OBSTETRICS & GYNECOLOGY

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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

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

**Date:** Jul 12, 2019
**To:** "Adam Korrick Lewkowitz" [redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-19-1058

RE: Manuscript Number ONG-19-1058

Association between Stillbirth at ≥ 23 weeks gestation and Severe Intrapartum Maternal Morbidity

Dear Dr. Lewkowitz:

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 Aug 02, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The authors aim to evaluate if stillbirth is associated with severe maternal morbidity. I have the following comments regarding the manuscript:

Precis
1. Consider adding the comparison group to the precis (eg when compared to livebirths).

Intro
1. I completely understand the rationale for your introduction. But I would be cautious here. You are essentially building an argument that all women with a stillbirth should be delivered at a level III or IV center. This is tricky. Removing women from care providers they know in this particular circumstance could be quite detrimental. Instead building a case for increased vigilance in the context of existing incomplete literature may be preferred.

Methods
1. Why such a broad age range for inclusion? 13-55 yo. Seems more pertinent to look at maybe 16-45yrs. Very young and very old gravidas are at increased risk of complications, and the extremes are rare. Also, the abstract says up to age 55 and the methods say up to age 54. Please clarify which is correct.

Results
1. Do the authors have data about gestational age at delivery?

2. What about any data with codes for infection? Need for D&C for retained placenta?

3. Table 1. I am surprised that 12% of stillbirths were delivered by cesarean. Do you have codes for history of cesarean delivery? It seems like a really high proportion delivered by cesarean even if you account for women with multiple prior cesarean deliveries who would be relatively poor candidates for TOLAC.

Discussion
1. Line 270-3. I am not sure that the criteria for level III and IV centers are relevant. If the authors opt to keep this information in the Discussion, would try to delineate the importance for this particular study.

2. Line 281-4. I do not think that the findings can be extrapolated to saying women with stillbirths should deliver at level III or IV centers. 95% of the women with stillbirths and no comorbidities did not have SMM (when transfusion was excluded).

3. Line 279. Two of the examples given (trach and vent) for delivering at a higher level center did not occur in any of the stillbirths per Table 2 and 3.

4. Line 320-23. Would stick to the findings of this paper in your conclusions. This paper did not evaluate if higher levels of care reduce SMM. Don't lose sight of the really important points that can be made without tackling the levels of care issue. The odds ratios for SMM here are quite impressive. This is important for providers to know, we need to understand this association and be clinically vigilant.

Reviewer #2: The presented manuscript by Lewkowitz et al aims to identify risk factors for maternal morbidity associated with stillbirth in the peri-viable gestational age. My point by point comments are as follow:

-Stillbirth is luckily very uncommon, thus a cohort approach such as the one performed by the authors appears to be the logical approach. Yet, the limitations from this approach overshadow any conclusions that could ever be drawn. Within the cohort, the indexed pregnancy of stillbirth is assumed to be the first pregnancy of the patient. This disregards parity, history of losses/stillbirth, and inter pregnancy timeframes, all of which are known to be risk factors for poor obstetric outcomes.

-In addition, causality cannot be be drawn from this study. Women with poorly controlled diabetes and hypertension are also known to have increased morbidity and poor fetal outcomes.

-It does not appear that the authors excluded or accounted for fetal anomalies. The presence of fetal anomalies (anencephaly & T18 for example) are known to affected SMM.

-The nature of intrapartum complications such as abruption and infection are not mentioned. Thus the need for hysterectomy or transfusion cannot be independently deemed a morbidity without context.

-A patients prior history of cesarean section or myomectomy may also affect SMM and outcomes.

-A number of the co-morbidities and conditions were not present in either livebirth or stillbirth.

-The major conclusion from this manuscript is to support ACOG's recommendation for stillbirth management in higher levels of care, yet there is no mention if the SMM was more pronounced outside of Level III-IV centers. Thus, the data presented is not supporting of this recommendation.

Reviewer #3: The authors aim to assess whether women with fetal deaths at ≥ 23 weeks gestation have a higher likelihood of experiencing SMM. They do so through an analysis that stratifies by presence of maternal comorbid conditions using a validated obstetric co-morbidity index. This stratification appears to be problematic in these data given that a similar proportion of women with SB and LB have a comorbidity reported. This was surprising and intriguing for me, but apparently not so much for the authors who report this finding as any other without aiming to provide a justification beyond data quality or asking themselves if they've chosen an adequate set of comorbidities for their analysis - of note, only part of the comorbidities considered were found by others in the literature to be associated with SB.

Abstract/conclusion - authors assess associations not actual "risk"; the clinical conclusion is problematic as phrased - providers should be prepared to manage SMM in all patients not "especially" for those with SBs.

Introduction - CDC did not "redefine" the SMM measure - it is the same as originally proposed.

Methods - authors should specify the outcome variables for all regressions models and denote the "primary model". The sensitivity analyses are not well described - what type of analyses, what interactions were considered and why.

Page 14 line 284 -- statement "[…] transfer to higher levels of care, particularly for women with medical comorbidities" is not supported by their data.

Page 14 line 288 - unclear how this analysis supports clinical practice, if at all. What specific comorbidities were identified as putting women at "higher risk" of SMM during SB delivery?

Page 15 line 305 - the comparison with general population in FL re obesity status us incorrect - authors should look at PRAMS data for FL or another source that includes obesity in pregnancy for such comparison.

Limitations -- Fetal deaths may include abortions - no statement regarding this potential misclassification is included in the manuscript. Also, no discussion re type of SB - fresh or macerated - associations with both maternal comorbidities and SMM are expected to be different for the 2 groups of SBs.

Table 1 - why "baseline" characteristics in the table title?

Table 4 - If SMM without co-morbidity is shown in last column, why do you report comorbidities for that column? What analyses were conducted to arrive at results in this table? Numbers shown do not add up.

Overall, there are indeed many limitations to conducting a meaningful analysis of the relationships between maternal comorbidities, SB and SMM using this data source. This analysis and manuscript can be seen as a first step towards our gaining a better understanding of these relationships, in which case, it should be framed as such first step, clearly listing all data limitations, and providing recommendations for future studies. To me, making clinical recommendations based on this study's findings is not appropriate.

Reviewer #4: Using a state wide inpatient database, the authors conducted a retrospective study comparing SMM among women with history of still birth (>23 weeks) vs Women with normal singleton birth. Overall the study was conducted well and it reads well. Therefore, i would like to commend and congratulate the authors.

However, I have a recommendation to make the method a little more robust. The authors could select group of women that match the stillbirth group in selected variables that might impact the outcome of the study. In other words, the authors may consider applying a propensity score matching (perhaps 1:2 matching). Given the availability of adequate sample size, the application of propensity score matched approach is compelling and it will ensure that the two groups are similar in terms of variables such as age, race, parity, chronic illness, pregnancy related complication, and other demographic factors.

STATISTICAL EDITOR COMMENTS:

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

General: Much depends on the validity of the data base, especially over 2005-2014. What evidence is there of uniform quality control over the interval and if year were entered into the model, was it associated with any of the outcomes?

Table 1: Need to enumerate all missing data, could be in supplemental if needed.

Table 2: Should include a column of unadjusted ORs to contrast with aORs. For some of the specific morbidities, the counts among the stillbirth cohort are too few to adjust with 5 variables (eg, acute renal failure, ARDS, shock or hysterectomy). Although many of the odds are statistically significant and strong associations, few of the women with stillbirth had a composite morbidity (~ 5% of stillbirth and ~ 1% of livebirth), so although the relative increase was large, the absolute risk was small and the differences between relative and absolute risks became even more striking if transfusion were eliminated from morbidities.

