Date: Sep 27, 2018
To: "Sindhu K Srinivas" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1623

RE: Manuscript Number ONG-18-1623

The impact of delivery volume and high-risk condition volume on maternal morbidity among high-risk obstetric patients

Dear Dr. Srinivas:

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 Oct 18, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a retrospective cohort study with the objective to examine the relationship between hospital delivery volume, high-risk condition volume, and combined effects of both types of volumes on maternal outcomes for patients with high-risk OB conditions. Objective is clearly stated and conclusions do meet the objective. Major concern is the age of the data used for this study as it is from 2005-2009 and may not accurately reflect current practices and outcomes at the facilities included in the study. Large volume of deliveries included a strength. study findings support the fact that volume is not the only factor to consider in quality of care provided to patients.

Line 62-63 - Is this all patients, high-risk or low-risk? Please specify.

Line 68-71 - please describe what investigations were done

Line 89-90 - was number of deliveries from each state the same? How many deliveries in each state? Did findings differ by geographic location?

Line 124-133 - please quantify here what is low, mid, and high volume number of deliveries at a facility for overall deliveries and also high-risk deliveries

Line 136-137 - please quantify this

Line 215-216 - Please expand and explain this sentence further, also include other factors that may account for this (increased staffing, more experienced staff, etc.)

Reviewer #2: In the manuscript under review, the authors report a cohort study of over 10 million deliveries using linked state and discharge records from California, Missouri and PA from 2005-2009. They identified subjects as "high risk" if they had chronic abruption, placenta previa or accreta and vasa previa or a variety of medical complications such as congenital heart disease, DM, HTN (including preeclampsia), etc. They then look at the effect of having these conditions on a composite outcome including: eclampsia, shock, transfusion and/or postpartum hemorrhage using 1CD-9 codes. These results were stratified into an analysis by delivery hospitals divided into quartiles:

1) Annual delivery volume in quartiles

2) Annual high risk patient delivery volume in tertiles

Strengths of the current study include a large number of study patients in the analysis. The study question that is being asked is original and clinically applicable and is well written. The choices that lead to the creation of both the exposure and outcome variables require more explanation as several significant SMM's as defined by CDC were not included in the analysis so using the term "severe maternal morbidity" is misleading for those familiar with these definitions and literature.

The high-risk surgical conditions are really "placental" issues and do not include others such as hyst, multiple prior cesarean deliveries, adhesions, obesity, and other issues that could lead to adverse outcomes. They are clinical situations which place the subjects at high risk of the specific outcome defined as part of the "composite" outcome which really center around bleeding (except for eclampsia)... I think that it would benefit this paper to either 1)narrow the hypothesis to placental conditions and outcomes in high and low volume centers. OR 2) combine the surgical and medical groups and expand the outcome to include other SMMs and simplify the analysis.

Specific comments include:

1) Double check that the corresponding authors are assigned to the correct locations in the first page (Dr. Srinivas is noted to be from Wisconsin)

2) Methods, I am interested to know why the authors chose the surgical/medical complications and also why they selected both the complications and the outcomes they chose to include from the CDC SMM list. In particular I would be interested in hyst/heart failure/trac/vent (https://www.cdc.gov/reproductivehealth/maternalinfanthealth/smm/severe-morbidity-ICD.htm). Blood transfusion is sometime contraversal as an outcome esp when looking at accreta. What ICD-9 codes other than the CDC SMM (of note PPH not included in this list) were used to define the outcome?

3) This data set includes both birth certificate and ICD-9 date. Please note how the variables included in the adjustment were derived (from what data source). How was consideration given if some of the exposure variables differed in birth certificate data from ICD-9 codes (for examine diabetes or HTN)?

4) It would be important to include weight (pre-pregnancy) or weight gain in pregnancy as a covariate if available.

5) See above re: defining the outcome as SMM, in the traditional sense (as defined by Callaghan et al and other papers on this subject) this outcome is misleading

Reviewer #3: This article addresses a topic that may be useful to hospital planners: does regionalization of care, based upon medical acuity volume and overall volume, potentially improve maternal morbidity?

The article is extremely difficult to read because 1. It is confusing sorting out the terms high volume and high-risk and 2. The paper reads like an article for statisticians.

It might be more succinct (easier to read) if instead of reporting all of the unadjusted conclusions in detail and then following that with the (usually) different adjusted conclusions, to just report the adjusted and significant conclusions.

Line 82 The aims would be clearer if you addressed in the objectives that you are including both medical and surgical risk conditions in your high risk population. As it reads now, I had to go back to understand if you left out a third objective (surgical population) or what?

In general, the verbiage is too dense for the average reader who will read your abstract and perhaps, the conclusions. The KISS principle might be applicable: if there are more high risk patients, the morbidity worsens and if there is a larger delivery volume, the hospital has better outcomes, unless there are an extremely large number of very sick patients.

I am not a statistician, but I wonder if you could tease out more of the confounders. For example, BMI is not mentioned but it must be higher in the Midwest than the two coastal hospitals or perhaps within some of the high risk patients but not the sickest ones? Can you not use the ICD codes for more Su Analyses? It seems sorting out why the highest volume lowest risk hospitals have best outcomes. Is there more than volume at play here? For example, a hospital full of high SES high resource using patients who may be older but more heAlthy may do better than an indigent population hospital in the suburbs (lower volume)?

Line 114 Please clarify your term socioeconomic status - is that a conglomerate of education and insurance status?

It would be helpful to postulate more why your middle medical textile had the highest morbidity. You mention in lines 211 and 212 that volume may not reflect resources. I am left wondering if the entire study is missing the key differences that should be explored further, rather than just assuming that it is volume and/or medical complications. In lines 214-216 you allude to medical complications or perhaps special programs (like invasive placentation surgical teams?)but it seems,even

with the codes at your disposal, (acuity ranking or number of codes perhaps?) that this could be explored further.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:
lines 96-99: How was transfer during hospitalization ascertained from the database? For example, if she were evaluated at an outside ER or clinic, but not admitted elsewhere, would that show up as a transfer or as a primary admit to the hospital of record? Was there a relationship between complication rates and the distance from the woman's home to the center where delivery occurred, which might account for severity of illness upon arrival?

Methods: If a sensitivity analysis were done, using only the singleton births, what would the analysis be? (the adjustment model did not include multiple gestation as a variable, but perhaps was too infrequent to be included overall in model.)

Tables 2, 3: Should explain in column headings or in footnote what range of volume were in the tertiles. Need units for age. Should explain that "Mean high risk patients per year" is count per hospital unit. Were the distributions non-normal? If so, should cite as median(range), rather than mean ± SD. If any continuous variables were non-normally distributed, then should use Kruskal-Wallis, rather than usual ANOVA.

Table 4, 5: The discrepancy between the crude vs adjusted ORs implies the large difference in baseline characteristics for the cohorts, which led to completely inverting the association from (+) to (-). The data sets are large, so an alternative suggestion would be to supplement analysis with propensity matching (not mandatory, just a suggestion to strengthen the analysis and additionally show that the high delivery cohorts indeed have a different patient risk profile, but after matching, their complication rates are actually lower.)

Table 6: As the Authors note, here the narrative is less clear and adjustment either ablates the associations found in crude ORs (for mid tertile among surgical high-risk or high tertile among medical high risk), while leaving the high risk surgical high tertile and high risk medical mid tertile essentially unchanged. Hard to reconcile, may be unidentified covariates

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, as well as subsequent author queries. 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:
   1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
   2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Molly Passarella, MS did not indicate a conflict of interest disclosure on her Author Agreement Form. Her updated form may be submitted with the revision.

