OBSTETRICS & GYNECOLOGY

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

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

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

Personal or nonessential information may be redacted at the editor's discretion.

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

Date: Nov 14, 2019
To: "Ellen Marie Hartenbach"[redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1984

RE: Manuscript Number ONG-19-1984

More Blood Transfusions for Rural Women Delivering

Dear Dr. Hartenbach:

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 14 days from the date of this letter. If we have not heard from you by Nov 28, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Precis - Odds of peripartum blood transfusion higher for low risk women in rural US than in more urban areas

Abstract - Objective - maternal morbidity and mortality is increasing - goal was to evaluate outcome based on race and geography and evaluate transfusion rates as a marker of morbidity
Methods - 2014-2016 - birth records reviewed, information on rural versus urban counties, difference in blood transfusion in vertex, term deliveries
controlled for age, race, nativity, education, insurance, prenatal care, BMI, DM, HTN, tobacco use, gestational age, intrapartum care, mode of delivery, peripartum factors, county of delivery
Results - 3,346,816 eligible births - transfusion increases as counties become increasingly more rural from 2.5 versus 8.5 / 1000
county of delivery counted more than county of residence
Conclusion - odds of transfusion is higher in a more rural area - county of birth matters which reflect a difference in maternity care services

Introduction - Maternity morbidity and mortality are increasing and OB hemorrhage constitutes 11.5% of pregnancy related deaths in US; hypothesis: rural areas have an increase rate of transfusion

Methods - US population based retrospective cohort - 2014-2016 - transfusions listed on birth certificates
impact from county of residence and county of delivery - hospital births, nulliparous, single, term, vertex
socioeconomic and demographic factors - age, race, education, insurance, cigarette use, BMI, DM, HTN, induction, antibiotic use, chorioamnionitis, mode of delivery
looked at the association between urbanicity and transfusion, then added socioeconomic and demographic issues, then added maternal health, then L&D conditions, then the county of deliver

Results - 3,346816 eligible NTSV births - overall transfusion 3/1000
transfusion rate increased as county became more rural - from 1.9 to 5.3 per 1000 births
increase in transfusion if deliver in a more rural county than a hospital and county of delivery matters more than county of residency
after all adjustments, main driver is county of delivery

Discussion - transfusion as an indicator of maternity morbidity
risk is higher for low risk women in rural areas
individual risk factors for transfusion did not account for difference in rural women so thereis something at the health

system level
less prompt recognition of hemorrhage or lower threshold to transfuse
increase risk of hemorrhage at low volume hospitals - disparities not based on race but rather ruralness of hospital
guidelines for best practices could help rural hospitals since difference seems to be in maternity care not maternal characteristics

Comments -
1. This is an interesting evaluation of an important topic.

2. Rural hospitals, certain demographics of patients, lower volume hospitals are known to have poorer outcomes

3. This study reinforces the idea that higher volume of service leads to lower risks

4. Furthermore, this illustrates that discrepancies are not based on race or socioeconomic issues but rather delivery in rural hospitals therefore, opportunities to address these shortcomings exist

5. It is also important to note that this difference is not due to maternal characteristics but rather location of hospital.

6. This problem is then more easily addressed with practice guidelines and education than if it were related to race.

7. This is helpful in understanding that health care disaprities are not just race related but rather related to site of care.

Reviewer #2:

1) The authors note increasing maternal morbidity and mortality nationwide, as well as apparent demographic differences that define groups at the highest risk.

2) The hypothesis of the authors is that transfusion is the most common indicator of severe peripartum maternal morbidity and can serve as a surrogate marker to identify populations, situations, or conditions at risk for other adverse maternal outcomes.

3) This manuscript describes a retrospective cohort study that examines multiple factors potentially associated with peripartum transfusion.

4) The study consists of an analysis of data extracted by the National Center for Health Statistics from birth certificates between 2014 and 2016.

5) From a total of 11.9 million births, data was analyzed from 3.3 million births from nulliparous women with singleton, term, vertex presentations.

