, the direction, or what intervention is better, should be crystal clear. The reader has to backtrack to line 221-222 to figure this out; having readers have to reference back to former text and figure stuff out is not ideal.

Discussion
* In the first paragraph here, I would like to see more discussion of the main, positive findings. For example, there is moderate effect regarding shoulder dystocia in outpatient versus inpatient ripening, and that is not mentioned adequately in the Discussion. The reader should leave the first paragraph of the Discussion with a very clear picture of what main positive findings were, other than "limited evidence".

Reviewer #2:
I thank the authors for their efforts and interest, because systematic review takes a surprising amount of time and effort.
The authors conducted a systematic review and meta-analysis to assess the comparative effectiveness and potential adverse events of cervical ripening in the outpatient versus the inpatient setting or in the outpatient setting alone. The certainty of the evidence was generally low.
The study addresses an important topic to obstetric patients and providers.
I have several general and specific comments and suggestions.

General comments
A major challenge is assessing quality of the studies in a systematic review, which can strongly influence the findings of the review.

Major strength of the study: Pre-induction cervical ripening is an important part of the labor induction process in women with an unfavorable cervix.
ACOG Practice Bulletin 107. Are cervical ripening methods appropriate in an outpatient setting?
Limited information is available on the safety of outpatient management of induction of labor.

Major weaknesses: (a) Sources and Study Selection; (b) primary outcomes - confusing, because the perinatal and maternal adverse events were related to labor and delivery management rather than to pre-induction cervical ripening.

1. Suggest separate analysis of:
(a) Include studies after 2009 only;
(b) Studies from United States (e.g., Ausbeck EB, et al. Obstet GYnecol 2020; 136:597)
(c) Studies from other developed countries. Hence, the results are generalizable or applicable to a particular target population!
Risk of adverse events during the period between insertion and expulsion of a balloon catheter in cervical ripening to be low. These data facilitate further evaluation and implementation of this procedure in an outpatient setting for low-risk pregnancies. limited by small sample size but suggest longer time to delivery compared with Foley and misoprostol or oxytocin.

Specific comments and suggestions by page(s) and line(s):

INTRODUCTION
2. Page 4 lines 85-104. Expand background with addition of the following:
Ausbeck EB, et al. Outpatient Foley Catheter for Induction of Labor in Nulliparous Women: A Randomized Controlled Trial. Obstet Gynecol 2020; 136:597.

METHODS
3. Pages 4-5, lines 108-147. (See general comments above).

DISCUSSION
4. Pages 11-16, lines 249-383. Too long, and suggest focused analysis.
Suggest restructuring to:
Statement of main findings
Strengths and limitations
Implications for clinical practice

REFERENCES
5. Check for accuracy, relevance, current, and format for Green Journal
Tables 3 and 4
6. Pages 23-24. Labor and delivery management outcomes rather than pre-induction cervical ripening related outcomes.

Reviewer #3: lines 194-195: There is no Figure 3 attached.

Table 3: Most adverse outcomes had low incidence. Those proportions, in relation to the total sample sizes of the pooled studies, result in low power to discern a difference. This can be inferred from the wide CIs of the RRs. For example, for uterine infection, comparing prostaglandins vs placebo, 7% vs 10% among N = 771: the RR would have to be > 1.8 or < 0.38 to fulfill 80% power and the usual $p < .05$ threshold. In other words, the NS finding cannot be generalized from these data. The sample sizes and incidence rates make the math even worse for the other comparisons.

Figures: Should include funnel plots, which could be on-line material.

Figures: Should omit the test for I^2 and conclusions re: heterogeneity when there are only 1 or 2 studies being pooled. And in the case of 1 study, the subgroup simply recapitulates the single study, so that "pooling" is redundant and should be omitted. Rather, simply show the single study with its CI. Need to show a column of the weights within each subset and separate column of weights for the overall pooling.

EDITOR COMMENTS:

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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 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.

2. 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.

3. If your study is based on data obtained from the National Center for Health Statistics, please review the Data Use Agreement (DUA) for Vital Statistics Data Files that you or one of your coauthors signed. If your manuscript is accepted for publication and it is subsequently found to have violated any of the terms of the DUA, the journal will retract your article. The National Center for Health Statistics may also terminate your access to any future vital statistics data.

