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 31, 2020
To: "Morgen S Doty" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-74

RE: Manuscript Number ONG-20-74

Neonatal Seizures among Low Risk Pregnancies at Term: Risk Factors and Adverse Outcomes

Dear Dr. Doty:

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

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

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Feb 21, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Doty and colleagues present a retrospective cohort study comparing adverse outcomes in neonates and mothers when neonatal seizures do and don't occur. I have the following questions/comments for the authors.

1 - The abstract and full text are very well written and clear.

2 - The inclusion of maternal outcomes is intriguing but the authors themselves comment on the fact that a temporal relationship is unclear. Why did the authors choose to include maternal outcomes? Is it more likely that there is possible confounding such as a difficult birth that cannot be gleaned from the dataset being used? Consider addressing this possibility in the discussion section.

3 - The limitations inherent in such a population based retrospective study are appropriately addressed. However, the supposition that the associations identified with certain risk factors could lead to preventive interventions is overstated. (Lines157-58)

4 - The authors suggest that the identified associations could be evaluated prospectively; however, with the occurrence rate noted, prospective work in this area would not likely be prudent. Consider altering the language to remove prospective. (Lines 180-81)

Reviewer #2: No comments to authors.

Reviewer #3: Thank you for the opportunity to review, "Neonatal Seizures among Low Risk Pregnancies at Term: Risk Factors and Adverse Outcomes." The authors objective was to examine risk factors and adverse outcomes for neonatal-maternal dyad among low risk pregnancies at term (37-41 weeks) with subsequent neonatal seizures.

The authors performed a retrospective population based cohort study utilizing the U.S. vital statistics dataets (2013-2017). The utilization of this data set address issues that may have otherwise been difficult to address but are more easily done so due to the large number included in the cohort. More than 11.7 million patients met inclusion criteria and were included in this study.

Neonatal seizures are a reason for NICU admissions. Term NICU admissions are a quality measure for the Joint Commission. To be able to address what potential risk factors are by addressing maternal and neonatal characteristics may help when embarking on further research to address issues that may be modifiable.

The authors describe a clear hypothesis which was addressed in the study design and the paper.

This is a very well designed study and well written manuscript.

Specific Comments:
1. It is important that modifiable risk factors were identified to prevent neonatal morbidity and mortality. Smoking and pre-pre pregnancy BMI are modifiable risk factors and this information helps to further educate physicians who may share this information with their patients which maybe utilized during preconception and antenatal counseling.

2. The rate of neonatal risk factors is lower than what was previously assessed (.2/1000 vs. .9-3.0 per 1000 live births). In important comment that the authors addressed was that this number is addresses low risk term deliveries vs. all gestational ages and conditions.

3. It is important that the maternal factors are also addressed which was unique to this study. In past studies, there is a focus on neonatal risk factors, however, research has shown that maternal health plays a role on fetal outcomes.

4. The risk of neonatal seizures was higher in cesarean sections and operative deliveries vs. spontaneous vaginal deliveries. This may be confounded due to other factors including the indications for these delivery options including fetal heart rate abnormalities (which may cause shifts in acid/base status of the neonate), maternal exhaustion, etc.

5. Study limitations are important and were acknowledged.

STATISTICAL EDITOR COMMENTS:

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

Table 2: Either in Table or as supplemental, should include the rates of seizures per 1000 births, with CIs, for each subset. Need to put the RRs and aRRs in context. For example, the strongest association (chorioamnionitis vs neonatal seizures) had RR and aRR of 5.04 and 3.27, respectively, each was highly statistically significant. However, among cases of chorioamnionitis, only 0.12% of them had neonatal seizures, which comprised 7.9% of all seizures. Should either report as attributable risk or as NNT. It would also be helpful to calculate the risk among all those with lowest risk. That is, how many neonatal seizures occurred among women who represented the referent in all the categories identified in Table 2? What was the rate of seizures among them and what proportion of all seizures occurred in that "all referent" group.

Table 3: Similarly, although these RRs and aRRs are obviously extremely high, each of these risk factors represent from 7% to 43% of all neonatal seizures. That is, most seizures are not associated with these individual risk factors, even though the relative risks are very increased.

Table 4: Same observation, but here the math is more extreme, with the majority of neonates having mothers with maternal adverse outcomes did not have seizures, despite the elevated RRs and aRRs.

