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.

Date:	Dec 18, 2020
To:	"K S Joseph"
From:	"The Green Journal" em@greenjournal.org
Subject:	Your Submission ONG-20-3002

RE: Manuscript Number ONG-20-3002

Maternal mortality in the United States: Recent trends, current status and future considerations

Dear Dr. Joseph:

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

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

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jan 08, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This manuscript contains vital information concerning obstetrical care in the USA. Revealing that the national data set has multiple flaws is the first step on the road to correction and obtaining the information so badly needed to develop an effective response. With their deep dive, the authors are able to discern some useful information and are also able to offer some thoughts on how to remediate the data collection for the future. Although dense with information and difficult for the casual reader to utilize all the results fully, there is no doubt that this paper will be used by other researchers and program developers to plan their efforts.

Reviewer #2:

Overall comments to author
1)   A review of maternal morality measurement issues will be useful to readers of the Green journal. Digesting and synthesizing the NCHS reports for Green J readers will be useful. The commentary would be improved by clarifying the focus (measurement) and more attention to disparities and social determinants of health using data from the US. Consider using a framework to organize the commentary? (WHO direct/indirect/late?)
2)   Help readers understand the motivation behind adding the checkbox in the first place, as the NCHS report does. I don't think the authors can assume that Green J readers have read the NCHS reports, so more detail on what they say would be helpful. Sometimes the authors make leaps that may be explained in the NCHS report but will not be clear to readers unfamiliar with the NCHS reports
3)   For example, this commentary could do 3 things as a primer on MM surveillance:
a.   Describe measurement issues - motivation for adding checkbox and what we now know about the impact of adding checkbox
b.   Discuss how to improve measurement/surveillance
c.   Discuss what to do about persistent disparities in MM
4)   Please revise language to precise and clear (see below for examples)
5)   Is there any concern that prior to the pregnancy checkbox, maternal deaths were under-reported (especially related to chronic conditions and late maternal deaths)? That misclassification could go both ways? There seems to be an assumption that the pre-pregnancy checkbox period is a gold standard. Can this be justified?

Title
6)   Is this commentary about maternal mortality trends and status or is it maternal mortality measurement? I would

focus on the measurement - what we've learned about the checkbox and how use of the checkbox impacted observed trends, implications for data collection and measurement going forward, and needs to improve surveillance.

Abstract
7)   Line 37: is this a commentary? Replace "paper" with commentary if so
8)   Line 43-45: I might delete the info about specific causes of maternal deaths and replace with something about persistent disparities and their causes. "Reducing disparities" is in the precis but does not appear anywhere in the abstract.
9)   Line 50: this sentence is confusing, please clarify: does this mean that the situation is not as dire as we recently thought?
10)   Line 52: mention of reducing disparities but no data/info presented abut disparities in the abstract. Seems a bit of a throw-away line here and a large oversight.

Introduction
11)   Line 57: "recent turn in the maternal mortality narrative" is wordy and awkward - what do you mean here?
12)   Line 58-61: do the authors privilege WHO estimates over IHME estimates? If so, why?
13)   Line 61: "The steady stream of depressing news was contradicted..." - wordy. "These findings were contradicted..." or "Recent reports from NCHS have contradicted these findings" to make it active voice
14)   Line 70: "obstetric and other substantive issues" - what does this mean?
15)   Line 75: "a comprehensive description of maternal mortality in the US" - is this commentary a comprehensive description of maternal mortality? I would argue not - this commentary is a description and synthesis of the measurement challenges, the impact of changes in measurement, and implications for ongoing surveillance. Please clarify the focus and purpose of this commentary.
16)   Line 76-66: "residual challenges" is vague - state them here so the reader knows where we are headed?

17)   Line 88-89: late maternal death. This seems really important. Being able to capture late maternal deaths will give us a more complete picture of the burden of maternal causes of death, especially in the context of increasing chronic conditions. The commentary seems to suggest that most late maternal deaths are misclassified - is this the intent?
18)   Line 91 - also O99? It is not clear to me why coding would change for these after introduction of the checkbox - I think I'm missing something.
19)   Line 95-97: Put each citation next to the relevant cause. Clarify "Journalists and researchers have suggested diverse causes..." This is about causes of the observed increase in maternal death, correct? "implicated diverse factors " is vague.
20)   Line 115-119: indirect causes and less specific causes, late maternal deaths. As above - are the authors saying these are spurious? It is possible they were under-/missed previously? That the trends prior to the checkbox are not a gold standard? Please include a few examples of the types of conditions that might be coded this way (ie is it PE? VTE? What was getting captured as pregnancy related conditions that may not have been actually related to pregnancy?) In other settings, indirect and late deaths have been found to increase - they were previously missed - after review processes, e.g: Hogan, M. C., Saavedra-Avendano, B., Darney, B. G., Torres-Palacios, L. M., Rhenals-Osorio, A. L., Sierra, B. L., . . . Lozano, R. (2016). Reclassifying causes of obstetric death in Mexico: a repeated cross-sectional study. Bull World Health Organ, 94(5), 362-369B. doi:10.2471/BLT.15.163360
21)   Line 132-136: Was there any positive impact from this 2018 restriction on the age use for the pregnancy checkbox? Did this help improve the quality of the data?
22)   Line 140: Vague statement - list the "issues" you will discuss here so reader knows where we are headed.

23)   Line 142-144: without pregnancy checkbox and also without late maternal deaths and "other" codes? I was confused here.

24)   Line 148: change "mothers" to "women giving birth" Change "mothers" throughout. Individual giving birth have rich identities that go beyond motherhood.

25)   Line 164-171: These are interesting figures. These indicate that increases in conditions like cHTN or DM likely explain many of these trends. Is that what the reader is to infer? Do the authors have any thoughts regarding an explanation? There is some description of the discrepant trend with CHTN later, but a reference to this may be helpful as the reader is left wondering about why the trend might have occurred.

26)   Line 165: I think in this paragraph you are referring to Fig 2, not Fig 1?

27)   Line 169-171: is there a justification for these groupings? Embolism and CNS/mental disorders - how/why do they go together?

28)   Line 189-190: disparities in MMR by race/ethnicity simply cannot just be mentioned in passing.

29)   Line 193-195: Again, are there examples of the types of conditions that might be included in this other specific pregnancy related condition

30)   Line 195: Does Fig 3A show fractions of deaths due to causes/cause groupings or MMR for each cause? Also see below.