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

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Review articles should not exceed 25 typed, double-spaced pages (6,250 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. 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. 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; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and

Instruments is 200 words. Please provide a word count.

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

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

11. ACOG 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 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.

14. 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.

In addition, 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. Figures 1-4: Please upload as figure files on Editorial Manager.

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

appropriate by the editors). If you have questions prior to submission, please contact the journal's production editor at obgyn@greenjournal.org.

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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 12, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Torri Metz, MD
Associate Editor, Obstetrics

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

Obstetrics & Gynecology

Please accept our submission of a revised manuscript Number ONG-20-3300 (entitled **Cervical Ripening in the Outpatient Setting: A Systematic Review and Meta-analysis)** for consideration for publication in *Obstetrics & Gynecology*. Also submitted are the reviewer comments and our responses to each, below. We appreciated the reviewer's comments and the opportunity to revise our manuscript.

We confirm that the Agency of Healthcare Research and Quality (AHRQ) is currently holding the publication of the final report that is related to this manuscript (contract no. 290-2015-00009-I, PCORI Publication No. 2020-SR-03). While AHRQ has approved the assertion of copyright by the authors, AHRQ retains a license to display, reproduce, and distribute the data first produced under this task order according to the contract terms and the Federal Acquisition Regulations (FAR). We are grateful to the journal for considering an expedited review of this resubmission. If you are interested in co-publication with the AHRQ final report, we request a decision by March 12, 2021.

Sincerely,

Marian McDonagh

Reviewer Comments and Author Responses RE: Manuscript Number ONG-20-3300

Cervical Ripening in the Outpatient Setting: A Systematic Review and Meta-analysis

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AUTHOR RESPONSE: We have streamlined the discussion.

2. Consider tempering your conclusion in the abstract. It seems that with the available data, definitive statements about safety cannot be made.

AUTHOR RESPONSE: We agree that there are a number of limitations to the evidence for fetal/neonatal and maternal harms. We described these in the discussion and have edited the conclusion statement in the abstract to better reflect this.

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).

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REVIEWER COMMENTS:

Reviewer #1:

This is a systematic review evaluating types of cervical ripening (inpatient versus outpatient and one type versus another) in induction of labor for any indication on obstetrics practice. I appreciate the authors' contribution to the field and undertaking a challenging systematic review, and appreciate the editors giving me the change to evaluate this interesting manuscript.

Strengths:

* This is an extremely important systematic review…on a topic where increasing focus is being placed. Outpatient cervical ripening is becoming an important trend in obstetric practice, and this systematic review highlights important findings in that sphere. The amount of evidence/study on the topic is appropriate for systematic review, with a large number of high-quality studies and a large number of participants contributing to the evidence.
* The study adheres to guidelines for systematic review methodology and appropriate screening and study identification procedures.
* The authors do an excellent job reviewing the strength/validity of the studies and highlighting to what types of populations the results of this review apply.

AUTHOR RESPONSE: *Thank you for your comments on the review's strengths*

Limitations

* The study seems to lack a clear sense of focus. What is the main comparison that the authors sought to evaluate? Inpatient versus outpatient? Or what type of ripening is best if outpatient is done? Just doing a search for all forms of ripening is too broad, and does not make it clear to the reader what the overarching question of the review is.

AUTHOR RESPONSE: *We acknowledge this review was complex and thus required a broad and comprehensive literature search. The objective stated in the abstract is: "To assess the comparative*

effectiveness and potential harms of cervical ripening in the outpatient versus the inpatient setting or in the outpatient setting alone." Similarly, the final purpose statements at the end of the introduction state: "Therefore, we conducted a systematic review and meta-analysis comparing the effectiveness and potential harms of outpatient versus inpatient cervical ripening. We also compared the effectiveness and potential harms of different methods of outpatient cervical ripening." Thus, the purpose was indeed two-fold. We have attempted to clarify wording throughout the manuscript. The complete Key questions are articulated in the full AHRQ report.

* As there are a lot of things being compared here, there needs to be much clearer language around what is being compared to what when "no differences" are found. Particularly in the abstract, the way the sentences read makes it very hard to interpret.