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. 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.

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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

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 appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

7. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

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

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

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

10. 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.

11. 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.

12. Please express outcome data as both absolute and relative effects since information presented this way is much more useful for clinicians. In both the Abstract and the Results section of the manuscript, please give actual numbers and percentages in addition to odds ratios (OR) or relative risk (RR). 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 dollar amounts.

13. Line 194: 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 on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

14. 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.

15. Figures 1 and 2 may be resubmitted as-is.

16. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

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 Oct 18, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

In response to the EU General Data Protection Regulation (GDPR), you have the right to request that your personal information be removed from the database. If you would like your personal information to be removed from the database, please contact the publication office.

_____
In compliance with data protection regulations, please contact the publication office if you would like to have your personal information removed from the database.

October 18, 2018

Dr. Nancy Chescheir
Editor-in-Chief
Obstetrics & Gynecology

Dear Dr. Chescheir:

Please find enclosed the revised manuscript entitled "The impact of delivery volume and high-risk condition volume on maternal morbidity among high-risk obstetric patients," to be considered for publication in *Obstetrics & Gynecology*.

As the lead author, I affirm 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 there are no discrepancies from the study as planned.

Appended below please find the reviewers comments with our responses noted in blue. We have addressed the reviewers' comments to the best of our ability and revised the manuscript accordingly. All edits can be found using the tracked changes feature of Microsoft Word. We believe that this research is of significant interest to the readership of *Obstetrics and Gynecology*.

Thank you for your consideration of our work.

Sincerely,

Sindhu K. Srinivas, MD, MSCE
[redacted]

<u>Reviewer 1:</u> This is a retrospective cohort study with the objective to examine the relationship between hospital delivery volume, high-risk condition volume, and combined effects of both types of volumes on maternal outcomes for patients with high-risk OB conditions. Objective is clearly stated and conclusions do meet the objective.

Major concern is the age of the data used for this study as it is from 2005-2009 and may not accurately reflect current practices and outcomes at the facilities included in the study.

We appreciate the reviewer's comment. The database utilized has the benefit of capturing all deliveries at all facilities in three diverse states over a 5-year time period. In order for these data to be accurately collected and verified, there is a significant delay between the present and the available, verified data. While we do admit there could be changes in the outcomes of specific facilities, the object of this study was to examine the interplay between facility volume of types of deliveries, rather than specific practice patterns at specific hospitals.

Large volume of deliveries included a strength. study findings support the fact that volume is not the only factor to consider in quality of care provided to patients.

1. Line 62-63 - Is this all patients, high-risk or low-risk? Please specify.

We appreciate the reviewer's question. Due to space limitations, this line has been removed.

2. Line 68-71 - please describe what investigations were done

We appreciate the reviewer's comment. Due to space limitations, these lines have been edited for brevity. These lines have been clarified to reflect the current body of literature on obstetric volume, which has focused on outcomes for low-risk populations or unstratified groups.

This has been changed in lines 80-82.

3. Line 89-90 - was number of deliveries from each state the same? How many deliveries in each state? Did findings differ by geographic location?

We thank the reviewer for the opportunity to clarify this. The breakdown of deliveries by state is included in Tables 2 and 3. We have further emphasized the contribution of each state to the cohort in the results section. While we acknowledge the role of geographic variation in practice, we chose not perform analyses stratified by state or region as part of this investigation in order to maintain robust numbers for volume analysis and to maintain representation of diverse practice contexts. We determined regional variation was beyond the scope of this project, but would be notable for future investigations.

The changes noted have been made to lines 214-215.

4. Line 124-133 - please quantify here what is low, mid, and high volume number of deliveries at a facility for overall deliveries and also high-risk deliveries

We thank the reviewer for the opportunity to clarify this. Tables 2 and 3 do report the mean volume of high-risk deliveries for each tertile. We have added statements of these volumes in the manuscript text. We additionally removed the delivery ranges from Table 6 to more clearly demonstrate the differences by grouping.

Table 5 contains the delivery volume quartiles for the hospital total obstetric volume. We have added the information regarding the mean and standard deviation for each quartile to the table.

The changes have been made to lines 209-212 and to Tables 5 and 6.

5. Line 136-137 - please quantify this

We thank the reviewer for the opportunity to clarify this. We have included the odds ratios in the text as well as referred to the table containing the results.

This change has been made to lines 222-225.

6. Line 215-216 - Please expand and explain this sentence further, also include other factors that may account for this (increased staffing, more experienced staff, etc.)

We appreciate the reviewer's comment. We have edited the manuscript to reflect some of the potential characteristics of the low total obstetric volume centers with high high-risk obstetric volumes and their lower complication rates. They may represent specialized referral centers or hospital centers with high volumes high-risk transfers (ie specialty centers in otherwise rural locations). While outside the scope of this paper to further characterize, this may be a subject for further inquiry.

This change has been made to lines 340-342

Reviewer #2: In the manuscript under review, the authors report a cohort study of over 10 million deliveries using linked state and discharge records from California, Missouri and PA from 2005-2009. They identified subjects as "high risk" if they had chronic abruption, placenta previa or accreta and vasa previa or a variety of medical complications such as congenital heart disease, DM, HTN (including preeclampsia), etc. They then look at the effect of having these conditions on a composite outcome including: eclampsia, shock, transfusion and/or postpartum hemorrhage using 1CD-9 codes. These results were stratified into an analysis by delivery hospitals divided into quartiles:
1) Annual delivery volume in quartiles
2) Annual high risk patient delivery volume in tertiles
Strengths of the current study include a large number of study patients in the analysis. The study question that is being asked is original and clinically applicable and is well written.

The choices that lead to the creation of both the exposure and outcome variables require more explanation as several significant SMM's as defined by CDC were not included in the analysis so using the term "severe maternal morbidity" is misleading for those familiar with these definitions and literature. The high-risk surgical conditions are really "placental" issues and do not include others such

as hyst, multiple prior cesarean deliveries, adhesions, obesity, and other issues that could lead to adverse outcomes. They are clinical situations which place the subjects at high risk of the specific outcome defined as part of the "composite" outcome which really center around bleeding (except for eclampsia)… I think that it would benefit this paper to either 1)narrow the hypothesis to placental conditions and outcomes in high and low volume centers. OR 2) combine the surgical and medical groups and expand the outcome to include other SMMs and simplify the analysis.

We thank the reviewer for the comments.

We utilized the CDC definition to identify maternal outcomes at high risk for maternal compromise (hysterectomy, eclampsia, shock, transfusion, hemorrhage). We do acknowledge these may be biased surgically and have revised the outcome to reflect the complete list of CDC SMMs. To address this issue, we have re-coded the outcome and re-analyzed the results to include all diagnoses included in the CDC definition of SMM.

We have chosen to maintain the separation in the medical and surgical cohorts as we believe the resources and systems of care may differ in dealing with these differing patient needs, therefore the interaction with volume may be different. Prior to examining the results, we hypothesized that the high surgical condition volume would improve outcomes (increased practice) whereas high medical condition volume would worsen outcomes (increased complexity), which was why these groups were separated.

Regarding the surgical conditions selected, we chose conditions with the ability to diagnose prior to delivery. We appreciate and would have wanted to include adhesions or operative complexity but we thought this would be unlikely to be determined preoperatively. Likewise, higher order multiple cesarean deliveries could not be reliably identified based on the data source as ICD coding does not include this information.

These changes are found in lines 176-178, Table 4, and lines 510-516.

