Date: Jan 30, 2019
To: "Morgen S Doty" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2408

RE: Manuscript Number ONG-18-2408

Non-Macrosomic Large for Gestational Age Neonates: Maternal and Neonatal Morbidity

Dear Dr. Doty:

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

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

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Feb 20, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Abstract -

Objective - to compare the rate of adverse outcomes in non-macrosomic LGA infants - >90th%, < 4000 gm versus AGA 10-89% between 37-39 wks of gestation

Methods - Retrospective cohort with US Vital Statistics Dataset from 2011-2013 - inclusion singleton, non-anomalous, AGA/LGA < 4000 gm, laboring, between 37-39 weeks
Primary outcome - maternal morbidity and neonatal morbidity

Results - 3.9 million, 1.3% non-macrosomic-LGA infants
composite maternal morbidity was 53% higher in NM-LGA than in AGA with an increased risk in diabetics and non-diabetics
composite neonatal morbidity was 83% higher for NM-LGA than AGA - higher in diabetics and non-diabetics
Conclusion - NM-LGA pregnancies/babies still have higher maternal and neonatal morbidities than AGA

Introduction - There are known risks with macrosomia but there is a gap in knowledge regarding morbidity/ mortality of NM-LGA pregnancies
The primary outcome was to compare maternal morbidity and neonatal morbidity with NM-LGA vs AGA infants and the secondary objective was outcome stratified by status of diabetics

Materials/ Methods - population based retrospective study
period linked birth-infant death data files from 2011-2013 and birth certificate data
statistical models were used to evaluate fetal growth status and risk of composite maternal/neonatal morbidity outcomes

Results - 3,917,831 live births meeting the inclusion criteria
NM-LGA consistutes 1.3% of these
NM-LGA likely to be older, non-hispanic whites, overweight, GDM, hypertensive while AGA more likely to be primiparous and smokers
Maternal morbidity - 53% higher in NM-LGA than AGA in both diabetics and nondiabetics
neonatal morbidity is 83% higher in NM-LGA than AGA - increased risk in both diabetics and nondiabetics

Discussion - NM-LGA consistutes 1% of births but with a 37-39% increased risk of an adverse outcome over AGA
50% increased rate maternal morbidity, 80% increased rate neonatal morbidity

The management to address this is problematic because accelerated growth is not often recognized, this would increase

c/s rate, induction prior to 39 weeks has not been evaluated, ACOG does not recommend indcution for accelerated growth

To study and address a decreased risk of 1/3, 29,000 women would have to be randomized for induction so this is not an achievable study

Comments - This is an interesting and well done study to show that with or without diabetes/ GDM, there is still and increased risk of neonatal and maternal morbidity in NM-LGA babies as compared to AGA babies
It is not clear to me if the proposal for a study would be elective induction prior to 39 weeks. This still shows an increased risk with delivery 37-39 weeks, so how early would delivery need to be performed to decrease the risk, and then the risk of prematurity would affect the neonatal risk, so any benefit would be outweighed by risk of prematurity.

While the increased risk is interesting, please clarify in discussion what the proposal is - it is not clear to me if the thought is to proceed with earlier delivery. This is not feasible given risks of prematurity, particularly given poor ability to estimate fetal weight.

Also, these NM-LGA are identified after delivery, but how many were even known prior to delivery to even help guide management - either suggesting earlier delivery or to guide management if progress in labor is slower than anticipated. If not identified prior to labor, which often they aren't, there isn't much to be done. Please address how these were identified and if it was prior to labor or just with weight after delivery.

Reviewer #2: THis is a well done meticulous study evaluating the significane of maternal and perinatal morbidity of non macrosomic LGA neonates with AGA neonates

In the materials and methods I did not understand on page 9, lines 136-140 why sensitivity analysis was done for adverse outcome excluding matneral transfusion for the association of adverse outcomes?

Reviewer #3: OVERALL

The authors conducted a study to compare maternal and neonatal morbidities between NM-LGA and AGA. They found NM-LGA neonates compared to AGA neonates had higher risk of maternal and neonatal morbidities.

The findings provided additional knowledge for health care providers because this study was conducted in a specific population. The study helps us to better understand non-macrosomic LGA pregnancies.