AUTHOR RESPONSE: *We have attempted to clarify wording throughout the manuscript, and particularly in the abstract. Please see the track changes version for these revised sentences.*

* It appears that the authors "meta-analyzed" (Tables 2-3) anytime there were results, and this is misleading. There should only be meta-analysis done where 3 or more different studies made the same comparison (same two interventions being compared) on the same outcome. See comments below.

AUTHOR RESPONSE: *Meta-analysis was undertaken if at least two studies could be pooled, using a random effects profile likelihood model. While some suggest performing meta-analysis where three or more studies are available, pooling when there are two studies is considered acceptable and widely practiced for estimating effects when results are ~~expected to be~~ similar and studies are reasonably homogeneous. This also allows for visual representation of individual study data. Neither Cochrane Handbook (https://training.cochrane.org/handbook/current/chapter-10) or AHRQ methods guide (https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/methods-guide-quantitative-synthesis-update.pdf) recommends 3 studies as the cutoff for meta-analyses. We want to clarify that meta-analyzing two studies in itself does NOT violate any particular assumption, though we acknowledge that pooling a small number of studies will make it hard to adequately check model assumptions, which is true for either 2 or 3 studies. We acknowledge that results of pooling a small number of studies with small sample sizes should be interpreted with caution, and all meta-analyses, regardless of the number of studies may have limitations that need to be considered. Single studies, by definition, were not meta-analyzed, but have been included in forest plots where subgroup analyses were performed, and one of the groups contained only 1 study. Including these on the plots helps with visual representation of the results, but these single studies are also part of the overall combined estimate, and therefore belong on the plots. We note that the tables clearly indicate the number of studies pooled (i.e. meta-analyzed)*

Comments for authors by section:

Abstract

* Line 63-65: The first part of this sentence a bit unclear to the reader. Was there no difference in Cesarean between inpatient VERSUS outpatient dinoprostone, or dinoprostone (either inpatient or outpatient) was not different VERSUS single balloon catheters in regard to Cesarean. This sentence may need to be broken up and reworded so the reader can tell exactly what is being compared to what in

which Cesarean section was not different. As this is one of the main comparisons/outcomes of the review, this is key to keep clear.

AUTHOR RESPONSE: *Yes, we appreciate the difficulty in interpreting the comparisons as worded. As noted above, there were many comparisons, and summarizing for an abstract is a challenge. We have revised the wording for clarity - Please see the track changes for a comparison.*

* Line 70-73: It is very hard to tell from reading this sentence what was compared to what when "no differences" were found. For neonatal infection, for example, what was dinoprostone "not different" from? For birth trauma, what was single-balloon catheter not different from? This sentence is very difficult to understand.

AUTHOR RESPONSE: *Here, to, we can see the difficulty in interpreting the comparisons as worded and we have revised the wording for clarity - Please see the track changes for a comparison.*

Introduction

* Line 86: It would be key to briefly summarize here what the ARRIVE trial studied and what the key findings were. I agree it is important to mention here, but the reader that is not as familiar with the ARRIVE trial needs to hear a short summary.

AUTHOR RESPONSE: W*e agree that some readers may not be as familiar with the findings of the ARRIVE trial as other. Hence, we have added a very brief description of the findings, and moved the citation for ARRIVE to immediately following this description so that a reader can easily locate the study if they would like more information.*

* Line 101-104: These are two very large goals, and it might be key to emphasize which was the PRIMARY aim of the study. If comparing outpatient versus inpatient ripening is the primary aim of the review, then all emphasis and comparisons should emphasize that, and then secondarily compare different types of ripening. That would also help with clarity around what is being compared to what in results.

AUTHOR RESPONSE: *We can understand the desire to be able to focus the paper on only one comparison. In the context of a systematic review, there is often not a single primary question. In this case all questions were deemed equally important. To the nominator of the topic (ACOG). As such, we have put our efforts into being more clear on the comparisons being reported in the results section. Please see track changes in the manuscript for these edits.*

* The introduction should include slightly more information about past systematic reviews on this topic (not just the Cochrane), and why this review is necessary at this time.