6) Using a stepwise logistic regression method, the effects of multiple variables on the transfusion rate were determined.

7) These variables included rurality of both the county of residence and the county of delivery.

8) Other demographic variables included race, nativity, age, education, marital status, insurance, and prenatal care initiation.

9) Health related variables included antepartum medical conditions, intrapartum complications, and delivery complications.

10) Multivariable regression control for all factors continued to show higher transfusion rates related to rurality of county of delivery, with a smaller effect related to the county of residence.

11) The county of delivery was more important than any other factor except for the need for facility transfer and the use of forceps, which were similar in effect to facility rurality.

12) The authors conclude that possible explanations for this observation include less aggressive prevention of hemorrhage, delays in diagnosis, and a lower threshold for transfusion in rural facilities.

13) The authors conclude that declining rural deliveries and disproportionate allocation of resources may be underlying causes of the observed differences.

14) More research on the applications of practice guidelines and maternal care resources to rural facilities is suggested.

15) The data presented in this paper is extensive and essentially represents a national cohort. The dominant influence of the rurality of delivery on this important morbidity indicator is surprising.

16) The conclusions are important and justified and suggest a need for more research on issues related to quality of maternal care in rural facilities.

17) The paper is well organized and written in a style that is engaging and easy to understand.

Reviewer #3: In this manuscript, the authors present an analysis of birth certificate data to explore the impact of rural delivery location and residence on blood transfusion rates as a marker of severe maternal morbidity. This is a well described analysis. The authors present the limitations well also.

1. Abstract conclusion states that county of where the birth occurred "largely explains" higher transfusion rates. However, in the multivariable model, multiple other factors which were taken into consideration were still significantly associated with transfusion, notably labor and delivery characteristics and being of Asian descent. Thus, it does not seem the results support this ranking of explanation of transfusion rates.

2. The sensitivity analyses are appropriate. Perhaps an appendix would be useful for these data.

3. the finding of delivering in a more rural county than one's residence being associated with a higher risk of transfusion is interesting and was striking when looking at table 2 when women who lived in LMC delivered in non-Core places (rate of 18.5 per 1,000 women).

4. Describing 5 models in the methods and results but only having 3 of them in the Table is somewhat confusing.

5. The authors mention bundles that are coming out now. Postpartum hemorrhage is a popular bundle to be implemented. Is it possible that these bundles are more rigorous or recommend lower transfusion thresholds at more rural facilities? This could be a follow up study on how they are being implemented possibly differently.

STATISTICAL EDITOR COMMENTS:

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

Fig 2: Should add CIs for the transfusion rates.

Table 1: Need units for maternal age, BMI.

Table 2: Could include this in supplemental material with concise description in main text.

Table 3: Need units for maternal age, BMI. These models each are multivariable and should be referred to as aORs or adjusted ORs. Should round all ORs and their CIs to nearest 0.01. Is row entry, M5 OR is missing a decimal. Given the number of comparisons in this Table, should use a stricter inference threshold than $p < .05$, due to multiple hypothesis testing. Could omit the log-likelihood and BIC from the Table (could cite in supplemental if desired).

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.

- Perhaps "the rate of peripartum blood transfusion...."?

- 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.

As an example, the Objective of the Abstract should be a simple "to" statement without background.

As well, tables and figures are not to be placed within the text--see instructions for authors for further information,.

- Line 43: In your precis you use the phrase "low risk women"; in your title you use "low risk infants" and in your abstract you use neither. Please be consistent and define your population. Of course, just because a woman is a NSTV (which you define as your patient population on line 50 and which I'm guessing is your definition of "low risk woman") doesn't make her low risk for post partum hemorrhage--she may have fibroids, a clotting disorder, polyhydramnios, anemia, which makes her at increased risk for needing a transfusion.

- Line 65: Impact implies causation. Your paper can report associations only. Please revise your paper to include associative language throughout.