Specific comments include:

1) Double check that the corresponding authors are assigned to the correct locations in the first page (Dr. Srinivas is noted to be from Wisconsin)

We appreciate this correction and apologize for this oversight. Dr. Srinivas' affiliation has been corrected.

This change has been made in lines 9-10.

2) Methods, I am interested to know why the authors chose the surgical/medical complications and also why they selected both the complications and the outcomes they chose to include from the CDC SMM list. In particular I would be interested in hyst/heart failure/trac/vent (https://www.cdc.gov/reproductivehealth/maternalinfanthealth/smm/severe-morbidity-ICD.htm). Blood transfusion is sometime contraversal as an outcome esp when looking at accreta. What ICD-9 codes other than the CDC SMM (of note PPH not included in this list) were used to define the outcome?

We thank the reviewer for this comment. Please see the response outlined to Reviewer 2's above comment.

3. This data set includes both birth certificate and ICD-9 date. Please note how the variables included in the adjustment were derived (from what data source). How was consideration given if some of the exposure variables differed in birth certificate data from ICD-9 codes (for examine diabetes or HTN)?

We thank the reviewer for the comment. We preferentially utilized ICD coding data where available. If discrepancies between the two sources existed, ICD codes were utilized due to prior literature showing concern for the accuracy of birth certificate reports for maternal conditions.[1,2,3]

This change has been made to lines 199-200.

[1] Josberger RE, Wu M, Nichols EL. BirthCertificate Validity and the Impact on Primary Cesarean Section Quality Measure in New York State. J Community Health. 2018 Oct 15. doi: 10.1007/s10900-018-0577-y. [Epub ahead of print]

[2] Li Q, Jenkins DD, Kinsman SL. Birth Settings and the Validation of Neonatal Seizures Recorded in Birth Certificates Compared to Medicaid Claims and Hospital Discharge Abstracts Among Live Births in South Carolina, 1996-2013. Matern Child Health J. 2017 May;21(5):1047-1054.

[3] Dietz P, et al. Validation of selected items on the 2003 U.S. standard certificate of live birth: New York City and Vermont. Public Health Rep. 2015 Jan-Feb;130(1):60-70. Erratum in: Public Health Rep. 2015 May-Jun;130(3):192.

4. It would be important to include weight (pre-pregnancy) or weight gain in pregnancy as a covariate if available.

We appreciate the reviewer's comment. We acknowledge that weight and weight gain may be an important covariate in the analyses, but unfortunately this information was not available in this data source. We also did not utilize coding based on BMI or obesity related codes in this data set due to the unreliable nature of this variable. Other researchers have observed the lack of validity of BMI or obesity related coding in ICD data with significant undercoding based on ICD records.[1] Prior researchers have observed that unless obesity is a primary reason for hospital admission, it is often not included in hospital discharge coding.[2] For these reasons, we felt it would be unreliable to include this measure in the analysis.

[1] Martin BJ, Chen G, Graham M, Quan H. Coding of obesity in administrating hospital discharge abstract data: accuracy and impact for future research studies. BMC Health Services Research. 2014;14:70.

[2] Mocarski M, Tian Y, Smolarz BG, McAna J, Crawford A. Use of International Classification of Diseases, Ninth Revision Codes for Obesity: Trends in the United States from an Electronic Health Record-Derived Database. Population Health Management. 2018;21:222-230.

5. See above re: defining the outcome as SMM, in the traditional sense (as defined by Callaghan et al and other papers on this subject) this outcome is misleading

We thank the reviewer for this comment. We have re-defined the outcome to more comprehensively reflect the SMM definition. Please see the above response to Reviewer 2's first comment and noted changes.

Reviewer #3: This article addresses a topic that may be useful to hospital planners: does regionalization of care, based upon medical acuity volume and overall volume, potentially improve maternal morbidity?
The article is extremely difficult to read because 1. It is confusing sorting out the terms high volume and high-risk and 2. The paper reads like an article for statisticians.

1. It might be more succinct (easier to read) if instead of reporting all of the unadjusted conclusions in detail and then following that with the (usually) different adjusted conclusions, to just report the adjusted and significant conclusions.

We thank the reviewer for the comment. We acknowledge these results are complex to present. We believe the unadjusted results are important to include as they demonstrate the role of patient mix in changing the direction of association for the results (high volume centers change from increased complications to lower complications after adjustment).

No changes were made.

2. Line 82 The aims would be clearer if you addressed in the objectives that you are including both medical and surgical risk conditions in your high risk population. As it reads now, I had to go back to understand if you left out a third objective (surgical population) or what?

We thank the reviewer for this comment. We have clarified this language to reflect the objectives were analyzed in both medical and surgical populations.

This change can be found in lines 112-113.

3. In general, the verbiage is too dense for the average reader who will read your abstract and perhaps, the conclusions. The KISS principle might be applicable: if there are more high risk patients, the morbidity worsens and if there is a larger delivery volume, the hospital has better outcomes, unless there are an extremely large number of very sick patients.

We thank the reviewer for this comment. We have clarified the conclusions to highlight this point more directly.

These changes can be seen in lines 353-362.

4. I am not a statistician, but I wonder if you could tease out more of the confounders. For example, BMI is not mentioned but it must be higher in the Midwest than the two coastal hospitals or perhaps within some of the high risk patients but not the sickest ones? Can you not use the ICD codes for

more Su Analyses? It seems sorting out why the highest volume lowest risk hospitals have best outcomes. Is there more than volume at play here? For example, a hospital full of high SES high resource using patients who may be older but more heAlthy may do better than an indigent population hospital in the suburbs (lower volume)?

We thank the reviewer for the comment. We have utilized a large database of discharge codes to analyze patient volume. While this has the benefits of providing a population level information, it does have limitations as to the degree to which we are able to draw specific conclusions about patient differences. While we acknowledge that there are likely additional patient level variables that may further illustrate hospital differences, we have attempted to correct for these systematic differences by clustering the analysis by hospital.

See the above response to Reviewer 2 comment #4 for specific comments regarding BMI. While we did control for state of delivery, we also did not include geographic area as this was beyond the scope of this paper. We agree with the reviewer that it would be interesting to look more in depth at characteristics of hospitals that performed particularly well or poorly as well as exploring specific volume cut offs for performance. At this time we feel this investigation is beyond the scope of this current paper. We will consider this suggestion for future work.

No changes were made.

5. Line 114 Please clarify your term socioeconomic status - is that a conglomerate of education and insurance status?

We thank the reviewer for the comment. We have clarified the language to reflect that the adjustment was made for both level of education and insurance status.

This change is made on lines 219-220.

6. It would be helpful to postulate more why your middle medical textile had the highest morbidity. You mention in lines 211 and 212 that volume may not reflect resources. I am left wondering if the entire study is missing the key differences that should be explored further, rather than just assuming that it is volume and/or medical complications. In lines 214-216 you allude to medical complications or perhaps special programs (like invasive placentation surgical teams?)but it seems,even with the codes at your disposal, (acuity ranking or number of codes perhaps?) that this could be explored further.

We appreciate the reviewer's comment. The strength of this study is that it utilizes a large database to enable examination of the effect of hospital level volume on patient outcomes. While there are likely additional confounders, these may necessitate a more detailed examination of hospital records not available in these data (ie creation of a registry).

No changes were made.

STATISTICAL EDITOR COMMENTS:

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

1. lines 96-99: How was transfer during hospitalization ascertained from the database? For example, if she were evaluated at an outside ER or clinic, but not admitted elsewhere, would that show up as a transfer or as a primary admit to the hospital of record? Was there a relationship between complication rates and the distance from the woman's home to the center where delivery occurred, which might account for severity of illness upon arrival?