AUTHOR RESPONSE: *While we screened several prior systematic reviews, we did not find other systematic reviews that cover the same questions as this review, those that were posed by ACOG. For example, we identified a 2018 review "Safety of the balloon catheter for cervical ripening in outpatient care: complications during the period from insertion to expulsion of a balloon catheter in the process of labour induction: a systematic review (Dierderen, BJOG)," which only included 2 RCTs with outpatient single balloon catheter use, but included 23 inpatient studies. Hence the findings of the review relate almost entirely to inpatient use of Foley catheters. Another review we identified was a 2017 non-*

systematic review "Outpatient induction of labour with prostaglandins: Safety, effectiveness and women's views. (Smith, British Journal of Midwifery) " Since this was a non-systematic review, we only screened the included studies list to insure we did not miss anything. The review included 11 studies (6 RCTs, all of which were "part of the OPRA trial", so not independent trials). Given both the limitations of these reviews, and the word-count restrictions, we have added only a mention of, and cite these reviews.

Sources

* Line 112: Define for the reader what "gray literature search" means. Not all readers will be familiar with this term. Also, gray literature is not all that is found in ClinicalTrials.gov (ClinicalTrials.gov includes literature from both traditional and non-traditional sources), so I am not sure if this is the best term to use here.

AUTHOR RESPONSE: *Thank you for this comment, "gray literature" is certainly a jargon term in systematic reviews, and its definition is not completely agreed upon. Also, the reviewer's point about some ClinicalTrials.gov entries not being truly unpublished, at least at some point in time, is also a helpful reminder. We have removed the term "gray literature" and simply stated that "ClinicalTrials.gov registry was searched in December 2020 for both completed and on-going studies." To avoid confusion and reduce word count.*

* Did you search for references that were not found within the citation lists of identified systematic reviews and studies on the topic? Be clear about how other relevant systematic reviews were utilized to identify primary papers.

AUTHOR RESPONSE: *The bibliographies of systematic reviews and of included studies were searched to identify potentially relevant articles for include. Our original statement of: "References of included studies and systematic reviews were searched to locate additional studies." To lessen confusion regarding inclusion of systematic reviews, we altered the sentence to: ". References of included studies and prior systematic reviews were searched to locate additional studies."*

Study Selection

* The PICOS ("population, intervention, comparator(s), outcomes, and study types") could be a bit clearer here, particularly in regard to whether or not the study was required to have an arm that included outpatient ripening? Or did any study that compared two types of ripening, regardless of inpatient/outpatient, get included? As it appears that the primary focus of the study is to compared inpatient to outpatient, that should have been the focus of the PICOS, with secondary plans to compare different types of ripening within inpatient or outpatient. The PICOS should clearly follow the focus of the study, and not be quite so broad.

AUTHOR RESPONSE: *Thank you for pointing out the lack of clarity in this sentence. As we noted above, there were two equal questions/parallel goals of the review:*

- *Evaluating the effectiveness and safety of outpatient versus outpatient cervical ripening and*
- *Comparing the effectiveness and safety of various CR methods against each other as applied in the outpatient setting only.*

To clarify the PICOTS, we have edited the sentence to: "To evaluate risks and benefits of outpatient cervical ripening, we included randomized controlled trials (RCTs) and observational (i.e., cohort) studies with concurrent controls that enrolled women ≥37 weeks gestation undergoing cervical ripening in the outpatient setting (any method available in the US), comparing either to an inpatient setting or another

method in the outpatient setting." We will also include the full PICOTS table, which reflects both of these goals, in the Supplemental Digital Material;

* Did you include all women with pregnancies in the "population" part of the PICOS? In other words, did you put any clinical parameters on what populations are appropriate for induction, or say that any study with any maternal or pregnancy characteristics that compared one type of ripening to another was appropriate for this review?

AUTHOR RESPONSE: *The population criteria was limited only to women at 37 or more weeks gestation. Otherwise, we did not limit the study inclusion criteria. We collected data on important maternal subgroups, such as parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational). Note that we are now including the full PCIOTS criteria in a table as a part of the supplementary materials.*

Results

* Grouping by outcomes rather than interventions gets quite messy and confusing for the reader. I highly suggest grouping the parts of the results by COMPARISON between two different interventions, so a subheading would be "inpatient versus outpatient dinoprostone" rather than "Cesarean section". That way, when clinicians are choosing between two available interventions and want to know what benefits/harms there are, they can go the comparisons that have evidence to support them rather than sorting through a large paragraph on "Cesarean section" that has many different comparisons embedded in the text.

