

# OBSTETRICS & GYNECOLOGY



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

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

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](mailto:obgyn@greenjournal.org).

**Date:** 02/16/2023  
**To:** "Marie Thoma" [REDACTED]  
**From:** "The Green Journal" em@greenjournal.org  
**Subject:** Your Submission ONG-23-183

RE: Manuscript Number ONG-23-183

The rise and differential impact of the COVID-19 pandemic on pregnancy-related mortality in the United States

Dear Dr. Thoma:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

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 submission will be maintained in active status for 14 days from the date of this letter. If we have not heard from you by 03/02/2023, we will assume you wish to withdraw the manuscript from further consideration.

#### EDITOR COMMENTS:

Thank you for submitting your work to the Green Journal. We are interested in publishing a revised version of this manuscript.

1) The reviewers and Statistical Editor have suggested additional details to aid in the interpretation and significance of these findings. The Editorial Board believes this work would be better formatted as an Original Research article (not Research Letter) to allow space to address the concerns below and highlight the nuances in ascertainment and interpretation of the mortality data. The revised article can still remain brief and concise. With this change, please also update the abstract to the Original Research article format (<https://journals.lww.com/greenjournal/Pages/InformationforAuthors.aspx#II-A>).

2) Since submission, it appears that the 2021 natality and mortality data have now been finalized (no longer provisional). Please update your manuscript with the final data.

3) 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](https://journals.lww.com/greenjournal/Documents/RevisionChecklist_Authors.pdf) and making the applicable edits to your manuscript.

#### REVIEWER COMMENTS:

##### Reviewer #1:

This is an analysis of publicly available national vital statistics data obtained from CDC Wonder for 2019-2021 in which the authors calculate pregnancy-related mortality ratio (PRMR) before and after the onset of the COVID-19 pandemic in the United States. The authors illustrate indirectly how COVID-19 has been a contributory cause to rising maternal mortality

over time. The authors go on to sub-categorize the PRMR data by race/ethnicity and report that the American Indian/Native people (AIAN) had the largest increase in PRMR after the onset of the COVID-19 pandemic.

A main concern with this paper relates to strategy of analyzing the data obtained from the National Center for Health statistics and applying definitions for pregnancy-related mortality that are broader (up to 1 year postpartum) without the added in-depth review of vital records by a medical epidemiologist for this group of late postpartum deaths.(1) To calculate the PRMR rates, the authors used the same ICD-10 codes as the National Center for Health Statistics (NCHS) (codes A34, O00-O95, O98-O99) but also add the ICD-10 code O96 to include maternal deaths between 43 days and 1 year postpartum. Addition of the O96 code makes this data set different from what is reported by NCHS(1) which uses the 42 day limit, although this difference is not clearly stated in the methods. Please clarify in the manuscript and include a justification of why this approach was chosen, and the potential pitfalls of the approach.

For example, the authors report that in 2020, there were 999 pregnancy-related deaths with a mortality ratio of 36.7 per 100,000 live births; however in February 2022, the NCHS reported that 861 women died from maternal causes with a maternal mortality ratio of 23.8 deaths per 100,000 live births.(2) I presume that the difference in these values is due to the addition of the O96 ICD-10 code. Because this could cause confusion to the reader trying to compare these rates to those already published(2), I would recommend including a figure that sub-categorizes the PRMR into a (a) deaths during pregnancy to 42 days postpartum and (b) deaths 43 days - 1 year postpartum. How is this report novel compared to what is already published?

Additionally, in the limitations, please address potential discrepancies that accompany data ascertainment from ICD-10 codes. The NCHS itself has reported on the high degree of misclassification of pregnancy status on death certificates due to incorrect documentation and limitations of ICD-10 code accuracy.(3) Validation studies found that for 21-50% of death certificates marked as pregnant-postpartum, the woman was not pregnant or postpartum at the time of death.(4,5)

Finally, please address that the large relative change seen in PRMR for the AIAN group is limited by the very small numbers in this group.

1. <https://www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm#about-pmss>
2. Hoyert DL. Maternal mortality rates in the United States, 2020. NCHS Health E-Stats. 2022. DOI: <https://dx.doi.org/10.15620/cdc:113967>.
3. MacDorman MF, Declercq E, Thoma ME. Making Vital Statistics Count: Preventing U.S. Maternal Deaths Requires Better Data. *Obstet Gynecol.* May 2018;131(5):759-761. doi:10.1097/AOG.0000000000002598
4. Catalano A, Davis NL, Petersen EE, et al. Pregnant? Validity of the pregnancy checkbox on death certificates in four states, and characteristics associated with pregnancy checkbox errors. *Am J Obstet Gynecol.* Mar 2020;222(3):269 e1-269 e8. doi:10.1016/j.ajog.2019.10.005
5. Baeva S, Saxton DL, Ruggiero K, et al. Identifying Maternal Deaths in Texas Using an Enhanced Method, 2012. *Obstet Gynecol.* May 2018;131(5):762-769. doi:10.1097/AOG.0000000000002565

#### Reviewer #2:

The authors conducted a retrospective assessment of pregnancy-related mortality in the US before and during the COVID-19 pandemic (2019-2021).