General: As stated on line 49, etc, the study design and analysis reveals associations, not causation. Therefore, although some of the cited risk factors may be modifiable, this study can only conjecture as to whether modifying those factors would lower the subsequent risk of neonatal seizures.

EDITOR'S COMMENTS:

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

PRESENTATION OF STATS INFORMATION
P Values vs Effect Size and Confidence Intervals

While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.
This is true for the abstract as well as the manuscript, tables and figures.

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

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

Line 39: what do you mean by "prenatal care"? Inadequate prenatal care? No prenatal care?

Line 29: how did you define "Low risk women".

Line 41 and 42: are routes of delivery risk factors or associations? A bit of quibble, but the reason for the non-spontaneous delivery may be the risk factor (non reassuring fetal status, for instance).

Line 79: Please clearly articulate that these criteria (Lines 79-81) are your criteria for low risk women (if in fact they are the criteria.) If these are not, please list the criteria.

In discussion, please provide some information about validation of Vital Statistics for accuracy of identification of neonatal seizures.

Line 283: isn't it neonates with seizures, not neonatal seizures.

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. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

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

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by

manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

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

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

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

10. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

11. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

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

13. Figure 1 may be resubmitted with the revision as-is.

14. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a

publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

15. If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Feb 21, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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

_____

[redacted]

February 18, 2020

Nancy C. Chescheir, MD
Editor-in-Chief
Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

RE: Neonatal Seizures among Low Risk Pregnancies at Term: Risk Factors and Adverse Outcomes

Dear Dr. Chescheir:

Thank you for considering revisions to the above-mentioned manuscript for publication in *Obstet Gynecol*.

Based on the your and reviewers' suggestions, we have revised the manuscript. In the subsequent pages, you will see our point-by-point response to the comments.

We have attached:

1. The red ink copy of the manuscript and tables.
2. The clean copy of the revised manuscript.

All co-authors of this paper have read and approved the revised version of the manuscript being submitted. There are no potential conflicts of interest for all co-authors to disclose. No external funding was received for conducting this study. Since this study was not considered as "human subjects research", this study was in exempt status from review by the institutional review boards at the University of Texas Health Science Center at Houston.

In addition, the lead author, Morgen Doty, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Revisions to the original manuscript are in attachments, both track changes and clean copy. Within this letter, you will find responses to the editor comments (see red for responses). Line numbers correspond to the track change copy. If you have any questions or further suggestions, please do not hesitate to contact us.

Sincerely,

Morgen S. Doty, DO
Maternal-Fetal Medicine Fellow
Department of Obstetrics, Gynecology & Reproductive Sciences
McGovern Medical School
University of Texas Health Science Center at Houston
[redacted]

Reviewer #1

Doty and colleagues present a retrospective cohort study comparing adverse outcomes in neonates and mothers when neonatal seizures do and don't occur. I have the following questions/comments for the authors.

1. The abstract and full text are very well written and clear.

Thank you for your compliment, which, at least, the senior author is unaccustomed to!

2 - The inclusion of maternal outcomes is intriguing but the authors themselves comment on the fact that a temporal relationship is unclear. Why did the authors choose to include maternal outcomes? Is it more likely that there is possible confounding such as a difficult birth that cannot be gleaned from the dataset being used? Consider addressing this possibility in the discussion section.

The reviewer has a poignant question about the maternal outcomes associated with neonatal seizures. We chose to include maternal complications for it is often overlooked, even though our specialty is "Maternal." Additionally, over the years, though we noticed that neonatal seizures followed maternal complications, we were unable to identify any prominent publication on the topic. We agree with the reviewer that unmeasured confounders may have introduced bias. In lines 245-247, we added: "Seventh, unmeasured confounders may have introduced bias.[24] Hence, we consider our analysis to be hypothesis generating, and not hypothesis testing.[25]"

3 - The limitations inherent in such a population based retrospective study are appropriately addressed. However, the supposition that the associations identified with certain risk factors could lead to preventive interventions is overstated. (Lines157-58)

Thank you. We have added the word "may" in line 192 so as not to overstate our findings.

4 - The authors suggest that the identified associations could be evaluated prospectively; however, with the occurrence rate noted, prospective work in this area would not likely be prudent. Consider altering the language to remove prospective. (Lines 180-81)

The reviewer had a good point that prospective identification of an uncommon event is

unlikely. Thus, we have deleted the word “prospective” from line 218.

Reviewer #2
No comments to authors.