31)   I am confused by why some causes are included in 3A and 3B. e.g. abortive outcomes is 7.6/million and included in

3A but HTN is 7.9/million and in 3B. And ectopic (an abortive outcome? Is abortive outcome O00-O08? On Table 2, specific abortive outcomes are included but not ectopic or molar. Are these cause of death groupings/larger categories/buckets vs specific causes? I think this is it, but can you confirm and clarify?

32) Why sometimes do you use deaths per 100,000 live births (the standard measure) and sometimes per 1,000,000 live births? Is that also standard?

33) Line 201-206: this is a very long sentence and I got lost in the middle of it.

34) Line 202: "potential misclassification of non-maternal deaths among women 10-44 as maternal deaths in 2018 data is suggested by..." clarify what the misclassification was?

35) Line 203: do we expect deaths to be higher in 45+ compared to 40-44? Tell the reader why this discrepancy suggests misclassification?

36) Line 204: declines in pre-eclampsia: how much of this is a coding artifact and how much due to better diagnosis of HTN? See comment on Fig 2.

37) Line 208-210: but how many young women die of these causes OUTSIDE pregnancy? Young women do not die very much, pregnancy is one of the riskiest things they do.

38) Line 213: is citation #20 correct? Should it be #19?

39) Line 214: or substitution of HTN for eclampsia in coding?

40) Line 222: why? Clearly state why (re: raising the possibility that such deaths occurred among non-pregnant women)

41) Line 223: But doesn't pregnancy exacerbate all conditions? Is an "incidental association" even possible? I suppose it is for some conditions.

42) Line 227: subtitle says 40-44

43) Line 233: again not clear if Fig 3A are fractions or MMR

44) Line 244: obstetric embolism - I see blood clot and amniotic embolism on Fig 3B - which one? Both?

45) Line 254: more likely reflects increases in these conditions and in pregnancies among women with CNS/mental disorders, no?

46) Line 260: Are there any examples of the impact of these ACOG/state based maternal mortality review efforts? The example of the UK is nice,but a US example would be helpful.
47) Line 267: Please elaborate on the impact of mental health issues and discontinuation of prenatal care and maternal mortality. Is the reader to assume that mental health issues leads to stopping prenatal care which leads to maternal mortality?

48) Line 271: social determinants: this needs to be included in the abstract. Cite data from the US in this section in additional to general statements from WHO and Marmot?

49) Line 272: Can change to race differences or the differences between black and white, but "racial black white" is confusing
50) Line 276: #33 is not in reference list

51) Line 278: Does "exceeded" here refer to the 5 fold higher death rate in England vs the 2.5 fold higher death rate in the US? Please be explicit
52) Line 280: cite for "factors arising from racism"

53) Line 286-295:

a. The discussion of racial disparities feels tacked on and not well developed.
b. 31% of maternal deaths are to Blacks. So a larger proportion of maternal deaths are to white women as you state (44%) - but what is the distribution in the population? Among reproductive age women? Among pregnant women? That is, are Black women 31% of the population or are they disproportionately represented among maternal deaths? This is a tone deaf statement at best.
c. Please review and incorporate US literature - I'm intrigued by all the UK data. It is good data, but this is about US maternal mortality rates.
54) Line 291-295: What should be the takeaway from this statement? That both race and SES status impact maternal mortality and health? I think some discussion of how race and SES are correlated / interact might be helpful here?

55)   Conclusion: This appears to just be the intro/abstract repeated. What is the reader to take away from this article?
56)
57)   Line 304: The methods to improve maternal mortality surveillance can be reiterated here in more detail as a specific call to action. 1) review committees 2)physicians education 3) pregnancy checkboxes with better data / more detail. In addition, the specific action items related to SDH and methods to address broader issues of maternal mortality should be spelled out: 1) investment in racial disparities 2)equitable access to healthcare (whatever other ideas are thought to be helpful)
58)

59)   Figure 1:

a.   Was ICD-10 adopted on death certificates in 1999? It was not widely adopted in the US until later.
b.   Why does panel A start at 1993 and panel B at 1999?
c.   Could A & B be presented in 1 figure? 3 classifications, 1993-2014, with arrows for checkbox implementation? Not clear to me why this needs 2 figures.

60)   Figure 2:
a.   Why per million here? Or is that a typo of 100,000 on the Y axis?
b.   Make the Y axis the same for all panels?
c.   Panel A: I wonder if women with pre-eclampsia have HTN and is gets diagnosed earlier now? Thus the switch we see of eclampsia going down and HTN going up?
61)   Figure 3:
a.   Panel A: very hard to read and interpret. Not clear if the numbers are ratios per 100,000 or proportions (pie chart). In general, avoid pie charts. Use a stacked bar instead? Clarify if these are MMR per cause or proportions of deaths.
b.   Panel A: Is there any insight into what types of conditions are "puerperal complications"? It seems like things could be classified in a number of these categories, what are examples of cases for some of these. An appendix with exemplar cases would be very helpful to gain insight into the discrepancies related to coding.
c.   Panel B: are these the same data as in Table 2? Why per 1 million births? Ectopic pregnancy is not on Table 2 - I got confused.
d.   Panel B: Are the components of mental /CNS disorders inclusive of suicide? I think this was referenced earlier in the paper, but again, what Is an example of the disease states included here?

Reviewer #3:

The authors present a reasonable review of causes of maternal mortality in the US. While I appreciate the work here, much of what is being presented is not novel and is well known. The database used has been used in many works on the causes of maternal mortality. Additionally, health care disparities are well known to be determinants of poor outcomes in pregnant women.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. 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. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

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

3. 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.

4. 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.

5. If 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.

6. 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.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

8. 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).

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

10. 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 Current Commentary articles is 250 words. Please provide a word count.

11. 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.

12. 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.

13. 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%").

14. 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.

15. 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 reference you are citing is still current and available. If the reference you are citing has been updated (ie,

replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

16. Figures 1-2: Okay.
Figure 3: Please add color to A.
Please cite figures in order in the manuscript, this includes A and B labels.

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.

17. 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.

18. 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.

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

* * *

If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:
     * A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
     * A point-by-point response to each of the received comments in this letter. 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 Jan 08, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
John O. Schorge, MD
Associate Editor, Gynecology

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

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January 8, 2021

To
John O. Schorge, MD
Associate Editor, Gynecology
Obstetrics and Gynecology

Re Manuscript No. ONG-20-3002

Dear Madam/Sir,

On behalf of my coauthors, I am submitting a revised manuscript after having addressed issues raised by Reviewers and the Editor in your letter dated 18, December 2020. A point-by-point response to the Reviewers' and Editor's comments is provided below. I confirm that we have read the Instructions to Authors and that this revision has been developed in consultation with all coauthors.