Table 3: Same issue with need for unadjusted ORs and the aORs for eclampsia,, sepsis, shock and hysterectomy each have too few adverse events to adjust for 5 variables. Same issue, to a lesser extent, for these cohorts, although since they already were identified as having medical comorbidities, their risk (both stillbirth and livebirth) were higher, but again, most high risk women who had stillbirth (87%) did not have overall morbidity composite and 95% did not have morbidity, if transfusion were eliminated for consideration.

Table 4: Same issue with unadjusted ORs and the counts are too few for multiple adjustment for placenta previa, chronic kidney disease, SS disease, asthma, pre-gestational DM and GDM.

General: The reference by Bateman et al was from 2013, not 2014.

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you

are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

***The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.***

- 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.

- missing a hyphen

- I'm curious and honestly don't know the answer. I think its "Delivering a stillborn" while it would be correct to say "attending stillbirth delivery".

- I agree with one of your reviewers that providers attending any delivery has to be prepared to manage SMM. While your data suggests significant increased risk in deliveries of stillborns, it still happens with liveborns and one doesn't want to suggest otherwise.

- not sure "unexpected" was necessary to have SMM

- note reviewer comment

- Please put the CDC components of SMM into a box.

- In the introduction, you specifically talk about SMM INTRAPARTUM which is a subset of SMM. Its really important that you maintain this distinction if your study is specifically about intrapartum SMM.

- were you studying long term outcomes? I thought this was a study of intrapartum SMM.

- Picky editing thing. You either identified pregnancies which resulted in stillbirths OR you identified deliveries of stillborns or liveborns

- Clearly it is unlikely that women who are at Level 1 or 2 center who shows up with an abruption bad enough to have a stillborn will likely deliver at that center. I think its important to temper your discussion abit because you don't want to box in the providers at lower LoMC hospitals who deliver a stillborn infant and then have an intrapartum SMM. Perhaps given the more then 3 fold higher rate of SMM in women with stillborn infants in association with co-morbidity v not, perhaps offer greater emphasis that its those with medical comorbidities for who one should consider referral for delivery to a higher level of care in These women should be considered. Its also important, in my opinion, to make sure you make some shout out to those at the level 3 and 4 hospitals reminding them that they may need to be generous in accepting these patients in order to avoid feeling like its a transfer of a patient who is hard to care for and can feel like a "dump".

- please consider the additional analyses requested by your reviewers.

- move to primary paper

- move to primary paper

2. 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.

3. 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.

Any author agreement forms previously submitted will be superseded by the eCTA. During the resubmission process, you are welcome to remove these PDFs from EM. However, if you prefer, we can remove them for you after submission.

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

5. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works.

A significant portion of this manuscript is copied and pasted from a previous publication (https://doi.org/10.1016/j.ajog.2019.06.027). Please add variance to the materials and methods section (lines 111-124 and 138-148).

6. 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.

7. 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, tables, boxes, figure legends, and print appendixes) but exclude references.

8. 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).

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

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

15. If you choose to revise your manuscript, please submit your revision 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 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 Aug 02, 2019, 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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In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

Washington University in St. Louis
SCHOOL OF MEDICINE

July 26, 2019

Dr. Chescheir,

Thank for the opportunity to revise our manuscript ONG-19-1058 (entitled, "Association between Stillbirth at ≥ 23 weeks gestation and Severe Intrapartum Maternal Morbidity") according to the comments from the reviewers and editors. We greatly appreciate their thoughtful comments and have revised the manuscript accordingly. We hope you find the result improved.

Of note, since submission, I graduated from MFM fellowship Washington University in St. Louis. Though I will not start at Brown University until August 1, 2019, I have updated my contact information to reflect my future credentials. Please note that this is my personal email, which, should the manuscript be accepted for publication, I would like to have revised to my Brown work email prior to publication.

**Revised Text (Title Page)**

Our responses are below:

1. Response to Reviewers, Statistical Editor, and Editor

Reviewer 1

REVIEWER 1, COMMENT 1:
*Precis. Consider adding the comparison group to the precis (eg when compared to livebirths).*

We have added the comparison group and changed the précis to abide by journal requirements.

**Revised Text (Precis, Page 3, Lines 50-51)**:

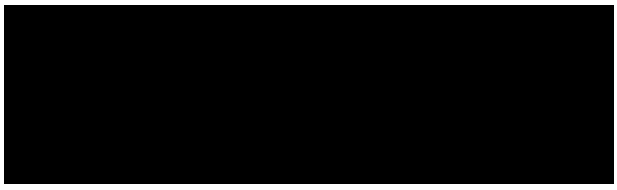
"Compared to delivering livebirth, delivering stillbirth ≥23 weeks gestation is associated with increased risk of severe maternal morbidity, particularly in the setting of maternal comorbidities.

REVIEWER 1, COMMENT 2:
*Intro. I completely understand the rationale for your introduction. But I would be cautious here. You are essentially building an argument that all women with a stillbirth should be delivered at a level III or IV center. This is tricky. Removing women from care providers they know in this particular circumstance could be quite detrimental. Instead building a case for increased vigilance in the context of existing incomplete literature may be preferred.*

Thank you for this comment. We did not mean to imply that all women with stillbirth should be delivered at a level III or IV maternity center but instead tried to frame our manuscript exactly in the way you recommend: that those with stillbirth may be at higher risk of SMM and, if so, may require additional vigilance during delivery. We have removed all references to levels of care in the manuscript and revised the introduction.

**Revised Text (Introduction, Page 6, Lines 91-94)**:

"Given stillbirth occurs in 1 in 160 deliveries in the United States,[8] it is of crucial importance to determine whether there is an association between stillbirth and SMM and if this association differs for women with medical comorbidities. This insight could help providers appropriately triage their patients' risk for SMM during stillbirth delivery."



REVIEWER 1, COMMENT 3:

*Methods. Why such a broad age range for inclusion? 13-55 yo. Seems more pertinent to look at maybe 16-45yrs. Very young and very old gravidas are at increased risk of complications, and the extremes are rare. Also, the abstract says up to age 55 and the methods say up to age 54. Please clarify which is correct.*

We included a broad age range specifically because very young and very old gravidas are at increased risk of either stillbirth or SMM (and comorbidities among elderly gravidas), and this manuscript describes the association between stillbirth and SMM, stratified by comorbidities. Thus, while women at these extreme age ranges are less likely to become pregnant compared to women in their 20s and 30s, they still do become pregnant, and we wanted to provide insight for clinicians as to their potential risks should they then develop a stillbirth.

Thank you for noticing the discrepancy between the abstract and methods—we included women aged 13-54 and have edited the abstract accordingly.

**Revised Text (Abstract, Page 4, Lines 57-58)**:

"The first delivery of female Florida residents aged 13 to 54 years old from 2005 - 2014 was included."

REVIEWER 1, COMMENT 4:

*Results 1. Do the authors have data about gestational age at delivery?*

Unfortunately, the HCUP database does not include the lack of gestational age at delivery. One of the ICD-9-CM codes we used to identity deliveries (650) is supposed to be utilized only in setting of term deliveries, but the other (V270) does not specify gestational age. One ICD-9-CM code does specifically describe preterm delivery, this this code does not specify exact gestational age and has not been well-validated. We agree that the lack of gestational age at delivery may confound our findings and have added this as a limitation to our analyses.

**Revised Text (Discussion, Page 13, Lines 276-278)**:

"Second, though stillbirth is defined in the United States as pregnancy loss at or after 20 weeks gestation,[8] our study defined stillbirth as ≥ 23 weeks gestation due to ICD-9-CM diagnosis code definitions and because the HCUP database does not include gestational age at delivery. The lack of inclusion of stillbirth between 20 and 22 weeks and specific gestational age at delivery may have impacted our results.."