The current draft is organized but readers can only obtain limited information from the Method section. The authors need to further describe the dataset and study design. The reviewer's comments mainly focus on the Method section. The comments/suggestions are listed below:

METHOD

Data source

1. The data source and study design were not clearly described in this section. Readers can only have limited information to know this study because they are not quite familiar with the dataset. For example, what is the type of the dataset? Is it a survey dataset, administration claim dataset, or a registration dataset? The authors only mentioned the data were annually reported by CDC. This is not enough.

2. The authors also need to address the advantage/disadvantage of the dataset. It could help the readers to understand the strength and weakness of the study.

3. In addition, in the first paragraph, the authors mentioned the data file (Period linked Birth-infant Death Data File) was from 2011-2013. However, in the second paragraph, they mentioned the 2003 revised birth certificate. This is confusing. What is the link between the data file and the birth certificate? Furthermore, they mentioned the data of maternal morbidity was added in 2011 and dropped in 2014. Again, this is confusing. What is the purpose of doing so? Please clarify. Would the lack of information (maternal morbidity) have impact on the study validity?

4. The data were from 38 states. Did the rest of 12 states not provide the data? This part is not clear, either. Please clarify. (Again, how did the data form?) Will the finding be generalized to the whole U.S. population? Please explain.

5. The paragraph "The 2003 revision …" created more questions than answers. What is the main message that the authors wanted to deliver in this paragraph? Please explain. Are these two estimates distinct? Please clarify.

Study design

6. The outcome of this study was a composite measure of several maternal morbidities or neonatal morbidities. The reviewer suggests the authors to conduct an analysis of each maternal morbidity and neonatal morbidity first. Then, they

can look at the composite measure. Doing so would obtain a more comprehensive result.

7. Is this a cohort study or a cross-sectional study? This goes back to the previous question that the reviewer mentioned regarding the type of the dataset.

Covariate adjustment

8. How did these covariates identify? Did the dataset contain the information of these variables? What are the operational definitions of these variables? Were these variables measured before or during pregnancy? If they were measured before pregnancy, what was the period of the measurement? Please explain/clarify.

9. In this dataset, would it be possible to identify prescription use among pregnant women? Comorbidities can be identified and adjusted. The authors did so. How about the prescription use? Medication use before and during pregnancy can also be a confounder.

10. The statement of the sensitivity was not clear. What was the sensitivity analysis that the authors conducted? This part was not clear. The authors only mentioned the sensitivity analysis in one sentence, and without any further clarification. Please clarify.

STATISTICAL EDITOR'S COMMENTS:

1. If the cases were comprised of singletons with BW ≥ 90th centile, but < 4000 grams, then the reference criteria (1996-1999) seem unsuitable to this cohort, since only 1.3% were NM-LGA, while 7% were LGA with macrosomia. Also, the differential between 90th percentile for GA vs 4000 grams would represent a smaller proportion for males, since their BWs are skewed to higher values compared to females. This results in a higher proportion of males in the cases studied and males are known to have higher neonatal morbidity/mortality.

2. Tables 3 and 5: Need to include a column citing the counts for composite morbidities for all row entries. The samples are large, but for the GDM and pre-GDM strata, the counts are respectively ~50 and ~13 for maternal morbidity. These are too few to allow precise correction for 12 covariates in the aRR models. So, the conclusion holds for all and for non-diabetic, but there are too few counts to be assured of the same conclusion for the smaller subsets. Could attempt a matching algorithm, given the large sample of AGA. Also, should include a column of crude RR.

3. Table 4:Need to include CIs for rates.

4. For Table 5: The counts of neonatal morbidity for pre-GDM and for GDM are ~ 41 and 85, respectively, again too few for 12 covariates as adjustors in the aRR model.

5. Table 6: Same issue as with Tables 3 and 5 re: counts of adverse events and aRR models and need to include crude RR column and column of actual counts of morbid events.

6. General: To what extent are the increases in maternal and neonatal morbidities associated with increased rate of cesarean?

ASSOCIATE EDITOR'S COMMENTS:

Please, if you choose to revise (and I hope you do)

1) Include actual birthweights of the LGA, non-macrosomic infants --median (range)
2) Use only standard abbreviations
3) Pay special heed to the comments of the Statistical Editor.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, 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. 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.