Précis and abstract well written. The last sentence in the abstract does not add to the already clear section above it. Would recommend removing it.

#### Introduction

-The problem is well illustrated and the objective/study plan is clear.

#### Methods

A weakness: Provisional counts for 2021 are used. Historically how do provisional counts compare to the predicted and final counts?

#### Results

It is important to provide relative and absolute mortality counts in parentheses after statements regarding increasing rates are made (lines 62-64).

#### Discussion

No concerns

#### STATISTICAL EDITOR COMMENTS:

lines 13-15 and Fig 1: Please also report whether the differences in PRMR without a Covid-19 code significantly changed over the period examined. From the figure, the changes appear small and likely NS.

lines 34-35: Although inclusion of late maternal deaths is an accepted inclusion to pregnancy related mortality, the effect of Covid-19 on population mortality in general is difficult to disentangle from the usual causes of late maternal mortality. Please separate out those cases of late mortality with/without a Covid-19 diagnosis. That may mitigate the difference from previous years, or at least allow a more precise estimate of Covid's effect on maternal mortality.

General: Please provide more detail in terms of actual counts, so that the reader can be better informed re: interpretation of the various mortality ratio estimates. This could be shown in supplemental material. This is particularly important for the smaller subsets examined, e.g., indigenous Alaskans or American Indians, whose denominators are likely  $< 100,000$  per quarter, thus the estimates of maternal mortality are subject to much more stochastic variability and imprecision.

General: The Authors need to include in limitations the general issues of obtaining accurate, consistent (across time) estimates of maternal mortality from the various States and the issue of accurate ascertainment of Covid-19 during the early part of the pandemic, when testing was unavailable, restricted or inaccurate.

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Sincerely,  
Mark A. Clapp, MD, MPH  
Editorial Fellow

The Editors of Obstetrics & Gynecology

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

## EDITOR COMMENTS:

Thank you for submitting your work to the Green Journal. We are interested in publishing a revised version of this manuscript.

**Response: Thank you for the opportunity to address the thoughtful critiques and make revisions. We think the suggestions by the editors and reviewers have improved the overall manuscript and interpretation of the findings.**

1) The reviewers and Statistical Editor have suggested additional details to aid in the interpretation and significance of these findings. The Editorial Board believes this work would be better formatted as an Original Research article (not Research Letter) to allow space to address the concerns below and highlight the nuances in ascertainment and interpretation of the mortality data. The revised article can still remain brief and concise. With this change, please also update the abstract to the Original Research article format

(<https://journals.lww.com/greenjournal/Pages/InformationforAuthors.aspx#II-A>).

**Response: We have updated the manuscript to reflect the Original Research article format. We have revised the manuscript as an Original Research article and, thus, updated the sections of the manuscript to better reflect the journal guidelines for this type of article, including a more detailed Introduction and Discussion section. Given the new format, we also moved some supplementary figures to the main manuscript and created new supplementary figures.**

2) Since submission, it appears that the 2021 natality and mortality data have now been finalized (no longer provisional). Please update your manuscript with the final data.

**Response: We compared all of our prior calculations for 2021 to the updated final data in CDC Wonder. All estimates remained the same and no changes were needed.**

3) 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](https://journals.lww.com/greenjournal/Documents/RevisionChecklist_Authors.pdf) and making the applicable edits to your manuscript.

**Response: We have reviewed the Revision Checklist and updated the manuscript accordingly.**

## REVIEWER COMMENTS:

Reviewer #1:

This is an analysis of publicly available national vital statistics data obtained from CDC Wonder for 2019-2021 in which the authors calculate pregnancy-related mortality ratio (PRMR) before and after the onset of the COVID-19 pandemic in the United States. The authors illustrate indirectly how COVID-19 has been a contributory cause to rising maternal mortality over time. The authors go on to sub-categorize the PRMR data by race/ethnicity and report that the American Indian/Native people (AIAN) had the largest increase in PRMR after the onset of the COVID-19 pandemic.

A main concern with this paper relates to strategy of analyzing the data obtained from the National Center for Health statistics and applying definitions for pregnancy-related mortality that are broader (up to 1 year postpartum) without the added in-depth review of vital records by a medical epidemiologist for this group of late postpartum deaths.(1) To calculate the PRMR rates, the authors used the same ICD-10 codes as the National Center for Health Statistics (NCHS) (codes A34, O00-O95, O98-O99) but also add the ICD-10 code O96 to include maternal deaths between 43 days and 1 year postpartum. Addition of the O96 code makes this data set different from what is reported by NCHS(1) which uses the 42 day limit, although this difference is not clearly stated in the methods. Please clarify in the manuscript and include a justification of why this approach was chosen, and the potential pitfalls of the approach.