REVIEWER 1, COMMENT 5:

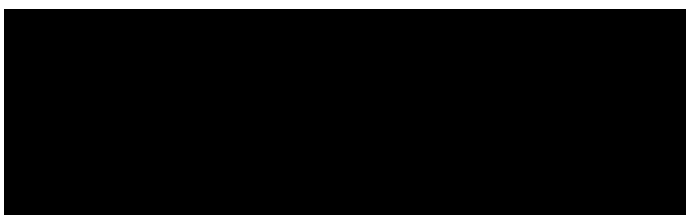
*Results 2: What about any data with codes for infection? Need for D&C for retained placenta?*

Our composite SMM outcome did include data with ICD-9-CM codes for severe infection like sepsis and shock (which could be due to infectious or non-infectious causes). However, we did not capture data on less clinically meaningful infections like endomyometritis for two main reasons. First, the HCUP database is built on standard discharge billing data, and it is less likely that providers enter diagnoses codes for common conditions that do not change payment structure like EMM. Second, our analyses focused on severe maternal morbidity using a well-validated composite created by the CDC. Neither minor infections like EMM nor D&C for retained placenta were included in the SMM composite so were not included in our analyses.

**Revised Text (None)**:

REVIEWER 1, COMMENT 6:

*Results 3: Table 1. I am surprised that 12% of stillbirths were delivered by cesarean. Do you have codes for history of cesarean delivery? It seems like a really high proportion delivered by cesarean even if you account*



*for women with multiple prior cesarean deliveries who would be relatively poor candidates for TOLAC.*

We agree! This statistic is even more remarkable given that history of cesarean section was one of the conditions included within the comorbidity composite. In other words, the 12% of women without any comorbidities who delivered their stillbirth via cesarean section did so in the setting of not having ICD-9-CM coding for a prior cesarean. Conversely, more than 1/3 of women who had comorbidities (including history of cesarean) were delivered via cesarean section. We have edited our manuscript to emphasize this finding.

**Revised Text (Results, Page 9, Lines 165-167)**:

"Among women who delivered a stillbirth, 12% of those without any comorbidities and 37% of those with at least one comorbidities delivered via cesarean section.."

**AND**

**Revised Text (Discussion, Page 13, Lines 258-261)**:

"Of note, though ACOG recommends reserving cesarean section for stillbirth delivery for unusual circumstances,[8] more than one third of women with comorbidities and more than one tenth of women without comorbidities delivered their stillbirth via cesarean. Clinical practice regarding stillbirth mode of delivery does not appear to align with ACOG recommendations."

REVIEWER 1, COMMENT 7:

*Discussion 1: Line 270-3. I am not sure that the criteria for level III and IV centers are relevant. If the authors opt to keep this information in the Discussion, would try to delineate the importance for this particular study.*

We agree that this criteria is irrelevant to the manuscript and have removed this sentence from the text.

**Deleted Text (Discussion, Page 13, Line 262)**:

REVIEWER 1, COMMENT 8:

*Discussion 2: Line 281-4. I do not think that the findings can be extrapolated to saying women with stillbirths should deliver at level III or IV centers. 95% of the women with stillbirths and no comorbidities did not have SMM (when transfusion was excluded).*

Thank you for this comment. We agree completely and have reframed our conclusions to better align with our findings.

**Revised Text (Discussion)**:

REVIWER 1, COMMENT 9:

*Discussion 3: Line 279. Two of the examples given (trach and vent) for delivering at a higher level center did not occur in any of the stillbirths per Table 2 and 3.*

We believe this reviewer may have misinterpreted the table—as per HCUP guidelines, we are unable to report the specific number of women if less than 11 had a particular condition to ensure patient confidentiality and instead present n<11 for outcomes as "—" in the table. However, to better frame our findings, and in response to Editor Comment 1, we heavily revised our discussion and deleted this sentence from the manuscript.

**Deleted Text (Discussion, Page 12, Line 239)**

REVIEWER 1, COMMENT 10:

*Discussion 4: Line 320-23. Would stick to the findings of this paper in your conclusions. This paper did not evaluate if higher levels of care reduce SMM. Don't lose sight of the really important points that can be made without tackling the levels of care issue. The odds ratios for SMM here are quite impressive. This is important for providers to know, we need to understand this association and be clinically vigilant.*

Thank you for this comment. We agree and have edited the discussion accordingly

**Revised Text (Discussion, Page 12, Lines 237-242)**:

"In addition, we identified specific medical conditions including chronic kidney disease, hypertensive disease, sickle cell disease, and placenta previa that significantly increased the risk of SMM among women delivering stillbirth. Thus, though the majority of women who have a stillbirth ≥ 23 weeks will have delivery unaffected by SMM, our findings suggest providers must be vigilant about the increased risk of SMM during stillbirth delivery, particularly for women with the medical comorbidities placing them at highest risk for SMM."

**AND**

**Revised Text (Discussion, Page 14, Lines 304-305)**

"Taken together, these findings could help providers triage their patients' risk of SMM during stillbirth delivery while increasing their vigilance for all SMM, not just blood transfusion."

Reviewer 2

REVIEWER 2, COMMENT 1:

*Stillbirth is luckily very uncommon, thus a cohort approach such as the one performed by the authors appears to be the logical approach. Yet, the limitations from this approach overshadow any conclusions that could ever be drawn. Within the cohort, the indexed pregnancy of stillbirth is assumed to be the first pregnancy of the patient. This disregards parity, history of losses/stillbirth, and inter pregnancy timeframes, all of which are known to be risk factors for poor obstetric outcomes.*

We respectfully disagree that the limitations of our study overshadow any possible conclusions. We found a strong association between stillbirth and SMM, particularly among women with medical comorbidities, and identified specific comorbidities associated with particularly high risk of SMM during delivery of stillbirth. We do agree that our initial framing of the manuscript with clinical recommendations for delivery levels of care unintentionally overstepped our findings and have heavily revised the manuscript to more accurately describe the clinical significance of our findings. In addition, we identified and acknowledged additional limitations that should be considered in response to Reviewer and Editor's comments. We hope the Editors and reviewers agree that these modifications strengthened the manuscript.

In terms of disregarding parity, history of losses/stillbirth, and interpregnancy timeframe in our analyses, we agree that these are risk factors for poor obstetric outcomes. However, the aim of the manuscript was not to identify all risk factors for poor obstetric outcomes but instead compare rates of SMM after stillbirth delivery to that after livebirth delivery. Limiting our study population to the index pregnancy during the study time period ensured that each woman was included only once in our analyses. Had we included all deliveries during the time period, it is possible that our findings would have been skewed by a minority of women with multiple comorbidities who had recurrent stillbirth. Thus, we believe our strict inclusion criteria is a study strength.

**Revised Text (none)**:

REVIEWER 2, COMMENT 2:

*In addition, causality cannot be be drawn from this study. Women with poorly controlled diabetes and hypertension are also known to have increased morbidity and poor fetal outcomes.*

We agree that causality cannot be drawn from this study, which is why we mentioned this first in our list of study limitations (Discussion, Page 13, Lines 269-271). We also agree that women with these morbidities are at increased risk of SMM and that our data does not capture this; we have added this as a limitation.

**Revised Text (Discussion, Page 15, Lines 271-276)**:

"In addition, as in any retrospective study, there is a residual risk of confounding. For example, ICD-9-CM coding utilized in our analyses did not account for disease severity, though factors like uncontrolled diabetes or hypertension are associated with stillbirth[18] and prolonged duration of stillbirth

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prior to delivery may be associated with increased risk of SMM.[8] The lack of causality and potential for confounding require our findings to be confirmed with prospective data."

REVIEWER 2, COMMENT 3:
*It does not appear that the authors excluded or accounted for fetal anomalies. The presence of fetal anomalies (anencephaly & T18 for example) are known to affected SMM.*

This is correct. Fetal anomalies are also associated with increased risk of stillbirth. We have added this as a limitation.