We thank the reviewer for the question. Only patients who were coded as having a hospital admission were included. Transfers were determined by comparing the hospital identification number at admission and at discharge. If patients were evaluated in a clinic setting, that would not be reflected in this analysis as no outpatient records were available in this dataset. We chose to limit the scope of this paper to the inpatient setting only. Additionally, please see the response to Reviewer 3, question 4 regarding geography.

Changes made in response on lines 196-198.

2. Methods: If a sensitivity analysis were done, using only the singleton births, what would the analysis be? (the adjustment model did not include multiple gestation as a variable, but perhaps was too infrequent to be included overall in model.)

We thank the reviewer for this comment. In response we performed a sensitivity analysis limiting the cohort to only singleton births. In the singleton only analysis, there were no differences in the adjusted outcomes for the surgical population. Likewise there was no significant change when looking at risk of the primary outcome by total hospital volume. However, in the medical population analysis of high-risk volume, there was a change for the high volume high-risk delivery tertile (see table below).

	As reported	Singletons only
Hosp Quartile Medical	Adjusted OR	Adjusted OR
Q1	1	1
Q2	0.77	0.76
Q3	0.61	0.65
Q4	0.47	0.47
HR tertile Medical		
Low	1	1
Mid	1.25	1.30
High	0.98	1.81

Based on this we have revised the adjustments to include multiple births.

These changes found in lines 193, Table 5, Table 6.

Tables 2, 3: Should explain in column headings or in footnote what range of volume were in the tertiles. Need units for age. Should explain that "Mean high risk patients per year" is count per hospital unit. Were the distributions non-normal? If so, should cite as median(range), rather than mean ± SD. If any continuous variables were non-normally distributed, then should use Kruskal-Wallis, rather than usual ANOVA.

We thank the reviewer for this comment. We have edited the tables for clarity. Due to the size of the data, we made the assumption by the central limit theorem that the data were normally distributed. The only continuous variable used was age, which was normally distributed, therefore, we used ANOVA.

Changes were made to tables 2 and 3 and to lines 493 and 526.

Table 4, 5: The discrepancy between the crude vs adjusted ORs implies the large difference in baseline characteristics for the cohorts, which led to completely inverting the association from (+) to (-). The data sets are large, so an alternative suggestion would be to supplement analysis with propensity matching (not mandatory, just a suggestion to strengthen the analysis and additionally show that the high delivery cohorts indeed have a different patient risk profile, but after matching, their complication rates are actually lower.)

We thank the reviewer for the comment. Propensity score matching is a potential option that we have used in other work for this particular issue. As shown in Tables 2 and 3, there are substantial and expected differences in the baseline covariates of patients in the different cohorts, which would give us the result that we show in adjusted results shown in Tables 4 and 5. We hypothesize that the propensity score matching would give us similar results to Tables 4 and 5, with potentially larger effect sizes that may or may not be clinical different from those shown in our regression analyses. If the editors would like us to pursue this sensitivity/supplemental analysis, we will be willing to consider it. However, the analysis will take a couple of months to implement given the size of the dataset, and thus is outside of the time frame of this resubmission.

No changes were made.

Table 6: As the Authors note, here the narrative is less clear and adjustment either ablates the associations found in crude ORs (for mid tertile among surgical high-risk or high tertile among medical high risk), while leaving the high risk surgical high tertile and high risk medical mid tertile essentially unchanged. Hard to reconcile, may be unidentified covariates

We thank the reviewer for the comment. We agree this is unclear. There are likely unidentified covariates that are unable to be assessed with the limitations of a coding level database. We also posit this relationship may also represent different volume cut-offs that may influence outcomes. We have included in the discussion some of these potential confounders and limitations.

See response and changes made to Reviewer 2, comment 4 and Reviewer 3, comment 4.

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, as well as subsequent author queries. 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:

1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.

2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

We agree to OPT-IN.

2. Molly Passarella, MS did not indicate a conflict of interest disclosure on her Author Agreement Form. Her updated form may be submitted with the revision.

We apologize for this oversight. Molly Passarella's does not have any conflicts of interest and her revised Agreement form is submitted with this revision.

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.

We appreciate the opportunity to make this transparency declaration. This statement has been added to the cover letter as submitted above.

4. 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.

We thank the editor for the opportunity to clarify this. All information was obtained through a linked record of vital statistics, inputted by each state's vital statistics program under the purview of the national and hospital administrative data. We assessed the accuracy of the data by examining the distributions of each variable constructed within the dataset and changed to missing any variable with values outside the ranges of normal, such as gestational ages < 20 weeks or > 48 weeks, or birth weights < 300 grams or > 8000 grams, or birth weights </> 5 SD for the reported GA. This methodology has previously been reported by Murthy et al.[1]

[1] Murthy K, Macheras M, Grobman WA, Lorch SA. Hospital of Delivery and the Racial Differences in Late Preterm and Early-Term Labor Induction. Am J Perinatol 2015;32(10):952–9.

Change made to lines 184-186.

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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

We affirm that we have familiarized ourselves and used the reVITALize definitions in this work.

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 appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

We thank the editor for the guidance on space limitations.
The manuscript has been edited for length.
The introduction has been edited for length and clarity. The current word count is 249.
The discussion has been edited for length and clarity. The current word count is 740.

Changes made throughout the introduction, lines 97-115, as well as to the discussion, lines 322-413.

7. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).**

We thank the editor for this comment. We have no financial support or additional acknowledgements to report. No portion of this paper has been previously presented.

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

This has been changed to: Hospital high-risk OB volume and maternal morbidity

The change has been made to line 24

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

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

We thank the editor for this guidance. The abstract word count is 260.

10. 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.

We thank the editor for the guidance. We have made changes to the abstract and manuscript.

Changes made to lines 41 and 190-191.

11. 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.

We thank the editor for the correction. We have removed any occurrences from the manuscript.

These changes were made in Table 1, Table 2, and Table 3.

12. Please express outcome data as both absolute and relative effects since information presented this way is much more useful for clinicians. In both the Abstract and the Results section of the manuscript, please give actual numbers and percentages in addition to odds ratios (OR) or relative risk (RR). 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 dollar amounts.

We thank the editor for the guidance. We have presented complication data in percentages in table 4 in addition to reporting odds ratios.

13. Line 194: 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 on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

We thank the editor for the comment. We have removed this phrase from the manuscript.

Change made to line 331.

14. 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.

We thank the editor for the guidance. The tables have been edited.

15. Figures 1 and 2 may be resubmitted as-is.

These figures have been edited for content based on the revised outcome measures and are resubmitted with the revised document.

16. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

We appreciate the opportunity to submit our revisions. A Word document with track changes has been submitted along with this cover letter outlining these changes.

From: [redacted]
To:
Cc:
Subject: Re: [External] Your Revised Manuscripts 18-1623R1
Date: Sunday, October 28, 2018 11:35:35 PM
Attachments: 18-1623R1 ms (10-25-18v2) LB SS.docx
editor comment responses.docx

Please see attached word document for responses and well as tracked changes manuscript.

Thank you.

Sindhu K. Srinivas, MD, MSCE
Associate Professor
Director of Obstetrical Services at the Hospital of the University of Pennsylvania
Vice Chair for Quality and Safety
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine
5 Dulles
[redacted]

From: Randi Zung <RZung@greenjournal.org<mailto:RZung@greenjournal.org>>
Date: Thu, 25 Oct 2018 12:55:28 +0000
To: Sindhu Srinivas [redacted]
Subject: [External] Your Revised Manuscripts 18-1623R1

Dear Dr. Srinivas:

Your revised manuscript is being reviewed by the Editors. Before a final decision can be made, we need you to address the following queries. Please make the requested changes to the latest version of your manuscript that is attached to this email. Please track your changes and leave the ones made by the Editorial Office. Please also note your responses to the author queries in your email message back to me.