- line 77: "Is increasing" seems less colloquial than "is on the rise".

- Line 92: Are the infant outcomes "poor" or just not as good as in urban setting?

- It is the CENTERS for Disease Control and Prevention. Note the plural in Centers and the full name.

- Line 95: Please provide the ratio between maternal mortality and SMM

- Line 116: Can you provide this schema in a box in the manuscript or in Supplemental Digital Content?

- Line 121: please state why the IRB exempted this

- Line 134: This is an oversimplification. Not all NTSV pregnancies are low risk by any means. This really needs to be addressed. Women in rural settings may be at higher risk for diabetes, substance use, hypertension, etc etc based on their rural settings. If you wish to make an argument that you used NTSV to define a comparable group of patients for the different settings, that's fine, but its a big reach to describe them as low risk.

Line 136: Its the American College of Obstetricians and Gynecologists.

- Line 138: please consolidate this information with introduction of this information on line 116

- "Moms" is colloquial. Perhaps "Women" or "Mothers"?

- Line 197: please provide some statistical evidence that these are something other than numerically higher. "Generally higher" is very vague and non informative.

- Line 202 and throughout: As these abbreviations will be relatively unfamiliar to our readers, please spell these out rather than abbreviate them.

- Line 211: another example of causal language.

- Line 246: causal language. Of note, I've not pointed out all instances of causal language, just some examples. You need to edit throughout

- For all tables, please embolden all significant rows.

- Line 260: The discussion can be shortened by about 10%.

- Line 268: Please see my prior strong concerns about this statement.

- Line 269: Please provide a reference for this statement. While I believe this is good practice, please provide evidence that it is "generally" done.

- Line 295: Please provide some description of available blood banking resources at rural vs urban hospitals. Limited resources may result in practice pattern to transfuse at a lower threshold in order to "stay ahead".

- Line 297: Please delete "dramatically" and let the reader decide how different they are. Is 6 more per 1000 dramatic?

- Line 315: causal. Please provide a reference for "healthy mothers lead to healthy communities"

- please either use the abbreviation or correctly use the name.

- Line 333: again, refrain from this here.

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.

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

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

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

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

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

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

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

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and

acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

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

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

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

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

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

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

14. Figures

Figure 1: Please add exclusion boxes. Upload figure as a separate figure file on Editorial Manager.

Figure 2: Upload figure as a separate figure file on Editorial Manager.

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

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

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

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

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

Again, your paper will be maintained in active status for 14 days from the date of this letter. If we have not heard from you by Nov 28, 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

[redacted]

[redacted]

December 5, 2019

Nancy C. Chescheir, MD
Editor-in-Chief
Obstetrics & Gynecology

RE: **Manuscript Number ONG-19-1984**

Dear Dr. Chescheir,

I am resubmitting our manuscript with significant revisions based on the suggestions and questions provided by you and the reviewers. The revised manuscript is entitled, "**More Peripartum Blood Transfusions for Rural Women in the United States"**. I am very hopeful you will find the revised manuscript suitable and worthy of publication in Obstetrics & Gynecology. The topic of disparities in maternal care in rural counties in the United States is timely and I believe we have addressed the concerns you noted in the first submission.

We presented our work at the annual meeting of the American College of Obstetrics and Gynecology in Nashville. We are only submitting the manuscript to Obstetrics & Gynecology and it is not under consideration elsewhere nor will we will submit elsewhere unless a final negative decision is made by the Editors of Obstetrics & Gynecology. I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. The University of Wisconsin Minimal Risk Institutional Review Board (Health Sciences) declared this research exempt since it does not involve human subjects as defined under federal regulation 45 CFR 46.102(e)(l). All authors listed in the byline meet the criteria recommended by the International Committee of Medical Journal Editors. I carefully read the Instructions for Authors provided at this website: http://edmgr.ovid.com/ong/accounts/authors.pdf.

