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: Oct 08, 2021
To: "Claire E Margerison" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-1835

RE: Manuscript Number ONG-21-1835

Pregnancy-associated deaths due to drugs, suicide, and homicide in the U.S. 2010-2019

Dear Dr. Margerison:

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).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

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 Oct 22, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Obstetrics and Gynecology
Manuscript # ONG-21-1835
"Pregnancy-associated deaths due to drugs, suicide, and homicide in the U.S. 2010-2019"

GENERAL

The submitted manuscript constitutes a review of existing United States death records from 2010-2019 to specifically determine incidences of pregnancy-associated deaths due to substance-related causes, suicide, and homicide.

1. The general article structure should be formatted to meet journal submission requirements.
2. The opening sentence of the abstract proposes that "…evidence suggests pregnancy-associated deaths due to drug-related causes, homicide, and suicide represent a substantial and increasing burden of mortality during pregnancy", followed the ostensibly contradictory "but no recent national estimates exist". This sentence should be rephrased, perhaps omitting the "evidence suggests" as this is the intent of the study.
3. It is unclear to the reader why data from the Maryland and California populations were included, given that the reporting methodology is significantly different than the other 32 states include and increases the heterogeneity of the data analysis (utilizing ICD-10 codes instead of the standard revised form). Did the authors consider these two states to include unique patient populations or expect incidences to vary substantially?
4. Line 24: Would the listing of preventative strategies be perhaps better characterized as "systemic" or "socioeconomic" (instead of "structural") barriers?
5. The authors extrapolation of under-reporting (listed in the Misclassification and Discussion sections) suggests 41.2% of all pregnancy-related deaths occur are either drug-related, suicide, and homicide, yet (Line 138) 54.6% of deaths are due to obstetrical etiologies; do the authors feel that 4.2% are actually not classifiable (instead of current 19%)?
6. Another manner to represent Figure 2 would be to substitute time intervals along the Y axis (i.e. antepartum, death <43 days postpartum, death 43-360 days postpartum, exact timing unknown) and show percentages of each etiology specific to time intervals.

Reviewer #2:

The authors provide to us a studythat addresses the paucity of current data on pregnancy-associated mortality due to drugs, suicide, and homicide. This manuscript highlights the rise in the prevalence of mortality in these groups and finds that minority groups were at higher risk for pregnancy-associated deaths due to these specific circumstances. This further defines the disparate pregnancy-related mortality among racially diverse groups in the United States and adds to the body of data that requires reaction.

Ln 86 the authors chose to list any death where Hispanic ethnicity is chosen as Hispanic seemingly regardless of other racial contributions; this should be elaborated upon; what precedent was referenced in making this distinction? If there is no precedent the thought-process needs to be described.

Ln 92 it is unclear which variable is unavailable on the CA death certificate; please elaborate

Ln 95 it is helpful to include a sentence or two that includes not only the statistical software that was used, but also what statistical tests were used for nominal and interval data.

Ln 130 again, CA is excluded in a calculation; did the authors consider not including CA in the data set?

Ln 142 these couple of sentences are unclear; while I was eventually able to glean the meaning, it could be presented in a clearer manner.

Ln 154 230% vs 220% on Ln 16 and Ln 194- verify and correct

Ln 180 missing is not an accurate descriptor; per the manuscript this is a factor that estimates the under-reported values. If so, then state it as such.

Ln 185-187 back to a prior point, it seems that eliminating CA and possibly MD would lead to your data set being cleaner using only the revised death certificate

Ln 204 it is known that IPV increases in pregnancy; it is worth addressing this with respect to homicide in pregnancy

Reviewer #3:

Critical information for OBGYN and also primary care. It was surprising and important to see some of the differences with California compared to other States. This article is a must; getting this into the public eye. I do hope that there is a 2.0 type of version looking at differences after the pandemic too.