Reviewer #3
Thank you for the opportunity to review, "Neonatal Seizures among Low Risk Pregnancies at Term: Risk Factors and Adverse Outcomes." The authors objective was to examine risk factors and adverse outcomes for neonatal-maternal dyad among low risk pregnancies at term (37-41 weeks) with subsequent neonatal seizures.

The authors performed a retrospective population based cohort study utilizing the U.S. vital statistics datasets (2013-2017). The utilization of this data set address issues that may have otherwise been difficult to address but are more easily done so due to the large number included in the cohort. More than 11.7 million patients met inclusion criteria and were included in this study.

Neonatal seizures are a reason for NICU admissions. Term NICU admissions are a quality measure for the Joint Commission. To be able to address what potential risk factors are by addressing maternal and neonatal characteristics may help when embarking on further research to address issues that may be modifiable.

The authors describe a clear hypothesis which was addressed in the study design and the paper.

This is a very well-designed study and well written manuscript.
We appreciate the complement from the reviewer.

Specific Comments:
1. It is important that modifiable risk factors were identified to prevent neonatal morbidity and mortality. Smoking and pre-pregnancy BMI are modifiable risk factors and this information helps to further educate physicians who may share this information with their patients which maybe utilized during preconception and antenatal counseling.
Thank you. We also feel it is important to identify these modifiable risk factors.

2. The rate of neonatal risk factors is lower than what was previously assessed (.2/1000 vs. .9-3.0 per 1000 live births). In important comment that the authors addressed was that this number is addresses low risk term deliveries vs. all gestational ages and conditions.
Thank you. We would expect it to be lower in the low risk population, and may lead to future work among high-risk pregnancies. In lines 240-242, we noted “Fifth, we excluded preterm births, multiple gestations, and high-risk pregnancies; thus, our findings are not applicable to these populations who are at risk for neonatal seizures.[20,23]” Additionally in lines 197-202, we provide the four possible reasons why the rate of seizure was lower than previously published.

3. It is important that the maternal factors are also addressed which was unique to this study. In past studies, there is a focus on neonatal risk factors, however, research has shown that maternal health plays a role on fetal outcomes.

Again, thank you. We concur with the reviewer that with interdependence of maternal-neonatal dyad, identification of maternal factors is important.

4. The risk of neonatal seizures was higher in cesarean sections and operative deliveries vs. spontaneous vaginal deliveries. This may be confounded due to other factors including the indications for these delivery options including fetal heart rate abnormalities (which may cause shifts in acid/base status of the neonate), maternal exhaustion, etc.

This is an excellent point. Although previous literature has also reported this as a risk factor, we have included an additional sentence (lines 204-208) to address this possible confounder. Specifically we note that: "Route of delivery – specifically, operative vaginal and cesarean delivery – were found to have higher incidence of neonatal seizures; it is important to note that these findings may not be directly related to delivery route, and may be influenced, at least in part, by the reason for operative delivery (non-reassuring fetal status, etc.)."

5. Study limitations are important and were acknowledged.

We appreciate the reviewer's complement.

STATISTICAL EDITOR COMMENTS:

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

Table 2: Either in Table or as supplemental, should include the rates of seizures per 1000 births, with CIs, for each subset. Need to put the RRs and aRRs in context. For example, the strongest association (chorioamnionitis vs neonatal seizures) had RR and aRR of 5.04 and 3.27, respectively, each was highly statistically significant. However, among cases of chorioamnionitis, only 0.12% of them had neonatal seizures, which comprised 7.9% of all seizures. Should either report as attributable risk or as NNT. It would also be helpful to calculate the risk among all those with lowest risk. That is, how many neonatal seizures occurred among women who represented the referent in all the categories identified in Table 2? What was the rate of seizures among them and what proportion of all seizures occurred in that "all referent" group.

As suggested by the statistic editor, in this revision, we have added CI's of the rates of seizures per 1,000 births (Table 2).

In this study, we used relative risk to examine the association between maternal factors and neonatal seizure. Relative risk is a common measure used to estimates the magnitude of an association between exposure and disease. Because our study did not examine any treatment, we did not use a NNT measure. Also, we did not use attributable risk (AR), as this measure calculates the number of cases of disease among the exposed that could be eliminated if the exposure were eliminated; however, AR may not be appropriate for some non-modifiable factors, such as race and infant sex, in our study. In addition, AR tends to imply a causal effect relationship, but our goal was to examine association.

