OBSTETRICS & GYNECOLOGY

NOTICE: This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

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

Date: Feb 14, 2020
To: "Emily DeFranco" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-119

RE: Manuscript Number ONG-20-119

Factors associated with maternal and neonatal interventions at the threshold of viability

Dear Dr. DeFranco:

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 Mar 06, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

1. One of the major issue with this analysis is it does not take into consideration intent of the providers and patients. Many cases do not receive any interventions but deliver a stillborn baby. Since this is for livebirth, we would never know how many patients did not receive any interventions and ended up with a stillborn or a delivery not coded as livebirth.

2. Somewhat related to the issue above, this analysis does not account for interventions (excluding cesarean) in cases that deliver after the periviable period. In essence, this analysis only accounts for interventions in those who delivered, and therefore gives a biased assessment.

3. I have concerns about the accuracy of the data in these birth records, particularly when it comes to pregnancy complications and GWG.

4. Given the very large sample size, statistically significant differences are bound to be found, with limited clinical applicability or clinical significance.

5. We always assume that the interventions are for fetal benefit, but some of the interventions could have been for maternal benefit, particularly considering preeclampsia.

6. This manuscript may be more appropriate for an epidemiology journal as it has very minimal clinical implications.

Reviewer #2: This is a retrospective case control study using vital statistics databases evaluating sociodemographic, medical and pregnancy characteristics of pregnancies at periviability (22-23 weeks).

I think this is a very important article that will be well received by Green journal readers. I think the author does a nice job describing the many limitations of vital stats databases but sheds light on a rare and difficult patient population.

I know you report that "hospital or birth place" information was not known, however it would be very interesting and relevant to know if state of delivery was known. If so, I would suggest you stratify outcomes/interventions by legal gestational age limits to assess if this changed provider/patient decisions changed based on this.

line 98: data/reference to suggest shift in aggressive resuscitation?

line 99: in decisions to receive intervention, I think state laws is important to consider adding as resuscitation at 23 weeks is not an option in some states.

line 126: can you stratify based on state laws? ie gestational age at which termination is illegal

line 157: why was GWG adjusted for time pregnant?

line 242: I dont think we can say anything about potential influence of counseling as this is not evaluated in a retrospective study. I think your prior use of language on patient and provider decisions is more appropriate.

line 268: itd be interesting to look at NH black women alone at the patient level to see what number of them had combined intervention.

line 295: i would also argue that women undergoing assisted reproduction have higher educational levels which has been shown to be a reason one chooses against resuscitation.

In the discussion, I think it is important that many of the studies and data referenced include implicit provider biased as is evidenced by ref 27. An important aspect of you study is to demonstrate that these data highlight disparities in our care and importance of patient centered care and decision making over provider. Another important and truly valuable aspect that this study provides is the lack of cohesion between maternal and neonatal care and the importance of optimizing antenatal care if neonatal resuscitation is desired. It highlights the importance of multidisciplinary discussion and communication among teams (ie why would a neonate that is planned to get resuscitation not receive BMTZ?)

Tables: some numbers have 2 digits following decimal point, others one. Be consistent with author instructions

Table 4: Id suggest SGA over FGR given it was after delivery

Figure 1 is not referenced in the text. Also the first series in Figure 1, does "all deliveries" mean 22-23 weeks? if so, I'd clarify that.

Reviewer #3:

1. Thank you for the opportunity to review your Manuscript "Factors associated with maternal and neonatal interventions at the threshold of viability".In this study, the authors perform a retrospective case control study of US live births at 22-23 weeks and compare the influence of maternal sociodemographic, medical and pregnancy characteristics that could predict or be associated with receiving or deferring antepartum / neonatal intervention. Outcomes were grouped into three categories namely maternal, neonatal or combined. The authors noted 0.12 % of US live births between 2012-2016 to have occurred between 22-23 weeks. > 50 % of these patients at least received one intervention. Pre eclampsia was the factor positively associated with both interventions. Increasing age, Medicaid, Low SE status, multiparity, twin and ART were noted be positively associated as well. Black race was noted to be negatively associated with maternal but positively associated with neonatal intervention. Fetal birth defects showed the opposite.

2. The study is indeed novel and has not been addressed in many papers.
Some portion of the maternal characteristics and associations were noted in some articles (referenced). However, the question of positive and negative association was not independently studied.

3. Methodology, as listed by the authors in their limitations, is retrospective and does not allow causal relationship to be studied. There is also significant scope for bias and deficient documentation since US live birth data was used. The co morbidities and other socio demographic factors may not be accurately documented or may not be available.
The advantages of studying such a database cannot be restrained as it adds the strength of numbers, reduction of risk of loss of patient privacy, generalizability to an extent etc.

4. I believe the study to be of significance as this is a question that often comes to mind when counseling patients who have similar clinical circumstances. We are often left wondering if there are any factors that influence patent decision. Although this study does not show causal relationship, it provides an overview of social determinants of health.