STATISTICS EDITOR COMMENTS:

Abstract: Needs to include more information, specifically that these data are not from the entire US, but rather based on data from DC + 33 States, representing ~ 75% of all US births. That is, it does not enumerate all births in US. Need to clarify this for transparency.

Table 2, Fig 1 and lines 154-158: Need to include a legend for Figure 1 which includes a summary of relevant statistics. It appears that the drug-related deaths increased significantly, while the change in suicides did not, and the change in homicide was possibly statistically significant. Need to address whether the rates changed vs year.

Table 3: Need to include CIs for the rate ratios to establish whether the numerical differences vs the referents were statistically significant. In part due to small counts for some subsets, I suspect that some of the rate ratios are NS different from their referent. Need units for age.

Table 4 and lines 177-187: This part of the analysis is not based on actual data, but a hypothetical extrapolation. This part of the article should be in supplemental material and can be referenced in results and discussion, but should be a secondary outcome, not a primary conclusion of the study.

Figure 2: Elsewhere in the text, Tables etc, the Authors say that there were 33 US States + DC in the data analysis, but title to Figure 2 says 32 States. Need to clarify.

EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased 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.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors).
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

4. If your study is based on data obtained from the National Center for Health Statistics, please review the Data Use Agreement (DUA) for Vital Statistics Data Files that you or one of your coauthors signed. If your manuscript is accepted for publication and it is subsequently found to have violated any of the terms of the DUA, the journal will retract your article. The National Center for Health Statistics may also terminate your access to any future vital statistics data.

5. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research

instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

6. Your study uses ICD-10 data, please make sure you do the following:
a. State which ICD-10-CM/PCS codes or algorithms were used as Supplemental Digital Content.
b. Use both the diagnosis and procedure codes.
c. Verify the selected codes apply for all years of the study.
d. Conduct sensitivity analyses using definitions based on alternative codes.
e. For studies incorporating both ICD-9 and ICD-10-CM/PCS codes, the Discussion section should acknowledge there may be disruptions in observed rates related to the coding transition and that coding errors could contribute to limitations of the study. The limitations section should include the implications of using data not created or collected to answer a specific research question, including possible unmeasured confounding, misclassification bias, missing data, and changing participant eligibility over time.
f. The journal does not require that the title include the name of the database, geographic region or dates, or use of database linkage, but this data should be included in the abstract.
g. Include RECORD items 6.3 and 7.1, which relate to transparency about which codes, validation method, and linkage were used to identify participants and variables collected.

7. 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 data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

8. 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 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

9. 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).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

10. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

11. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

12. 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 limit for Original Research articles is 300 words. Please provide a word count.

13. 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.

14. 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.

15. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

16. 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%").

17. Your manuscript contains a priority claim. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

18. 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.

19. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, 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 references you are citing are still current and available. Check the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

If the reference you are citing has been updated and 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.

18. Figure 1: Please upload as figure files to Editorial manager. Please add tick marks along the x- and y-axes and consider adding color.
Figure 2: Please upload as figure files to Editorial manager. Please consider adding color.

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

19. Each supplemental file in your manuscript should be named an "Appendix," numbered, and ordered in the way they are first cited in the text. Do not order and number supplemental tables, figures, and text separately. References cited in appendixes should be added to a separate References list in the appendixes file.

20. 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 https://wkauthorservices.editage.com/open-access/hybrid.html.

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 open access, you will receive an Open Access Publication Charge letter from the Journal's Publisher, Wolters Kluwer, and instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line, "Please Submit Your Open Access Article Publication Charge(s)." Please complete payment of the Open Access charges within 48 hours of receipt.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded as a Microsoft Word document. 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. Do not omit your responses to the Editorial Office or Editors' comments.

