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

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.

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

Date: Sep 30, 2022

To: "Lorie Harper"

From: "The Green Journal" em@greenjournal.org

Subject: Your Submission ONG-22-1654

RE: Manuscript Number ONG-22-1654

All-Cause Mortality in Reproductive Age Females by State: An Analysis of the Impact of Abortion Legislation

Dear Dr. Harper:

Thank you for your submission to Obstetrics & Gynecology. Your manuscript was reviewed and we believe may be acceptable for publication if the reviewers' comments can be adequately addressed. Given the public health importance of your findings, we ask that you complete your revisions within 7 days if possible.

When revising your manuscript please ensure that your comments in the abstract and manuscript are supported by the study data (ie, statements regarding reduced maternal, fetal and infant mortality for moderate and supportive abortion legislation states when the findings in supportive state were not statistically significantly different than restrictive states for two of these three metrics).

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, and STATISTICAL EDITOR COMMENTS (if applicable) below. The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your revised submission is due in Editorial Manager by Oct 07, 2022. If you need an extension, please contact Randi Zung (rzung@greenjournal.org).

EDITOR COMMENTS:

Please note the following:

- * Help us reduce the number of queries we add to your manuscript after it is revised by reading the Revision Checklist at https://journals.lww.com/greenjournal/Documents/RevisionChecklist_Authors.pdf and making the applicable edits to your manuscript.
- * Figures:
- Figure 1: The current file may be resubmitted as-is, unless changes have been requested by the Statistical Editor.

Figure 2: This will likely not fit in print. Please move this to supplemental digital content (an appendix) or please rework into another format.

* Since you are using data from WONDER, please make sure you have reviewed the CDC's Data Use Restrictions at https://wonder.cdc.gov/datause.html. Most notably, do not present or publish statistics representing nine or fewer births or deaths, including rates based on counts of nine or fewer births or deaths, in figures, graphs, maps, tables, etc.

REVIEWER COMMENTS:

Reviewer #1: ONG 22-1654

In the manuscript under review, we evaluate the results of a retrospective cohort analysis evaluating the impact of abortion legislation on maternal and infant mortality. Using the WONDER data, the authors found that infant mortality was lower in both moderate and supportive states, however the maternal mortality only decreased in moderate states.

A few comments on the manuscript are as follows:

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ABSTRACT

1. No major issues identified.

INTRODUCTION

The authors make a compelling argument for the need for this type of analysis.

METHODS

- 3. The authors need to add a statement justifying the timelines used for this study. Could a reliable answer be obtained by including fewer years? One consideration is to add something to the effect of "since most outcomes are rare, several years' worth of data are required to show a significant trend".
- 4. If fetal death included deaths 20 weeks and over and made no distinction between spontaneous and induced, how did the authors account for states allowing abortions at gestational ages after 20 weeks? This could help explain the lack of difference in fetal mortality noted in supportive states (more legal abortions conducted after 20 weeks). This is especially important since the authors have data that goes back to 2000.
- 5. Is there any reference that can be added explaining how the authors could use a classification that reduced an itemized list from 7 down to 3 (restrictive. moderate and supportive)?
- 6. Please add a sentence stating the STROBE guidelines were followed throughout.

RESULTS

- 7. The data in Figure 2 is hard to follow and should be presented in another format or split into 4 figures instead of one. It may be that adding a line for trend also highlights the fact that no changes were seen
- 8. What time interval is used for table 1? Is it the data for one specific year, all years or a certain timeframe? Please clarify.
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- 10. For table 2, 3 and 4, are the authors considering when these laws went into effect? Its clear that a very restrictive law on insurance coverage in the books for 10 years will have a more profound impact than a law that was added this year.
- 11. Please add a reference to table 5 on the last sentence of the results section.
- 12. How did the authors account for changes in classification among the states? For example, Arizona was classified as supportive in 2000, Moderate in 2010 and restrictive in 2020. Same is true for West Virginia.

DISCUSSION

13. As a general comment, adding a time trend analysis to all types of mortality may help solidify the conclusions. If there is an association between restrictive laws and any type of mortality, this may become more evident with more time. It would also give the reader a better understanding of the nature of the association that is being reported here.