We would be grateful if you could consider our manuscript for possible publication in the *Journal*.
Yours sincerely.

K.S. Joseph MD, PhD
Professor
Department of Obstetrics and Gynaeology
School of Population and Public Health
University of British Columbia

Maternal mortality in the United States: Recent trends, current status and future considerations

Response to Reviewers' comments

<u>**Reviewer #1:**</u>

Comment: **This manuscript contains vital information concerning obstetrical care in the USA. Revealing that the national data set has multiple flaws is the first step on the road to correction and obtaining the information so badly needed to develop an effective response. With their deep dive, the authors are able to discern some useful information and are also able to offer some thoughts on how to remediate the data collection for the future. Although dense with information and difficult for the casual reader to utilize all the results fully, there is no doubt that this paper will be used by other researchers and program developers to plan their efforts.**
<u>Response:</u> *Thank you.*

<u>**Reviewer #2:**</u>
Overall comments to author
Comment 1): **A review of maternal morality measurement issues will be useful to readers of the Green journal. Digesting and synthesizing the NCHS reports for Green J readers will be useful. The commentary would be improved by clarifying the focus (measurement) and more attention to disparities and social determinants of health using data from the US. Consider using a framework to organize the commentary? (WHO direct/indirect/late?)**
<u>Response:</u> *The NCHS reports, which have overturned the prevailing view regarding rising rates of maternal mortality in the US, constitute the background around which this manuscript is framed. The manuscript provides an overview of the obstetric and public health issues related to maternal mortality after accounting for distortions in the data caused by the introduction of the pregnancy checkbox. Some intricacies arise because examination of obstetric issues reveals what appear to be unrecognized errors in the recent 2018 data due to pregnancy checkbox issues. These pregnancy checkbox errors affect direct, indirect and late maternal deaths. In the revised manuscript, we have emphasized this categorization of maternal deaths*
Page 6
"On the other hand, the pregnancy checkbox profoundly impacted the identification of some less informative <u>direct</u> (e.g., 'Other specified pregnancy-related conditions', ICD-10 O268), and <u>indirect</u> causes of death (e.g., 'Other obstetric conditions not elsewhere classified', O99) and <u>late maternal deaths (ICD-10 O96, O97)."</u>
The focus of the manuscript is now clearly stated at the outset
Page 4
"This Commentary provides the background to the NCHS reports, summarizes their findings, describes temporal trends and the current status of maternal mortality in the United States, identifies surveillance and clinical concerns, and discusses issues related to the identification and prevention of maternal death."

<u>**Comment:**</u> **2) Help readers understand the motivation behind adding the checkbox in the first place, as the NCHS report does. I don't think the authors can assume that Green J**

2

readers have read the NCHS reports, so more detail on what they say would be helpful. Sometimes the authors make leaps that may be explained in the NCHS report but will not be clear to readers unfamiliar with the NCHS reports.

<u>Response:</u> *Under the heading 'Background to the NCHS reports' we provide the reason for the introduction of the checkbox, namely, that studies had showed under-ascertainment of maternal deaths when surveillance was based solely on death certificate information. Individual states' experience with the pregnancy checkbox was another reason.*
Page 4 bottom
"Studies carried out prior to 2003 showed that identification of maternal deaths based solely on death certificate information resulted in substantial numbers of missed maternal deaths [13-16]. These studies and the experience of a few states with a pregnancy checkbox on death certificates led the NCHS to introduce a standard pregnancy checkbox on the revised 2003 death certificate."

<u>**Comment 3):**</u> **For example, this commentary could do 3 things as a primer on MM surveillance:**
a. Describe measurement issues - motivation for adding checkbox and what we now know about the impact of adding checkbox.
<u>Response:</u> *As mentioned in #2, the NCHS' motivation for adding the checkbox is explained on page 4. The impact of the checkbox is also explained*
Page 4 bottom and page 5 top
"The staggered implementation of the pregnancy checkbox by the states resulted in a progressive increase in the number of reported maternal deaths (Figure 1A [17]."
Page 5-6
"The pregnancy checkbox led to an increase in MMRs by about 9.6 maternal deaths per 100,000 live births between 2003 and 2017 [7]. However, the impact of the checkbox differed by maternal age, race and Hispanic origin, and underlying cause of death [7]. The contribution of the pregnancy checkbox was negligible (increase of <0.5 deaths per 100,000 live births or modest (increase of <1 death per 100,000 live births) for several cause-of-death categories (e.g., complication of labor and delivery), though mortality rates within some such categories increased or decreased due to unrelated factors [7; pp. 13, 24]. On the other hand, the pregnancy checkbox profoundly impacted the identification of some less informative direct (e.g., 'Other specified pregnancy-related conditions', ICD-10 O268), and indirect causes of death (e.g., 'Other obstetric conditions not elsewhere classified' and late maternal deaths, ICD-10 O95–O99).

Although the pregnancy checkbox improved the detection of some maternal deaths, it was also incorrectly identified some deaths to non-pregnant women as maternal deaths or late maternal deaths. The most egregious checkbox errors occurred among older women e.g., in 2013, 187 women aged ≥85 years were identified by the checkbox as pregnant at the time of death or within one year of death [8]. Pregnancy checkbox misclassification of some non-maternal deaths as maternal deaths was also suggested by the change in age-specific (non-maternal) deaths from 2003 to 2017 due to unintentional injury, suicide, drug overdose, homicide and unknown causes. Whereas deaths due to such non-maternal causes increased significantly among women <10 years or 55-59 years of age, they decreased significantly among (non-pregnant) women aged 15-44 years (indicating that some such deaths among nonpregnant women aged 15-44 years had been misclassified as maternal deaths [7])."

Comment 3b: Discuss how to improve measurement/surveillance
Response: *Analysis by cause of death categories seemingly unaffected by the pregnancy checkbox shows false positive errors associated with the checkbox. We propose the following solutions*
Page 10-11
"There is a strong case for corrective measures aimed at minimizing the misclassification of non-maternal deaths among women aged 10-44 years. Potential remedies include requiring specification of at least one pregnancy-related cause of death for all cases where the pregnancy checkbox is ticked, and a manual review of the causes of death listed on the death certificate or on the corresponding medical record in a hospitalization database ('database autopsy' [29]). A related issue pertains to enhanced physician education regarding the 'underlying cause of death' concept and the importance of accurately completing death certificates."