As requested, the following pages outline a point by point response to the comments made by you and the reviewers. The revised manuscript indicates the position of all changes made and I utilized the "track changes" feature in my word processing software. The revised manuscript was developed in consultation with my co-authors and each author has given approval to the final form of this revised manuscript. On behalf of my co-authors, I want to thank you in advance for reviewing our work.

Sincerely,

Ellen Hartenbach MD, FACOG
[redacted]

RE: Manuscript Number ONG-19-1984

More Peripartum Blood Transfusions for Rural Women in the United States

Reviewer #1: Precis - Odds of peripartum blood transfusion higher for low risk women in rural US than in more urban areas

Abstract - Objective - maternal morbidity and mortality is increasing - goal was to evaluate outcome based on race and geography and evaluate transfusion rates as a marker of morbidity Methods - 2014-2016 - birth records reviewed, information on rural versus urban counties, difference in blood transfusion in vertex, term deliveries controlled for age, race, nativity, education, insurance, prenatal care, BMI, DM, HTN, tobacco use, gestational age, intrapartum care, mode of delivery, peripartum factors, county of delivery Results - 3,346,816 eligible births - transfusion increases as counties become increasingly more rural from 2.5 versus 8.5 / 1000 county of delivery counted more than county of residence Conclusion - odds of transfusion is higher in a more rural area - county of birth matters which reflect a difference in maternity care services

Introduction - Maternity morbidity and mortality are increasing and OB hemorrhage constitutes 11.5% of pregnancy related deaths in US; hypothesis: rural areas have an increase rate of transfusion

Methods - US population based retrospective cohort - 2014-2016 - transfusions listed on birth certificates impact from county of residence and county of delivery - hospital births, nulliparous, single, term, vertex socioeconomic and demographic factors - age, race, education, insurance, cigarette use, BMI, DM, HTN, induction, antibiotic use, chorioamnionitis, mode of delivery looked at the association between urbanicity and transfusion, then added socioeconomic and demographic issues, then added maternal health, then L&D conditions, then the county of deliver

Results - 3,346816 eligible NTSV births - overall transfusion 3/1000 transfusion rate increased as county became more rural - from 1.9 to 5.3 per 1000 births increase in transfusion if deliver in a more rural county than a hospital and county of delivery matters more than county of residency after all adjustments, main driver is county of delivery

Discussion - transfusion as an indicator of maternity morbidity risk is higher for low risk women in rural areas individual risk factors for transfusion did not account for difference in rural women so thereis something at the health system level less prompt recognition of hemorrhage or lower threshold to transfuse increase risk of hemorrhage at low volume hospitals - disparities not based on race but rather ruralness of hospital guidelines for best practices could help rural hospitals since difference seems to be in maternity care not maternal characteristics

Comments -
1. This is an interesting evaluation of an important topic.

2. Rural hospitals, certain demographics of patients, lower volume hospitals are known to have poorer outcomes
3. This study reinforces the idea that higher volume of service leads to lower risks
4. Furthermore, this illustrates that discrepancies are not based on race or socioeconomic issues but rather delivery in rural hospitals therefore, opportunities to address these shortcomings exist
5. It is also important to note that this difference is not due to maternal characteristics but rather location of hospital.
6. This problem is then more easily addressed with practice guidelines and education than if it were related to race.
7. This is helpful in understanding that health care disaprities are not just race related but rather related to site of care.

We appreciate the positive comments of Reviewer #1.