Reviewer #2:

Overall:

This is a retrospective cohort student looking at the association between state laws regulating abortion and all cause mortality in reproductive age females. Secondary analysis looked at maternal, infant and fetal mortality. I thank the authors for posing this important public health question. The paper has some important take home points that are important for physicians and the general public to understand. I do have some recommendations to make the paper stronger.

Introduction:

"Abortion regulations and restrictions also focus on protecting the life of the fetus (and a subsequent newborn infant)."
Please use a citation. Consider rephrasing to "protecting the fetus" as there is much political debate surrounding the word "life". Consider rewording to something like " abortion regulations and restrictions have been enacted to protect the fetus (citation), yet previous studies have demonstrated...".

Methods:

"Fetal deaths are defined as fetal death at 20 weeks gestation or more;6 the database makes no distinction between spontaneous and induced fetal deaths": Does this mean that induced abortion after 20 weeks would be categorized as a fetal death? If so, this seems like information that would be quite variable state to state where abortions after 20 weeks are more limited. Due to significant confounding, the authors may want to consider removing this outcome from the paper. The authors point this out as a limitation in the discussion, but I favor removing it entirely.

Results:

Second paragraph: this text "with non-significantly fewer deaths in supportive states (2.5 fewer maternal deaths per 100,000 live births, 95% CI [-6.7, 1.7])" is confusing. Is maternal mortality lower in moderate states compared to restrictive but not supportive compared to restrictive? Or is the non-significant finding in supportive states above and beyond the already lower rate in maternal mortality in moderate states?

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If permitted by the journal, the results would benefit from subheadings for clarity "all cause mortality, maternal mortality, etc."

Discussion:

The authors reference the "recent Supreme Court decision". To ensure the paper can be helpful for years to come, please outline that the authors mean the June 2022 Dobbs decision. While the timeframe of this analysis cannot review the impact of the Dobbs decision, what can the authors extrapolate from the analysis of those states with Trigger laws? Those patients were the first ones impacted by the Dobbs decision.

I would encourage the authors to be more robust in the discussion about the implications of these findings. Why is it important to know that increasing abortion restrictions raises maternal mortality? Why is it important to know that all cause mortality is unchanged?

Last line: yes countermeasures would be appropriate, but what are the implications of this? Can we justify a car that puts out abundant carbon emissions if we plant trees? Can we justify abortion restrictions if there are abundant resources for pregnant patients? The authors might consider either expounding on countermeasures or rewriting the last line.

Additional, minor comments:

Please use line numbers in future submissions. It helps for reviewers to give feedback about specific parts of the paper. Consider transitioning from "prior to" to "before". It helps with word count and readability.

STATISTICAL EDITOR COMMENTS:

Table 1: Need to round the estimates to less precise numbers. An estimate to the 0.0001 place per 100,000 females or births implies denominators of 1,000,000,000. Suggest rounding to the second decimal place for point estimates and CIs.

Tables 2-5: Same issue re: precision of estimates and CIs. There are multiple hypotheses being tested in these Tables, with no adjustment for multiple hypothesis testing. Should set a stricter inference threshold. Most of inferences will remain significant, but some of the likely spurious ones would be eliminated.

General: For the all-cause mortality rate in females of reproductive age, were the rates adjusted, based on the age distribution within each state? If not, need to adjust. Also, the States differ in terms of availability of health care, particularly before implementation of the Affordable Healthcare Act. States also differ in terms of income, education, etc which could impact maternal, fetal and infant mortality rates.

Methods, para 3, sentence 2: The Authors state that all-cause mortality was selected as the primary outcome because data on maternal mortality was unreliable. Therefore, should present in Results and in Tables the primary outcome first and clearly separated from the secondary ones.

