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: Jan 08, 2021
To: "Alison D Gernand" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-3165

RE: Manuscript Number ONG-20-3165

Chorioamnionitis and Risk for Maternal and Neonatal Sepsis: A Systematic Review and Meta-analysis

Dear Dr. Gernand:

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 Jan 29, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Overall, this is a well-written systematic review and meta-analysis of maternal and neonatal sepsis in relation to chorioamnionitis. The study is clinically relevant and follows appropriate methods for the most part, but there are some limitations as listed below:

Major comments:
1) While it is appropriate to report Odds Ratios, clinicians do not normally think in terms of ORs but in terms of potential risk/probability of sepsis (Eg. a 1 in 100 risk or 1 in 10 risk). While it is useful to know that OR is 3-6, it is very different if the baseline rate is 1 in a 1000 (the difference in exposed group will still be <1%) versus 1 in 10 (much higher risk). In addition to providing the ORs, it would be useful to also provide the overall unadjusted incidence rates of early onset sepsis etc with exposure to chorio vs. no chorio etc to get an idea of the absolute risk.
2) Studies were not included in meta-analyses if no sepsis events were reported in both the exposed and non-exposed groups. Why is this? Given that sepsis is a low-frequency event, it is highly likely that many studies with lower sample sizes may not have any episodes of sepsis. Selecting only studies with sepsis events will cause a selection bias towards studies with higher rates of outcome. This is especially important as the data that is currently shown (e.g. Figure 2) indicates a very high risk of EONS even in infants without HCA (as high as 12 in 168 or 13 in 236, which is >5%, while most population studies indicate the risk of EONS is <2 per 1000 live births, and only about 2 per 100 live births even in extremely preterm infants.
3) As most of the studies involved preterm infants, and few term infants were included, given that term infants are less likely to develop sepsis compared to preterm infants, it is not clear how well the data can be extrapolated to term infants. This is mentioned in the Discussion and Analysis but should be emphasized.

Minor comments:
1) Abstract: It is not clear what is meant by "Studies were included in meta-analysis if >=3 studies had a shared exposure of....."
2) Abstract: Multiple locations: Odds Ratios (ORs) are abbreviated as OR's....this is incorrect as it is the plural (Odds Ratios), not possessive (not belonging to the Odds Ratio)
3) Introduction: Line 72: suggest changing "following delivery" to "after birth"
4) Many references have typos: eg. Ref 56 (Author's name truncated), 81, 93

Reviewer #2:

This manuscript is a systematic review and meta-analysis to estimate the risk of
Maternal and neonatal sepsis associated with chorioamnionitis. The authors screened 1,251 studies from three data bases (Pub Med, BIOSIS, and clinicaltrials.gov) that quantified the association between chorioamnionitis with maternal and neonatal sepsis. Studies were included in meta-analyses if ≥3 studies had a Shared exposure of histological or clinical chorioamnionitis, and a shared outcome of maternal or neonatal sepsis. They found that Histological and clinical chorioamnionitis were strongly associated with increased risk of maternal and early neonatal sepsis. There was weak association with between chorioamnionitis and preterm infants with late onset sepsis. They concluded that the findings support current guidelines for preventative neonatal care, and plead that future research on chorioamnionitis and maternal sepsis is needed.

General Comments

Chorioamnionitis as a risk factor for infection in the mothers and infants is well known to obstetric and neonatal clinicians. They often use this risk factor in clinical management and decision. This practice evolved over time with multiple publications that provide the evidence for the clinical practice. The authors are correct in stating that except for one report (listed as reference #17), a systematic review and meta-analysis of the association has not been done in the past. The current report is an attempt to provide this gap of knowledge. The authors followed the usual methodology in performing the review and analysis. The outcome is not surprising and add credence to the current guidelines in managing mothers and infants with clinical or histological chorioamnionitis. The manuscript is very long and needs some editing to shorten and save editorial space. There are also some issues listed in the comments below that needs attention.