Reviewer #2:

1) The authors note increasing maternal morbidity and mortality nationwide, as well as apparent demographic differences that define groups at the highest risk.
2) The hypothesis of the authors is that transfusion is the most common indicator of severe peripartum maternal morbidity and can serve as a surrogate marker to identify populations, situations, or conditions at risk for other adverse maternal outcomes.
3) This manuscript describes a retrospective cohort study that examines multiple factors potentially associated with peripartum transfusion.
4) The study consists of an analysis of data extracted by the National Center for Health Statistics from birth certificates between 2014 and 2016.
5) From a total of 11.9 million births, data was analyzed from 3.3 million births from nulliparous women with singleton, term, vertex presentations.
6) Using a stepwise logistic regression method, the effects of multiple variables on the transfusion rate were determined.
7) These variables included rurality of both the county of residence and the county of delivery.
8) Other demographic variables included race, nativity, age, education, marital status, insurance, and prenatal care initiation.
9) Health related variables included antepartum medical conditions, intrapartum complications, and delivery complications.
10) Multivariable regression control for all factors continued to show higher transfusion rates related to rurality of county of delivery, with a smaller effect related to the county of residence.
11) The county of delivery was more important than any other factor except for the need for facility transfer and the use of forceps, which were similar in effect to facility rurality.

There are many variables that are significantly associated with increased transfusion in our analysis including the use of forceps in vaginal birth and facility transfer as noted by this reviewer. The purpose of our study, however, was to examine the blood transfusion rates across rural-urban gradients. The use of forceps and maternal transfer was treated as a control variable along with numerous other predictors. We took into account the associations between blood transfusion and the use of forceps, maternal transfer, and an array of variables related to maternal socioeconomic and demographic background,

maternal health, morbidities, and adverse labor processes. In the final model, the significant association of delivery in a more rural facility remained.

12) The authors conclude that possible explanations for this observation include less aggressive prevention of hemorrhage, delays in diagnosis, and a lower threshold for transfusion in rural facilities.
13) The authors conclude that declining rural deliveries and disproportionate allocation of resources may be underlying causes of the observed differences.
14) More research on the applications of practice guidelines and maternal care resources to rural facilities is suggested.
15) The data presented in this paper is extensive and essentially represents a national cohort. The dominant influence of the rurality of delivery on this important morbidity indicator is surprising.
16) The conclusions are important and justified and suggest a need for more research on issues related to quality of maternal care in rural facilities.
17) The paper is well organized and written in a style that is engaging and easy to understand.

We appreciate the favorable comments of Reviewer #2

Reviewer #3: In this manuscript, the authors present an analysis of birth certificate data to explore the impact of rural delivery location and residence on blood transfusion rates as a marker of severe maternal morbidity. This is a well described analysis. The authors present the limitations well also.
1. Abstract conclusion states that county of where the birth occurred "largely explains" higher transfusion rates. However, in the multivariable model, multiple other factors which were taken into consideration were still significantly associated with transfusion, notably labor and delivery characteristics and being of Asian descent. Thus, it does not seem the results support this ranking of explanation of transfusion rates.

We were mainly interested in examining the association between rurality and blood transfusion. The influence of the other variables was taken into consideration in our analysis. We do not intend to suggest that the rural-urban gradients of the delivery/residence are the only explanation. We did not rank variables by their impact. The results do indicate that the rurality of the county where the birth occurred accounts for more of this disparity than does the rurality of the mother's residence county.

2. The sensitivity analyses are appropriate. Perhaps an appendix would be useful for these data.

The sensitivity analyses were included as supplemental digital content and are now cited in the manuscript as Appendix 1.

3. The finding of delivering in a more rural county than one's residence being associated with a higher risk of transfusion is interesting and was striking when looking at table 2 when women who lived in LMC delivered in non-Core places (rate of 18.5 per 1,000 women).

4. Describing 5 models in the methods and results but only having 3 of them in the Table is somewhat confusing.

We agree with this reviewer that it would be preferable to include the details of all the models in Table 3. Given space limitations on a page, we decided to include the data on the last three models in Table 3. The information about the details of all the models is included in the text and an abbreviated version at the bottom of Table 3. If upon further review, the editorial office desires the full data on all 5 models in Table 3 or in supplementary materials, we are happy to provide these.

5. The authors mention bundles that are coming out now. Postpartum hemorrhage is a popular bundle to be implemented. Is it possible that these bundles are more rigorous or recommend lower transfusion thresholds at more rural facilities? This could be a follow up study on how they are being implemented possibly differently.