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Jason D. Wright, MD Editor-in-Chief

The Editors of Obstetrics & Gynecology

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

3 10/11/2022, 2:23 PM

Dear Editors,

To follow, please find revisions of the manuscript entitled, "All-Cause Mortality in Reproductive Age Females by State: An Analysis of the Impact of Abortion Legislation." My co-authors and I would like to thank you in advance for your consideration for publication in *Obstetrics and Gynecology*. This manuscript is submitted to review only at *Obstetrics and Gynecology*. If there are any additional materials needed, please do not hesitate to contact the corresponding author (Lorie M. Harper).

Title: All-Cause Mortality in Reproductive Age Females by State: An Analysis of the Impact of Abortion Legislation

Submission: We affirm that this study is not under review at any other journal or institution.

Clinical Trial Registration: Not applicable

IRB: This study was exempt from IRB review.

Authors: All authors meet the two stated author requirements.

Conflicts of interest: None

Thank you again for your consideration.

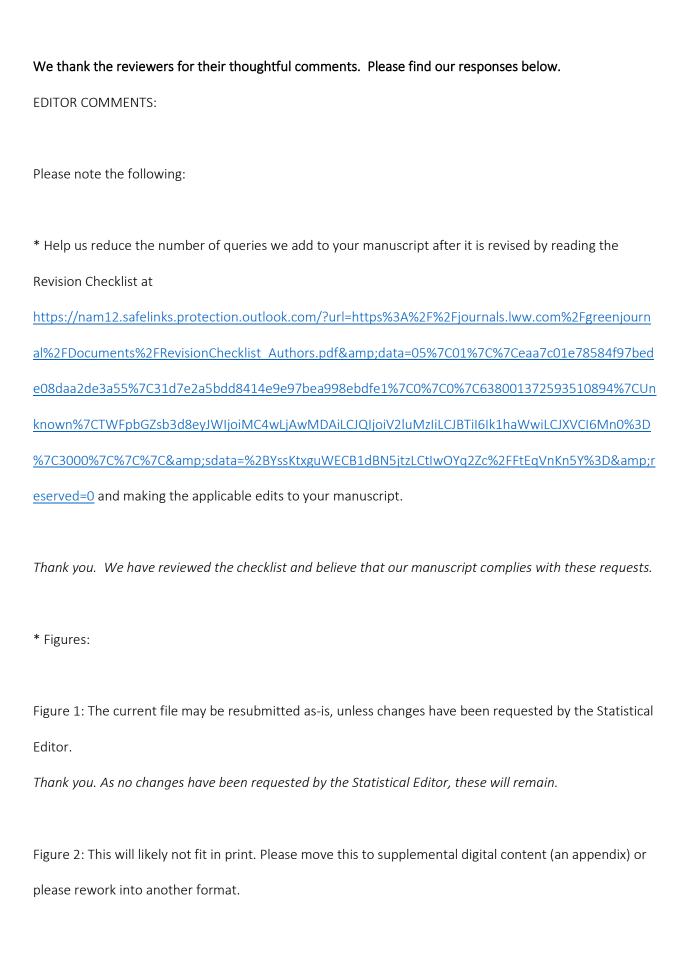
Best regards,

Lorie M. Harper, M.D., M.S.C.I.

Corresponding Author

The University of Texas at Austin Dell Medical School, Department of Women's Health, Austin, TX

Address: 1301 W 38th St, Ste 705, Austin, TX, 78705



Thank you. This will be removed from the manuscript and changed to supplemental digital content Figures

1-4.

* Since you are using data from WONDER, please make sure you have reviewed the CDC's Data Use

Restrictions at

https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwonder.cdc.gov%2Fdatause.html

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VTVpi5s1G4xC%2FJGvsbyd3bMHp0qsg1dcl%3D&reserved=0. Most notably, do not present or

publish statistics representing nine or fewer births or deaths, including rates based on counts of nine or

fewer births or deaths, in figures, graphs, maps, tables, etc.

Thank you. These have been reviewed. While we utilize the data based on counts of nine or fewer to obtain

our estimates, we are not publishing these raw data in order to be compliant with the CDC's Data Use

Restrictions.

REVIEWER COMMENTS:

Reviewer #1: ONG 22-1654

In the manuscript under review, we evaluate the results of a retrospective cohort analysis evaluating the

impact of abortion legislation on maternal and infant mortality. Using the WONDER data, the authors

found that infant mortality was lower in both moderate and supportive states, however the maternal mortality only decreased in moderate states.