1. General: The Editor has made edits to the manuscript using track changes. Please review them to make sure they are correct.

2. Title: The journal avoids using “impact” other than to mean “to strike.” Please change “impact” to “effect,” “affect,” or “association with” throughout your paper.

3. Please ask Molly Passarella to respond the authorship confirmation email we sent. We sent an email from em@greenjournal.org<mailto:em@greenjournal.org>. The message contains a link that needs to be clicked on. We emailed Dr. Passsarella at [redacted] – is this the correct address?

4. Precis (and elsewhere): Just saying something is “influenced” doesn’t tell us which direction the influence goes. Could you provide some further information here?

5. Abstract-Objective (and elsewhere): The journal avoids using “impact” other than to mean “to strike.” Please change “impact” to “effect,” “affect,” or “association with” throughout your paper. Your paper cannot address causation. Please look at all verbiage to avoid causal language, and instead substitute with associative language.

6. Abstract-Results: In the abstract, please provide absolute numbers as well as whichever effect size you are reporting + Confidence intervals. P values may be omitted for space concerns. By absolute values, I mean

something like: “xx (outcome in exposed) / yy (outcome in unexposed) (zz%) (Effect size= ; 95% CI=.).” An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4).

7. Line 47: Please write this more clearly. I read this to mean that among high risk patients, as hospital total delivery volume increased, there was an associated declined in risk for maternal mortality. As I’ve written it—if it is what you intended—it is clearer than just saying volume was associated with risk. Please edit for this type of clarity throughout. In the last sentence of results, this might look like: “As total volumes of deliveries increased the rate of maternal complications for women at risk for surgical as well as medical complications decreased. Conversely, as the increased odds of adverse maternal outcomes with higher volumes of high-risk patients.”

8. Line 57: What kind of role? Can you be more specific?

9. Line 84: Tongue in check, but I looked up “Inputted” on Google as it just sounded funny to me. My favorite result from that search:

The past tense of put is put; the past tense of putt is putted. Since input is formed from "put" rather than "putt", it seems logical that its past tense should be input, rather than "inputted"; "inputted" sounds like a demented golfing term. My NOAD lists input and inputted both as acceptable participles.
The writer of that posting appears to agree with me. Would you consider something like: “Data were obtained through a linked record of vital statistics programs, under the purview of....”

10. Line 90: This coding was found where?

11. Line 102: Please use the full name is the Centers for Disease Control and Prevention. Please list the components of the maternal outcome measure, perhaps in a box. If you add a box, please cite it here in the text and then create it at the end of the file where the tables are located.

12. Line 103: I don’t know what this means. “Within the defined cohorts....
Do you mean you had 3 categories:

1. Annual total delivery volume (quartiles)
2. Annual medical high-risk patient delivery volumes (tertiles)
3. Annual surgical high-risk patient delivery volumes (tertiles)

13. Line 110: Are there 2 or 3 volume types?

14. Abstract-Results: For data presented in the text, please provide the raw numbers as well as data such as percentages, effect size (OR, RR, etc) as appropriate and 95% CI’s.

15. Line 129: Please round these up to whole numbers. # of deliveries has be an integer. Please make sure any edits to the data are made consistently in the rest of your manuscript, tables, and figures.

16. Line 130: True for both surgical and medical high risk?

17. Line 132: Just to be clear, so we know what your comparison group is, would you consider something like “compared to women delivering at hospitals with low (can you provide a tertile level??) high-risk volume center, women delivering a higher high-risk centers tended to be older....

Please note we don’t allow authors to describe something as different unless there is a statistical difference. When you say on line 130 that group TENDED to be older—was that numerically or statistically? If not statically different, these data needed to be excluded or presented as similar.

18. Line 133: What does this mean?

19. Line 137: I keep coming up against descriptions of surgical and medical cohorts. It’s just not clear what you mean. I think you mean—for instance, higher rate of diabetes, etc for the medical patients.

20. Line 207: What does this mean?

To facilitate the review process, we would appreciate receiving a response by October 29.

Best,
Randi Zung

_ _
Randi Zung (Ms.)
Editorial Administrator | Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th Street, SW
Washington, DC 20024-2188
T: 202-314-2341 | F: 202-479-0830
http://www.greenjournal.org<http://www.greenjournal.org/>

Your revised manuscript is being reviewed by the Editors. Before a final decision can be made, we need you to address the following queries. Please make the requested changes to the latest version of your manuscript that is attached to this email. Please track your changes and leave the ones made by the Editorial Office. Please also note your responses to the author queries in your email message back to me.

1. General: The Editor has made edits to the manuscript using track changes. Please review them to make sure they are correct.

We thank the editor for the changes made. We have reviewed and agree.

2. Title: The journal avoids using “impact” other than to mean “to strike.” Please change “impact” to “effect,” “affect,” or “association with” throughout your paper.

We thank the editor for the comment. We have changed this vocabulary throughout the paper.

3. Please ask Molly Passarella to respond the authorship confirmation email we sent. We sent an email from em@greenjournal.org<mailto:em@greenjournal.org>. The message contains a link that needs to be clicked on. We emailed Dr. Passsarella at [redacted] – is this the correct address?

We apologize for the delay. Her correct email is passarellam@email.chop.edu.

4. Precis (and elsewhere): Just saying something is “influenced” doesn’t tell us which direction the influence goes. Could you provide some further information here?

We thank the editor for the comment. We have changed the Precis to read: “Adverse maternal outcomes for high-risk obstetric patients decreased as total obstetric delivery volume increased, but increased in centers with high volumes of high-risk patients.” (word count: 24)

5. Abstract-Objective (and elsewhere): The journal avoids using “impact” other than to mean “to strike.” Please change “impact” to “effect,” “affect,” or “association with” throughout your paper. Your paper cannot address causation. Please look at all verbiage to avoid causal language, and instead substitute with associative language.

We thank the editor for the comment. We have changed this vocabulary throughout the paper.

6. Abstract-Results: In the abstract, please provide absolute numbers as well as

whichever effect size you are reporting + Confidence intervals. P values may be omitted for space concerns. By absolute values, I mean something like: “xx (outcome in exposed) / yy (outcome in unexposed) (zz%) (Effect size= ; 95% CI=.).” An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4).

We thank the editor for the comment. Changes have been made to the reporting in lines 52-56.

The results section of the abstract now reads: “We identified 142,194 high-risk surgical deliveries and 1,322,276 high-risk medical deliveries for evaluation. Among surgical high-risk patients, higher hospital total obstetric delivery volume was associated with 22% decreased risk for maternal morbidity (Q4 AOR 0.78; 95% CI 0.64-0.94); likewise for medical high-risk patients, higher total delivery volume was associated with a 28% decreased risk (Q4 AOR 0.72; 95% CI 0.59-0.86). The adjusted odds ratio for severe morbidity for high-risk patient volume in the medical cohort was 1.27 (95% CI 1.10-1.48). There was a significant combined effect of both types of volume on maternal complications for both surgical (p=0.006) and medical high-risk patients (p<0.001).”