Comment 3c: Discuss what to do about persistent disparities in MM
Response: This section has been revised and includes additional citations to the literature.
Pages 13-14
"Racial disparities in MMRs reflect many factors arising from racism [38] including closely connected social determinants of health such as income, social status, education, access to health care, housing, the physical environment, social supports, health behaviors, and culture [12,38-41]. The strong correlations and synergism between these factors ensure that vulnerable populations experience disproportionately high risks of outcomes such as maternal death.

Racial and ethnic disparities in MMRs need to be addressed on an urgent basis through broad-based public health initiatives. Although the etiologic role of the social determinants of maternal death has been recognized for decades, the relative impact of these factors appears to be increasing [37]. Vulnerable segments of the population, especially non-Hispanic Black women, need to be supported through comprehensive and sustained public health programs that address preconceptional health and chronic conditions (at the individual level), implicit racial bias among health care providers (at the interpersonal level), quality of care in hospitals predominantly serving non-Hispanic Black women (at the community level) and paid parental leave and extended health insurance (at the societal level) [38]. Such initiatives are also required to support vulnerable women and address social determinants of health across the entire population. This need is highlighted by the distribution of maternal deaths in 2018: 287, 205 and 105 deaths occurred among non-Hispanic White, non-Hispanic Black and Hispanic women, respectively [8]."

Comment 4): Please revise language to precise and clear (see below for examples)
Response: *We have attempted to make the language more precise and clearer (see responses below).*

Comment 5): Is there any concern that prior to the pregnancy checkbox, maternal deaths were under-reported (especially related to chronic conditions and late maternal deaths)? That misclassification could go both ways? There seems to be an assumption that the pre-pregnancy checkbox period is a gold standard. Can this be justified?
Response: *We have stated that studies carried out prior to 2003 showed that the pregnancy checkbox was able to identify maternal deaths that were otherwise missed. This statement is*

supported by 4 relevant studies. The experience of states that introduced the pregnancy checkbox in the 1990s was congruent with this finding.
Page 4
"Studies carried out prior to 2003 showed that identification of maternal deaths based solely on death certificate information resulted in substantial numbers of missed maternal deaths [13-16]. These studies and the experience of a few states with a pregnancy checkbox on death certificates led the NCHS to introduce a standard pregnancy checkbox on the revised 2003 death certificate."

We have also stated that the pregnancy checkbox was responsible for a large number of false positive maternal deaths.
Page 6
"Although the pregnancy checkbox improved the detection of some maternal deaths, it was also incorrectly identified some deaths to non-pregnant women as maternal deaths or late maternal deaths. The most egregious checkbox errors occurred among older women e.g., in 2013, 187 women aged ≥85 years were identified by the checkbox as pregnant at the time of death or within one year of death [8]."
Page 10
"Several recent studies have shown that the pregnancy checkbox leads to a substantial misclassification of non-maternal deaths as maternal deaths [23-28]."

Title
<u>Comment 6)</u>: **Is this commentary about maternal mortality trends and status or is it maternal mortality measurement? I would focus on the measurement - what we've learned about the checkbox and how use of the checkbox impacted observed trends, implications for data collection and measurement going forward, and needs to improve surveillance.**
<u>Response</u>: *The 3 NCHS reports focus on measurement of maternal mortality in the United States. In the section providing the Background to the NCHS reports and in the section summarizing the NCHS reports, we discuss issues related to measurement of maternal mortality in the United States. The rest of the manuscript provides an obstetric and public health perspective on temporal trends, current status and future concerns related to maternal mortality after accounting for the measurement issues raised by the NCHS reports. The examination of temporal trends in underlying causes of death and details related to causes of death in 2018 suggest continued misclassification of maternal deaths due to the pregnancy checkbox. In response to these findings, we have made recommendations regarding further steps needed to improve maternal mortality measurement. Since the focus of the manuscript is on providing an accurate obstetric and public health perspective on maternal mortality, we feel the title is appropriate.*

Abstract
<u>Comment 7)</u>: **Line 37: is this a commentary? Replace "paper" with commentary if so**
<u>Response</u>: *This change has been made.*

<u>Comment 8)</u>: **Line 43-45: I might delete the info about specific causes of maternal deaths and replace with something about persistent disparities and their causes. "Reducing disparities" is in the precis but does not appear anywhere in the abstract.**

Response: *The Abstract has been edited, the information on specific causes of death has been abbreviated and the disparity in maternal mortality between non-Hispanic Blacks and non-Hispanic Whites is mentioned.*
"Specific causes of maternal death, which were not impacted by the pregnancy checkbox, such as preeclampsia, showed substantial temporal declines. However, in 2018, non-Hispanic Blacks had a 2.5-fold higher maternal mortality rate compared with non-Hispanic Whites."

Comment 9): Line 50: this sentence is confusing, please clarify: does this mean that the situation is not as dire as we recently thought?
Response: *The intended meaning of this sentence was to convey that the temporal increases in maternal mortality reported in recent years were artefacts and not real. However, improvements in surveillance have identified more maternal deaths than previously. To avoid confusion, we have revised the sentence which now states*
"Challenges with ascertaining maternal deaths notwithstanding, several causes of maternal death (unaffected by surveillance artefacts) show significant temporal declines, even though there remains substantial scope for preventing avoidable maternal death and reducing disparities."

Comment 10): Line 52: mention of reducing disparities but no data/info presented abut disparities in the abstract. Seems a bit of a throw-away line here and a large oversight.
Response: *As mentioned in response to Comment 8, a sentence has been added on the issue of disparities in the revised manuscript.*
Page
"However, in 2018, non-Hispanic Blacks had a 2.5-fold higher maternal mortality rate compared with non-Hispanic Whites."

Introduction
Comment 11): Line 57: "recent turn in the maternal mortality narrative" is wordy and awkward - what do you mean here?
Response: *We have revised the sentence to clarify the meaning.*
"The recent change in the maternal mortality narrative in the United States likely surprised many obstetricians, epidemiologists and public health experts."
The rest of the paragraph expands on this sentence and explains how after an extended period when maternal mortality rates were reported to have been rising, NCHS reports showed that there has in fact been no increase in maternal death rates in the United States.

Comment 12): Line 58-61: do the authors privilege WHO estimates over IHME estimates? If so, why?
Response: *The citation of WHO reports was not intended to cast doubt on the quality of the work carried out by the Institute for Health Metrics and Evaluation. In fact, estimates and temporal trends in maternal mortality in the United States published by the IHME also showed high and rising rates of maternal mortality in the United States. We have edited the sentence and added references to the IHME publications in the revised manuscript.*
"Page 3

For over a decade, several articles, and publications from reputable organizations documented temporal increases in maternal mortality rates (MMR) in the United States, and MMRs in the United States that were higher than those in many other countries [1-5].