AUTHOR RESPONSE: *We acknowledge that there may be multiple ways for reporting and organizing results and different readers may prefer different organizations. Cesarean delivery and harms were the primary outcomes for which there was sufficient evidence. Tables 2 and 3 provide detail for cesarean delivery and harms respectively by intervention/comparator pairs. For each outcome, results are organized first by the outpatient vs. inpatient comparison then for the comparison of cervical ripening method with each other in the outpatient setting in an effort to make best use of space. Table 4 has a listing of all intervention/comparator pairs and strength of evidence. Combined with the other tables, and figures, the reader may readily see which interventions may be associated (or not) which harms at a glance. Given the somewhat long list of intervention/comparator pairs, reorganizing the results by these pairs may substantially increase word count and may increase confusion.*

* Line 171-172: This is really a point about Methods, but I would recommend only performing meta-analysis when 3 or more studies make the same comparison on the same outcome. This is pretty standard practice in systematic review, as reporting the results of only one or two studies as "meta-analysis" violates some assumptions.

AUTHOR RESPONSE: *Meta-analysis was undertaken if at least two studies could be pooled, using a random effects profile likelihood model. While some suggest performing meta-analysis where three or more studies are available, pooling when there are two studies is considered acceptable and is widely practiced for estimating effects when results are expected to be similar and studies are reasonably homogeneous. This also allows for visual representation of individual study data. Neither the Cochrane Handbook (https://training.cochrane.org/handbook/current/chapter-10) or AHRQ methods guide (https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/methods-guide-quantitative-synthesis-update.pdf) recommends 3 studies as the cutoff for meta-analyses. We want to clarify that meta-analyzing two studies in itself does NOT violate any particular assumption, though we acknowledge that*

pooling a small number of studies will make it hard to adequately check model assumptions, which is true for either 2 or 3 studies. We also acknowledge that results of pooling a small number of studies with small sample sizes should be interpreted with caution, and that all meta-analyses, regardless of the number of studies may have limitations that need to be considered. Single studies, by definition, were not meta-analyzed but may have been included in forest plots to provide a visual representation of the results.

* Line 171-172: There is very limited reporting of meta-analysis in the results; I would like to see more OR and numbers from relevant meta-analysis where this is sufficient evidence highlighted in the text.

AUTHOR RESPONSE: *We attempted to make best use of allotted space and focus on reporting relevant analyses which were supported by the most evidence. These data are in the tables; we chose not to repeat the data in the text to stay within space limitations. Additional information on the meta-analyses, including additional figures, are available in the full AHRQ report.*

* Line 235-236: It would be helpful in this sentence to list what interventions had evidence around infection, so we know what interventions were being compared here and found "no difference". This sentence does not help the reader evaluate, when choosing between interventions, which ones have evidence of non-different infection rates. This also furthers my case for grouping by intervention in the results, rather than by outcome and saying "no difference was found", which does not help the reader.

AUTHOR RESPONSE: *This sentence has been edited to include what is being compared. The intention was for the reader to refer to Table 3 for specifics but we understand that it is more helpful to the reader to have this information up front in the text.*

* Line 246-247: This sentence does not make clear which intervention (outpatient or inpatient) was favored (better) for avoiding shoulder dystocia, only that there was a different that was moderate. In all statements of a different in results, the direction, or what intervention is better, should be crystal clear. The reader has to backtrack to line 221-222 to figure this out; having readers have to reference back to former text and figure stuff out is not ideal.

AUTHOR RESPONSE: *This sentence has been revised to indicate that the incidence was lower in the outpatient group than in the inpatient group.*

Discussion

* In the first paragraph here, I would like to see more discussion of the main, positive findings. For example, there is moderate effect regarding shoulder dystocia in outpatient versus inpatient ripening, and that is not mentioned adequately in the Discussion. The reader should leave the first paragraph of the Discussion with a very clear picture of what main positive findings were, other than "limited evidence".

AUTHOR RESPONSE: *We have made edits to the Discussion as the reviewer suggested. Please see the revised text.*

Reviewer #2:

I thank the authors for their efforts and interest, because systematic review takes a surprising amount of time and effort.