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 Oct 22, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Dwight J. Rouse, MD
Associate Editor, Obstetrics

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

MICHIGAN STATE
UNIVERSITY

Dwight J. Rouse, MD MSPH
Editor-in-Chief, *Obstetrics & Gynecology*

Original Research entitled: "Pregnancy-associated deaths due to drugs, suicide, and homicide in the United States 2010-2019"

Dear Dr. Rouse,

Thank you for the opportunity to revise and resubmit our manuscript (ONG-21-1835). We appreciated the thoughtful comments from the reviewers and editors. We have edited the manuscript using track changes and responded to the comments in our point-by-point response at the end of this letter. We also note that we found a small typo in our original coding assigning cause of death by ICD-10 code that identified 87 additional pregnancy-associated deaths due to drug-related causes that had previously been identified as "other causes". We have updated all tables, figures, and text to reflect this change.

These data have not been previously published, in whole or in part; we have no similar paper in press or under review elsewhere; this paper will not be submitted elsewhere unless a final negative decision is made by the Editors of Obstetrics & Gynecology. We have no conflicts of interest to declare. This research was approved by the Institutional Review Board of Michigan State University.

I, Claire Margerison, have reviewed and edited the submission to omit any identifying information. I hereby submit this self-blinded manuscript for consideration in Obstetrics & Gynecology. I have read the Instructions for Authors.

Sincerely,

Claire E Margerison

Claire Margerison, Ph.D.
Associate Professor, Department of Epidemiology and Biostatistics
Michigan State University
East Lansing, MI
[redacted]

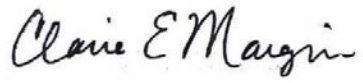
The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

COLLEGE OF
HUMAN MEDICINE

Department of Epidemiology and Biostatistics

Michigan State University
[redacted]

Signed by:



*The manuscript's guarantor.

Point-by-point response to reviewer and editor comments

Note to all reviewers and editor:
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Reviewer #1:

Obstetrics and Gynecology
Manuscript # ONG-21-1835
"Pregnancy-associated deaths due to drugs, suicide, and homicide in the U.S. 2010-2019"

GENERAL

The submitted manuscript constitutes a review of existing United States death records from 2010-2019 to specifically determine incidences of pregnancy-associated deaths due to substance-related causes, suicide, and homicide.

1. The general article structure should be formatted to meet journal submission requirements.
   For our initial submission, we used *Obstetrics & Gynecology's* Essential Requirements only. We have now formatted to meet the full set of requirements.

2. The opening sentence of the abstract proposes that "…evidence suggests pregnancy-associated deaths due to drug-related causes, homicide, and suicide represent a substantial and increasing burden of mortality during pregnancy", followed the ostensibly contradictory "but no recent national estimates exist". This sentence should be rephrased, perhaps omitting the "evidence suggests" as this is the intent of the study.
   In editing the abstract to meet formatting requirements, we removed this sentence.

3. It is unclear to the reader why data from the Maryland and California populations were included, given that the reporting methodology is significantly different than the other 32 states include and increases the heterogeneity of the data analysis (utilizing ICD-10 codes instead of the standard revised form). Did the authors consider these two states to include unique patient populations or expect incidences to vary substantially?

   To clarify, as in the other states included in the analysis, pregnancy-associated deaths from MD and CD are also <u>primarily identified through use of a checkbox on death certificates</u>, with additional deaths from obstetric causes identified by ICD10 codes.

As noted at the end of the section titled "Data and Study Population", we wanted to include as much of the birthing population of the United States as possible to obtain estimates of the burden of pregnancy-associated mortality due to these causes. We have edited this sentence to clarify that the unrevised Maryland birth certificate includes a pregnancy checkbox that reports whether the death was pregnancy-associated—and the timing of the death relative to pregnancy—in much the same way as the standard pregnancy checkbox on the 2003 revised birth certificate. Although California unfortunately did not use this standard question throughout the study period, we still wanted to include data from that state because it includes approximately 1/6 of all births in the US in a given year. Because California does include an indicator for whether the decedent was pregnant within the last year, we chose to include this information where possible. We note that California is excluded from analyses regarding more precise timing of death relative to pregnancy. We also include a secondary analysis excluding both California and Maryland (See final paragraph of Results and Appendix Tables 5 and 6).