We also identified pregnancies with the lowest risk (a combination of the lowest risk category for each factor). Overall, only 0.4% (n=48,853) of pregnancies met the criteria; among them, only 2 cases had neonatal seizure. Therefore, this number is not useful for clinicians, and we choose not to report it.

Table 3: Similarly, although these RRs and aRRs are obviously extremely high, each of these risk factors represent from 7% to 43% of all neonatal seizures. That is, most seizures are not associated with these individual risk factors, even though the relative risks are very increased.

In table 3 and 4, we examined and presented the association between neonatal seizure and adverse outcomes, not risk factors. In this revision, we added CI's of the rates of seizures per 1000 births.

Table 4: Same observation, but here the math is more extreme, with the majority of neonates having mothers with maternal adverse outcomes did not have seizures, despite the elevated RRs and aRRs.

In table 3 and 4, we examined and presented the association between neonatal seizure and adverse outcomes, not risk factors. In this revision, we added CI's of the rates of seizures per 1000 births.

Of note, we also added CI's into Table 5 as well.

General: As stated on line 49, etc, the study design and analysis reveals associations, not causation. Therefore, although some of the cited risk factors may be modifiable, this study can only conjecture as to whether modifying those factors would lower the subsequent risk of neonatal seizures.

We appreciate and agree with this comment. Our study aimed to examine the association, and did not imply causation. In the manuscript we use the word associate/association nineteen times and never use the word cause or causation.

EDITOR'S COMMENTS:

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

PRESENTATION OF STATS INFORMATION

P Values vs Effect Size and Confidence Intervals

While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

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

We have used RR and aRR in abstract, manuscript and tables. We have consistently avoided P values.

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

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

RR was added to aRR variables in the abstract and text – see lines 39-41, 43-44, 65, 161-163, 169, 172-173, 177, 184.

Line 39: what do you mean by "prenatal care"? Inadequate prenatal care? No prenatal care?

Our apologies for the omission. This what meant to be "no" prenatal care. This was added to line 37.

Line 29: how did you define "Low risk women".

The editor has a very good point that we should define low-risk. In the abstract we note: "…were low risk women (without hypertensive disease or diabetes) with non-anomalous singletons, who delivered after labor at 37-41 weeks" which describes our cohort (lines 29-30). Additionally, we note (in lines 102-105), "Our criteria for low risk pregnancies were non-anomalous singletons, who did not have hypertensive disorders, pre-gestational or gestational diabetes, who labored (vaginal delivery or labor with subsequent cesarean delivery), delivered at term (37 to 41 weeks), and had cephalic presentation at birth."

Line 41 and 42: are routes of delivery risk factors or associations? A bit of quibble, but the reason for the non-spontaneous delivery may be the risk factor (non reassuring fetal status, for instance).

This is a good point. Please see lines 204-208 which states "Route of delivery – specifically, operative vaginal and cesarean delivery – were found to have higher incidence of neonatal seizures; it is important to note that these findings may not be directly related to delivery route, and may be influenced, at least in part, by the reason for operative delivery (non-reassuring fetal status, etc.). "

Line 79: Please clearly articulate that these criteria (Lines 79-81) are your criteria for low risk women (if in fact they are the criteria.) If these are not, please list the criteria.

The editor has a good point that we should articulate the inclusion criteria. In lines 102-107, we have specifically written: "Our criteria for low risk pregnancies were non-anomalous singletons, who did not have hypertensive disorders, pre-gestational or gestational diabetes, who labored (vaginal delivery or labor with subsequent cesarean delivery), delivered at term (37 to 41 weeks), and had cephalic presentation at birth. Additional criteria for inclusion were data on neonatal seizures, and had birth data recorded using the 2003 revised birth certificate."

In discussion, please provide some information about validation of Vital Statistics for accuracy of identification of neonatal seizures.

We have added the following to the limitations part of the discussion (lines 234-239): "Third, a recent validation study of the 2003 birth certificate revision did not include neonatal seizures[22]; thus, future studies of national validation of birth certificates are warranted. "

Line 283: isn't it neonates with seizures, not neonatal seizures.

I am not sure which line this actually refers to (283 is part of the references in the copy I see). If it is referring to the last paragraph, however, I believe the term could be used either way. If something needs to be changed, however, we would be happy to comply.

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.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

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

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

This is written above in the letter to the editor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your

point-by-point response to this letter.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
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* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

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10. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms

of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

11. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

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

13. Figure 1 may be resubmitted with the revision as-is.

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