The authors conducted a systematic review and meta-analysis to assess the comparative effectiveness and potential adverse events of cervical ripening in the outpatient versus the inpatient setting or in the outpatient setting alone. The certainty of the evidence was generally low.

The study addresses an important topic to obstetric patients and providers.

I have several general and specific comments and suggestions.

General comments

A major challenge is assessing quality of the studies in a systematic review, which can strongly influence the findings of the review.

AUTHOR RESPONSE: We agree, no response appears to be needed.

Major strength of the study: Pre-induction cervical ripening is an important part of the labor induction process in women with an unfavorable cervix.

ACOG Practice Bulletin 107. Are cervical ripening methods appropriate in an outpatient setting?

Limited information is available on the safety of outpatient management of induction of labor.

AUTHOR RESPONSE: No response appears to be needed.

Major weaknesses: (a) Sources and Study Selection; (b) primary outcomes - confusing, because the perinatal and maternal adverse events were related to labor and delivery management rather than to pre-induction cervical ripening.

AUTHOR RESPONSE:

(a) I*t is not clear what concern is being raised about sources and study selection. We followed the AHRQ Methods Guide for performing systematic review.*

(b)*The review is only able to report on and analyze outcomes as reported in the included studies. During the process of review development, specific outcomes, their definitions, and their prioritization were discussed extensively with the sponsor (PCORI), ACOG, AHRQ, Key Informants and a Technical Expert Panel. The expert panel included physicians, midwives, nurses and patient advocates in addition to the perspectives of clinician team members. The full report was also peer reviewed and made available for public comment. Generally, though, the clinical experts felts that cervical ripening is the first step in labor induction management and can contribute to outcomes investigated. Moreover, clinically relevant outcomes specific to cervical ripening in itself have not yet been well-defined. Therefore, we felt it more important to focus on clinically relevant labor and birth outcomes, with the understanding that cervical ripening is the first step in these overall processes. We acknowledge that some outcomes may be surrogate for outcomes more directly related to the efficacy of ripening; for example, cervical ripening is important to achieve successful vaginal delivery, thus an equivalent cesarean delivery rate implies equivalent ripening efficacy in both groups.*

*1. Suggest separate analysis of:

(a) Include studies after 2009 only;

(b) Studies from United States (e.g., Ausbeck EB, et al. Obstet GYnecol 2020; 136:597)

(c) Studies from other developed countries. Hence, the results are generalizable or applicable to a particular target population!

AUTHOR RESPONSE: *The rationale and need for the suggested additional analyses are unclear. Doing them, we feel, would compromise the ability to draw meaningful conclusions across studies. Separate*

analysis for different populations may decrease generalizability and limit the available evidence to smaller studies (and/or poor-quality studies) and thus decrease confidence in the findings and limit ability to draw conclusions across studies.

(a) *We are not aware that there are substantial changes in understanding or practices related to cervical ripening after 2009. Further, limiting studies to those published after 2009 would substantially reduce the evidence base which in turn would limit meaningful conclusions that can be drawn across studies. This issue, of a temporal change in practice was discussed with our clinical expert panel during the development of the protocol.*

(b and c). Across key questions, 60% of the included studies were done in the U.S. (Table below). For Key Question 3, 82% of studies (and 18/22 RCTs) were performed in the U.S. Nearly all included RCTs were conducted in developed countries. Restricting studies to those performed in the United States would eliminate a large number of RCTs which may be applicable. We are not aware of any data or rationale to suggest that the physiologic process of cervical ripening would differ by nation such that it would influence women's responses, or the primary outcomes reported in this review. Practically, practice patterns and extreme variability regarding cervical ripening exists even within the US. Thus, separate analyses would likely not add insight into our findings. These issues were also discussed with our expert panel a priori, and not deemed to rise to the level of separate analysis. The AHRQ report had both peer review and a public comment period, neither of which raised these issues.

We note that the Ausbeck study was published after our search, and that adding it would not reflect a systematic process. The results of this manuscript, not including this study, are consistent with the full AHRQ report, which is being used by ACOG's guideline committee. We have added a short description of the study's findings – that they are consistent with our findings - in the discussion.