Specific Comments
Abstract
Objective: Should revise to state what the objective of the study is and not stating what is being done
Results: There should be a sentence emphasizing the fact the odds ratio and relative risk are all unadjusted which is a significant weakness of the data.
Conclusion: The reference to strong and weak association is based on the values of the odds ratio. The authors might simply state that there is significant statistical association between chorioamnionitis and maternal as well as neonatal sepsis and leave the interpretation of strong and weak association for the readers to make.
Introduction: Well written, no comments
Methods: Page 10-Lines 173-188 This description is for neonatal sepsis. How about maternal sepsis, how was it defined in the studies
Results: Figure 1: Please bullet list the reasons for the exclusion of 905 studies.
Page 14: Please indicate that the appendices are published on line (I assume this is the case) Also, there is no need to list all the countries that published the studies. The description of the contents of the appendices can also be shorten and save some editorial space. There are similar problems with the presentation of study results. The forest graphs (figure 2-6) very clearly show the data. The authors may want to try shorten the description of each figure for ease of reading and save editorial space.
Comments: Well done. no comment

Reviewer #3:

Beck and colleagues present a systematic review and meta-analysis evaluating association between chorioamnionitis, antibiotics, and early and late neonatal sepsis. I have the following comments for the authors.

1 - The methodology is clearly described.

2 - The work is well done and the results appreciated. The issue of overtreatment of neonates after birth is one of concern.

STATISTICS EDITOR COMMENTS:

Abstract: Should include estimates of actual rates of neonatal rates of sepsis, in addition to the increase in odds. This will give the reader a better appreciation of the clinical magnitude of the problem in absolute terms.

Fig 2: The last column (weight %) refers to the overall OR, need to also include the weights in a separate column for the subsets (confirmed vs suspected cases). Also, the studies by Cakir and Wang appear to have the same total number of entries, merely reclassified as to whether confirmed or presumed. Those are being counted twice and should be eliminated from either one or the other of the groups, when aggregating for the overall ORs.

Figs 3, 4: Same issue with the weights% column.

Need to include funnel plots with the forest plots, which could be in on-line supplemental material.

EDITOR COMMENTS:

1. Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, the editors would like you to add information about maternal treatment of chorioamnionitis (at least to the Discussion). Currently, the Discussion is very focused on neonatal treatment, but most of our readers are obstetricians (not neonatologists or pediatricians) and will want to know how your findings affect their practices.
2. Please ensure that the revision meets journal specifications with an abstract that is 300 words or less and a manuscript that is 6250 words or less (approx. 25 pages) to meet journal specifications. This will require a substantial reduction in length.
3. Rather than consolidating histologic and clinical chorioamnionitis into a group, we suggest that they are presented separately in the manuscript and the abstract.
4. In your abstract, it is unclear what you mean by “shared” when describing exposures and outcomes. Do you mean “either”? Please clarify.

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 applicable: In order for an administrative database study to be considered for publication in Obstetrics & Gynecology, the database used must be shown to be reliable and validated. In your response, please tell us who entered the data and how the accuracy of the database was validated. This same information should be included in the Materials and Methods section of the manuscript.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Methods section of the body text, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

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 Reviews is 300 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. 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%").

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

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.

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).

14. Figures 1-6: 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.

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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.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded 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 Jan 29, 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

_____

[redacted]

Torri Metz, MD
Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

January 29, 2021

Dear Dr. Metz:

Thank you for the review of our original manuscript and the opportunity to submit a revision. On behalf of my co-authors, I am pleased to share our revised paper, “Chorioamnionitis and Risk for Maternal and Neonatal Sepsis: A Systematic Review and Meta-analysis”, for further consideration in *Obstetrics & Gynecology*.

We greatly appreciate the detailed comments from the expert referees and editorial board. We have carefully reviewed and addressed all feedback. Please find below our point-by-point response to each of the reviewer, statistician, and editor comments received. Line numbers refer to lines when all markup is viewed inline in the Word document.

Reviewer #1:
Overall, this is a well-written systematic review and meta-analysis of maternal and neonatal sepsis in relation to chorioamnionitis. The study is clinically relevant and follows appropriate methods for the most part, but there are some limitations as listed below:

Major comments:
1) While it is appropriate to report Odds Ratios, clinicians do not normally think in terms of ORs but in terms of potential risk/probability of sepsis (Eg. a 1 in 100 risk or 1 in 10 risk). While it is useful to know that OR is 3-6, it is very different if the baseline rate is 1 in a 1000 (the difference in exposed group will still be <1%) versus 1 in 10 (much higher risk). In addition to providing the ORs, it would be useful to also provide the overall unadjusted incidence rates of early onset sepsis etc with exposure to chorio vs. no chorio etc to get an idea of the absolute risk.