3. 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.

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

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

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 26 typed, double-spaced pages (6,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

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

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

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

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

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

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

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

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

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

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If you choose to revise your manuscript, please submit your revision 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 Feb 20, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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

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March 5, 2019

The Editor
Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

RE: Manuscript Number ONG-18-2408
Non-Macrosomic Large for Gestational Age Neonates: Maternal and Neonatal Morbidity

Dear Dr. Rouse:

Thank you kindly for considering the above-mentioned manuscript for publication in *Obstet Gynecol*. We truly appreciate the opportunity to revise the manuscript and resubmit.

Per your instructions, we have:

1. Responded to the three reviewers' comments, the statistical editor's comment, and the associate editor's comments (please see below and note that the line numbers mentioned refer to the "red ink" manuscript and not the clean copy).
2. Attached a red ink manuscript highlighting the multitude of revisions
3. Attached a clean copy of the revised manuscript

All the authors have reviewed the revisions.

We look forward to hearing from you and your staff.

Sincerely,

Morgen S. Doty, D.O.
The University of Texas Health Science Center at Houston
Department of Obstetrics, Gynecology and Reproductive Sciences
6431 Fannin Street, MSB 3.262
Houston, Texas 77030
[redacted]

RE: Manuscript Number ONG-18-2408
Non-Macrosomic Large for Gestational Age Neonates: Maternal and Neonatal Morbidity

REVIEWER COMMENTS:

Reviewer #1:

Objective - to compare the rate of adverse outcomes in non-macrosomic LGA infants - >90th%, < 4000 gm versus AGA 10-89% between 37-39 wks of gestation

Methods - Retrospective cohort with US Vital Statistics Dataset from 2011-2013 - inclusion singleton, non-anomalous, AGA/LGA < 4000 gm, laboring, between 37-39 weeks
Primary outcome - maternal morbidity and neonatal morbidity

Results - 3.9 million, 1.3% non-macrosomic-LGA infants composite maternal morbidity was 53% higher in NM-LGA than in AGA with an increased risk in diabetics and non-diabetics composite neonatal morbidity was 83% higher for NM-LGA than AGA - higher in diabetics and non-diabetics

Conclusion - NM-LGA pregnancies/babies still have higher maternal and neonatal morbidities than AGA

Introduction - There are known risks with macrosomia but there is a gap in knowledge regarding morbidity/ mortality of NM-LGA pregnancies
The primary outcome was to compare maternal morbidity and neonatal morbidity with NM-LGA vs AGA infants and the secondary objective was outcome stratified by status of diabetics

Materials/ Methods - population based retrospective study period linked birth-infant death data files from 2011-2013 and birth certificate data statistical models were used to evaluate fetal growth status and risk of composite maternal/neonatal morbidity outcomes

Results - 3,917,831 live births meeting the inclusion criteria NM-LGA constitutes 1.3% of these NM-LGA likely to be older, non-Hispanic whites, overweight, GDM, hypertensive while AGA more likely to be primiparous and smokers
Maternal morbidity - 53% higher in NM-LGA than AGA in both diabetics and nondiabetics neonatal morbidity is 83% higher in NM-LGA than AGA - increased risk in both diabetics and nondiabetics

Discussion - NM-LGA constitutes 1% of births but with a 37-39% increased risk of an adverse outcome over AGA 50% increased rate maternal morbidity, 80% increased rate neonatal morbidity.

The management to address this is problematic because accelerated growth is not often recognized, this would increase c/s rate, induction prior to 39 weeks has not been evaluated,

ACOG does not recommend indcution for accelerated growth.

To study and address a decreased risk of 1/3, 29,000 women would have to be randomized for induction so this is not an achievable study.

Response: We appreciate the reviewer's summary of our manuscript. Since there does not seem to be a comment or a question in the summary above, we have not modified the manuscript.

Comments - This is an interesting and well-done study to show that with or without diabetes/ GDM, there is still and increased risk of neonatal and maternal morbidity in NM-LGA babies as compared to AGA babies.

Response: We truly appreciate the complement by the reviewer.