A few comments on the manuscript are as follows:

ABSTRACT

1. No major issues identified.

INTRODUCTION

2. The authors make a compelling argument for the need for this type of analysis.

METHODS

- 3. The authors need to add a statement justifying the timelines used for this study. Could a reliable answer be obtained by including fewer years? One consideration is to add something to the effect of "since most outcomes are rare, several years' worth of data are required to show a significant trend".

 Thank you for this observation. The following has been added to the methods section:

 "We selected this twenty-year period to evaluate as data were available for both maternal and infant mortality for all years selected and the state-level abortion legislation shifted dramatically over the twenty-year period. A large time period was required to account for changes in state legislation (resulting in changing exposure groups) and to provide adequate power for detecting differences in rare outcomes."
- 4. If fetal death included deaths 20 weeks and over and made no distinction between spontaneous and induced, how did the authors account for states allowing abortions at gestational ages after 20 weeks? This could help explain the lack of difference in fetal mortality noted in supportive states (more

legal abortions conducted after 20 weeks). This is especially important since the authors have data that goes back to 2000.

Thank you. We have added a sentence to highlight this point in the Discussion section:

"As we could not differentiate between spontaneous fetal death versus termination of pregnancy after 20 weeks, this may account for the lack of difference in fetal death rates between supportive and restrictive states."

5. Is there any reference that can be added explaining how the authors could use a classification that reduced an itemized list from 7 down to 3 (restrictive. moderate and supportive)?

Thank you. Unfortunately, there is no reference for our classification system, which is why we also evaluated the impact of each individual type of law. We elected to condense from seven categories to three due to anticipated sample size/power issues. However, the 7-category classification is equally without foundation and was created by the Guttmacher Institute. In order to minimize confusion/concerns over this issue, we have re-written this section to describe how we classified into our three categories:

"The Guttmacher Institute has analyzed the abortion policy landscape in each state.¹⁴ The laws of each state were reviewed, and scored on a scale of -6 to +6 based upon the number of supportive policies (+1 point) and the number of restrictive policies (-1 point). Based on this score from -6 to +6, states were classified either restrictive (-6 through -2), moderate (-1, 0, or +1), or supportive (+2 through +6) for every year from 2000-2019. Policies were not counted in effect if they were blocked by a court order or if the effective date had not been reached."

6. Please add a sentence stating the STROBE guidelines were followed throughout.

This statement has been added to the methods section.

"The STROBE guidelines for reporting cohort studies was followed. 11"

RESULTS

7. The data in Figure 2 is hard to follow and should be presented in another format or split into 4 figures instead of one. It may be that adding a line for trend also highlights the fact that no changes were seen.

Thank you. We have altered the Figure to be included only as a supplemental/appendix file and have altered to include trend lines.

8. What time interval is used for table 1? Is it the data for one specific year, all years or a certain timeframe? Please clarify.

Thank you. The estimates presented are for all 20-years examined. The title of the table has been altered to reflect this.

- 9. Please explain what is meant by a type III p value (table 1). Most readers will be unfamiliar with this term. Also, please reduce the decimal points down to just 2, it's makes the tables easier to read *Thank you. These changes have been made.*
- 10. For table 2, 3 and 4, are the authors considering when these laws went into effect? Its clear that a very restrictive law on insurance coverage in the books for 10 years will have a more profound impact than a law that was added this year.

Thank you. For Tables 2-4, we considered only the effect of the law for a given year. So, for example, a law restricting insurance coverage that passed in 2010 was not in effect in 2000-2009 and was assumed to have the same impact from 2010-2019. Your point that laws that are in effect longer may have a more profound impact is interesting and we have examined the cumulative impact of laws (eg accounting for the length of time that a law was in place). On the whole, this analysis altered the point estimates but not

the direction of effect and generally did not alter whether or not the effect was statistically significant.

Given the already large amount of data being presented, we had elected not to include this secondary analysis of cumulative effect of the laws. However, if the reviewers request, it can be included in an appendix.