5. Tables and Figures do add detail to the work. The manuscript is well written and easy to read.

6. References are pertinent. However, there are some newer articles that have been published since and may need mention.

Reviewer #4: Case-control study of US live births at 22-23 weeks gestation using vital statistics birth records from 2012-2016. Analyzed three outcomes in the treatment of periviable delivery: (1) maternal interventions (cesarean delivery, maternal hospital transfer or antenatal corticosteroid administration), (2) neonatal interventions (NICU) admission, surfactant administration, antibiotic administration, or assisted ventilation), and (3) combined interventions (≥1 maternal and ≥1 neonatal intervention).

Demographics were compared between 22-23-weeks with 24-40 weeks

Objective well stated and consistent

Introduction is good/ Please confirm early in the manuscript that the range in gestation from 22-0/7-23-6/7 weeks? You state this in the Results and I think best for reader to define in Introduction/Abstract.

Can you discuss the limitations of the maternal hospital transfer as a defined maternal intervention broad category. The changing landscape of medicine and transfers is not always about the periviable delivery but even for OBGYN and obstetric services. Sometimes women present to a hospital with no Obstetric services. Transfers happen for all sorts of reasons.

Results: "factors positively associated with interventions were increasing maternal age, Medicaid, low educational attainment, multiparity, twin gestation and infertility treatment " These factors represent a broad swath of society from low educational attainment and medicaid to higher age and Infertility. There does not seem to be a commonality to this group? I think discussing there is no single stereotype or profile of woman.

I think Table 3 is compelling and informative and deserves a little more highlighting and discussion in the manuscript. What kind of interventions. example someone may be willing to give ANCS but not perform a cesarean, one can see how this willingness changes between 22-23 weeks. I suggest discussing the complexity of this decision making would add to your discussion. Not all interventions are thought to be equal as the risk/benefit scenario plays out

STATISTICAL EDITOR COMMENTS:

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

lines 161-162: Although 0.13% is a small percentage, it represents . 25,000 births during the study period, which exceeds the number of 22-23 wk live births. If the missing data re: GA were not randomly allocated, there is the potential to have biased the analysis.

Tables 1 and 2 aggregate live births at 22 wks with those at 23 wks. As can be seen in Table 3, the intervention rates varied significantly between 22 and 23 wks. Should provide analysis comparing the baseline characteristics of live births at 22 vs 23 wks, as in Table 1.

Table 2: There are many comparisons in this Table, so use of $p < .05$ for drawing inferences very likely will include some spurious associations. Need to use a stricter inference threshold.

Table 4: Need to clarify the referent or index for each covariate. For example, is maternal age per year increase? Black race vs all non-black or vs Caucasian? Again, there are multiple comparisons in this table and many do not show high strength of association with the intervention and become statistically significant due to the large sample sizes. Also, according to Table 3 and Fig 1, there should be an association with GA = 22 vs 23, but any such differences are aggregated in this analysis.

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.

Line 42: The précis is a single sentence of no more than 25 words, written in the present tense and stating the

conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstracts conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Precis should be the "hook" for people who scan the Table of Contents to see what to read. It shouldn't not include statements like "in this study" or "we found". Just state what you found.

Line 48: The journal style does not support the use of the virgule (/) except in mathematical expressions. Please remove here and elsewhere.

Line 48: How do you know these are "maternal decisions"? Maybe some patients were not offered the full range of care and so what was done as documented in the birth records actually has as much to do with provider decisions as it does "maternal decisions" ?

Line 51: The abstract should be written in complete sentences. For instance, Line 52 should read "We analyzed three outcomes…in the treatment of delivery of a periviable neonate "

Line 88: you did not include magnesium sulfate administration for neonatal neuroprotection. Oversight or is that data not available? '

Line 103: Back to my comment at line 48…are these all decision to "receive…interventions" or also to "offer interventions"?

Line 123: It's not clear here. If a patient received 1 maternal intervention vs all of them, how was that considered? Same for neonatal interventions.

Lines 130+. The use of ranges here is problematic due to the differences between 22 and 23. You need to explain this a bit and justify not looking at 22 weeks, 23 weeks, 24 weeks, etc. as separate times.

Lines 138: Can you do an analysis excluding twins?

Line 156: Please note this is now the National Academy of Medicine. Please check their website to determine best way of referencing the Gest. Weight Gain recommendations, which were made prior to the name change.

Line 188: 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 190: There is no "Between 22-23 weeks". Do you mean at 22-23 weeks? Same is true on line 194: Do you mean "from 24-42 weeks"?

We have a paper in process, using a different data base, looking at regional and patient level differences in interventions for periviable deliveries. It's a different data base but looking at similar patients. Their data set is 2006-2017; yours is 2012-2016 and includes more patients.

I'd like to suggest that you add an analysis by region. They used the census bureau definitions of location: Northeast, South, midwest, etc. It would be interesting to add this analysis to your data set. Not required, but if easy to do would augment this study which found significant differences by region of birth in both neonatal and maternal interventions.

EDITOR 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. Please submit a completed STROBE checklist with your revision.

Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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 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.

6. 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.

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 limits for different article types are as follows:

Original Research articles, 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. 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.

13. 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.

14. Figure 1 may be resubmitted with the revision.

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 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.

16. 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 Mar 06, 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

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