It is not clear to me if the proposal for a study would be elective induction prior to 39 weeks. This still shows an increased risk with delivery 37-39 weeks, so how early would delivery need to be performed to decrease the risk, and then the risk of prematurity would affect the neonatal risk, so any benefit would be outweighed by risk of prematurity.

While the increased risk is interesting, please clarify in discussion what the proposal is - it is not clear to me if the thought is to proceed with earlier delivery. This is not feasible given risks of prematurity, particularly given poor ability to estimate fetal weight.

Response: The reviewer requests a clarification of a hypothetical randomized trial to determine if the increased morbidity associated with non-macrosomic LGA is reducible. In line 224, we have added that in the planned randomized trial the intervention would be induction at 39 week, as compared to expectant management.

Also, these NM-LGA are identified after delivery, but how many were even known prior to delivery to even help guide management - either suggesting earlier delivery or to guide management if progress in labor is slower than anticipated. If not identified prior to labor, which often they aren't, there isn't much to be done. Please address how these were identified and if it was prior to labor or just with weight after delivery.

Response: The reviewer requests clarification of when the newborns were identified as being non-macrosomic LGA or AGA. In the revised manuscript, we have added: "The categorization of newborns being non-macrosomic LGA versus AGA was based on actual birthweight and the the dataset does not permit determination of whether the clinicians were aware of the accelerated growth, which may influence the management of labor.[14,15]" (lines 246-247).

Reviewer #2:

This is a well-done meticulous study evaluating the significance of maternal and perinatal morbidity of non-macrosomic LGA neonates with AGA neonates

Response: We truly appreciate the complement by the reviewer.

In the materials and methods I did not understand on page 9, lines 136-140 why sensitivity analysis was done for adverse outcome excluding maternal transfusion for the association of adverse outcomes?

Response: The reviewer asks an excellent question about why the sensitivity analysis was done. In the revised manuscript, we have added the following sentence, along with four references (lines 149-153): "Since the birth certificate data did not collect information regarding the number of units given in a blood transfusion, the reasons for doing the sensitivity analysis were as follows: 1) transfusion of 1-2 units has false positives[15]; 2) some investigators opine that transfusion of less than 4 units is subjective and not necessarily a "severe" morbidity[16,17]; and 3) we desired to be congruent with other publications on the topic[18]."

Reviewer #3:

The authors conducted a study to compare maternal and neonatal morbidities between NM-LGA and AGA. They found NM-LGA neonates compared to AGA neonates had higher risk of maternal and neonatal morbidities.

The findings provided additional knowledge for health care providers because this study was conducted in a specific population. The study helps us to better understand non-macrosomic LGA pregnancies.

Response: We truly appreciate the nuanced complimentary comments by the reviewer.

The current draft is organized but readers can only obtain limited information from the Method section. The authors need to further describe the dataset and study design. The reviewer's comments mainly focus on the Method section. The comments/suggestions are listed below:

METHOD

Data source

1. The data source and study design were not clearly described in this section. Readers can only have limited information to know this study because they are not quite familiar with the dataset. For example, what is the type of the dataset? Is it a survey dataset, administration claim dataset, or a registration dataset? The authors only mentioned the data were annually reported by CDC. This is not enough.

Response: We appreciate the reviewer's request for additional information about data source and study design. We have added "cohort" to the abstract, and have added the following sentence in line 84: "This was a population-based retrospective cohort study using the Period Linked Birth-Infant Death Data Files of the United States Vital Statistics Data from 2011-2013 assembled by the National Center for Health Statistics and reported annually by the Centers for Disease Control and Prevention (CDC). These data, ascertained through birth certificates, comprised all live births in the United States between 2011 and 2013 and were linked to infant deaths within the first year."

2. The authors also need to address the advantage/disadvantage of the dataset. It could help the readers to understand the strength and weakness of the study.

Response: The reviewer's request to provide strengths and weakness is understandable. In lines 230-234, we describe the strengths of our dataset, and in lines 235-252 the weaknesses, or "limitations".