- 11. Please add a reference to table 5 on the last sentence of the results section.

 Thank you. This has been added.
- 12. How did the authors account for changes in classification among the states? For example, Arizona was classified as supportive in 2000, Moderate in 2010 and restrictive in 2020. Same is true for West Virginia.

Thank you. As described the methods section, the number and types of laws in each state were assessed yearly (only 2000, 2010, 2019 are depicted for brevity). States were classified for each year and may have transitioned from supportive to moderate to restrictive any given year. These classifications were then taken into account using the generalized estimating equations. We have added an additional statement to this effect in the methods section.

DISCUSSION

As a general comment, adding a time trend analysis to all types of mortality may help solidify the conclusions. If there is an association between restrictive laws and any type of mortality, this may become more evident with more time. It would also give the reader a better understanding of the nature of the association that is being reported here.

We have added trend lines to what used to be figure 2 and are now supplementary figures 1-4. In addition, the GEE models used to obtain the estimates, 95% Cl's, and p-values accounts for time (See above comment), so we believe that an additional analysis is not necessary.

Reviewer #2:

Overall:

This is a retrospective cohort student looking at the association between state laws regulating abortion and all cause mortality in reproductive age females. Secondary analysis looked at maternal, infant and fetal mortality. I thank the authors for posing this important public health question. The paper has some important take home points that are important for physicians and the general public to understand. I do have some recommendations to make the paper stronger.

Introduction:

"Abortion regulations and restrictions also focus on protecting the life of the fetus (and a subsequent newborn infant)." Please use a citation. Consider rephrasing to "protecting the fetus" as there is much political debate surrounding the word "life". Consider rewording to something like " abortion regulations and restrictions have been enacted to protect the fetus (citation), yet previous studies have demonstrated...".

Thank you. The phrase has been reworded and a reference added.

"Abortion regulations and restrictions also focus on protecting the fetus (and a subsequent newborn infant).4"

Methods:

"Fetal deaths are defined as fetal death at 20 weeks gestation or more;6 the database makes no distinction between spontaneous and induced fetal deaths": Does this mean that induced abortion after 20 weeks would be categorized as a fetal death? If so, this seems like information that would be quite variable state to state where abortions after 20 weeks are more limited. Due to significant confounding, the authors may want to consider removing this outcome from the paper. The authors point this out as a limitation in the discussion, but I favor removing it entirely.

Thank you. We have also considered this issue at length. We have added additional commentary in the Discussion that this inability to differentiate may account for the lack of difference in fetal death. However, we feel it important to include because, although supportive states do not have a reduced risk of fetal death, allowing abortion after an arbitrary gestational age limit does not increase fetal deaths. However, in order to address this concern, we also performed an analysis of fetal death overall excluding the states that would allow for termination at any gestational age in order to address this potential discrepancy. This analysis is not significantly different than the original analysis; however, we elect not to include in the publication as nearly half of supportive states were removed from this analysis. If the editors desire, it can be included in Supplemental materials.

	Estimate	95% CI		p-value
Number of laws	0.16	-0.0013	0.32	0.0518
Trigger Law (Bans abortion upon overturn of <i>Roe v Wade</i>)	1.60	-1.0019	4.21	0.23
Laws that require certain types of counseling	0.56	-0.32	1.43	0.21
Laws requiring in person counseling and/or consent	0.91	-0.24	2.06	0.12
Laws that require an ultrasound prior to abortion procedure	0.97	-0.61	2.54	0.23
Laws that prohibit insurance coverage abortions	0.60	-0.04	1.24	0.067

Laws that prohibit Medicaid coverage of abortion	0.13	-0.50	0.76	0.69
Laws that limit access to medication abortion	0.42	-0.26	1.11	0.23
Laws that require parental consent for abortions in those <18 years of age	0.56	-0.054	1.18	0.074
Targeted regulations of abortion providers (TRAP Laws)	0.86	0.20	1.53	0.011

^{*}No tests remained significant after Benjamini-Hochberg correction to control False Discovery Rate at q = 0.05.