Response: The reviewer makes an excellent point. We agree with the importance of evaluating the absolute risk for clinical relevance. To address this issue, we calculated overall unadjusted incidence rates for each exposure and outcome. The following sections of the manuscript were updated:

- Abstract: A statement was added that absolute risk was higher among preterm infants (see line 51). Incidence varied among the various exposures and outcomes reported in the manuscript, and due to space limitations within the abstract, we could not include further details here.
- Methods: We added a statement in the statistical analysis section to explain that random effects methods were used to generate pooled incidence rates for each exposure and outcome (line 194).
- Results: Incidence rates were added for each exposure and outcome within the results text to describe absolute risk (lines 307-312, 354-357, 384-387, 407-409, 431-433).

2) Studies were not included in meta-analyses if no sepsis events were reported in both the exposed and non-exposed groups. Why is this? Given that sepsis is a low-frequency event, it is highly likely that many studies with lower sample sizes may not have any episodes of sepsis. Selecting only studies with sepsis events will cause a selection bias towards studies with higher rates of outcome. This is especially important as the data that is currently shown (e.g. Figure 2) indicates a very high risk of EONS even in infants without HCA (as high as 12 in 168 or 13 in 236, which is >5%, while most population studies indicate the risk of EONS is <2 per 1000 live births, and only about 2 per 100 live births even in extremely preterm infants.

Response: The reviewer shared concerns regarding potential for selection bias and our decision to exclude studies with zero events in exposed and non-exposed groups. Each are discussed below.
Concern about number of studies excluded: The reviewer shared the concern that many studies may report zero events in both groups, leading to potential bias in selection of studies. Surprisingly, we only came across two studies that would have otherwise met criteria for inclusion in meta-analyses, but which reported zero events. One study, by Mu et al., reported events of late-onset neonatal sepsis (that were included in the meta-analysis for late-onset sepsis), but reported no events of early-onset neonatal sepsis as confirmed by blood culture in either group. Ykema et al. reported cases of presumed early-onset neonatal sepsis (included in our meta-analysis), but no events of early-onset neonatal sepsis as confirmed by blood culture in both the exposed and non-exposed groups. Both studies were in relation to histological chorioamnionitis.
Reason for exclusion of non-event studies: We chose to exclude studies with zero events in accordance with best practice guidelines for meta-analyses of odds ratios, as outlined in the Cochrane handbook for conducting systematic reviews and meta-analyses (Deeks, Jonathan J., et al. "Analysing data and undertaking meta-analyses." *Cochrane handbook for systematic reviews of interventions* (2019): 241-284.). Deeks et al. point out that when odds ratios are the effect measure being used for meta-analyses, that studies with no events in both groups provide no indication of either the direction or magnitude of the relative effect between groups. The handbook also gives direction pertaining to studies with rare events such as our study of sepsis, stating that while it may be clear that events are very rare in both groups (when zero events are reported in both groups), “no information is provided as to which group is likely to have a higher risk, or on whether the risks are of the same or different orders of magnitude.” Thus, it is recommended that studies not providing this information not be included in meta-analyses of odds ratios. We added a statement on line 123 that this exclusion criterion was used in accordance with best practice guidelines (with appropriate reference to the Cochrane handbook).

3) As most of the studies involved preterm infants, and few term infants were included, given that term infants are less likely to develop sepsis compared to preterm infants, it is not clear how well the data can be extrapolated to term infants. This is mentioned in the Discussion and Analysis but should be emphasized.

Response: We thank the reviewer for pointing out the importance of extrapolating results to infant groups across different gestational ages at birth. We agree that this is an important distinction. In response, we added statements throughout our manuscript to emphasize in our findings that incidence rates of sepsis were much lower for late preterm and term infants when compared to rates reported in preterm only infant studies. Please see statements added to the following locations: lines 307-312, 354-357, 384-387.

Minor comments:
1) Abstract: It is not clear what is meant by "Studies were included in meta-analysis if >=3 studies had a shared exposure of....."

Response: This statement was modified in the abstract to say: “Studies were grouped for meta-analyses according to exposures of histological or clinical chorioamnionitis and outcomes of maternal or neonatal sepsis.” See lines 34-36.

2) Abstract: Multiple locations: Odds Ratios (ORs) are abbreviated as OR's....this is incorrect as it is the plural (Odds Ratios), not possessive (not belonging to the Odds Ratio)

Response: Thank you for bringing this inadvertent error to our attention. “OR’s” were changed to “ORs” on lines 46, 48, 50.