3. In addition, in the first paragraph, the authors mentioned the data file (Period linked Birth-infant Death Data File) was from 2011-2013. However, in the second paragraph, they mentioned the 2003 revised birth certificate. This is confusing. What is the link between the data file and the birth certificate? Furthermore, they mentioned the data of maternal morbidity was added in 2011 and dropped in 2014. Again, this is confusing. What is the purpose of doing so? Please clarify. Would the lack of information (maternal morbidity) have impact on the study validity?

Response: The reviewer requests clarification about the data. The National Center for Health Statistics (NCHS) has been collaborating with colleagues in state vital statistics offices to revise the certificates of live birth and death, and the report of fetal death. This process is generally carried out every 10 to 15 years. Prior to 2003, the most recent revisions in effect were implemented in 1989. In 2003, the birth certificate was revised again to include more detailed obstetric, medical and demographic information. The 2003 birth certificate is the most current form of the NCHS birth certificate. Maternal morbidity measures were initially collected in the 2003 version of birth certificate and have been added to the Period linked Birth-infant Death Data Files since 2011, and some measures were dropped in 2014. We chose to use data from 2011-2013 in order to utilize the most available data of maternal morbidity. This is addressed in lines 97, and by the addition of "and is the currently used birth certificate by the CDC" to the manuscript.

4. The data were from 38 states. Did the rest of 12 states not provide the data? This part is not clear, either. Please clarify. (Again, how did the data form?) Will the finding be generalized to the whole U.S. population? Please explain.

Response: The reviewer requests clarification about the number of states included and about generalizability. As we have described in the paper (lines 96-103), we used the 2003 revised

birth certificate. The revised birth certificate was used by 36 states and the District of Columbia (D.C.) in 2011, 38 states and D.C. in 2012, and 41 states and D.C. in 2013, which represented 83%, 86%, and 90% of live births in the U.S., respectively. Therefore, our findings may not be generalizable to the whole U.S. population. We have included this in the limitation section (lines 237-240).

5. The paragraph "The 2003 revision …" created more questions than answers. What is the main message that the authors wanted to deliver in this paragraph? Please explain. Are these two estimates distinct? Please clarify.

Response: The reviewer requests clarification about gestational age. The paragraph "The 2003 revision …" intends to explain the definition of gestational age we used in this manuscript. As we stated in the manuscript, detailed information of the methods for this obstetric estimate of gestation is available in the Vital Statistics data set guidelines. (Please see reference 13). Additionally, we have added the following sentence (lines 111-115) in the revised manuscript: "The reason for selecting obstetric estimate, over clinical estimate, is due to increasing evidence of greater validity of the obstetric estimate compared with the LMP-based estimate. The National Center for Health Statistics transitioned to the obstetric estimate as the standard for estimating the gestational age of a newborn in 2014.[14]"

Study design

6. The outcome of this study was a composite measure of several maternal morbidities or neonatal morbidities. The reviewer suggests the authors to conduct an analysis of each maternal morbidity and neonatal morbidity first. Then, they can look at the composite measure. Doing so would obtain a more comprehensive result.

Response: We appreciate the reviewer's comment. But the primary goal was to examine the association between fetal growth and composite morbidity. Since some individual morbidity outcomes have very few cases, conducting multivariable regression analysis in individual morbidity may not have meaningful results. Therefore, we choose not to present analysis of individual morbidity.

7. Is this a cohort study or a cross-sectional study? This goes back to the previous question that the reviewer mentioned regarding the type of the dataset.

Response: The reviewer has an excellent question about the type of the study we conducted. As we stated in the Methods section, this was a retrospective cohort study. We used the Period Linked Birth-Infant Death Data Files of the United States Vital Statistics Data. In the linked birth and infant death data set, the information from the death certificate is linked to the information from the birth certificate for each infant within 1 year of age who dies in the United State. Also see response to Q1 in STATISTICAL EDITOR'S COMMENTS.

Covariate adjustment

8. How did these covariates identify? Did the dataset contain the information of these variables? What are the operational definitions of these variables? Were these variables measured before or during pregnancy? If they were measured before pregnancy, what was the period of the measurement? Please explain/clarify.

Response: The reviewer asks a good question about the covariates. The covariates were selected a priori as they are known potential confounders. All variables were obtained from birth certificate data.