The postpartum hemorrhage bundle is not a strict guideline and there are not specific transfusion thresholds for obstetrical patients in various hospital facilities based on rurality. Patient safety bundles recommend best practices based on existing guidelines and suggest an approach to hemorrhage management in each facility based on the four action items of readiness, recognition and prevention, response, and reporting and systems.

The reviewer brings up a good point that some rural providers may have a lower threshold for recommending a blood transfusion and that these quality bundles are likely to be implemented differently at different facilities. This is now clearly noted in the discussion section as a possible explanation for the association of higher rates of transfusion in rural hospitals.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:
Fig 2: Should add CIs for the transfusion rates.

The confidence intervals for the county of residence and county of delivery variable depicted in Figure 2 (now Figure 3) were added as requested.

Table 1: Need units for maternal age, BMI.

The units were added to Table 1 for the categorical variables of maternal age and BMI. Maternal age is measured in years (less than 18 years old, 18-19 years, 20-24 years, 25-29 years (reference group), 30-34 years, 35-39 years, and 40 years old and older). BMI is measured in units of kg/m^2 (BMI < 18.5 underweight, 18.5-24.9 normal weight, 25-29.9 overweight), 30-34.9 Obese I, 35-39.9 Obesity II, >40 Obesity III).

Table 2: Could include this in supplemental material with concise description in main text.

The distinction of the association of transfusion rates based on county of residence in comparison to county of delivery is most easily seen in the women who move between counties. The complexity of the data included in Table 2 is difficult to translate to text. We believe that discerning readers will likely seek this information and thus would prefer to keep Table 2 in the main body of the manuscript. If this is important to the editor, Table 2 could certainly be moved to a supplemental data file and additional text added to the manuscript.

Table 3: Need units for maternal age, BMI. These models each are multivariable and should be referred to as aORs or adjusted ORs. Should round all ORs and their CIs to nearest 0.01. Is row entry, M5 OR is missing a decimal. Given the number of comparisons in this Table, should use a stricter inference threshold than $p < .05$, due to multiple hypothesis testing. Could omit the log-likelihood and BIC from the Table (could cite in supplemental if desired).

In Table 3, the units were added for both maternal age and BMI. The odds ratios were relabeled as aORs. The aORs and their CIs were rounded to the nearest 0.01. The mistake in the decimal was corrected in M5.

The Table was revised to use a stricter inference threshold than $p < .05$. This was changed to a threshold for significance of $p < .01$. The log-likelihood and BIC were deleted.

EDITOR COMMENTS:

- Perhaps "the rate of peripartum blood transfusion...."?

The word "odds" was replaced with "rate" in the precis.

- 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. As an example, the Objective of the Abstract should be a simple "to" statement without background.

Having reviewed the Instructions for Authors in detail, I believe formatting should be correct at this time. The Objective portion of the abstract was revised to be a simple "to" statement.

As well, tables and figures are not to be placed within the text--see instructions for authors for further information.

All table and figures were removed from the text and placed into separate files and labeled appropriately.

- Line 43: In your precis you use the phrase "low risk women"; in your title you use "low risk infants" and in your abstract you use neither. Please be consistent and define your population. Of course, just because a woman is a NSTV (which you define as your patient population on line 50 and which I'm guessing is your definition of "low risk woman") doesn't make her low risk for post partum hemorrhage--she may have fibroids, a clotting disorder, polyhydramnios, anemia, which makes her at increased risk for needing a transfusion.

We appreciate the editor's comment about clarifying that NTSV women are not all "low risk". This is absolutely correct. The term low risk women was removed from the title, the precis and throughout the manuscript. The rationale for selecting the NTSV cohort was explained in more detail in the methods section. Performing the detailed analysis for the cohort of NTSV women allowed us to exclude those with a prior cesarean section. These women have the highest risk for peripartum transfusion based on a prior study of a 59,282 women without medical diagnoses associated with anemia or coagulopathy that was performed by one of the co-authors (ref # 22). As prior cesarean section and undergoing cesarean section for breech presentation are known mediators, excluded them from the analysis should reduce bias. In addition, limiting to term pregnancies and singleton gestations allowed us to focus on the cohort most appropriate for delivery in rural areas.