3) Introduction: Line 72: suggest changing "following delivery" to "after birth"

Response: The recommended change was made (now lines 77 and 78 in revised document).

4) Many references have typos: eg. Ref 56 (Author's name truncated), 81, 93

Response: Thank you for bringing this to our attention. We have carefully checked the references and corrected any typographical errors.

Reviewer #2:

This manuscript is a systematic review and meta-analysis to estimate the risk of maternal and neonatal sepsis associated with chorioamnionitis. The authors screened 1,251 studies from three data bases (PubMed, BIOSIS, and clinicaltrials.gov) that quantified the association between chorioamnionitis with maternal and neonatal sepsis. Studies were included in meta-analyses if ≥3 studies had a shared exposure of histological or clinical chorioamnionitis, and a shared outcome of maternal or neonatal sepsis. They found that histological and clinical chorioamnionitis were strongly associated with increased risk of maternal and early neonatal sepsis. There was weak association with between chorioamnionitis and preterm infants with late onset sepsis. They concluded that the findings support current guidelines for preventative neonatal care, and plead that future research on chorioamnionitis and maternal sepsis is needed.

General Comments

Chorioamnionitis as a risk factor for infection in the mothers and infants is well known to obstetric and neonatal clinicians. They often use this risk factor in clinical management and decision. This practice evolved over time with multiple publications that provide the evidence for the clinical practice. The authors are correct in stating that except for one report (listed as reference #17), a systematic review and meta-analysis of the association has not been done in the past. The current report is an attempt to provide this gap of knowledge. The authors followed the usual methodology in performing the review and analysis. The outcome is not surprising and add credence to the current guidelines in managing mothers and infants with clinical or histological chorioamnionitis. The manuscript is very long and needs

some editing to shorten and save editorial space. There are also some issues listed in the comments below that needs attention.

Response: We have taken the reviewer's suggestion to shorten the manuscript. Within the results section of the manuscript, we have shortened descriptions pertaining to supplemental tables. Other specific comments are addressed individually below.

Specific Comments

Abstract
Objective: Should revise to state what the objective of the study is and not stating what is being done

Response: We thank the reviewer for this comment. The objective statement has been revised to state that our objective is to estimate the risk of maternal and neonatal sepsis associated with chorioamnionitis.

Results: There should be a sentence emphasizing the fact the odds ratio and relative risk are all unadjusted which is a significant weakness of the data.

Response: We thank this reviewer for the comment, as we agree that adjusted estimates are highly preferred over unadjusted estimates, particularly in observational research of this nature when confounding is expected to be present. In the abstract, we would point the reviewer to lines 45 and 48, which state that the odds ratios are unadjusted. We also added that "most studies only reported unadjusted results". Due to the word limitation on the abstract, discussion that unadjusted odds ratios are a weakness is included in the main text of the paper. In the "Strengths and Limitations" section of the manuscript, we state that one of the main limitations of our study is that the majority of studies only provided unadjusted odds ratios (see lines 544-545). We did summarize and report adjusted ORs when available in the main body of the paper.

Conclusion: The reference to strong and weak association is based on the values of the odds ratio. The authors might simply state that there is significant statistical association between chorioamnionitis and maternal as well as neonatal sepsis and leave the interpretation of strong and weak association for the readers to make.

Response: We thank the reviewer for this comment. References to "strong" and "weak" have been removed from the abstract and also the précis.

Introduction: Well written, no comments

Response: We appreciate the reviewer's feedback.

Methods: Page 10-Lines 173-188 This description is for neonatal sepsis. How about maternal sepsis, how was it defined in the studies

Response: Thank you for this point of clarification. On line 172, we added to the first statement to

specify that confirmed versus presumed sepsis definitions were applied to both maternal and neonatal sepsis. We added an additional statement that maternal sepsis was defined as occurring postpartum (lines 181-182).

Results: Figure 1: Please bullet list the reasons for the exclusion of 905 studies.

Response: While we kept close records of each study excluded at every stage, we did not record individual reasons for each study that was excluded at the title and abstract review stage. This was done according to standard practice for the selection process within a systematic review. To clarify that the 905 records were excluded at the title and abstract phase, we added language to indicate this to the box in Figure 1.