	KQ 1 RCTs	KQ 1 Cohort Studies	KQ 2 RCTs	KQ 2 Cohort Studies	KQ 3 RCTs	KQ 3 Cohort Studies
Number of studies	2	6	6	3	22	1
# Conducted in United States	0	2	2	2	18	0

*Risk of adverse events during the period between insertion and expulsion of a balloon catheter in cervical ripening to be low. These data facilitate further evaluation and implementation of this procedure in an outpatient setting for low-risk pregnancies. limited by small sample size but suggest longer time to delivery compared with Foley and misoprostol or oxytocin.

AUTHOR RESPONSE *No response appears to be needed.*

Specific comments and suggestions by page(s) and line(s):

*INTRODUCTION

2. Page 4 lines 85-104. Expand background with addition of the following:

Ausbeck EB, et al. Outpatient Foley Catheter for Induction of Labor in Nulliparous Women: A Randomized Controlled Trial. Obstet Gynecol 2020; 136:597.

AUTHOR RESPONSE: *Thank you for pointing this study out. We have added a brief mention of it to the Discussion section. Word limits and lack of a systematic search for other new studies did not allow a more in-depth discussion of this study.*

*METHODS

3. Pages 4-5, lines 108-147. (See general comments above).

AUTHOR RESPONSE: *Please see responses above*

*DISCUSSION

4. Pages 11-16, lines 249-383. Too long and suggest focused analysis.

Suggest restructuring to:

Statement of main findings
Strengths and limitations
Implications for clinical practice

AUTHOR RESPONSE: *We have edited and streamlined the discussion as per the reviewer's suggestions.*

*REFERENCES

5. Check for accuracy, relevance, current, and format for Green Journal

Tables 3 and 4

AUTHOR RESPONSE: *Thank you, we have checked formatting and updated any areas that did not meet the journal's requirements.*

6. Pages 23-24. Labor and delivery management outcomes rather than pre-induction cervical ripening related outcomes.

AUTHOR RESPONSE: *We note that this comment is also noted above; please also see our full response above. In brief, our view is that cervical ripening is the first step in labor induction management and can contribute to outcomes investigated. Moreover, clinically relevant outcomes specific to cervical ripening in itself have not yet been well-defined. Therefore, we felt it more important to focus on clinically relevant labor and birth outcomes, with the understanding that cervical ripening is the first step in these overall processes. We acknowledge that some outcomes may be surrogate for outcomes more directly related to the efficacy of ripening; for example, cervical ripening is important to achieve successful vaginal delivery, thus an equivalent cesarean delivery rate implies equivalent ripening efficacy in both groups*.

Reviewer #3: lines 194-195: There is no Figure 3 attached.

AUTHOR RESPONSE: *These figures appear to be included in our version but may not have been uploaded to site. When we re-submit will verify that all figures were uploaded as separate files.*

*Table 3: Most adverse outcomes had low incidence. Those proportions, in relation to the total sample sizes of the pooled studies, result in low power to discern a difference. This can be inferred from the

wide CIs of the RRs. For example, for uterine infection, comparing prostaglandins vs placebo, 7% vs 10% among N = 771: the RR would have to be > 1.8 or < 0.38 to fulfill 80% power and the usual p < .05 threshold. In other words, the NS finding cannot be generalized from these data. The sample sizes and incidence rates make the math even worse for the other comparisons.

AUTHOR RESPONSE: *We are very much in agreement with this comment. The assessment of the strength of the evidence for each outcome/intervention pair reflects consideration of this as part of precision of the estimate. That is why the evidence is low strength at best, but often insufficient. We have numerous notes throughout the manuscript and discussion regarding sample size concerns and limitations of the data. We have also edited the conclusion statement in the abstract to better reflect the problem of this issue (inadequate sample size/power).*

*Figures: Should include funnel plots, which could be on-line material.