4. Line 24: Would the listing of preventative strategies be perhaps better characterized as "systemic" or "socioeconomic" (instead of "structural") barriers?

   While this sentence has been removed from the abstract, it is still in the Discussion. We chose the word 'structural' here to reflect the concept that social ideologies, hierarchies, and policies structure individuals' access to and experiences within systems such as housing, health care, and the legal system. We draw from Crear-Perry et al (Crear-Perry J, Correa-de-Araujo R, Lewis Johnson T, McLemore MR, Neilson E, Wallace M. Social and Structural Determinants of Health Inequities in Maternal Health. J Womens Health (Larchmt). 2021 Feb;30(2):230-235) and Bailey et al (Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. Lancet. 2017 Apr 8;389(10077):1453-1463) who emphasize upstream, 'structural' determinants of health such as racism and institutional policies.

5. The authors extrapolation of under-reporting (listed in the Misclassification and Discussion sections) suggests 41.2% of all pregnancy-related deaths occur are either drug-related, suicide, and homicide, yet (Line 138) 54.6% of deaths are due to obstetrical etiologies; do the authors feel that 4.2% are actually not classifiable (instead of current 19%)?

   No, the proportion of deaths that are not classifiable would not be 4.2% after the adjustment because the denominator changes after accounting for misclassified deaths (from 11,782 deaths to 15,895 deaths). If we recalculate the cause-specific distribution using this adjusted denominator, the proportion of pregnancy-related deaths due to obstetric causes (n=6,989) would be 44.0% (vs. 59.3% prior to the adjustment) and the proportion not classifiable (n=2,174) would be 13.7% (vs. 18.5% prior to adjustment.)

6. Another manner to represent Figure 2 would be to substitute time intervals along the Y axis (i.e. antepartum, death <43 days postpartum, death 43-360 days postpartum, exact timing unknown) and show percentages of each etiology specific to time intervals.

   We note that those values (percent of deaths during pregnancy, in the first 43 days postpartum, etc.) due to each etiology are presented in Table 1. We therefore use Figure 2 to

present the proportion of each etiology that occurs in each time period, which we believe is valuable information in terms of identifying when and how to prevent these deaths.

Reviewer #2:

The authors provide to us a study that addresses the paucity of current data on pregnancy-associated mortality due to drugs, suicide, and homicide. This manuscript highlights the rise in the prevalence of mortality in these groups and finds that minority groups were at higher risk for pregnancy-associated deaths due to these specific circumstances. This further defines the disparate pregnancy-related mortality among racially diverse groups in the United States and adds to the body of data that requires reaction.

Ln 86 the authors chose to list any death where Hispanic ethnicity is chosen as Hispanic seemingly regardless of other racial contributions; this should be elaborated upon; what precedent was referenced in making this distinction? If there is no precedent the thought-process needs to be described.
This is standard procedure for death certificate data, as well as in studies that evaluate racial/ethnic disparities in maternal health. We now provide a citation for clarification.

Ln 92 it is unclear which variable is unavailable on the CA death certificate; please elaborate
We now clarify that the specific timing of PAD relative to pregnancy is not available on the CA death certificate.

Ln 95 it is helpful to include a sentence or two that includes not only the statistical software that was used, but also what statistical tests were used for nominal and interval data.
As noted at the end of the section entitled Statistical Analysis, "Analyses were conducted using Stata MP." We have added details on how we calculated the 'rate ratios' comparing pregnancy-associated death ratios over time (2019 compared to 2010) and between racial/ethnic and age groups.

Ln 130 again, CA is excluded in a calculation; did the authors consider not including CA in the data set?
We have clarified why CA was excluded as follows:
"These calculations excluded deaths in California, for which we did not have data on specific timing of death relative to pregnancy information."