In addition, we performed an additional sensitivity analysis since the original submission on the entire population without any exclusion based on parity, gestational age, number of fetuses, or fetal position. The associations with rurality and transfusion noted in the NTSV cohort were also seen in the full population analysis. This additional sensitivity analysis and the 3 outlined in the original manuscript are now included as supplemental digital content and cited in the manuscript as Appendix 1

- Line 65: Impact implies causation. Your paper can report associations only. Please revise your paper to include associative language throughout.

It is definitely true that the association of higher transfusion rates for rural residence and delivery in a rural hospital do no prove causation in any way, thank you for this reminder. "Impact" was removed from the results section of the abstract and any overt or implied claim of causation was removed. In addition, we carefully removed any implication of causation from the manuscript and took extra effort to let the readers know the limitation of the analyses in this regard.

- line 77: "Is increasing" seems less colloquial than "is on the rise".

This sentence was changed to reflect the preference of the editor.

- Line 92: Are the infant outcomes "poor" or just not as good as in urban setting?

Infant outcomes are not as good as in urban settings in the US. The manuscript was changed to reflect that distinction.

- It is the CENTERS for Disease Control and Prevention. Note the plural in Centers and the full name.

This was changed to reflect the proper name for the Centers for Disease Control and Prevention.

- Line 95: Please provide the ratio between maternal mortality and SMM

The ratio between maternal mortality and severe maternal morbidity was added to the introduction.

- Line 116: Can you provide this schema in a box in the manuscript or in Supplemental Digital Content?

An overview of the NCHS rural-urban classification schema was add as Figure 1 to give some general information about the population density of the various counties.

- Line 121: please state why the IRB exempted this

Further explanation was added to the manuscript. The study was deemed exempt by The University of Wisconsin Institutional Review Board because it does not involve human subjects as defined under CFR 46.102(e)(I).

- Line 134: This is an oversimplification. Not all NTSV pregnancies are low risk by any means. This really needs to be addressed. Women in rural settings may be at higher risk for diabetes, substance use, hypertension, etc etc based on their rural settings. If you wish to make an argument that you used NTSV to define a comparable group of patients for the different settings, that's fine, but its a big reach to describe them as low risk.

Thank you for the opportunity to make this correction and clarification. Again, we agree that not all NTSV pregnancies are low risk. We added more detail about the rationale for studying the NTSV cohort in the methods section of the manuscript.

In addition, please see our explanation of changes noted above, in our response to your comment on line 43. As above, the additional sensitivity analysis on the entire population did corroborate the finding of the association of higher transfusion rates in the rural counties.

Line 136: Its the American College of Obstetricians and Gynecologists.

The manuscript was changed to reflect the appropriate name.

- Line 138: please consolidate this information with introduction of this information on line 116

The details for the NCHS Urban-Rural Classification Scheme for Counties that was previously in a separate paragraph (line 138) was moved, It was incorporated into the previous paragraph where the classification scheme was first introduced (line 116).

- "Moms" is colloquial. Perhaps "Women" or "Mothers"?

The word "moms" was removed from the Figure and replaced with "mothers" or "women" in the text boxes.

- Line 197: please provide some statistical evidence that these are something other than numerically higher. "Generally higher" is very vague and non informative.

The "generally higher" comment was removed and the text now refers the reader to the table to look at the background information on patients. A test statistic was not applied to this data as it is descriptive data of the entire population. Confidence intervals were added to Table 1.

- Line 202 and throughout: As these abbreviations will be relatively unfamiliar to our readers, please spell these out rather than abbreviate them.