The operational definitions of these variables were provided in "Birth Edit Specifications for the 2003 Revision of the U.S. Standard Certificate of Birth." For example, mother's education was defined as the highest degree or level of schooling completed by the mother at the time of this delivery. This variable was measured during pregnancy. For detailed information of all covariates, please see the document mentioned above.

9. In this dataset, would it be possible to identify prescription use among pregnant women? Comorbidities can be identified and adjusted. The authors did so. How about the prescription use? Medication use before and during pregnancy can also be a confounder.

Response: The reviewer has a good suggestion about being able to identify prescription use among pregnant women. There was, regretfully, no information of prescription use collected in birth certificate data. Thus, we could not adjust for unmeasured confounders. We have included that in the limitation section (lines 249-251): "Though we adjusted for several confounders, we could not adjust for unmeasured confounders like obstetric history, suspected LGA, medication use before and during pregnancy, and the type of hospital where the delivery occurred."

10. The statement of the sensitivity was not clear. What was the sensitivity analysis that the authors conducted? This part was not clear. The authors only mentioned the sensitivity analysis in one sentence, and without any further clarification. Please clarify.

Response: The reviewer understandably inquires about the reason for sensitivity analysis. In the revised manuscript, we have added the following sentence, along with four references (lines 149-153): "Since the birth certificate data did not collect information regarding the number of units given in a blood transfusion, the reasons for doing the sensitivity analysis were as follows: 1) transfusion of 1-2 units has false positives[15]; 2) some investigators opine that transfusion of less than 4 units is subjective and not necessarily a "severe" morbidity[16,17]; and 3) we desired to be congruent with other publications on the topic[18]."

STATISTICAL EDITOR'S COMMENTS:

1. If the cases were comprised of singletons with BW ≥ 90th centile, but < 4000 grams, then the

reference criteria (1996-1999) seem unsuitable to this cohort, since only 1.3% were NM-LGA, while 7% were LGA with macrosomia. Also, the differential between 90th percentile for GA vs 4000 grams would represent a smaller proportion for males, since their BWs are skewed to higher values compared to females. This results in a higher proportion of males in the cases studied and males are known to have higher neonatal morbidity/mortality.

Response: The statistical editor has an insightful question about how we categorized newborns as being LGA and why the rate of LGA was low (1.3%). We used fetal growth criteria promulgated by Alexander et al (reference #11), which has been widely used in the obstetric publications.

The reason for low rate of LGA and macrosomia in our study is that we restricted the analysis to women that were U.S. residents; who delivered between 2011 and 2013; had a singleton, non-anomalous gestation between 37 and 39 weeks; had labor; had a neonate that was AGA or LGA with birth weight < 4,000 g; had diabetes status recorded; and had birth data recorded using the 2003 revised birth certificate (Figure 1).

Lastly, though there is higher proportion of male newborns, our results were adjusted for several potential confounders, including infant sex.

2. Tables 3 and 5: Need to include a column citing the counts for composite morbidities for all row entries. The samples are large, but for the GDM and pre-GDM strata, the counts are respectively ~50 and ~13 for maternal morbidity. These are too few to allow precise correction for 12 covariates in the aRR models. So, the conclusion holds for all and for non-diabetic, but there are too few counts to be assured of the same conclusion for the smaller subsets. Could attempt a matching algorithm, given the large sample of AGA. Also, should include a column of crude RR.

Response: The statistical editor poignantly requests additional data for Table 3 and 5. In the revised manuscript, we have included a column citing the counts for composite morbidities for all row entries in Tables 3, 5, and 6. We also included crude RR.

Our multivariable regression models included data from mothers with AGA and non-macrosomic LGA live births; fetal growth (AGA vs. non-macrosomic LGA) was used as the exposure variable, and the numbers of our composite maternal morbidity outcomes ranged from 192 to 14,597 in diabetic subgroups, and the numbers of our composite neonatal morbidity outcomes ranged from 396 to 21,919. Therefore, model over-fit was less of a concern. Since our aim was to compare outcomes between fetal growth groups, we did not perform an analysis only within the non-macrosomic LGA group, as reviewer commented.

3. Table 4: Need to include CIs for rates.

Response: The statistical editor's suggestion of providing CI in Table 4 is excellent. In the revised manuscript, we included CIs for rates in Table 2 and Table 4.