**Response: We operationalized pregnancy-related mortality using ICD-10 codes consistent with the CDC definition: “the death of a woman while pregnant or within 1 year of the end of pregnancy from any cause related to or aggravated by the pregnancy.” ICD-10 O-codes delineate both the cause (an obstetric or pregnancy-related cause) and time. Pregnancy-related causes prior to 43 days are classified as maternal deaths (A34, O00-O95, O98-O99) and causes after 43 days up to 1 year are coded as O96 (late maternal deaths). Although NCHS reports only maternal mortality statistics, we think extending the time frame for examining maternal/pregnancy-related deaths out to one year is more appropriate in general and particularly in the analysis of data during the pandemic, given our previous findings of increases for maternal and late maternal deaths earlier in the pandemic (Reference 1 in the manuscript). We clarified this description in the Methods section, paragraph 1. We elaborate on limitations below and in the Discussion section, paragraphs 2 and 3.**

The coding of ICD-10 codes is conducted by highly-trained mortality medical coders/nosologists within NCHS and coded consistent with WHO ICD-10 guidelines (<https://blogs.cdc.gov/nchs/2013/04/18/162/>). Pregnancy-related causes of death with a pregnancy-checkbox indicating 43 days to 1 year are grouped as ICD-10 code, O96. These processes are conducted consistent with international standards. Other data sources have information on pregnancy-related mortality and, although rates have been shown to differ between sources, the relative patterns are generally consistent across data sources. These

**other systems rely on vital records as a starting point for ascertainment, but apply different processes to identify pregnancy-related deaths (Reference #38 in the revised manuscript). Currently, these other data sources are not publicly available nor been examined/reported for the data years in this study (2019-2021) (Reference #14 in revised manuscript). We make of note of these differences in the Discussion under limitations, paragraph 3.**

For example, the authors report that in 2020, there were 999 pregnancy-related deaths with a mortality ratio of 36.7 per 100,000 live births; however in February 2022, the NCHS reported that 861 women died from maternal causes with a maternal mortality ratio of 23.8 deaths per 100,000 live births.(2) I presume that the difference in these values is due to the addition of the O96 ICD-10 code. Because this could cause confusion to the reader trying to compare these rates to those already published(2), I would recommend including a figure that sub-categorizes the PRMR into a (a) deaths during pregnancy to 42 days postpartum and (b) deaths 43 days - 1 year postpartum. How is this report novel compared to what is already published?

**Response: The differences in the number of deaths is two-fold. 1) NCHS reports on maternal deaths (deaths during pregnancy or within 42 days) only and we report on pregnancy-related deaths, which include both maternal and late maternal deaths, as noted by the reviewer. 2) NCHS reports numbers for the totality of 2020, whereas, we partition our findings into pre-pandemic (2019-March 2020) and pandemic (2020) rates. Our prior paper, referenced in the manuscript, showed that the increase in maternal mortality and late maternal mortality occurred after the start of the pandemic, rather than in the first quarter of 2020. Compared to what has already been published, this new report includes data for 2021 (not previously reported) and we partition the data into groups and time periods not often examined by NCHS. For example, American Indian Alaska Native and Asian groups, rural/urban, COVID-19 contributory causes, and quarterly estimates were not reported in prior reports. Unlike NCHS reporting of maternal death only, pregnancy-related mortality ratios capture risk that extends beyond a 42-day cut-off. Based on reviewer and statistical editor feedback, we include a supplementary analysis that partitions the PRMR into maternal and late maternal deaths by pre-pandemic and during (2020, 2021) the pandemic and by COVID-19 contributory causes.**

Additionally, in the limitations, please address potential discrepancies that accompany data ascertainment from ICD-10 codes. The NCHS itself has reported on the high degree of misclassification of pregnancy status on death certificates due to incorrect documentation and limitations of ICD-10 code accuracy.(3) Validation studies found that for 21-50% of death certificates marked as pregnant-postpartum, the woman was not pregnant or postpartum at the time of death.(4,5)

**Response: We add additional detail to the limitations (Discussion paragraph 2) on prior validation studies among older data years and discuss the changes NCHS made to the data in 2018 and onward to address this misclassification. Because these studies found a large portion of the misclassification occurred among older age groups (45+ years), NCHS no longer relies on the checkbox (only the literal text) for coding obstetric causes for decedents**

**ages 45 and up. Although not a perfect correction, it does account for a significant proportion of the potential age-related misclassification maternal deaths.**

Finally, please address that the large relative change seen in PRMR for the AIAN group is limited by the very small numbers in this group.