Ln 142 these couple of sentences are unclear; while I was eventually able to glean the meaning, it could be presented in a clearer manner.
Unfortunately, we are not able to see the line numbers in our submitted files. We guessed that the reviewer was referring to the section on under-reporting, and we edited it for clarity (bottom of p8 and top of p9).

Ln 154 230% vs 220% on Ln 16 and Ln 194- verify and correct
Thank you for noting this inaccuracy. The correct value is 190% (rate ratio of 2.9). In the prior version, the correct value was 220%, but when we corrected the typo in our ICD-10 coding, this value changed to 190%.

Ln 180 missing is not an accurate descriptor; per the manuscript this is a factor that estimates the under-reported values. If so, then state it as such.
We have re-labeled these deaths 'misclassified' because these are deaths that we argue occurred within 1 year of pregnancy but were not recorded on the checkbox as such, so were 'misclassified' as not pregnancy-associated.

Ln 185-187 back to a prior point, it seems that eliminating CA and possibly MD would lead to your data set being cleaner using only the revised death certificate
We chose to include as many as states as possible because we wanted to obtain estimates of the burden of pregnancy-associated mortality due to these causes across the US. California, in particular, accounts for 1/6 of all births in the US. We do present the estimates without CA and MD in Appendix Tables 5 and 6. As noted at the end of the Results section: "Compared to our main analyses, when we excluded California and Maryland, we found slightly higher pregnancy-associated death ratios due to drugs, suicide, and homicide…"

Ln 204 it is known that IPV increases in pregnancy; it is worth addressing this with respect to homicide in pregnancy
Thank you for this suggestion. We have added a citation regarding the link between IPV and both pregnancy-associated homicide and suicide.

Reviewer #3:

Critical information for OBGYN and also primary care. It was surprising and important to see some of the differences with California compared to other States. This article is a must; getting this into the public eye. I do hope that there is a 2.0 type of version looking at differences after the pandemic too.

We appreciate the reviewer's support for our manuscript. We do intend to look at post-pandemic data as soon as possible.

STATISTICS EDITOR COMMENTS:

Abstract: Needs to include more information, specifically that these data are not from the entire US, but rather based on data from DC + 33 States, representing ~ 75% of all US births. That is, it does not enumerate all births in US. Need to clarify this for transparency.
We now note the number of states in the Abstract.

Table 2, Fig 1 and lines 154-158: Need to include a legend for Figure 1 which includes a summary of relevant statistics. It appears that the drug-related deaths increased significantly, while the change in suicides did not, and the change in homicide was possibly statistically significant. Need to address whether the rates changed vs year.

We have revised the section in the Results that describes Figure 1 to include rate ratios comparing pregnancy-associated death ratios by cause in 2019 to 2010 to determine which causes of death

increased significantly over this time period. Per the editor's suggestion, we have also added this information to a Figure 1 legend.

Table 3: Need to include CIs for the rate ratios to establish whether the numerical differences vs the referents were statistically significant. In part due to small counts for some subsets, I suspect that some of the rate ratios are NS different from their referent. Need units for age.
We have added the CIs for the rate ratios and the units for age.

Table 4 and lines 177-187: This part of the analysis is not based on actual data, but a hypothetical extrapolation. This part of the article should be in supplemental material and can be referenced in results and discussion, but should be a secondary outcome, not a primary conclusion of the study.
We have moved this table to the appendix as requested. We also note the limitations of the estimates of misclassification in the Discussion.

Figure 2: Elsewhere in the text, Tables etc, the Authors say that there were 33 US States + DC in the data analysis, but title to Figure 2 says 32 States. Need to clarify.
We have added a footnote to clarify that Figure 2 does not include California data. This is described in the text.

EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased 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.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors). **Done**
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript. **Done**
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable). **NA**
* Name the IRB or Ethics Committee institution in the Methods section (if applicable). **Done**
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context. **NA**

3. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.
Done

4. If your study is based on data obtained from the National Center for Health Statistics, please review the Data Use Agreement (DUA) for Vital Statistics Data Files that you or one of your coauthors signed. If your manuscript is accepted for publication and it is subsequently found to have violated any of the terms of the DUA, the journal will retract your article. The National Center for Health Statistics may also terminate your access to any future vital statistics data.
Done. We have labeled all counts <10 in concordance with our DUA.

5. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.
As these are death certificate data, race/ethnicity is indicated by the person filling out the death certificate. In the statistical analysis section, we provided citations for prior studies indicating inequities in these outcomes by race/ethnicity, justifying our assessment of race/ethnicity.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.
In this paper, we use the categories as indicated on the death certificate, following the Office of Management and Budget classifications.

6. Your study uses ICD-10 data, please make sure you do the following:
a. State which ICD-10-CM/PCS codes or algorithms were used as Supplemental Digital Content. **Done**
b. Use both the diagnosis and procedure codes. **Not relevant for death certificate data**
c. Verify the selected codes apply for all years of the study. **Done**
d. Conduct sensitivity analyses using definitions based on alternative codes. **We have added a comparison where we define "poisoning deaths of undetermined intent" as suicides instead of drug-related deaths (Appendix Table 7).**
e. For studies incorporating both ICD-9 and ICD-10-CM/PCS codes, the Discussion section should acknowledge there may be disruptions in observed rates related to the coding transition and that coding

errors could contribute to limitations of the study. **Not needed, we only use ICD-10 codes.** The limitations section should include the implications of using data not created or collected to answer a specific research question, including possible unmeasured confounding, misclassification bias, missing data, and changing participant eligibility over time. **Done**

f. The journal does not require that the title include the name of the database, geographic region or dates, or use of database linkage, but this data should be included in the abstract. **Done**

g. Include RECORD items 6.3 and 7.1, which relate to transparency about which codes, validation method, and linkage were used to identify participants and variables collected.

We did not use data linkage in this analysis (RECORD item 6.3).

We provide a complete list of ICD-10 codes used to identify and categorize pregnancy-associated deaths in Appendix Tables 1 and 2 (RECORD item 7.1).

7. 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 data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions__;!!HXCxUKc!iQQFt9jgdZDSekeccYkOlEHbWCc6FwqykgwQ_MOuOsdDaOYEeDnlf-75D2l_SeE$ and the gynecology data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions__;!!HXCxUKc!iQQFt9jgdZDSekeccYkOlEHbWCc6FwqykgwQ_MOuOsdDaOYEeDnlf-75YUC-L2U$. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

None of these definitions are used in our manuscript.

8. 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 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

The revised manuscript adheres to the length restriction.

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

* All financial support of the study must be acknowledged. **Done**
* 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. **NA**
* 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. **NA**
* 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). **NA**
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10. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.
Pregnancy-associated death in US, 2010-2019

11. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."
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12. 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.
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In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.
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13. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/abbreviations.pdf__;!!HXCxUKc!iQQFt9jgdZDSekeccYkOlEHbWCc6FwqykgwQ_MOuOsdDaOYEe Dnlf-75uiZx8eo$. 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.
Done

14. 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.
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15. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.
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16. 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%").
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We have edited the Abstract to fit the structured forma, and as such, it no longer says 'no recent national estimates' exist. Elsewhere, we believe that we indicate that our work builds on prior research and cite relevant studies. We are happy to make further edits upon request.

18. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here:
https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/table_checklist.pdf__;!!HXCxUKc!iQQFt9jgdZDSekeccYkOlEHbWCc6FwqykgwQ_MOuOsdDaOYEeDnlf-75ulVPcy4$.

We have edited our tables according to the checklist.

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inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.
We have edited our reference list.

In addition, 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 references you are citing are still current and available. Check the Clinical Guidance page at https://urldefense.com/v3/__https://www.acog.org/clinical__;!!HXCxUKc!iQQFt9jgdZDSekeccYkOlEHbWCc6FwqykgwQ_MOuOsdDaOYEeDnlf-75_xEHFFw$ (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

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NA

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