Page 14: Please indicate that the appendices are published on line (I assume this is the case) Also, there is no need to list all the countries that published the studies. The description of the contents of the appendices can also be shorten and save some editorial space. There are similar problems with the presentation of study results. The forest graphs (figure 2-6) very clearly show the data. The authors may want to try shorten the description of each figure for ease of reading and save editorial space.

Response: We thank the reviewer for the recommendations to shorten the manuscript to save editorial space. Several revisions have been made, in line with the reviewer's comments. In particular, we shortened descriptions of contents of forest plots, as well as supplemental tables. All of the countries are no longer listed individually when describing study characteristics. To address the concern of pointing the reader to the location of appendices, where each appendix is referred to within the manuscript, the following statement has been added: "available online as supplemental digital content".

Comments: Well done. no comment

Response: We thank the reviewer for this feedback.

Reviewer #3:

Beck and colleagues present a systematic review and meta-analysis evaluating association between chorioamnionitis, antibiotics, and early and late neonatal sepsis. I have the following comments for the authors.

1 - The methodology is clearly described.

2 - The work is well done and the results appreciated. The issue of overtreatment of neonates after birth is one of concern.

Response: We thank this reviewer for the positive comments and feedback.

STATISTICS EDITOR COMMENTS:

Abstract: Should include estimates of actual rates of neonatal rates of sepsis, in addition to the increase

in odds. This will give the reader a better appreciation of the clinical magnitude of the problem in absolute terms.

Response: Thank you for this recommendation, as we agree that inclusion of actual rates will help the reader to appreciate the clinical magnitude of our findings. Reviewer 1 made a similar comment and we refer to our response above.

Fig 2: The last column (weight %) refers to the overall OR, need to also include the weights in a separate column for the subsets (confirmed vs suspected cases). Also, the studies by Cakir and Wang appear to have the same total number of entries, merely reclassified as to whether confirmed or presumed. Those are being counted twice and should be eliminated from either one or the other of the groups, when aggregating for the overall ORs.

Response: We thank the reviewer for these recommendations regarding display of weights and the double counting of entries. The studies by Cakir and Wang, as previously displayed as presumed cases, represent a composite of both confirmed and clinically suspected cases, which is why some of the cases (those that were confirmed) are currently presented twice (in meta-analyses of confirmed and presumed cases). The composite of confirmed and clinically suspected cases was used for the studies by Cakir and Wang in order to be uniform in definition with the majority of studies in the "presumed" group in our systematic review, which used a composite definition of confirmed and presumed cases as the neonatal sepsis outcome. Only three studies (Jones et al., Martius et al., and Ykema et al.) reported cases of presumed sepsis separately (rather than a composite category of any presumed and/or confirmed). However, from authors' descriptions, it appears that the outcome represents a larger pool of infants with clinical signs and symptoms, from which any confirmed cases would be a subgroup. Upon review of this issue, we are clarifying our methods section, graph titles, graph footnotes, and results where applicable to clarify that the majority of cases in the "presumed" category actually represent a composite of all confirmed or clinically suspected cases.

To avoid double counting into one overall pooled odds ratio, we modified Figure 2 so that an overall pooled odds ratio is not shown. Pooled odds ratios are now shown separately for confirmed cases and for composite presumed and/or confirmed cases, now displayed as "Any sepsis" within the graph. Studies that used composite versus all presumed cases are now clearly indicated within the graph with appropriate footnotes to enhance clarity for the reader. As the reviewer recommended weights are now displayed as adding up to 100% for each subgroup.

Revisions were made in the following locations: Figure 2 graph and legend, Figure 4 title and legend, methods section line 176, abstract lines 36, 45, and 47 to indicate any early-onset sepsis rather than merely presumed cases, and to results sections describing Figures 2 and 4. Funnel plot subheadings to reflect the composite outcome of any confirmed or presumed sepsis cases (Appendix 10, as supplemental digital materials) were also updated appropriately.

Figs 3, 4: Same issue with the weights% column.

Response: While we agree that the addition of a subgroup weight column would add to the current display, the Stata 16 statistical package allows for graphical display of either within subgroup weights *or* contributions to the total weight in a graph (but not both). We feel it is most appropriate to include contributions of the weights to the overall pooled odds ratio, as we are displaying contributions of each study to the overall pooled odds ratio which is the main research question. If further requested, we can include additional graphs as supplemental digital materials showing contributions to the subgroups.

Need to include funnel plots with the forest plots, which could be in on-line supplemental material.