**Revised Text (Discussion, Page 16, Lines 280-281)**:

"Third, we did not include ICD-9-CM coding for fetal anomalies, though fetal malformations are associated with increased risk of stillbirth.[8]"

REVIEWER 2, COMMENT 4:
*The nature of intrapartum complications such as abruption and infection are not mentioned. Thus the need for hysterectomy or transfusion cannot be independently deemed a morbidity without context.*

We agree that it is important to know whether a woman's cesarean hysterectomy was due to abnormal placentation, uterine atony, uterine rupture, or a combination of all of these factors; in fact, determining the context behind each SMM is a very interesting idea for a subsequent manuscript. However, for this project, we did not aim to determine the context behind conditions within the SMM composite. Instead, we viewed SMM as an independent outcome (regardless of its lack of context) and attempted to determine whether stillbirth was associated with increased risk for this outcome compared to livebirth.

**Revised Text (None)**:

REVIEWER 2, COMMENT 5:
*A patients prior history of cesarean section or myomectomy may also affect SMM and outcomes.*

We are in agreement, which is why we stratified women by a well-validated comorbidity composite that included history of cesarean section as one of its comorbid conditions. History of non-obstetric surgery was not extracted for our analysis as this was not included within the composite utilized for our analyses.

**Revised Text (None)**:

REVIEWER 2, COMMENT 6:
*A number of the co-morbidities and conditions were not present in either livebirth or stillbirth.*

Per HCUP guidelines, we are not permitted to present the exact number of women if less than 11 suffered a particular comorbidity. This is mentioned in the methods (page 8, lines 146-147). However, multiple reviewers have misinterpreted the tables, so we have added an additional sentence in the results to remind readers. Should the editors believe this is not warranted, please feel free to remove this sentence. Thank you.

**Revised Text (Results, Page 9, Lines 171-172)**:

"In Tables 2 – 4, counts of less than 11 are marked as "—" whereas counts of 0 are demarcated as such."

REVIEWER 2, COMMENT 7:
*The major conclusion from this manuscript is to support ACOG's recommendation for stillbirth management in higher levels of care, yet there is no mention if the SMM was more pronounced outside of Level III-IV centers. Thus, the data presented is not supporting of this recommendation.*

We agree and have edited our introduction and conclusion significantly. Please refer to our response to Reviewer 1, Comments 2, 7, and 8 for how we have revised our manuscript in response to this and other concerns about our reference to levels of care in the initial manuscript submission.

Reviewer 3

REVIEWER 3, COMMENT 1:

*The authors aim to assess whether women with fetal deaths at ≥ 23 weeks gestation have a higher likelihood of experiencing SMM. They do so through an analysis that stratifies by presence of maternal comorbid conditions using a validated obstetric co-morbidity index. This stratification appears to be problematic in these data given that a similar proportion of women with SB and LB have a comorbidity reported. This was surprising and intriguing for me, but apparently not so much for the authors who report this finding as any other without aiming to provide a justification beyond data quality or asking themselves if they've chosen an adequate set of comorbidities for their analysis - of note, only part of the comorbidities considered were found by others in the literature to be associated with SB.*

One of the major limitations working with a billing dataset derived entirely from inpatient hospital records is that all not all medical comorbidities are available for analysis. In terms of stillbirth, the HCUP data do not include some known neonatal or maternal risk factors that are primarily managed in the outpatient setting like growth restriction or infection. We also highlighted the finding that there were similar proportions of comorbidities in the stillbirth and livebirth groups but believe this comment adds an additional dimension to how we discussed the implications of this finding. We have amended the manuscript accordingly.

**Revised Text (Discussion, Page 13, Lines 248-250)**:

"This similarity may reflect undercoding of medical comorbidities within the HCUP database,[17] actual demographic similarities between the two groups, or the fact that our inpatient database does not include any outpatient comorbidities associated with stillbirth like maternal infection.[8]"

REVIEWER 3, COMMENT 2

*Abstract/conclusion - authors assess associations not actual "risk"; the clinical conclusion is problematic as phrased - providers should be prepared to manage SMM in all patients not "especially" for those with SBs.*

We have removed the word "risk" from the abstract and have modified our clinical conclusions to better align with our findings.

**Revised Text (Abstract, Page 5, Lines 74-76)**:

"Though SMM is overall uncommon, delivering a stillbirth ≥ 23 weeks is associated with increased likelihood of SMM, particularly among women with comorbidities, suggesting providers must be vigilant about SMM during stillbirth delivery."

REVIEWER 3, COMMENT 3:

*Introduction - CDC did not "redefine" the SMM measure - it is the same as originally proposed.*

Thank you for this correction. We have updated the manuscript per this suggestion.

**Revised Text (Introduction, Page 6, Lines 82-84)**:

"The Centers for Disease Control and Prevention (CDC) defines severe maternal morbidity (SMM) as a composite including medical conditions occurring and procedures performed during delivery hospitalization (Box 1).[1]"

REVIEWER 3, COMMENT 4:

*Methods - authors should specify the outcome variables for all regressions models and denote the "primary model". The sensitivity analyses are not well described - what type of analyses, what interactions were considered and why.*

Thank you for this comment. We have clarified our methodology to better describe our analyses.

**Revised Text (Methods, Page 8, Lines 133-144)**:

"The primary multivariable regression models stratified women by the presence of comorbidities and type of delivery (stillbirth or livebirth) and analyzed both primary and secondary outcomes (i.e., SMM as a composite with and without blood transfusion and the individual conditions within the SMM composite). The secondary model limited the study population to women who delivered a stillbirth and stratified them by the presence of each condition within the comorbidity composite; again, the outcome was SMM. For composite outcomes, we utilized multivariable logistic regression models adjusted for age, race/ethnicity, payer, income quartile by zip code, and mode of delivery. In addition, we calculated attributable risk of SMM for stillbirth in the presence and absence of composite medical comorbidity as well as for each individual medical comorbidity. Finally, we tested whether significant interactions existed between independent variables (age, race/ethnicity, payer, income quartile by zip code, and mode of delivery) within the primary models."

REVIEWER 3, COMMENT 5:
*Page 14 line 284 -- statement "[…] transfer to higher levels of care, particularly for women with medical comorbidities" is not supported by their data.*

We agree. Please refer to our response to Reviewer 1, Comments 2, 7, and 8.

REVIEWER 3, COMMENT 6:
*Page 14 line 288 - unclear how this analysis supports clinical practice, if at all. What specific comorbidities were identified as putting women at "higher risk" of SMM during SB delivery?*

Table 4 describes the association between specific comorbidities and SMM during delivery of stillbirth. This table was presented in the results section, and we discuss specific comorbidities identified as putting women at higher risk of SMM during stillbirth delivery (pages 11 & 12, lines 224-231). Please refer to our response to Reviewer 3, Comment 5 as to how our analyses may support clinical practice.

REVIEWER 3, COMMENT 7:
*Page 15 line 305 - the comparison with general population in FL re obesity status us incorrect - authors should look at PRAMS data for FL or another source that includes obesity in pregnancy for such comparison.*

This is an excellent point; thank you. We have changed the citation and manuscript accordingly.