7. Line 47: Please write this more clearly. I read this to mean that among high risk patients, as hospital total delivery volume increased, there was an associated declined in risk for maternal mortality. As I’ve written it—if it is what you intended—it is clearer than just saying volume was associated with risk. Please edit for this type of clarity throughout. In the last sentence of results, this might look like: “As total volumes of deliveries increased the rate of maternal complications for women at risk for surgical as well as medical complications decreased. Conversely, as the increased odds of adverse maternal outcomes with higher volumes of high-risk patients.”

We thank the editor for the comment. We agree with the clarified language.

8. Line 57: What kind of role? Can you be more specific?

We thank the editor for the comment. We have changed this in line 74-74.

This line now reads: “These observations suggest that both types of hospital volume have interacting effects on maternal risk of severe morbidity.”

9. Line 84: Tongue in cheek, but I looked up “Inputted” on Google as it just sounded funny to me. My favorite result from that search:

The past tense of put is put; the past tense of putt is putted. Since input is formed from "put" rather than "putt", it seems logical that its past tense should be input, rather than "inputted"; "inputted" sounds like a demented golfing term. My NOAD lists input and inputted both as acceptable participles.
The writer of that posting appears to agree with me. Would you consider something

like: “Data were obtained through a linked record of vital statistics programs, under the purview of....”

We thank the editor for the comment. We have changed this wording on line 108.

10. Line 90: This coding was found where?

We thank the editor for the question. We have clarified this in line 114.

11. Line 102: Please use the full name is the Centers for Disease Control and Prevention. Please list the components of the maternal outcome measure, perhaps in a box. If you add a box, please cite it here in the text and then create it at the end of the file where the tables are located.

We thank the editor for the correction and comment. We have changed the name. We had listed the components of the outcome measure as part of table 4. I have added this reference for clarity. Please inform us if you would rather they be listed separately. This change was made to line 126.

12. Line 103: I don’t know what this means. “Within the defined cohorts....
Do you mean you had 3 categories:

1. Annual total delivery volume (quartiles)
2. Annual medical high-risk patient delivery volumes (tertiles)
3. Annual surgical high-risk patient delivery volumes (tertiles)

We thank the editor for the comment. We have clarified the language in line 129.

13. Line 110: Are there 2 or 3 volume types?

We thank the editor for the comment. We have clarified the language in lines 136-137.

14. Abstract-Results: For data presented in the text, please provide the raw numbers as well as data such as percentages, effect size (OR, RR, etc) as appropriate and 95% CI’s.

We thank the editor for the comment. These changes have been made throughout the results section.

15. Line 129: Please round these up to whole numbers. # of deliveries has be an

integer. Please make sure any edits to the data are made consistently in the rest of your manuscript, tables, and figures.
We thank the editor for the comment. This change has been made in lines 157-159, table 2, table 3.

16. Line 130: True for both surgical and medical high risk?

We thank the editor for this question. We have changed the order of this sentence to emphasize that these results were found in both groups.

17. Line 132: Just to be clear, so we know what your comparison group is, would you consider something like “compared to women delivering at hospitals with low (can you provide a tertile level??) high-risk volume center, women delivering a higher high-risk centers tended to be older....

Please note we don’t allow authors to describe something as different unless there is a statistical difference. When you say on line 130 that group TENDED to be older—was that numerically or statistically? If not statically different, these data needed to be excluded or presented as similar.

We thank the editor for the comments. We have changed the wording to clarify the comparison group as well as remove the word tended as there was a statistically significant difference between groups. We have address both of these issues in lines 160-163.

18. Line 133: What does this mean?

We thank the editor for the opportunity to clarify this. That line has been removed and replaced with more specific language. This change made to line 163-164.

19. Line 137: I keep coming up against descriptions of surgical and medical cohorts. It’s just not clear what you mean. I think you mean—for instance, higher rate of diabetes, etc for the medical patients.

We thank the editor for the comment. We refer to the surgical cohort and medical cohort separately in an attempt to emphasize the parallel analyses done in the paper for both groups of patients. These are separate cohorts.

20. Line 207: What does this mean?

We thank the editor for the comment. We have clarified the language in lines 251-252.

From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: Re: [External] Your Revised Manuscripts 18-1623R1
Date: Saturday, November 3, 2018 11:41:38 PM
Attachments: editor response 11-2-18.docx
18-1623R1 ms (10-31-18v4) -edited.docx
Importance: High

Hi Randi,
I had emailed Thursday asking if it would be possible to speak to Dr. Chescheir. I had not hear back but in the meantime we have responded to all of of the comments we received. We look forward to hearing from you. The edited manuscript and the letter with responses to the editor are attached as two separate files.

Thanks and please let me know if anything else is needed.

Sindhu

Sindhu K. Srinivas, MD, MSCE
Associate Professor
Director of Obstetrical Services at the Hospital of the University of Pennsylvania
Vice Chair for Quality and Safety
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine
5 Dulles
[redacted]

On 11/1/18, 8:21 AM, "Randi Zung" <RZung@greenjournal.org> wrote:

>Dear Dr. Srinivas:
>
>Apologies, there are two additional comments from Dr. Chescheir. She says
>the following:
>1. Please provide an analysis using a matching algorithm to eliminate
>baseline differences for all known confounding variables.
>2. Please make sure your discussion highlights the somewhat modest
>absolute value differences for these outcomes.
>
>Please include these with the queries sent on October 31.
>
>Thank you,
>Randi
>
>-----Original Message-----
>From: Randi Zung
>Sent: Wednesday, October 31, 2018 9:34 AM
>To: 'Srinivas, Sindhu' <SSrinivas@obgyn.upenn.edu>
>Cc: Laura Bozzuto <laura.bozzuto@gmail.com>

>Subject: RE: [External] Your Revised Manuscripts 18-1623R1
>
>Dear Dr. Srinivas:
>
>Dr. Chescheir has reviewed your latest version. She has some additional
>queries for you to address in the attached file (v4). The new comments
>are highlighted in yellow, and listed below:
>
>1. Line 52: This is where you might add something like, "Conversely, as
>the volume of high-risk patients increased, the adjust odds ratio for
>severe morbidity increased (aOR=1.27, 95% CI 1.1.-1.48)."
>
>2. Line 56: Please state what the combined effect is? Important to know
>since the differences move in opposite direction for the different types
>of volumes when assessed alone. Also, please note that statistical data
>should be completely presented, not just the p values.
>
>3. Line 62: Above, you report data to that shows both types of volumes DO
>have an effect on risk for morbidity. Why are you saying here that the
>separate volume analyses only suggest an interacting effect?
>
>4. Line 73: Correct as written? All comers is a bit of jargon
>
>5. Line 84: See the query at end of this manuscript regarding a table to
>perhaps clarify your objectives. I've made some additional notes on Page
>26. If you add a new Table here, your Tables must be renumbered (similar
>to the query below).
>
>6. Line 109: Your Tables must be numbered in order of appearance. You
>need to renumber your Tables to make this Table 3 if you intend to
>include the citation here and add the Table at the end of the
>Introduction per Dr. Chescheir's comment. The subsequent Tables should be
>adjusted accordingly.
>
>7. Line 132: Could a woman be represented more than one time?
>
>8. Line 137: You have used 3 different ways to name these groups:
>   High-risk surgical conditions
>   Surgical cohort
>   Surgical high-risk cohort Same for medically high risk
>group. In an attempt to really simplify your presentation as much as
>possible, would you consider choosing one of these (or no more than 2?).
>
>9. Discussion: In this section, the Statistical Editor would like you to
>discuss the following comment as a limitation: "The aORs and their CIs,
>while significant, have relatively modest absolute values, so much of the
>statistical significance is due, again, to the large samples in their
>study."
>
>10. Line 217: Is this ok?
>
>11. Page 26: Your study design is somewhat complex-as it needs to be to
>answer the questions you've posed. I'm not wedded to this idea, but it
>helped me to organize my thinking about your paper. Would you consider
>adding a table in the introduction section where you describe your
>primary and secondary aims something like this table here? (Editorial
>Office Note: After you have addressed Dr. Chescheir's comment, please