Response: Funnel plots were previously included as supplemental digital materials for histological chorioamnionitis and clinical chorioamnionitis and outcomes of early-onset neonatal sepsis. In line with the reviewer's recommendation, we have added funnel plots for the outcome of late-onset neonatal sepsis. Updated funnel plots are displayed in our resubmission of Appendix 10, which is referenced in the publication bias section of the paper (see line 504). Within that figure, funnel plots are now presented for each forest plot displayed within the results section of the manuscript.

EDITOR COMMENTS:

1. Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, the editors would like you to add information about maternal treatment of chorioamnionitis (at least to the Discussion). Currently, the Discussion is very focused on neonatal treatment, but most of our readers are obstetricians (not neonatologists or pediatricians) and will want to know how your findings affect their practices.

Response: Thank you for this feedback, as we also appreciate the importance of clinical application regarding obstetrical care. When we planned this analysis, we did not know there would be so few publications on maternal sepsis. We wholeheartedly agree that maternal treatment should be included and we have added statements to address maternal clinical treatment to the discussion section of the manuscript (lines 582-590).

2. Please ensure that the revision meets journal specifications with an abstract that is 300 words or less and a manuscript that is 6250 words or less (approx. 25 pages) to meet journal specifications. This will require a substantial reduction in length.

Response: Thank you for pointing out the need to reduce the length of the manuscript. The manuscript has now been reduced to meet the specified guidelines, particularly by reducing the text describing the supplemental material.

3. Rather than consolidating histologic and clinical chorioamnionitis into a group, we suggest that they are presented separately in the manuscript and the abstract.

Response: The abstract has been revised to present findings separately for histological and clinical chorioamnionitis (see revisions to lines 44-49, specifically). Within the manuscript, forest plots, associated odds ratios, and main findings are presented separately for histological and clinical chorioamnionitis.

4. In your abstract, it is unclear what you mean by "shared" when describing exposures and outcomes. Do you mean "either"? Please clarify.

Response: The statement on abstract lines 34-36 was revised for clarification to now say "Studies were grouped for meta-analyses according to exposures of histological or clinical chorioamnionitis and outcomes of maternal or neonatal sepsis." This is meant to convey that studies were grouped for meta-analyses according to whether they reported the same exposures and outcomes.

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:

Response: OPT-IN: Yes, please 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.

Response: We confirmed disclosures prior to submission.

3. If applicable: In order for an administrative database study to be considered for publication in Obstetrics & Gynecology, the database used must be shown to be reliable and validated. In your response, please tell us who entered the data and how the accuracy of the database was validated. This same information should be included in the Materials and Methods section of the manuscript.

Response: Authors CB, KG, and LT manually extracted data from the included studies and entered the extracted data in an Excel spreadsheet, which had been preformatted by CB with headings for each piece of data that would be extracted (each author extracted data from 1/3 of the included studies). Following data entry into the Excel spreadsheet, a second author validated data entered by manually referencing each article and checking for accuracy of data entered for each study. Specifically, author CB verified accuracy of data entered by authors KG and LT, and author LT verified accuracy of data entered by author CB. Details are included on lines 125-135 in the “Data extraction” section of the methods.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Methods section of the body text, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

Response: Our review has been determined by the Pennsylvania State IRB office to be non-human subjects research and to thus meet requirements for IRB exemption. The link to the website outlining criteria for exemption is https://www.research.psu.edu/irb/step1. A letter has also been provided to us by the IRB, which has been uploaded with our revision. A statement was added to the methods section of our manuscript to indicate that our study was exempt from IRB approval by the Pennsylvania State University IRB office (lines 97-98).

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://nam10.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-obstetrics-data-definitions&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329615169%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=ytEW%2FxRnaiE%2FptS7hFSq7vWB%2FybIKAug1R1yfdMQiEY%3D&reserved=0 and the gynecology data definitions at https://nam10.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-gynecology-data-definitions&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329615169%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=onhbY3psOLMM9LHcVkxyIF8D9L1c5BftsJHVVBMlJU8%3D&reserved=0. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response: Thank you for the link to these definitions. We have reviewed the definitions, which are consistent with those used in our study and described within our manuscript.

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.

Response: Our manuscript has been shortened to meet the specified guidelines.

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.
Response: An additional statement was added to indicate funding received from the NIH National Institute of Allergy and Infectious Diseases Award Number K23 AI139337 (title page, lines 11-15). All funding sources are listed.