**Revised Text (Discussion, Page 14, Lines 290-293)**:

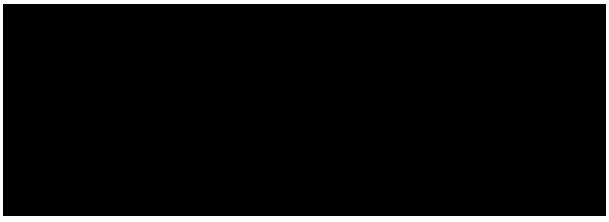
"For example, in our study population, 530 of the 9523 women who had stillbirth (5.6%) were coded with obesity, but, per the CDC Pregnancy Risk Assessment Monitoring System, almost 20% of mothers in Florida were obese prior to pregnancy in 2009-2011.[19]"

REVIEWER 3, COMMENT 8:
*Limitations -- Fetal deaths may include abortions - no statement regarding this potential misclassification is included in the manuscript. Also, no discussion re type of SB - fresh or macerated - associations with both maternal comorbidities and SMM are expected to be different for the 2 groups of SBs.*

The ICD-9-CM diagnosis codes for abortion range from 634.x to 639.x. Thus, we are confident that our study population of women with stillbirth do not have abortion, as these codes are distinct from those we used. Unfortunately, there is no ICD-9-CM differentiation for duration of time of stillbirth prior to delivery. We have added this as a potential limitation.

**Revised Text (Discussion, Pages 13, Lines 272-276)**:

"For example, ICD-9-CM coding utilized in our analyses did not account for disease severity, though factors like uncontrolled diabetes or hypertension are associated with stillbirth[18] and prolonged duration of stillbirth prior to delivery may be associated with increased risk of SMM.[8] The lack of causality and potential for confounding require our findings to be confirmed with prospective data."



REVIEWER 3, COMMENT 9:
*Table 1 - why "baseline" characteristics in the table title?*

We removed this word.

**Deleted Text (Table 1: Title)**:

REVIEWER 3, COMMENT 10:
*Table 4 - If SMM without co-morbidity is shown in last column, why do you report comorbidities for that column? What analyses were conducted to arrive at results in this table? Numbers shown do not add up.*

This table compares the presence of a specific condition within the comorbidity composite and its association with SMM during stillbirth delivery. The numbers in each row add up to 735, which is the number of women with stillbirth who had SMM. In the column that says "SMM without maternal comorbidity," the "n" represents all women with stillbirth who had SMM despite not having that individual comorbidity, and the percentage presented uses the total number of women with stillbirth (9523) as the denominator. As presented, we understand why this table may be confusing. Hopefully our footnote helps clarify

**Revised Text (Table 4)**:

"Each row sums to 735 women, the overall number of women with stillbirth who had SMM. In this column, the "n" presented is the number of women with stillbirth who did not have that specific comorbidity but did have SMM. The percentage presented is calculated using the denominator of total number of women with stillbirth (n=9523).

REVIEWER 3, COMMENT 11:
*Overall, there are indeed many limitations to conducting a meaningful analysis of the relationships between maternal comorbidities, SB and SMM using this data source. This analysis and manuscript can be seen as a first step towards our gaining a better understanding of these relationships, in which case, it should be framed as such first step, clearly listing all data limitations, and providing recommendations for future studies. To me, making clinical recommendations based on this study's findings is not appropriate.*

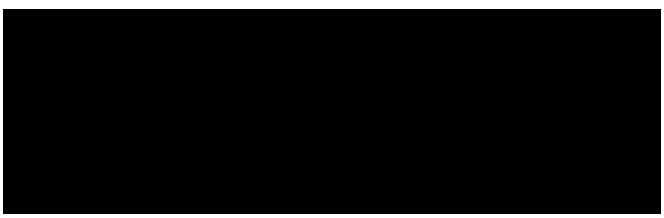
We agree that we provide an important first step and have removed our clinical recommendations. Please refer to our response to Reviewer 1, Comments 2, 7, and 8 as well as Editor, Comments 1 and 11.

<u>Reviewer 4</u>

REVIEWER 4, COMMENT 1:
*Using a state wide inpatient database, the authors conducted a retrospective study comparing SMM among women with history of still birth (>23 weeks) vs Women with normal singleton birth. Overall the study was conducted well and it reads well. Therefore, i would like to commend and congratulate the authors.*

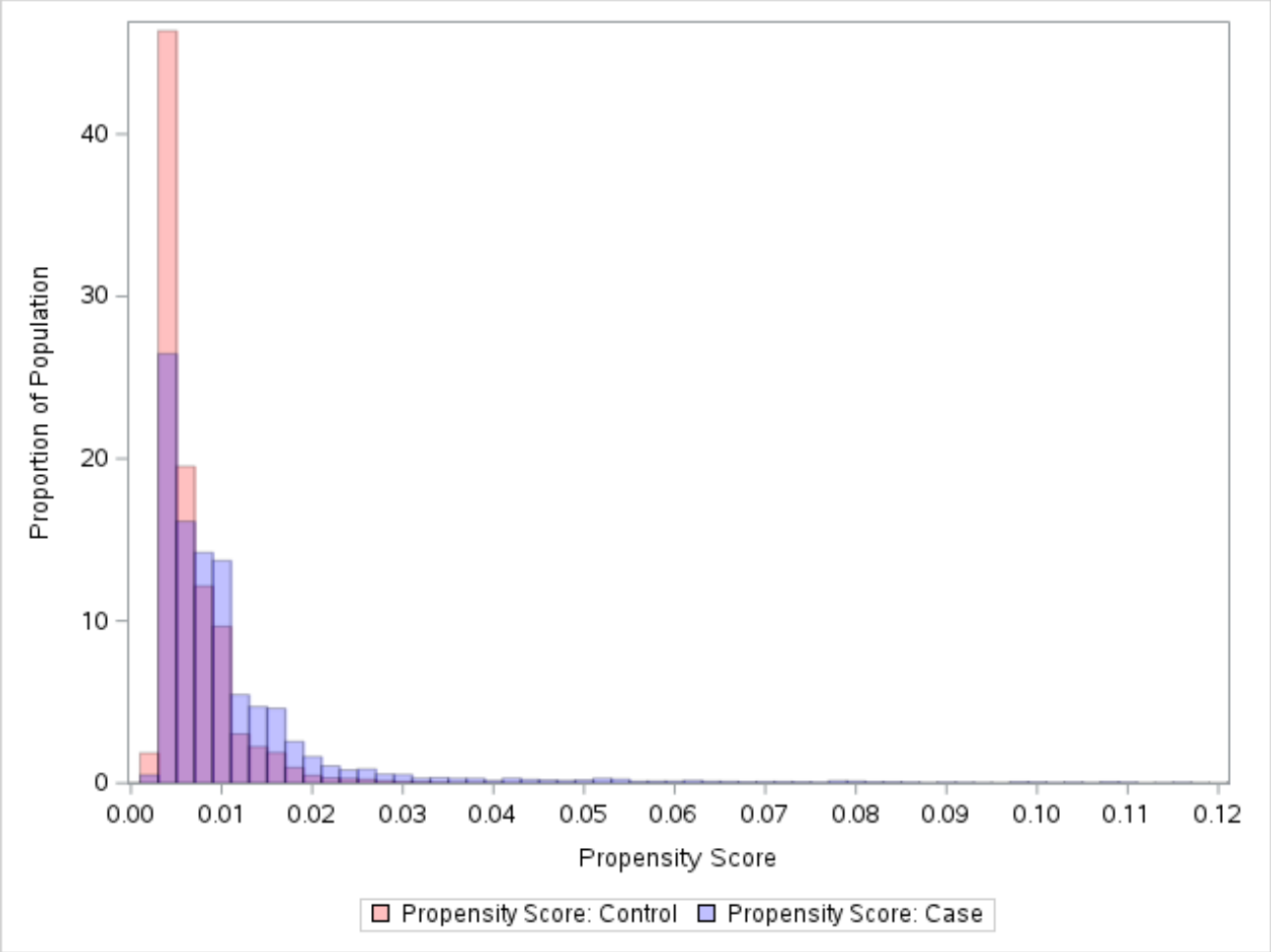
*However, I have a recommendation to make the method a little more robust. The authors could select group of women that match the stillbirth group in selected variables that might impact the outcome of the study. In other words, the authors may consider applying a propensity score matching (perhaps 1:2 matching). Given the availability of adequate sample size, the application of propensity score matched approach is compelling and it will ensure that the two groups are similar in terms of variables such as age, race, parity, chronic illness, pregnancy related complication, and other demographic factors.*