References

4. Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, et al. Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5. Lancet 2010;375:1609-23.

5. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Shackelford KA, Steiner C, Heuton KR, et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:980-1004.

Comment 13): **Line 61: "The steady stream of depressing news was contradicted…" - wordy. "These findings were contradicted…" or "Recent reports from NCHS have contradicted these findings" to make it active voice**

Response: *This sentence has been edited.*

Page 3

"More recently, three detailed reports published by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention contradicted these assessments [6-8]."

Comment 14): **Line 70: "obstetric and other substantive issues" - what does this mean?**

Response: *The term 'substantive' was used as an antonym to 'methodologic' (in this context 'measurement') issues. In response to this comment, the sentence has been deleted.*

Comment 15): **Line 75: "a comprehensive description of maternal mortality in the US" - is this commentary a comprehensive description of maternal mortality? I would argue not - this commentary is a description and synthesis of the measurement challenges, the impact of changes in measurement, and implications for ongoing surveillance. Please clarify the focus and purpose of this commentary.**

Response: *We restated the purpose and justification for this Commentary.*

Page 4

"This paper provides the background to the NCHS reports, summarizes their findings, describes temporal trends and the current status of maternal mortality in the United States, identifies surveillance and clinical concerns, and discusses issues related to the identification and prevention of maternal death. These topics merit consideration since the current literature [9-12] fails to recognize the full import of the NCHS reports, and because a description of maternal mortality that accounts for surveillance artefacts is important from an obstetric and public health standpoint. There is also a need to address the misclassification of non-maternal deaths which continues to compromise maternal mortality surveillance."

Comment 16): **Line 76-66: "residual challenges" is vague - state them here so the reader knows where we are headed?**

Response: *The revised version of the manuscript specifies what is meant by residual challenges.*

Page 4

"Additionally, there is a need to address the misclassification of non-maternal deaths which continues to compromise maternal death surveillance."

Comment 17): Line 88-89: late maternal death. This seems really important. Being able to capture late maternal deaths will give us a more complete picture of the burden of maternal causes of death, especially in the context of increasing chronic conditions. The commentary seems to suggest that most late maternal deaths are misclassified - is this the intent?

Response: *At this point in manuscript, the increase in specific cause-of-death categories that were responsible for the seeming rise in maternal deaths is highlighted (without commentary regarding misclassification). At a later stage in the manuscript, this is discussed in more detail. Specifically, it is stated that a majority of late maternal deaths were identified solely because of the pregnancy checkbox. Currently, it is not possible to quantify what proportion of such late maternal deaths were misclassified. It is important to identify late maternal deaths accurately and also to identify the causes of late maternal deaths. Toward this end a suggestion is made to require relevant non-O chapter codes to accompany non-specific O chapter codes including those for late maternal deaths.*

Page 11

"The high rates of maternal deaths with non-informative and less informative causes of death such as 'Other specified pregnancy-related conditions' (ICD-10 O268) and 'Disease of the circulatory system complicating pregnancy, childbirth and the puerperium' (ICD-10 O994) need to be addressed: insight into pathologic conditions of concern can only be obtained with greater specificity in cause-of-death information. This concern, which also applies to late maternal deaths, may be addressed by requiring less informative O (pregnancy) Chapter ICD-10 codes to be accompanied by relevant codes from other Chapters. For example, in cases of aortic dissection, the I Chapter code for this condition (viz., ICD-10 I710) should accompany the less informative O chapter code (ICD-10 O994) which merely identifies a pregnancy-related disease of the circulatory system."

18)   Line 91 - also O99? It is not clear to me why coding would change for these after introduction of the checkbox - I think I'm missing something.

Response: *Yes. O99 is mentioned in Figure 1B but not in the text (which provides only one example of a non-specific ICD10 code, namely O268). There are 2 reasons why the number of deaths assigned to ICD10 codes O268, O96, O97 and O99 increased after the introduction of the pregnancy checkbox*

1) *Correct use of the pregnancy checkbox. More complete identification of 'other specified pregnancy-related conditions', late maternal deaths and 'other maternal diseases classifiable elsewhere' would have occurred because the checkbox would have led to improved identification of women who died while pregnant or who were pregnant within the year before death. For example, if a pregnant woman died with aortic dissection as the underlying cause of death, she may have been misclassified as a non-maternal death in the absence of the pregnancy checkbox and correctly identified as a maternal death (O994) if the pregnancy checkbox had been ticked.*
2) *Erroneous use of the pregnancy checkbox. False identification of 'other specified pregnancy-related conditions', late maternal deaths and 'other maternal diseases classifiable elsewhere' would have resulted because erroneous use of the checkbox would have led to*

8

misclassification of non-maternal deaths as maternal deaths. For example, if a non-pregnant woman who had not been pregnant in the past year died with aortic dissection as the underlying cause of death, she would have been misclassified as a maternal death if the pregnancy checkbox was erroneously ticked. Note the large number of women ≥85 years of age for whom the pregnancy checkbox had been ticked.

Comment 19): **Line 95-97: Put each citation next to the relevant cause. Clarify "Journalists and researchers have suggested diverse causes…" This is about causes of the observed increase in maternal death, correct? "implicated diverse factors " is vague.**
Responses: *The diverse factors implicated are specified and references have been provided next to each implicated factor in the revised manuscript (one reference has been changed).*
Page 5
"Journalists and researchers implicated diverse factors as the cause for the temporal increase in MMRs including rising cesarean delivery rates [18,19], excessive use of ultrasound [19], systemic racism [20], reduced access to abortion services, and lack of funding for planned parenthood [21]."

Comment 20): **Line 115-119: indirect causes and less specific causes, late maternal deaths. As above - are the authors saying these are spurious? It is possible they were under-/missed previously? That the trends prior to the checkbox are not a gold standard? Please include a few examples of the types of conditions that might be coded this way (ie is it PE? VTE? What was getting captured as pregnancy related conditions that may not have been actually related to pregnancy?) In other settings, indirect and late deaths have been found to increase - they were previously missed - after review processes, e.g: Hogan, M. C., Saavedra-Avendano, B., Darney, B. G., Torres-Palacios, L. M., Rhenals-Osorio, A. L., Sierra, B. L., . . . Lozano, R. (2016). Reclassifying causes of obstetric death in Mexico: a repeated cross-sectional study. Bull World Health Organ, 94(5), 362-369B. doi:10.2471/BLT.15.163360**
Response: *This section of the manuscript provides a summary of the NCHS reports (as stated in the section heading). The effect of the pregnancy checkbox in terms of increasing the identification of less specific cause of maternal death categories is stated. This point is subsequently clarified by the sentence that follows.*
Page 6
"Although the pregnancy checkbox improved the detection of specific causes of maternal death, it also incorrectly identified some deaths to non-pregnant women as maternal deaths or late maternal deaths."