All of the abbreviations related to the county designations in the NCHS rural-urban classification schema were removed and they are now spelled out throughout the text of the manuscript.

- Line 211: another example of causal language.
- Line 246: causal language. Of note, I've not pointed out all instances of causal language, just some examples. You need to edit throughout

Thank you; causal language was removed from the manuscript and a statement that the final results only reveal associations was added to the discussion.

- For all tables, please embolden all significant rows.

We did add bold text to all the areas of significance in tables; however, we did not embolden every row that was "statistically significant" in Table 3. Since this is a large dataset, some data that is meeting "statistically significant" thresholds is merely a statistical artifact and should not be interpreted as truly meaningful information. If the editor prefers that all statistically significant rows be boldened, we can easily make that further edit.

In addition, we used a stricter inference threshold than $p < .05$, due to multiple hypothesis testing as suggested by the statistical editor. Table 3 was revised accordingly.

- Line 260: The discussion can be shortened by about 10%.

The discussion was shortened.

- Line 268: Please see my prior strong concerns about this statement.

The term "low risk" has been removed from the manuscript; see responses above for more detail.

- Line 269: Please provide a reference for this statement. While I believe this is good practice, please provide evidence that it is "generally" done.

This sentence was removed from the manuscript.

- Line 295: Please provide some description of available blood banking resources at rural vs urban hospitals. Limited resources may result in practice pattern to transfuse at a lower threshold in order to "stay ahead".

Thank you for highlighting this important consideration. There may be two issues at play in these circumstances. Indeed, providers may transfuse at a lower threshold to "stay ahead." Conversely, some smaller hospitals have only a limited "emergency supply" of blood products that could limit availability of blood products or the timely administration of blood transfusion. This information about blood banking resources at rural vs urban hospitals was added to the discussion section.

- Line 297: Please delete "dramatically" and let the reader decide how different they are. Is 6 more per 1000 dramatic?

The word "dramatically" was removed.

- Line 315: causal. Please provide a reference for "healthy mothers lead to healthy communities"

While this phrase is often noted on public health related websites, an academic citation was not identified to support this statement. It was removed from the manuscript.

- please either use the abbreviation or correctly use the name.

The ACOG abbreviation was chosen for brevity.

- Line 333: again, refrain from this here.

The term "low risk" was removed; see responses above for more detail.

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.

We chose to "OPT IN" so you may 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.
Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

All disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

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.

The IRB review process is documented in the cover letter and outlined in the Methods section of the manuscript. The IRB exemption (Submission ID number 2018-0598) was uploaded to editorial manager. The University of Wisconsin Madison Minimal Risk IRB (Health Sciences) exempted the study since it did not involve human subjects as defined under 45 CFR 46.102(e)(l). A copy of the Data Use Agreement (DUA) for Vital Statistics Data Files was also uploaded to editorial manager.

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

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

Our original research report including the title page, précis, abstract, text, and tables is 19 double-spaced pages and 5,198 words.

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).

All acknowledgements are in order for our manuscript. The financial acknowledgements are listed on the title page. Our work was presented as a poster at the American College of Obstetrics and Gynecology Annual Meeting, Nashville, TN, May 4, 2019. This is noted on the title page.

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.

The abstract was shortened to less than 300 words.

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.

Abbreviations and acronyms are 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.

The virgule symbol was removed from the manuscript.

11. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only

secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

The results are presented as odds ratio with appropriate confidence intervals.

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

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

The data was standardized as requested.

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.

The tables were revised to conform to the journal style according to the checklist.

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. Figures

Figure 2: Upload figure as a separate figure file on Editorial Manager.

Figure 1: Please add exclusion boxes. Upload figure as a separate figure file on Editorial Manager.

Exclusion boxes were added to the flowchart of Figure 1 (now Figure 2). All figures were uploaded as a separate figure file on Editorial Manager.

We were uncertain how to format the BOX that the Editor requested about the NCHS schema so this was included as Figure 1. This could be easily reformatted as desired by the editorial office.