Thank you for this comment! We initially thought of conducting our analyses using a propensity score approach but were worried that, despite our large patient population, we would not be able to find enough livebirth controls to match to our stillbirth cases on all factors that could contribute to SMM. However, we agree with the reviewer that this approach is compelling and, if successful, would make our analyses more



robust. Thus, we re-analyzed our data using a propensity score matched approach, matching women with stillbirth to those with livebirth, according to risk factors for SMM (age, race/ethnicity, income quartile by zip code, payer status, mode of delivery, maternal comorbidities within the morbidity composite, and other factors like smoking we identified in the literature). Unfortunately, our propensity score model to predict SMM was not robust. We think this is due to a combination of factors: the outcome of SMM was rare and often occurs without any risk factors, our population was limited to singletons, HCUP is limited to inpatient records, and not all factors (like smoking or non-severe infections like EMM) are rigorously coded in HCUP. The graph below shows the poor predictive ability of the variables we included in the propensity score model, for your reference.

One of the senior programmers conducted these additional analyses, and we have acknowledged him in the manuscript.




**Revised Text (Acknowledgements, Page 2, Lines 42-43)**

**"**We would like to acknowledge Dustin Stwalley for his statistical support."

STATISTICAL EDITOR

STATISICAL EDITOR, COMMENT 1:

*General: Much depends on the validity of the data base, especially over 2005-2014. What evidence is there of uniform quality control over the interval and if year were entered into the model, was it associated with any of the outcomes?*

This is an excellent point. The HCUP is derived of standard discharge billing data used by all hospitals for the purpose of collecting data for reimbursement While there is no quality control per se for billing data, the

main way HCUP maintains rigorous quality control is because entering incorrect data on the hospital bill constitutes fraud. We did look at the number of cases of SMM stratified by number of deliveries (stillbirth and livebirth) each year, and the number slightly increased but was overall consistent throughout the ten-year study period.

**Revised Text (None)**:

STATISTICAL EDITOR, COMMENT 2:

*Table 1: Need to enumerate all missing data, could be in supplemental if needed.*

We have added two additional supplemental tables to enumerate the missing data as well as referred to this in the manuscript.

**Revised Text (Results, Page 9, Lines 157-159)**:

"Sociodemographic and obstetric characteristics between women who delivered stillbirth ≥ 23 weeks gestation and livebirth stratified by the presence of maternal comorbidities are shown in **Table 1**; missing data are presented in **Appendices 3 and 4**."

**AND**

**Revised Text (Appendices 3,4)**

STATISTICAL EDITOR, COMMENT 3-5:

COMMENT 3: *Table 2: Should include a column of unadjusted ORs to contrast with aORs. For some of the specific morbidities, the counts among the stillbirth cohort are too few to adjust with 5 variables (eg, acute renal failure, ARDS, shock or hysterectomy). Although many of the odds are statistically significant and strong associations, few of the women with stillbirth had a composite morbidity (~ 5% of stillbirth and ~ 1% of livebirth), so although the relative increase was large, the absolute risk was small and the differences between relative and absolute risks became even more striking if transfusion were eliminated from morbidities.*

COMMENT 4: *Table 3: Same issue with need for unadjusted ORs and the aORs for eclampsia,, sepsis, shock and hysterectomy each have too few adverse events to adjust for 5 variables. Same issue, to a lesser extent, for these cohorts, although since they already were identified as having medical comorbidities, their risk (both stillbirth and livebirth) were higher, but again, most high risk women who had stillbirth (87%) did not have overall morbidity composite and 95% did not have morbidity, if transfusion were eliminated for consideration.*

COMMENT 5: *Table 4: Same issue with unadjusted ORs and the counts are too few for multiple adjustment for placenta previa, chronic kidney disease, SS disease, asthma, pre-gestational DM and GDM.*

We agree and have amended our tables, added the column of unadjusted ORs for all aORs and removed all aORs for individual conditions to avoid our models being overfit. Though the Statistical Editor did not explicitly state this, we believe s/he would prefer we added attributable risk to the table as well to highlight the difference between relative and absolute risk, which we have done. We have also revised the methods to reflect this updated methodology as well as the results and discussion.

**Revised Text (Methods, Page 8, lines 138-140)**:

"For composite outcomes, we utilized multivariable logistic regression models adjusted for age, race/ethnicity, payer, income quartile by zip code, and mode of delivery."

**AND**

**Revised Text (Methods, Page 8, Lines 140-142):**

"In addition, we calculated attributable risk of SMM for stillbirth in the presence and absence of composite medical comorbidity as well as for each individual medical comorbidity."

**AND**

**Revised Text (Results, Page 11, lines 221-224)**

"Overall, the risk of SMM was significantly higher for women who had stillbirth and at least one medical comorbidity compared to stillbirth and no medical comorbidities (n=390 (13.3%) for

comorbidities versus n=345 (5.2%) for no comorbidities; aOR 1.82 (95% CI 1.53 – 2.16); risk of SMM during stillbirth attributed to comorbidity: 8.1%)."

**AND**

**Revised Text (Results, Pages 11-12, lines 224-231)**

"The condition associated with the highest risk of SMM during delivery of stillbirth was chronic kidney disease (CKD): nearly two thirds of the 63 women with CKD who delivered stillbirths had SMM (n=39 (61.9%); Odds Ratio 20.46 (95% CI 12.23 – 34.22)), with 54.6% risk of SMM during stillbirth delivery attributed to CKD. Many more common comorbidities including preeclampsia with or without severe features, chronic hypertension, placenta previa, sickle cell disease, asthma, and history of cesarean section were also associated with increased risk of SMM during delivery of stillbirth. Conversely, gestational and pregestational diabetes and human immunodeficiency virus were not associated with increased risk of SMM during stillbirth delivery."

**AND**

**Revised Text (Tables 2, 3, and 4)**

STATISTICAL EDITOR, COMMENT 6:

*General: The reference by Bateman et al was from 2013, not 2014.*

Great catch. We have changed this throughout.

**Revised Text (Tables 1-4 and Appendix 2, 3, & 4 and Box 2)**:

EDITOR

EDITOR, COMMENT 1:

*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.*

Thank you. We have reviewed the instructions for authors again and have significant decreased the word count for the introduction and discussion. However, multiple reviewers brought additional limitations to our attention, and the discussion is slightly longer than the 750 word limit in order to incorporate their suggestions.

Please note that the introduction and discussion have essentially been rewritten.

**Revised Text (Introduction, Page 6, Lines 82-99)**:

**"**The Centers for Disease Control and Prevention (CDC) defines severe maternal morbidity (SMM) as a composite including medical conditions occurring and procedures performed during delivery hospitalization (Box 1).[1] SMM has been identified as a risk factor for both postpartum morbidity[2,3] and peripartum maternal mortality. [4] As such, multiple risk factors for SMM have been identified, including obstetric conditions like placental abruption, medical comorbidities like hypertensive disorders, and maternal demographic factors like black race.[3,5–7]

Though these same risk factors have also been associated with increased risk of stillbirth.[8,9] the association between stillbirth and SMM is less clear. Prior studies are limited by a lack of control group[10] or occur in resource-poor settings,[10–13] and the impact of underlying comorbidities on SMM during stillbirth delivery are unknown. Given stillbirth occurs in 1 in 160 deliveries in the United States,[8] it is of crucial importance to determine whether there is an association between stillbirth and SMM and if this association differs for women with medical comorbidities. This insight could help providers appropriately triage their patients' risk for SMM during stillbirth delivery.