**Response: We included a statement about conducting additional supplementary analyses to provide more reliable estimates among AIAN in the Methods section (paragraph 2). We also note that the rates for the main analysis meet standards of reliability. To address this comment and that of the statistical editor, we include an additional year of data (2018) and combine pre-pandemic (2018-Q1,2020) and all pandemic years (Q2-Q4 2020 and 2021) – the increase remained substantial. While annual variation was noted in the pre-pandemic years, this variation was minimal compared to what was seen for 2021 (the absolute change in PRMR between 2018 to 2019 and 2019 to 2020 was 18 and 4, respectively, while the absolute change between pandemic 2020 to 2021 was 81). We agree that it can be difficult to disentangle stochastic change from non-random change over time for smaller groups; however, we believe examination remains critical as we may miss concerning patterns that require further investigation.**

1. <https://www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm#about-pmss>
2. Hoyert DL. Maternal mortality rates in the United States, 2020. NCHS Health E-Stats. 2022. DOI: <https://dx.doi.org/10.15620/cdc:113967>.
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Reviewer #2:

The authors conducted a retrospective assessment of pregnancy-related mortality in the US before and during the COVID-19 pandemic (2019-2021).

Précis and abstract well written. The last sentence in the abstract does not add to the already clear section above it. Would recommend removing it.

**Response: We removed this sentence from the abstract.**

Introduction

-The problem is well illustrated and the objective/study plan is clear.

Methods

A weakness: Provisional counts for 2021 are used. Historically how do provisional counts compare to the predicted and final counts?

**Response: Final counts are now available on CDC Wonder. We compared our estimates and no changes were needed.**

Results

It is important to provide relative and absolute mortality counts in parentheses after statements regarding increasing rates are made (lines 62-64).

**Response: We have included both relative and absolute changes/differences between the rates.**

Discussion

No concerns

## STATISTICAL EDITOR COMMENTS:

lines 13-15 and Fig 1: Please also report whether the differences in PRMR without a Covid-19 code significantly changed over the period examined. From the figure, the changes appear small and likely NS.

**Response: We conducted z-tests of proportions to compare changes in PRMR across relevant quarterly time periods. Given the variability in COVID-19 testing over time (as noted as a limitation below), we do not want to rely on formal hypothesis testing for non-COVID PRMR over time. Rather, Figure 1 is meant to descriptively show how peaks in the overall PRMR correspond to a higher proportion of pregnancy-related mortality with a COVID-19 contributory cause relative to the non-COVID PRMR within each time period.**

lines 34-35: Although inclusion of late maternal deaths is an accepted inclusion to pregnancy related mortality, the effect of Covid-19 on population mortality in general is difficult to disentangle from the usual causes of late maternal mortality. Please separate out those cases of late mortality with/without a Covid-19 diagnosis. That may mitigate the difference from previous years, or at least allow a more precise estimate of Covid's effect on maternal mortality.

**Response: We partition out overall maternal and late maternal deaths with and without a COVID-19 contributory cause before and during (2020, 2021) the pandemic. We include this as supplementary material. The difference in previous years, difference in measures, and rationale for use of PRMR is explained above (Reviewer 1).**

General: Please provide more detail in terms of actual counts, so that the reader can be better informed re: interpretation of the various mortality ratio estimates. This could be shown in supplemental material. This is particularly important for the smaller subsets examined, e.g., indigenous Alaskans or American Indians, whose denominators are likely  $\ll 100,000$  per quarter, thus the estimates of maternal mortality are subject to much more stochastic variability and imprecision.

**Response: The supplemental table included counts of pregnancy-related deaths, rates of PRMR and % with COVID overall and by race/ethnicity and rural/urban differences, and we calculate absolute (p-values) and relative differences by pre-pandemic and pandemic (2020 and 2021 separately). Subgroup analyses (race/ethnicity and rural/urban) were compared by pre-pandemic and pandemic periods (2020 and 2021), not by quarter. To generate more reliable estimates of PRMR among AIAN birthing people, we included an additional pre-pandemic year (2018) and combined pandemic years into one group in a supplementary analysis. The prepandemic PRMR for AIAN were 60.8 (39 deaths per 64095 births) compared with pandemic PRMR of 125.0 (58 deaths per 46384 births). While some stochastic variation was noted per year in the pre-pandemic years (see response under Reviewer 1), it was not to the extent seen in 2021.**

General: The Authors need to include in limitations the general issues of obtaining accurate, consistent (across time) estimates of maternal mortality from the various States and the issue of

accurate ascertainment of Covid-19 during the early part of the pandemic, when testing was unavailable, restricted or inaccurate.

**Response: We have included a statement regarding the limitations of COVID-19 testing in the early part of the pandemic.**