>delete this text so that it does not accidentally end up in your final
>version.)
>
>Please send me your next version when you are finished.
>
>Thank you,
>Randi
>
>-----Original Message-----
>From: Srinivas, Sindhu [redacted]
>Sent: Sunday, October 28, 2018 11:35 PM
>To: Randi Zung <RZung@greenjournal.org>
>Cc: Laura Bozzuto [redacted]
>Subject: Re: [External] Your Revised Manuscripts 18-1623R1
>
>Please see attached word document for responses and well as tracked
>changes manuscript.
>
>Thank you.
>
>Sindhu K. Srinivas, MD, MSCE
>Associate Professor
>Director of Obstetrical Services at the Hospital of the University of
>Pennsylvania Vice Chair for Quality and Safety Department of Obstetrics
>and Gynecology, Division of Maternal Fetal Medicine
>5 Dulles
>[redacted]
>
>From: Randi Zung <RZung@greenjournal.org<mailto:RZung@greenjournal.org>>
>Date: Thu, 25 Oct 2018 12:55:28 +0000
>To: Sindhu Srinivas
[redacted]
>Subject: [External] Your Revised Manuscripts 18-1623R1
>
>WARNING: This email originated outside of the Penn Medicine email system.
>USE CAUTION with links or attachments in Unexpected emails from Unknown
>senders.
>_____
>Dear Dr. Srinivas:
>
>Your revised manuscript is being reviewed by the Editors. Before a final
>decision can be made, we need you to address the following queries.
>Please make the requested changes to the latest version of your
>manuscript that is attached to this email. Please track your changes and
>leave the ones made by the Editorial Office. Please also note your
>responses to the author queries in your email message back to me.
>
>1. General: The Editor has made edits to the manuscript using track
>changes. Please review them to make sure they are correct.
>
>2. Title: The journal avoids using "impact" other than to mean "to
>strike." Please change "impact" to "effect," "affect," or "association
>with" throughout your paper.
>
>3. Please ask Molly Passarella to respond the authorship confirmation
>email we sent. We sent an email from

>em@greenjournal.org<mailto:em@greenjournal.org>. The message contains a
>link that needs to be clicked on. We emailed Dr. Passsarella at
[redacted] - is this the
>correct address?
>
>4. Precis (and elsewhere): Just saying something is "influenced" doesn't
>tell us which direction the influence goes. Could you provide some
>further information here?
>
>5. Abstract-Objective (and elsewhere): The journal avoids using "impact"
>other than to mean "to strike." Please change "impact" to "effect,"
>"affect," or "association with" throughout your paper. Your paper cannot
>address causation. Please look at all verbiage to avoid causal language,
>and instead substitute with associative language.
>
>6. Abstract-Results: In the abstract, please provide absolute numbers as
>well as whichever effect size you are reporting + Confidence intervals. P
>values may be omitted for space concerns. By absolute values, I mean
>something like: "xx (outcome in exposed) / yy (outcome in unexposed)
>(zz%) (Effect size= ; 95% CI=.)." An example might be: Outcome 1
>was more common in the exposed than the unexposed 60%/20% (Effect
>size=3;95% CI 2.6-3.4).
>
>7. Line 47: Please write this more clearly. I read this to mean that
>among high risk patients, as hospital total delivery volume increased,
>there was an associated declined in risk for maternal mortality. As
>I've written it-if it is what you intended-it is clearer than just saying
>volume was associated with risk. Please edit for this type of clarity
>throughout. In the last sentence of results, this might look like: "As
>total volumes of deliveries increased the rate of maternal complications
>for women at risk for surgical as well as medical complications
>decreased. Conversely, as the increased odds of adverse maternal outcomes
>with higher volumes of high-risk patients."
>
>8. Line 57: What kind of role? Can you be more specific?
>
>9. Line 84: Tongue in check, but I looked up "Inputted" on Google as it
>just sounded funny to me. My favorite result from that search:
>
>The past tense of put is put; the past tense of putt is putted. Since
>input is formed from "put" rather than "putt", it seems logical that its
>past tense should be input, rather than "inputted"; "inputted" sounds
>like a demented golfing term. My NOAD lists input and inputted both as
>acceptable participles.
>The writer of that posting appears to agree with me. Would you consider
>something like: "Data were obtained through a linked record of vital
>statistics programs, under the purview of...."
>
>10. Line 90: This coding was found where?
>
>11. Line 102: Please use the full name is the Centers for Disease Control
>and Prevention. Please list the components of the maternal outcome
>measure, perhaps in a box. If you add a box, please cite it here in the
>text and then create it at the end of the file where the tables are
>located.
>
>12. Line 103: I don't know what this means. "Within the defined

>cohorts....
>Do you mean you had 3 categories:
>
> 1. Annual total delivery volume (quartiles)
> 2. Annual medical high-risk patient delivery volumes (tertiles)
> 3. Annual surgical high-risk patient delivery volumes (tertiles)
>
>13. Line 110: Are there 2 or 3 volume types?
>
>14. Abstract-Results: For data presented in the text, please provide the
>raw numbers as well as data such as percentages, effect size (OR, RR,
>etc) as appropriate and 95% CI's.
>
>15. Line 129: Please round these up to whole numbers. # of deliveries
>has be an integer. Please make sure any edits to the data are made
>consistently in the rest of your manuscript, tables, and figures.
>
>16. Line 130: True for both surgical and medical high risk?
>
>17. Line 132: Just to be clear, so we know what your comparison group is,
>would you consider something like "compared to women delivering at
>hospitals with low (can you provide a tertile level??) high-risk volume
>center, women delivering a higher high-risk centers tended to be older....
>
>Please note we don't allow authors to describe something as different
>unless there is a statistical difference. When you say on line 130 that
>group TENDED to be older-was that numerically or statistically? If not
>statically different, these data needed to be excluded or presented as
>similar.
>
>18. Line 133: What does this mean?
>
>19. Line 137: I keep coming up against descriptions of surgical and
>medical cohorts. It's just not clear what you mean. I think you mean-for
>instance, higher rate of diabetes, etc for the medical patients.
>
>20. Line 207: What does this mean?
>
>To facilitate the review process, we would appreciate receiving a
>response by October 29.
>
>Best,
>Randi Zung
>
>_ _
>Randi Zung (Ms.)
>Editorial Administrator | Obstetrics & Gynecology American College of
>Obstetricians and Gynecologists
>409 12th Street, SW
>Washington, DC 20024-2188
>T: 202-314-2341 | F: 202-479-0830
>http://www.greenjournal.org<http://www.greenjournal.org/>
>
>

Dr. Chescheir has reviewed your latest version. She has some additional queries for you to address in the attached file (v4). The new comments are highlighted in yellow, and listed below:

1. Line 52: This is where you might add something like, "Conversely, as the volume of high-risk patients increased, the adjust odds ratio for severe morbidity increased (aOR=1.27, 95% CI 1.1.-1.48)."

We thank the editor for this comment. We have incorporated this change in line 56.

2. Line 56: Please state what the combined effect is? Important to know since the differences move in opposite direction for the different types of volumes when assessed alone. Also, please note that statistical data should be completely presented, not just the p values.