Using a state database, we aimed to ascertain whether stillbirth ≥23 weeks gestation was associated with increased risk of SMM compared to singleton livebirth among women who were and were not coded with medical comorbidities during their delivery hospitalization. We hypothesized that stillbirth was associated with increased risk of SMM compared to livebirth regardless of maternal medical comorbidities."

**AND**

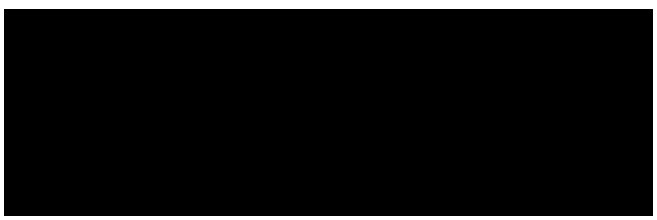
**Revised Text (Discussion, Pages 12-14, Lines 234-306)**

"In this large retrospective cohort study, we provide insight into the incidence of SMM during delivery of stillbirth at ≥ 23 weeks gestation versus liveborn singleton. Specifically, the risk of SMM was markedly higher for women who had stillbirth compared to livebirth regardless of maternal medical comorbidities (aOR 7.05 (95% CI 6.27 – 7.93) for no comorbidities; aOR 6.21 (95% CI 5.54 – 6.96) with at least one comorbidity). In addition, we identified specific medical conditions including chronic kidney disease, hypertensive disease, sickle cell disease, and placenta previa that significantly increased the risk of SMM among women delivering stillbirth. Thus, though the majority of women who have a stillbirth ≥ 23 weeks will have delivery unaffected by SMM, our findings suggest providers must be vigilant about the increased risk of SMM during stillbirth delivery, particularly for women with the medical comorbidities placing them at highest risk for SMM.

Our findings supporting prior studies identifying non-Hispanic black race and advanced maternal age as risk factors for stillbirth[8] while identifying additional risk factors for stillbirth: public insurance compared to private insurance and lower socioeconomic status. However, though ACOG states maternal comorbidities are associated with increased risk of stillbirth,[8] our study population had similar rates of maternal medical comorbidities coded during hospitalization for stillbirth delivery versus livebirth delivery (30.8%). This similarity may reflect undercoding of medical comorbidities within the HCUP database,[17] actual demographic similarities between the two groups, or the fact that our inpatient database does not include any outpatient comorbidities associated with stillbirth like maternal infection.[8] Additional prospective research is needed to confirm this finding to better clarify the association between comorbidities and stillbirth. Of note, though ACOG recommends reserving cesarean section for stillbirth delivery for unusual circumstances,[8] more than one third of women with comorbidities and more than one tenth of women without comorbidities delivered their stillbirth via cesarean. Clinical practice regarding stillbirth mode of delivery does not appear to align with ACOG recommendations.

Our study offers several strengths. First, we provide granular insight into the association between specific medical conditions and SMM during stillbirth delivery, which may help providers triage their patient's individual risk for SMM based on her specific comorbidities. Second, our data derive from a large, comprehensive, all-payer database that allowed us to analyze outcomes for all deliveries in Florida for a decade, increasing the generalizability of our findings. Third, our ICD-9-CM coding has been validated for all critical variables included in this analysis, including deliveries,[16] medical comorbidities,[7] and SMM.[1,3] This validation strengthens our findings.

Nevertheless, limitations should be considered. First, our analyses cannot determine causality. Because SMM and delivery type were coded in the same inpatient hospitalization, we cannot determine whether SMM occurred after the stillbirth or caused the stillbirth. In addition, as in any retrospective study, there is a residual risk of confounding. For example, ICD-9-CM coding utilized in our analyses did not account for disease severity, though factors like uncontrolled diabetes or hypertension are associated with stillbirth[18] and prolonged duration of stillbirth prior to delivery may be associated with increased risk of SMM.[8] The lack of causality and potential for confounding require our findings to be confirmed with prospective data. Second, though stillbirth is defined in the United States as pregnancy loss at or after 20 weeks gestation,[8] our study defined stillbirth as ≥ 23 weeks gestation due to ICD-9-CM diagnosis



code definitions and because the HCUP database does not include gestational age at delivery. The lack of inclusion of stillbirth between 20 and 22 weeks and specific gestational age at delivery may have impacted our results. Third, we did not include ICD-9-CM coding for fetal anomalies, though fetal malformations are associated with increased risk of stillbirth.[8] Fourth, some conditions within the comorbidity or SMM composites may have been under-coded in the HCUP dataset. For example, in our study population, 530 of the 9523 women who had stillbirth (5.6%) were coded with obesity, but, per the CDC Pregnancy Risk Assessment Monitoring System, almost 20% of mothers in Florida were obese prior to pregnancy in 2009-2011.[19] This risk of under-coding impacts all studies utilizing administrative dataset and may impact the association between stillbirth and SMM. Lastly, it is possible that providers were more likely to code for medical comorbidities during stillbirth versus livebirth delivery, resulting in selection bias. The impact of selection bias on our results is likely not significant given the association between SMM and stillbirth versus livebirth was similar among women with and without medical comorbidities but warrants additional prospective research.

In conclusion, women who have a stillbirth ≥ 23 weeks gestation have higher risk of SMM during their delivery hospitalizations compared to those who have a livebirth singleton, particularly in the setting of maternal comorbidities. In addition, the risk of nearly all conditions within the SMM composite—not just blood transfusion—was increased during delivery of stillbirth versus livebirth. Finally, specific medical comorbidities were identified with particularly high risk of SMM during stillbirth delivery. Taken together, these findings could help providers triage their patients' risk of SMM during stillbirth delivery while increasing their vigilance for all SMM, not just blood transfusion."

EDITOR, COMMENT 2:
*Missing a hyphen*

Thank you. We have deleted the extra digits.

**Deleted Text (Abstract, Page 4, Line 71)**:

EDITOR, COMMENT 3:
*I'm curious and honestly don't know the answer. I think its "Delivering a stillborn" while it would be correct to say "attending stillbirth delivery".*

We also do not know the exact language but think "delivering stillbirth" may flow better than "attending stillbirth delivery." However we defer to the Editor about this linguistic intricacy and would support her decision on this matter.

EDITOR, COMMENT 4:
*I agree with one of your reviewers that providers attending any delivery has to be prepared to manage SMM.*

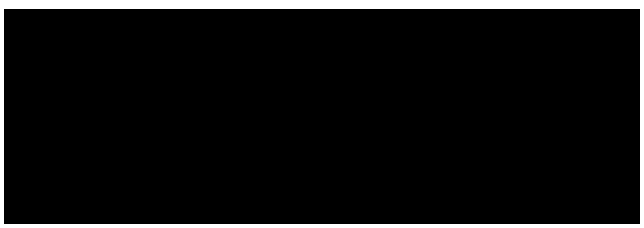
*While your data suggests significant increased risk in deliveries of stillborns, it still happens with liveborns, and one doesn't want to suggest otherwise.*

We agree and have believe our reframed manuscript more successfully describes the risk of SMM for both livebirth and stillbirth.

**Revised Text (Abstract, Page 5, Lines 74-76)**:

"Though SMM is overall uncommon, delivering a stillbirth ≥ 23 weeks is associated with increased likelihood of SMM, particularly among women with comorbidities, suggesting providers must be vigilant about SMM during stillbirth delivery."

EDITOR, COMMENT 5:
*Not sure "unexpected" was necessary to have SMM*



True. This sentence was deleted in our revision of the introduction as per our response to Editor, Comment 1.

EDITOR, COMMENT 6:
*Note reviewer comment*

We did and have updated our manuscript as per this feedback.