Comment 21): **Line 132-136: Was there any positive impact from this 2018 restriction on the age use for the pregnancy checkbox? Did this help improve the quality of the data?**
Response: *The age restriction eliminated the false positive checkbox errors involving women aged 45-54 years. As stated in the NCHS reports, the pregnancy checkbox was ticked in a large number of deaths among older women in 2013 and other years (also mentioned in the previous paragraph).*

Comment 22): **Line 140: Vague statement - list the "issues" you will discuss here so reader knows where we are headed.**

Response: *The sentence has been revised and the issues to be discussed are listed.*
Page 6-7.
"The following sections include data from the CDC Wonder Births and Detailed Mortality databases, and the Mortality Multiple Causes of Death files of NCHS (Appendix 1) and provide insights into temporal trends, current status, clinical and surveillance concerns and social determinants of maternal mortality."

Comment 23): Line 142-144: without pregnancy checkbox and also without late maternal deaths and "other" codes? I was confused here.
Response: *In order to assess if maternal mortality rates were truly increasing (as opposed to the pregnancy checkbox artefactually increasing rates), the NCHS carried out a study using pre-2003 methodology i.e., without using information from the pregnancy checkbox. Late maternal deaths were not excluded if they were identified as such in the death certificate's underlying cause of death information. We have attempted to clarify this by revising the sentence.*
Page 7
"The NCHS investigation showed that MMRs did not increase significantly between 2002 and 2015-16 and 2018 when all rates were estimated without using information from the pregnancy checkbox i.e., when pre-2003 methods were used [6-8]."

Comment 24): Line 148: change "mothers" to "women giving birth" Change "mothers" throughout. Individual giving birth have rich identities that go beyond motherhood.
Response: *This change has been made throughout.*

Comment 25): Line 164-171: These are interesting figures. These indicate that increases in conditions like cHTN or DM likely explain many of these trends. Is that what the reader is to infer? Do the authors have any thoughts regarding an explanation? There is some description of the discrepant trend with CHTN later, but a reference to this may be helpful as the reader is left wondering about why the trend might have occurred.
Response: *This is a key point being made in this Commentary: some or all of the increase in deaths from chronic hypertension and other such diseases is likely due to misclassification of non-maternal deaths. We have tried to alert the reader to this issue when Figure 2 is mentioned and the issue is discussed in more detail in the section on surveillance concerns.*
Page 8
"Some of the temporal patterns in related subcategories of maternal death (e.g., preeclampsia-eclampsia versus chronic hypertension and amniotic fluid embolism versus blood clot embolism) were discrepant and potentially indicative of misclassification problems (see below)."
Page 10
"Discrepant temporal trends between related causes of death (e.g., declines in preeclampsia deaths vs increases in deaths from chronic hypertension; Figure 2A) and the high proportion of maternal deaths due to less informative and potentially incidental causes of death are other indicators suggesting misclassification. Whereas obstetric causes of death on a death certificate (e.g., preeclampsia and amniotic fluid embolism) would be unaffected by the incorrect use of the pregnancy checkbox, non-obstetric causes of death among non-pregnant women (e.g., chronic hypertension and pulmonary embolism) would be misclassified as maternal deaths if the pregnancy checkbox was ticked erroneously."

Comment 26): Line 165: I think in this paragraph you are referring to Fig 2, not Fig 1?

10

Response: *This error has been corrected.*

Comment 27): Line 169-171: is there a justification for these groupings? Embolism and CNS/mental disorders - how/why do they go together?

Response: *Figure 2 highlights selected cause-of-maternal death subcategories of clinical interest (from among the cause-of-death categories that were unimpacted by the pregnancy checkbox) that showed substantial temporal change. Table 1 provides a list of all cause-of-maternal death subtypes that were unimpacted by the pregnancy checkbox and which showed significant temporal changes between 1999 and 2018 (and Appendix Table 2 provides all cause-of-maternal death subtypes that were unimpacted by the pregnancy checkbox irrespective of whether they showed significant temporal changes between 1999 and 2018).*

Comment 28): Line 189-190: disparities in MMR by race/ethnicity simply cannot just be mentioned in passing.

Response: *This section is on the 'Current status' of maternal mortality in the United States. The overall maternal mortality rate is provided here along with a quantification of racial disparities in maternal death rates. A discussion of racial disparities, and how disparities are to be interpreted and addressed is provided in the section titled 'Social determinants of health'.*

Comment 29): Line 193-195: Again, are there examples of the types of conditions that might be included in this other specific pregnancy related condition.

Response: *This code O268 includes heterogenous conditions including pregnancy related renal disease, peripheral neuritis, etc. However, unless other codes are used to provide further detail, this code provides no specific information on the condition per se. We point this out as being problematic as a substantial proportion of maternal deaths fall into this uninformative category. In the section on 'Surveillance concerns' we address this issue and recommend a potential remedy using an example to illustrate the problem.*
Page 11
"The high rates of maternal death with less informative causes of death such as 'Other specified pregnancy-related conditions' (ICD-10 O268) and 'Disease of the circulatory system complicating pregnancy, childbirth and the puerperium' (ICD-10 O994) needs to be addressed: insight into pathologic conditions of concern can only be obtained with greater specificity in cause-of-death information. This concern, which also applies to late maternal deaths, may be addressed by requiring less informative O (pregnancy) Chapter ICD-10 codes to be accompanied by relevant codes from other Chapters. For example, in cases of aortic dissection, the I Chapter code for this condition (viz., ICD-10 I710) should accompany the less informative O chapter code (ICD-10 O994) which merely identifies a pregnancy-related disease of the circulatory system."

Comment 30): Line 195: Does Fig 3A show fractions of deaths due to causes/cause groupings or MMR for each cause? Also see below.