4. For Table 5: The counts of neonatal morbidity for pre-GDM and for GDM are ~ 41 and 85, respectively, again too few for 12 covariates as adjustors in the aRR model.

Response: Please see our response to Q2 in STATISTICAL EDITOR'S COMMENTS.

5. Table 6: Same issue as with Tables 3 and 5 re: counts of adverse events and aRR models and need to include crude RR column and column of actual counts of morbid events.

Response: Please see our response to Q2 in STATISTICAL EDITOR'S COMMENTS

6. General: To what extent are the increases in maternal and neonatal morbidities associated with increased rate of cesarean?

Response: The statistical editor has an excellent question about cesarean delivery and associated morbidity. In this study, our primary goal was to examine the association between fetal growth and morbidity outcome. We did not examine the association between delivery method and morbidity outcome, since it may be in the causal pathway between fetal growth and morbidity outcome.

ASSOCIATE EDITOR'S COMMENTS:

Please, if you choose to revise (and I hope you do)

1) Include actual birthweights of the LGA, non-macrosomic infants --median (range)

Response: The Associate Editor's request to provide actual birthweight of LGA, non-macrosomic newborn is excellent. In the revised manuscript, we include the median (interquartile range) birth weight in Table 1.

2) Use only standard abbreviations

We have corrected the manuscript to only use standard abbreviations.

3) Pay special heed to the comments of the Statistical Editor.

See responses above to Statistical Editor's comments.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing.

If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, 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.

Response: We will OPT-IN.

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

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

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.

3. 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.

4. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of

randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 26 typed, double-spaced pages (6,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

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

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

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear

conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

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

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

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

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

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

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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.

***

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 Feb 20, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

Daniel Mosier

From: Doty, Morgen S [redacted]
Sent: Thursday, March 14, 2019 4:14 PM
To: Daniel Mosier
Subject: Re: [EXTERNAL EMAIL] Fwd: Manuscript Revisions: ONG-18-2408R1
Attachments: 18-2408R1 ms 3-14-19v5.docx

Daniel,
I have made a few minor edits, and changed Tables 5 and 6 to Appendix 1 and 2. See attached.
Thanks,
Morgen

From: Daniel Mosier <dmosier@greenjournal.org>
Sent: Thursday, March 14, 2019 2:46 PM
To: Doty, Morgen S
Subject: [EXTERNAL EMAIL] RE: [EXTERNAL EMAIL] Fwd: Manuscript Revisions: ONG-18-2408R1

Dr. Doty,

Thank you for addressing our questions in a timely manner. The editor on your manuscript has reviewed your latest revision, and has a couple of follow-up questions:

1. Several minor edits and deletions have been made to this version. Please review your manuscript carefully to ensure that no mistakes or discrepancies were accidentally introduced during the editing process.
2. TABLES 5 AND 6: Yes, our Journal commonly references supplemental tables in the Results and Discussion sections. You are correct: Please remove those tables from the paper, and rename the citations “Appendix 1, Appendix 2” throughout.

Please let me know if you have any other questions or concerns.

Sincerely,
-Daniel Mosier

Daniel Mosier
Editorial Assistant
Obstetrics & Gynecology
Tel: 202-314-2342

From: Doty, Morgen S [redacted]
Sent: Wednesday, March 13, 2019 8:22 PM
To: Daniel Mosier <dmosier@greenjournal.org>
Cc: Morgen Doty [redacted]
Subject: Re: [EXTERNAL EMAIL] Fwd: Manuscript Revisions: ONG-18-2408R1

Mr Dosier,

Attached are the corrections / comments for the manuscript **ONG-18-2408R1**.

I appreciate the comments, and have incorporated the edits. If there is anything further I can assist in getting this manuscript ready for print, please let me know. I also had a question regarding the tables becoming supplemental digital content - please see comments in the tracked change copy within this email.

Also, do I need to upload this to editorial manager? I could not find a place to upload these changes, but would be happy to if you guide me to the correct location.