**Revised Text (Introduction, Page 6, Lines 82-84)**:

"The Centers for Disease Control and Prevention (CDC) defines severe maternal morbidity (SMM) as a composite including medical conditions occurring and procedures performed during delivery hospitalization (Box 1).[1]"

EDITOR, COMMENT 7:
*Please put the CDC components of SMM into a box.*

We have done so.

**Revised Text (Box 2)**

EDITOR, COMMENT 8:
*In the introduction, you specifically talk about SMM INTRAPARTUM which is a subset of SMM. Its really important that you maintain this distinction if your study is specifically about intrapartum SMM.*

This is an excellent catch. Thank you. Our study captures SMM coded during delivery hospitalization, which does not necessarily mean the adverse outcomes were limited to intrapartum. We have removed all references to intrapartum SMM.

**Revised Text (Title, Page 1, Line 1)**:

"Association between Stillbirth at ≥ 23 weeks gestation and Severe Maternal Morbidity"

**AND**

**Revised Text (Short Title, Page 1, Lines 44)**

"Stillbirth and Severe Maternal Morbidity"

**AND**

**Revised Text (Precis, Page 2, Lines 50-51)**

**"**Compared to delivering livebirth, delivering stillbirth ≥23 weeks gestation is associated with increased risk of severe maternal morbidity, particularly in the setting of maternal comorbidities."

**AND**

**Revised Text (Abstract Page 4, Line 53-54)**

"To determine whether stillbirth ≥ 23 weeks gestation is associated with increased risk of severe maternal morbidity (SMM) compared to livebirth, when stratified by maternal comorbidities."

**AND**

**Revised Text (Abstract, Page 4, Lines 61-63)**

"The primary outcome was an ICD-9-CM diagnosis or procedure code during delivery hospitalization of any indices within the Centers for Disease Control and Prevention's SMM composite."

**AND**

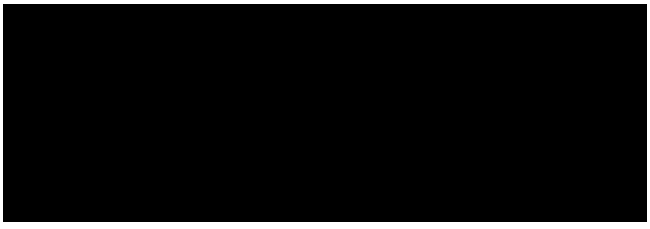
**Deleted Text (Keywords, Page 5, Line 79)**

**AND**

**Revised Text (Titles of Tables 2, 3, and 4)**

**AND**

EDITOR, COMMENT 9:
*Were you studying long term outcomes? I thought this was a study of intrapartum SMM.*



Again, excellent catch. There are no long-term outcomes, and we removed this portion of the sentence.

**Deleted Text (Methods, Page 7, lines 113-114)**:

EDITOR, COMMENT 10:

*Picky editing thing. You either identified pregnancies which resulted in stillbirths OR you identified deliveries of stillborns or liveborns*

Thank you for this comment; we identified this latter.

**Revised Text (Results, Page 8, Lines 154-155)**:

"A total of 1,362,567 singleton deliveries were identified: 9523 (0.7%) were stillbirths ≥ 23 weeks gestation and 1,353,044 (99.3%) were livebirths."

EDITOR, COMMENT 11:

*Clearly it is unlikely that women who are at Level 1 or 2 center who shows up with an abruption bad enough to have a stillborn will likely deliver at that center. I think its important to temper your discussion abit because you don't want to box in the providers at lower LoMC hospitals who deliver a stillborn infant and then have an intrapartum SMM. Perhaps given the more then 3 fold higher rate of SMM in women with stillborn infants in association with co-morbidity v not, perhaps offer greater emphasis that its those with medical comorbidities for who one should consider referral for delivery to a higher level of care in These women should be considered. Its also important, in my opinion, to make sure you make some shout out to those at the level 3 and 4 hospitals reminding them that they may need to be generous in accepting these patients in order to avoid feeling like its a transfer of a patient who is hard to care for and can feel like a "dump".*

In response to prior comments, we no longer frame our findings through the lens of ACOG's level of care centers, so we wholeheartedly agree with this Comment, it is less valid in the masnucript.

EDITOR, COMMENT 12:

*Please consider the additional analyses requested by your reviewers.*

We did. Please refer to our response to Reviewer 4, Comment 1.

EDITOR, COMMENTS 13 & 14:

Comment 13: *Move to primary paper*

Comment 14: *Move to primary paper*

We have created boxes for maternal comorbidities and SMM.

**Revised Text (Boxes 1 and 2)**:

2. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process:
**OPT-IN**

3. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works.

COMMENT 1: *A significant portion of this manuscript is copied and pasted from a previous publication (https://doi.org/10.1016/j.ajog.2019.06.027). Please add variance to the materials and methods section (lines 111-124 and 138-148).*

The lead author of the current manuscript also was the lead author for the manuscript mentioned above; both used the same methodological approach. The above article is now cited, and we have also added variance to the methods.

**Revised Text (Pages 6-7, Methods, Lines 105-118)**:

"Our methods have been published previously[15]; in brief, we identified deliveries in women aged 13-54 years using a validated algorithm of *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes.[16] We defined the index delivery as the first delivery within the database during the study timeframe, regardless of subsequent deliveries or parity. We restricted deliveries to stillbirth ≥23 weeks gestation (ICD-9-CM codes 656.40, 656.41, and V271) and liveborn singletons (ICD-9-CM codes 650 and V270). We excluded women whose index deliveries were coded as both live-born singletons and stillbirth ≥ 23 weeks gestation or as both singleton and multiple gestation (ICD-9-CM codes 651.00, 651.01, 651.10, 651.11, 651.20, 651.21, V272, and V275). Female non-Florida residents and patients listed as "male" were also excluded. Sociodemographic data analyzed included age, race/ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, and other), payer (private, public, or other), and income quartile by zip code.

Underlying maternal medical comorbidities coded during delivery hospitalization were identified using a maternal comorbidity composite validated for the HCUP databases[7] (**Box 2; Appendix 1**). "

**AND**

**Revised Text (Page 8, Methods, Lines 133-151):**

"Demographic and baseline clinical data were compared between women who had stillbirth versus livebirth using the $X^2$ test or Fisher's exact test for categorical variables as appropriate. The primary multivariable regression models stratified women by the presence of comorbidities and type of delivery (stillbirth or livebirth) and analyzed both primary and secondary outcomes (i.e., SMM as a composite with and without blood transfusion and the individual conditions within the SMM composite). The secondary model limited the study population to women who delivered a stillbirth and stratified them by the presence of each condition within the comorbidity composite; again, the outcome was SMM. For composite outcomes, we utilized multivariable logistic regression models adjusted for age, race/ethnicity, payer, income quartile by zip code, and mode of delivery. In addition, we calculated attributable risk of SMM for stillbirth in the presence and absence of composite medical comorbidity as well as for each individual medical comorbidity. Finally, we tested whether significant interactions existed between independent variables (age, race/ethnicity, payer, income quartile by zip code, and mode of delivery) within the primary models. Demographic data missing from the database was recoded as an indicator variable in order to ensure all patients were included in the multivariate analyses. All analyses considered a two-sided $p < 0.05$ as statistically significant. Due to HCUP restrictions aimed to preserve patient privacy, counts <11 are reported as "n<11" for exposures and "--" for outcomes.

The Washington University in St. Louis Human Research Protection Office exempted this study from review given HCUP data does not contain personally identifiable information. SAS version 9.3 (SAS Institute, Cary NC) was used for all analyses.

4. All ACOG documents cited are the updated versions.

Please let us know if there remain any questions or if you feel there are additional ways in which we could improve this manuscript.

Thank you for your consideration,

Adam K. Lewkowitz, MD, MPHS