Response: *Figure 3A shows the <u>rate of maternal death</u> by underlying cause of death category. The causes of death are presented in the pie chart in a clockwise manner starting with Abortive outcome (O chapter codes O00 to O08) and ending with "Other maternal diseases not elsewhere classified" (O chapter code O99). The Figure legend has been edited to clarify that maternal*

mortality rates are presented and that all O chapter codes for maternal death (not including late maternal death) are included in Figure 3A.
Page 23
"Figure 3. Maternal deaths within International Classification of Diseases (ICD-10) cause-of-death categories, United States 2018. Panel A shows maternal mortality rates (per million live births) within each ICD-10 cause-of-death category (all O chapter codes except those for late maternal death included) and Panel B shows cause-specific maternal mortality rates (per million live births) associated with specific conditions of obstetric interest. Note: Numbers in the pie chart (Panel A) represent cause-specific maternal mortality rates per million livebirths. The components are mutually exclusive and all inclusive, and sum to an overall maternal mortality rate of 17.4 per 100,000 live births."

Comment 31): **I am confused by why some causes are included in 3A and 3B. e.g. abortive outcomes is 7.6/million and included in 3A but HTN is 7.9/million and in 3B. And ectopic (an abortive outcome? Is abortive outcome O00-O08? On Table 2, specific abortive outcomes are included but not ectopic or molar. Are these cause of death groupings/larger categories/buckets vs specific causes? I think this is it, but can you confirm and clarify?**
Response: *The categories presented are ICD-10 categories. Pregnancy with abortive outcome is an ICD-10 category, while chronic hypertension is a subcategory of the category 'Hypertensive disorders of pregnancy'. The ICD-10 category 'Pregnancy with abortive outcome' includes the subcategories Ectopic pregnancies (ICD-10 code O00), Hydatiform mole (ICD-10 code O01), Other abnormal products of conception (ICD-10 code O02), Spontaneous abortion (ICD-10 code O03), etc. Table 2 is restricted to those cause of death subcategories that were unimpacted by the pregnancy checkbox and which showed a temporal change between 1999 and 2018.*

Comment 32): **Why sometimes do you use deaths per 100,000 live births (the standard measure) and sometimes per 1,000,000 live births? Is that also standard?**
Response: *Typically, overall maternal mortality rates are expressed per 100,000 live births. However, when quantifying cause-specific rates of maternal death, it is not uncommon to express rates per 1,000,000 live births because the rates tend to be small (less than 1 per 100,000).*

Comment 33): **Line 201-206: this is a very long sentence and I got lost in the middle of it.**
Response: T*his sentence has been edited. The simplified sentence now reads as follows.*
Page 10
"There are several reasons to suspect some degree of misclassification of non-maternal deaths (as maternal deaths) among women 10-44 years in 2018 including the lack of difference in MMRs between women aged 40-44 years versus 45-49 years. Restricting pregnancy checkbox use to women 10-44 years of age curtailed misclassification of non-maternal deaths among women 45-49 years only. However, uncorrected over-estimation of MMRs among women 40-44 years of age resulted in similar death rates in the two age groups. Discrepant temporal trends between related causes of death (e.g., declines in preeclampsia deaths vs increases in deaths from chronic hypertension; Figure 2A) and the high proportion of maternal deaths due to less informative and potentially incidental causes of death are other indicators suggesting misclassification. Whereas obstetric causes of death on a death certificate (e.g., preeclampsia and amniotic fluid embolism) would be unaffected by the incorrect use of the pregnancy checkbox, non-obstetric causes of death among non-pregnant women (e.g., chronic hypertension

and pulmonary embolism) would be misclassified as maternal deaths if the pregnancy checkbox was ticked erroneously."

Comment 34): Line 202: "potential misclassification of non-maternal deaths among women 10-44 as maternal deaths in 2018 data is suggested by…" clarify what the misclassification was?
Response: *This refers to the miss-classification of non-maternal deaths as maternal deaths and has been clarified.*
Page 10
"There are several reasons to suspect some degree of misclassification of non-maternal deaths (as maternal deaths) among women 10-44 years in 2018 including the lack of difference in MMRs between women aged 40-44 years versus 45-49 years."

Comment 35): Line 203: do we expect deaths to be higher in 45+ compared to 40-44? Tell the reader why this discrepancy suggests misclassification?
Response: *Maternal mortality is strongly associated with age and the lack of difference between maternal death rates among women 40-44 and 45-49 is unexpected and likely a consequence of the differential use of the pregnancy checkbox among women 10-44 and >=45 years of age. The revised manuscript provides this explanation.*
Page 9
"Restricting pregnancy checkbox use to women 10-44 years of age curtailed misclassification of non-maternal deaths among women 45-49 years. However, uncorrected over-estimation of MMRs among women 40-44 years of age resulted in similar death rates in the two age groups."

Comment 36): Line 204: declines in pre-eclampsia: how much of this is a coding artifact and how much due to better diagnosis of HTN? See comment on Fig 2.
Response: *It is not possible to estimate how much of the decline in maternal deaths from preeclampsia and chronic hypertension is because of coding artefacts. We have not speculated on this and merely asserted that the large decline in deaths from preeclampsia-eclampsia reflects improved care, while the increase in maternal deaths from chronic hypertension could represent a true increase or an increase in misclassification of non-maternal deaths.*
Pages 11
"The significant declines in deaths from preeclampsia-eclampsia (Figure 2A), medical and unspecified abortion, complications of anesthesia, intrapartum hemorrhage, and amniotic fluid embolism are highly encouraging developments (Table 2)."
*Page 12*
"The increases in maternal deaths from chronic hypertension, genitourinary tract infection, diabetes mellitus, malnutrition, liver disorders, mental and CNS disorders and diseases of the respiratory system could represent true increases in these conditions, increases in maternal deaths from these conditions, or (more likely) an increase in the misclassification of non-maternal deaths from these conditions."

Comment 37): Line 208-210: but how many young women die of these causes OUTSIDE pregnancy? Young women do not die very much, pregnancy is one of the riskiest things they do.
Response: *Healthy young women are at low risk of dying from nonpregnancy-related causes and*