Thanks you,
Morgen Doty

From: Msdoty [redacted]
Sent: Wednesday, March 13, 2019 11:18 AM
To: Doty, Morgen S
Subject: [EXTERNAL EMAIL] Fwd: Manuscript Revisions: ONG-18-2408R1

Sent from my iPhone

Begin forwarded message:

> **From:** Daniel Mosier <dmosier@greenjournal.org>
> **Date:** March 12, 2019 at 11:53:37 AM CDT
> **To:** Morgen Doty [redacted]
> **Subject: Manuscript Revisions: ONG-18-2408R1**
>
> Dear Dr. Doty,
>
> Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:
>
> 1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.
> 2. LINE 1: Note edits to title.
> 3. LINE 21: 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. Please provide a signed version of this statement.
> 4. LINE 28: Han-Yang Chen will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.
> 5. LINE 30: Newborns are aged one month to one year; neonates are aged birth to one month. Do you intend to say "neonates" here?
> 6. LINE 52: Note the edits to the first sentence of the Conclusion.

7. LINE 168: Please carry through the rest of the manuscript the phraseology that I have been using. Maternal morbidity can't occur in non-macrosomic LGA neonates--maternal morbidity occurs in the mothers who deliver such neonates.
8. TABLE 5: Please move this and the next table to supplemental digital content

When revising, use the attached version of the manuscript. Leave the track changes on, and do not use the "Accept all Changes"

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on **Thursday, March 14th**.

Sincerely,
-Daniel Mosier

Daniel Mosier
Editorial Assistant
Obstetrics & Gynecology
The American College of Obstetricians and Gynecologists
409 12th Street, SW
Washington, DC 20024
Tel: 202-314-2342
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Web: http://www.greenjournal.org

From: Daniel Mosier
To: Denise Shields; Eileen Chang (Temp)
Subject: FW: Figure Revisions: ONG-18-2408R1
Date: Tuesday, March 26, 2019 8:36:21 AM

Daniel Mosier
Editorial Assistant
Obstetrics & Gynecology
Tel: 202-314-2342

From: Morgen Doty [redacted]
Sent: Monday, March 25, 2019 4:56 PM
To: Daniel Mosier <dmosier@greenjournal.org>
Subject: Re: Figure Revisions: ONG-18-2408R1

Daniel,
Looks great!
Thanks,
Morgen

> On Mar 25, 2019, at 1:08 PM, Daniel Mosier <dmosier@greenjournal.org> wrote:
>
> Dr. Doty,
>
> Thank you for the timely reply. The Journal's staff had edited the figure based on your message, although we will not be using a hyphen for "Nonmacrosomic" as that would violate Journal style.
>
> Please let us know if you have any other questions or concerns.
>
> Sincerely,
> -Daniel Mosier
>
> **Daniel Mosier**
> Editorial Assistant
> *Obstetrics & Gynecology*
> Tel: 202-314-2342
>
> ---
>
> **From:** Morgen Doty [redacted]
> **Sent:** Wednesday, March 20, 2019 1:00 PM
> **To:** Daniel Mosier <dmosier@greenjournal.org>
> **Subject:** Re: Figure Revisions: ONG-18-2408R1
>
> Daniel,

Two changes for the figure:
1. In the lower left box, there should be a hyphen for “Non-macrosomic”
2. The box on the top right should have “Using 1989 revision of birth certificate”, using 1989 instead of 1987.

Otherwise, looks great!
Morgen

> On Mar 19, 2019, at 1:09 PM, Daniel Mosier <dmosier@greenjournal.org> wrote:
>
> Dear Dr. Doty,
> Your figures and legend have been edited and they have been attached for your review. Please review the attachments CAREFULLY for any mistakes.
> PLEASE NOTE: Any changes to the figures must be made now. Changes made 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 appreciate a reply no later than **Thursday, 3/21**.
> Thank you for your help.
> Sincerely,
> -Daniel MOsier
>
> **Daniel Mosier**
> Editorial Assistant
> *Obstetrics & Gynecology*
> The American College of Obstetricians and Gynecologists
> 409 12th Street, SW
> Washington, DC 20024
> Tel: 202-314-2342
> Fax: 202-479-0830
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> Web: http://www.greenjournal.org
>
> <18-2408 Fig 1 (03-18-19 v2).pdf><18-2408R1 figure legend.docx>

<18-2408 Fig 1 (03-25-19 v3).pdf>