We thank the editor for this comment. We report here in the abstract the overall interaction effect as significant for both the surgical and medical groups and refrain from more detailed description due to the complexity of this interaction and word limitations in the abstract. We feel the interaction effect is best illustrated by figures 1 and 2. Further, while both volumes are significantly associated, what is unique is evaluating them together. We are unsure of what additional statistical data the editor would like included for this-as the combined effect is demonstrated by the interaction p value.

3. Line 62: Above, you report data to that shows both types of volumes DO have an effect on risk for morbidity. Why are you saying here that the separate volume analyses only suggest an interacting effect?

We thank the editor for the comment and have changed the wording to reflect the significance of the results.

4. Line 73: Correct as written? All comers is a bit of jargon

We agree with the editor's rewording of this sentence.

5. Line 84: See the query at end of this manuscript regarding a table to perhaps clarify your objectives. I've made some additional notes on Page 26. If you add a new Table here, your Tables must be renumbered (similar to the query below).

We thank the editor for this suggestion. We have added this table to the document as Table 1**.**

6. Line 109: Your Tables must be numbered in order of appearance. You need to

renumber your Tables to make this Table 3 if you intend to include the citation here and add the Table at the end of the Introduction per Dr. Chescheir's comment. The subsequent Tables should be adjusted accordingly.

We thank the editor for the comment and have changed the numbering of the tables accordingly.

7. Line 132: Could a woman be represented more than one time?

We thank the editor for the question. Patients were included if they had a qualifying hospital admission leading to a delivery and as such could only have one delivery admission per pregnancy. Women could be represented more than one time, however, if they had more than one pregnancy during the 5 year time period. We have added this language to lines 133-136. We are unable to track women over time in all of the states included.

8. Line 137: You have used 3 different ways to name these groups:
High-risk surgical conditions
Surgical cohort
Surgical high-risk cohort
Same for medically high risk group. In an attempt to really simplify your presentation as much as possible, would you consider choosing one of these (or no more than 2?).

We thank the editor for the opportunity to clarify this. We have edited the manuscript throughout to use the term surgical (or medical) high-risk cohort.

9. Discussion: In this section, the Statistical Editor would like you to discuss the following comment as a limitation: "The aORs and their CIs, while significant, have relatively modest absolute values, so much of the statistical significance is due, again, to the large samples in their study."

We appreciate the comment from the editor. We have added a comment about this in the discussion.

10. Line 217: Is this ok?

We thank the editor for the clarification and agree with the edits.

11. Page 26: Your study design is somewhat complex-as it needs to be to answer the questions you've posed. I'm not wedded to this idea, but it helped me to organize my thinking about your paper. Would you consider adding a table in the

introduction section where you describe your primary and secondary aims something like this table here? (Editorial Office Note: After you have addressed Dr. Chescheir's comment, please delete this text so that it does not accidentally end up in your final version.)

We thank the editor for this comment. This table has been added.

12. Please provide an analysis using a matching algorithm to eliminate baseline differences for all known confounding variables.

We thank the editor and statistical editor for this comment. While propensity score matching is a potential option to account for systematic differences in the distribution of measured confounders between patients who attended hospitals of different surgical and medical volumes, which we have used in other work for this particular issue, we think that it is unlikely to give us a significantly different result for a few reasons 1) Matching would by definition force us to find like patients that go to each level of hospital and if that does not occur, would lead to elimination of patients from the analysis leading to a small sample size. There may be a significant loss of power with this decrease in sample size that is not outweighed by the improved statistical power that results from making the casemix of the different surgical and medical volume groups more similar. 2) from the JAMA article comparing propensity score matching to traditional multivariable regression: "Consistent with theoretical mathematical models, empirical evidence comparing propensity score approaches with multivariate risk adjustment show that results are usually very similar. A systematic review of 43 studies, including 78 exposure-outcome associations, found that 70 showed similar results between multivariate risk adjustment and propensity analysis; only 8 statistically significant associations with regression were not observed with propensity analysis. Propensity matching provided more conservative estimates, but the difference was small—on average,6.4%closer to finding no difference between the treatments being compared." (Thomas, A et al. Adjusted Analyses in Studies Addressing Therapy and Harm Users' Guides to the Medical Literature. JAMA February 21, 2017 Volume 317, Number 7). And 3) Such matching algorithms would not adjust for potential unmeasured differences between these groups. And it is most likely that the imbalance is possibly due to severity of disease which is unable to be captured by discharge data based on ICD codes. If the editor still would like us to consider this we would be happy to discuss this further.

13. Please make sure your discussion highlights the somewhat modest absolute value differences for these outcomes.

We thank the editor for the comment. We have added this discussion to the limitations section, lines 333-335.

From: [redacted]
To: Randi Zung
Cc: [redacted]
Subject: [External] Your Revised Manuscripts 18-1623R1
Date: Thursday, November 15, 2018 10:35:59 PM
Attachments: editor response 11_11.docx
18-1623R1 ms (11-6-18v6) 11-14 SS LB.docx

Dear Dr. Chescheir,

Thank you for speaking with us last week and for the opportunity to further edit our manuscript. We have addressed the enumerated comments and made significant edits to the discussion section to reflect our conversation. In reviewing the final manuscript, we found an error in the reporting of the dates of the data, which we have changed to correctly reflect the cohort of deliveries (1995-2009).

Thank you again for the chance to further edit our manuscript. We look forward to hearing from you.

Sindhu K. Srinivas, MD, MSCE
Associate Professor
Director of Obstetrical Services at the Hospital of the University of Pennsylvania
Vice Chair for Quality and Safety
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine
5 Dulles
[redacted]

In follow up from our phone discussion, we have made significant edits to the discussion to reflect our interpretation of the findings. Please refer to lines 395-476 and 495-519 for these changes.

We have responded to the additional comments in the manuscript and below:

1. Final sentence of the Abstract-Results: What is needed is to give the reader some idea about the direction and strength of the effect.

We thank the editor for the comment and have added the LR test value. Change made to lines 58-59.

2. Final sentence of the Abstract-Results: Please provide information for the statistical description of what this combined effect is. Just providing P values tells the reader nothing about the combined effect.

We thank the editor for the comment and have addressed this in the same lines as above.

3. Abstract-Conclusion: Your concluding statement states "These observations" which I read as referring to the individual associations, so I don't think that you can say that those individual observations support the interacting effect. If you want to, you need to mentions something about it in the first sentence of the conclusion.

We thank the editor for the comment. We have made changes to the abstract conclusion. These changes are found in lines 94-96.

4. Line 188: We don't allow authors to refer to "tendencies." If there was no statistical effect you have to say that here.

We thank the editor for the comment. We have removed this line from the manuscript.

5. Line 139: Please note this requested edit.

We thank the editor for the changes to this line.

From: [redacted]
To: Stephanie Casway
Subject: RE: O&G Figure Revision: 18-1623
Date: Tuesday, October 23, 2018 10:47:37 AM

No changes.

Thanks!

Sindhu K. Srinivas, MD, MSCE

[redacted]

From: Stephanie Casway [mailto:SCasway@greenjournal.org]
Sent: Monday, October 22, 2018 10:45 AM
To: Srinivas, Sindhu
Subject: [External] O&G Figure Revision: 18-1623

Good Morning Dr. Srinivas,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes.

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article's publication.

To avoid a delay, I would be grateful to receive a reply no later than Wednesday, 10/24. Thank you for your help.

Best wishes,

Stephanie Casway, MA
Production Editor

Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th St, SW
Washington, DC 20024
Ph: (202) 314-2339
Fax: (202) 479-0830
scasway@greenjournal.org