AUTHOR RESPONSE: *Funnel plots were created if there were sufficient numbers of studies to do so, based on AHRQ and Cochrane guidance, and due to inadequate numbers of studies, we were unable to conduct publication bias assessments for most outcomes. Only one of the meta-analyses for which we included forest plots met the criteria for creating a funnel plot. That plot is now included in the supplemental materials.*

*Figures: Should omit the test for I^2 and conclusions re: heterogeneity when there are only 1 or 2 studies being pooled.
And in the case of 1 study, the subgroup simply recapitulates the single study, so that "pooling" is redundant and should be omitted. Rather, simply show the single study with its CI.
Need to show a column of the weights within each subset and separate column of weights for the overall pooling.

AUTHOR RESPONSE: *We have edited the 2 figures that had a subgroup with only 1 study to eliminate reference to heterogeneity estimates, and removed the diamond that would show the pooled estimate. As the reviewer is most likely aware, the weights are indicated by the size of the point estimate square on the plots. This gives the readers a visual idea about the weights of each study. Visual presentation is more interpretable for many readers, saves space to make the plot less busy, and leaves space to show important study characteristics.*

EDITOR COMMENTS:

We understand that there is a desire to publish the full report of this systematic review and meta-analysis through AHRQ along with the submitted abbreviated report. The editors are interested in this possibility if your manuscript is ultimately accepted for publication. However, we anticipate that the proposed timeline for publishing will need to be pushed back to allow time for the authors to respond to the reviewers' and editors' comments.

AUTHOR RESPONSE: *We have confirmed with AHRQ that they are still interested in "co-publishing", and are holding their publication while the journal considers our resubmission.*

1. Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, please avoid simply restating the results in the Discussion section. The Discussion should be about 750 words, and should follow the format described in the Instructions for Authors.

AUTHOR RESPONSE: *Thank you, we have revised the Discussion section to better fit both the word limit and the outline for this journal. Please see the revised Discussion.*

2. Consider tempering your conclusion in the abstract. It seems that with the available data, definitive statements about safety cannot be made.

AUTHOR RESPONSE: *We agree that there are a number of limitations to the evidence for fetal/neonatal and maternal harms. We have edited the conclusion of the abstract to better reflect the nuances of this evidence.*

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 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.

AUTHOR RESPONSE: *Opt-In*

2. 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.

AUTHOR RESPONSE: *Thank you, we will do this.*

3. If your study is based on data obtained from the National Center for Health Statistics, please review the Data Use Agreement (DUA) for Vital Statistics Data Files that you or one of your coauthors signed. If your manuscript is accepted for publication and it is subsequently found to have violated any of the terms of the DUA, the journal will retract your article. The National Center for Health Statistics may also terminate your access to any future vital statistics data.

AUTHOR RESPONSE: *We confirm that this is not applicable to our manuscript.*

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.

AUTHOR RESPONSE: *If included studies provided information on race, ethnicity or both, the data were abstracted. The classification is as reported by the studies; the systematic review team did not alter any classifications*.

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.

AUTHOR RESPONSE: *We have checked and made the appropriate changes to capitalization. As above, the classification is as reported by the studies; the systematic review team did not alter any classifications.*

5. Standard obstetrics 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.

AUTHOR RESPONSE*: We are aware of these definitions, and discussed these with our Technical Expert panel, and clinician experts on our team, and our outcome categories and definitions reflect these definitions as much as possible – in some cases, we had to report outcomes as defined in the included studies.*

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Review articles should not exceed 25 typed, double-spaced pages (6,250 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.

AUTHOR RESPONSE: *We note that the description above includes references in the 25-page count, but then excludes them. We are assuming that the pages of references (bibliography) are not included. With this assumption, we have ensured that our submission meets these requirements.*

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).

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

8. 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.

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and Instruments is 200 words. Please provide a word count.

AUTHOR RESPONSE: *We have ensured that the abstract is 300 words. Please note that some of the requested additional explanations requested by reviewers cannot be accommodated in this word count. We have done our best to reframe and summarize.*

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

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

10. 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.

AUTHOR RESPONSE: *We have removed all use of the "/" symbol in the text.*

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.

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

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%").

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

13. 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.

AUTHOR RESPONSE: *We have ensured that our tables meet these requirements.*

14. 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.

In addition, 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).

AUTHOR RESPONSE: *We have ensured that our submission meets these requirements.*

15. Figures 1-4: Please upload as figure files on Editorial Manager.

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

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AUTHOR RESPONSE: *Thank you, we will.* ***

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Statement of Transparency:

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.
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