* 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.
Response: We did not pay for any manuscript preparation assistance.

* 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.
Response: All persons who contributed to the work reported in the manuscript have been acknowledged in accordance with these guidelines (see lines 17-20). Written permission was obtained from each person acknowledged in the manuscript.

* 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).
Response: Findings reported in this manuscript have not been previously presented at an organizational 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 Reviews is 300 words. Please provide a word count.

Response: We have carefully reviewed our revised abstract. It is 298 words and is consistent in content with findings reported in the manuscript.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://nam10.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fabbreviations.pdf&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329615169%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=%2BcSYH9TxTagDSkozpWz%2FGWNEoiYSzkx9o9hfUwAiTdQ%3D&reserved=0. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

Response: Thank you for these guidelines. We have reviewed them at the link you provided, which state the following: “If an unapproved abbreviation is used frequently in a manuscript and expansion of this abbreviation throughout the manuscript would detract from its readability, the abbreviation may be used after it has been defined. If there is any doubt about whether such an abbreviation would be acceptable, consult the Obstetrics & Gynecology editorial office.” We propose to use the following abbreviations for ease of readability and to reduce burden on manuscript length, as these lengthy terms

are used repeatedly throughout the manuscript, figures, and tables: clinical chorioamnionitis (CCA), histological chorioamnionitis (HCA), early-onset neonatal sepsis (EONS), and late-onset neonatal sepsis (LONS). In addition, we have seen these abbreviations used repeatedly in the papers reviewed for this study, and thus it seems that the audience for this type of study is accustomed to using the suggested abbreviations.

No abbreviations or acronyms are included in the title or précis. Abbreviations are spelled out the first time they are used, and only standard abbreviations (other than the four mentioned above) are used.

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.

Response: Sentences have been revised to remove the (/) symbol throughout the manuscript.

11. 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%").

Response: Effect sizes with associated confidence intervals are used as the main form of reported statistical results throughout our manuscript and tables. We have checked that reported percentages do not exceed one decimal place, and p-values do not exceed three decimal places. We have standardized the presentation of our data throughout our manuscript. Lastly, we did not evaluate treatments therefore NNTb or harm NNTh is beyond the scope of our review.

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

Response: While we carefully reviewed the literature, we did not conduct a systematic search for reviews on this topic. The claim referred to has been removed (lines 554-557).

13. Please review examples of our current reference style at https://nam10.safelinks.protection.outlook.com/?url=http%3A%2F%2Fong.editorialmanager.com%2F

&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329625160%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=MjvewlX5cwAeXHpB93QKhN2R2cX2dxA58G6fx%2FZzDSo%3D&reserved=0 (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://nam10.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fclinical&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329625160%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=Z3HA06D53xes1sZ%2Fj7v7RSpsRb0qg1pKwXWsnTidO38%3D&reserved=0 (click on "Clinical Guidance" at the top).

Response: We have reviewed ACOG committee opinions, and committee opinion 712 that is referenced within our manuscript is the most up to date opinion on intrapartum management of intraamniotic infection. References have been updated to be in concordance with referencing guidelines mentioned.

14. Figures 1-6: 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.

Response: Figures have been uploaded as PDF files, and tables created in Microsoft Word have been submitted in original source files.

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 https://nam10.safelinks.protection.outlook.com/?url=http%3A%2F%2Flinks.lww.com%2FLWW-ES%2FA48&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329625160%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=OqDGG6mjZayMsGhfidXlCVi3MuS5LJeD03oabR1o8qk%3D&reserved=0. The cost for publishing an article as open access can be found at https://nam10.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwkauthorservices.editage.com%2Fopen-access%2Fhybrid.html&data=04%7C01%7Ccxb1348%40psu.edu%7Cdd7d10b4585e494fe25e08d8b400741f%7C7cf48d453ddb4389a9c1c115526eb52e%7C0%7C0%7C637457261329625160%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=SSoXJg7xQYRtFgXXAESDpKSR%2BoAGlWAx8OPQ2mPYws0%3D&reserved=0.

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.

Response: Thank you for this information.

We developed our revision in consultation with co-authors. All authors have reviewed and approved this revised version. Thank you for considering our resubmission for potential publication. We appreciate your time and look forward to your response.

Sincerely,

Alison Gernand, PhD, MPH (Corresponding author)
Associate Professor of Nutritional Sciences,
The Pennsylvania State University
[redacted]