Results:

Second paragraph: this text "with non-significantly fewer deaths in supportive states (2.5 fewer maternal deaths per 100,000 live births, 95% CI [-6.7, 1.7])" is confusing. Is maternal mortality lower in moderate states compared to restrictive but not supportive compared to restrictive? Or is the non-significant finding in supportive states above and beyond the already lower rate in maternal mortality in moderate states?

Thank you. We agree this statement was confusing. We have separated into two sentences for clarity. "However, maternal mortality was significantly lower in moderate states (5.8 fewer maternal deaths per 100,000 live births, 95% CI: [-9.9, -1.7]) compared with restrictive states. The difference in maternal mortality between supportive states and restrictive states was not statistically significantly lower (2.5 fewer maternal deaths per 100,000 live births, 95% CI [-6.7, 1.7])."

If permitted by the journal, the results would benefit from subheadings for clarity "all cause mortality, maternal mortality, etc."

Thank you. We have not added subheadings as the second paragraph of the results section describes the main analysis by state classification, covering all types of mortality. The next four paragraphs cover each type of mortality and the individual types of laws. We did create a new paragraph for fetal mortality for clarity.

Discussion:

The authors reference the "recent Supreme Court decision". To ensure the paper can be helpful for years to come, please outline that the authors mean the June 2022 Dobbs decision. While the timeframe of this analysis cannot review the impact of the Dobbs decision, what can the authors extrapolate from the analysis of those states with Trigger laws? Those patients were the first ones impacted by the Dobbs decision. I would encourage the authors to be more robust in the discussion about the implications of these findings. Why is it important to know that increasing abortion restrictions raises maternal mortality? Why is it important to know that all cause mortality is unchanged?

Thank you. We changed the Supreme Court reference to have a month/year. We have added some lines about the current impact of trigger laws and awaiting data on the impact of the implementation of these trigger laws.

"However, it is important to note that the mere presence of trigger laws that were not yet enforced was associated with a substantial increase in all-cause mortality in reproductive age females, maternal mortality, and infant mortality. While data will not be available for several more years, it is reasonable to anticipate based on the information available that mortality rates will increase further with implementation of these laws."

Last line: yes countermeasures would be appropriate, but what are the implications of this? Can we

justify a car that puts out abundant carbon emissions if we plant trees? Can we justify abortion

restrictions if there are abundant resources for pregnant patients? The authors might consider either

expounding on countermeasures or rewriting the last line.

Thank you for this comment. We agree, but would like to limit our commentary to that clearly supported

by the evidence we present or that has been presented by others. We have altered the final statements,

which can be found below.

"While the relationship between abortion legislation and mortality rates is undoubtedly complex,

repealing certain types of laws may decrease all-cause mortality in reproductive age females and

maternal and infant mortality. Additionally, states with restrictive abortion laws should consider

countermeasures to offset increased mortality rates, including expansion of Medicaid or universal

healthcare."

Additional, minor comments:

Please use line numbers in future submissions. It helps for reviewers to give feedback about specific parts

of the paper. Consider transitioning from "prior to" to "before". It helps with word count and readability.

Thank you. Line numbers have been added.

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Table 1: Need to round the estimates to less precise numbers. An estimate to the 0.0001 place per 100,000 females or births implies denominators of 1,000,000. Suggest rounding to the second decimal place for point estimates and Cls.

Thank you. This has been changed.

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Thank you. This has been changed.

General: For the all-cause mortality rate in females of reproductive age, were the rates adjusted, based on the age distribution within each state? If not, need to adjust. Also, the States differ in terms of availability of health care, particularly before implementation of the Affordable Healthcare Act. States also differ in terms of income, education, etc which could impact maternal, fetal and infant mortality rates.

Methods, para 3, sentence 2: The Authors state that all-cause mortality was selected as the primary outcome because data on maternal mortality was unreliable. Therefore, should present in Results and in Tables the primary outcome first and clearly separated from the secondary ones.

Thank you. This change has been made in Table 1.

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Jason D. Wright, MD

Editor-in-Chief

The Editors of Obstetrics & Gynecology