pregnant women face specific obstetric risks. However, in the population non-pregnant women of reproductive age in fact die at <u>much higher rates</u> than pregnant women. The Confidential Enquiry into Maternal Deaths in the UK routinely published a Figure (see below) that contrasted death rates between pregnant and non-pregnant woman of reproductive age and showed this phenomenon in each age group in this range.
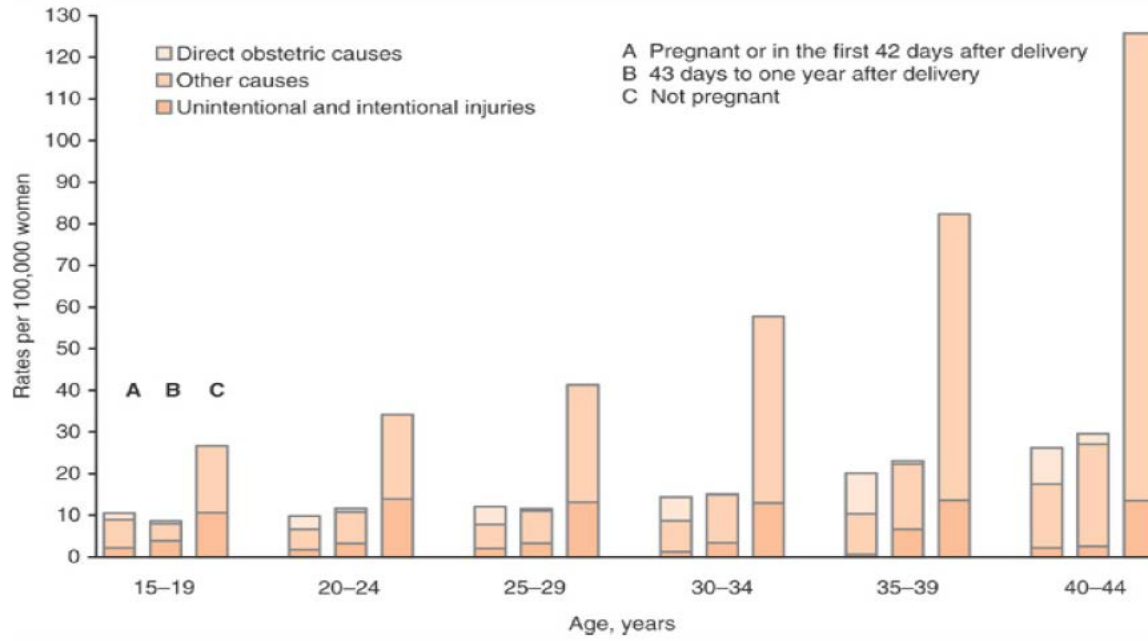
(Source: Why Mothers Die 2000-2002. The Sixth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom).

The reason for this difference is similar to the health worker effect: women who get pregnant tend to be healthier than women who do not get pregnant. The same phenomenon is evident in current data from the United States (see below).

An important and related point is that (both the rate and) the <u>number</u> of deaths to non-pregnant women in the reproductive age range is substantially larger than the number of deaths to pregnant women at the same age (because the number of pregnant women in a given year is far smaller than the number of all women of reproductive age in that year; see Table below). This means that a small misclassification of (non-maternal) deaths among non-pregnant women will lead to a substantial change in the maternal mortality rate. We have added a sentence in the manuscript clarifying this issue and have expanded on it in Appendix 4.
Page 10
"The number of non-maternal deaths from hypertensive diseases among reproductive age women far exceeds the number of maternal deaths from chronic hypertension so that a small misclassification of non-maternal deaths from hypertensive diseases (due to erroneous use of the pregnancy checkbox) will have a large impact on maternal deaths from chronic hypertension (Appendix 4)."

Appendix 4
Table 3. Numbers and rates of death from hypertensive diseases (i.e., non-maternal deaths, ICD-10 codes I10 to I15) and deaths from pre-existing hypertension complicating pregnancy, childbirth and the puerperium (i.e., maternal deaths ICD-10 codes O10 and O11) among women aged 15-44 years, United States, 2003-2018.

Year	Number of women aged 15-44 years	Non-maternal deaths from chronic hypertension (ICD-10 I10-I15)		Maternal deaths from chronic hypertension (ICD-10 O10, O11)	
		Number	*Rate per 1,000,000 women*	*Number*	*Rate per 1,000,000 women*
2003	61,887,915	793	12.8	7	0.11
2004	61,969,393	729	11.8	5	0.08
2005	62,070,636	785	12.6	15	0.24
2006	62,190,028	751	12.1	9	0.14
2007	62,292,084	750	12.0	11	0.18
2008	62,359,858	792	12.7	17	0.27
2009	62,373,024	846	13.6	19	0.30
2010	62,374,964	767	12.3	20	0.32
2011	62,517,048	805	12.9	26	0.42
2012	62,744,930	784	12.5	22	0.35
2013	62,939,772	794	12.6	27	0.43
2014	63,356,565	860	13.6	20	0.32
2015	63,606,765	884	13.9	20	0.31
2016	63,613,014	901	14.2	22	0.35
2017	63,958,243	923	14.4	24	0.38
2018	64,171,698	961	15.0	30	0.47

Comment 38): Line 213: is citation #20 correct? Should it be #19?
Response: *Thank you for identifying this error which has been corrected. Since we added 3 new references, previous reference 19 is now reference 22 and previous reference 20 is now reference 23.*

Comment 39): Line 214: or substitution of HTN for eclampsia in coding?
Response: *It is possible that preclampsia-eclampsia deaths could have been miscoded as maternal deaths due to chronic hypertension (and vice versa). However, any such occurrence would have been a longstanding issue and the need is to explain recent increases in maternal deaths from chronic hypertension. There is no reason to believe that deaths from preeclampsia-eclampsia are increasingly being coded as maternal deaths from chronic hypertension in recent years. The more likely explanation is that an increase in erroneous use of the pregnancy checkbox (following increasingly adoption of the checkbox by the states since 2003) led to a misclassification of non-maternal deaths from chronic hypertension (misclassified as maternal deaths from chronic hypertension) (see also response to Comment c on page 20 below).*

Comment 40): **Line 222: why? Clearly state why (re: raising the possibility that such deaths occurred among non-pregnant women).**
Response: *A sentence has been added to explain why.*
Page 10.
"It is likely that some such deaths occurred among non-pregnant women (or that pregnancy was incidentally associated with a fatal liver disorder) and that erroneous use of the checkbox led to misclassification of these non-maternal deaths."

Comment 41): **Line 223: But doesn't pregnancy exacerbate all conditions? Is an "incidental association" even possible? I suppose it is for some conditions.**
Response: *Determining the causal contribution of pregnancy to the cause of death is a challenge that the attending physician has to address and yes, pregnancy would likely exacerbate most conditions. However, there may be situations e.g., death due to a pre-existing condition in the early first trimester, where the physician may decide that pregnancy was incidental to the death.*

Comment 42): **Line 227: subtitle says 40-44**
Response: *The subtitle refers to women 10-44 years of age, though one of the indicators suggesting misclassification of maternal deaths in the 10-44 year age group is the lack of difference in maternal mortality rates among women 40-44 years versus women 45-49 years of age.*

Comment 43): **Line 233: again not clear if Fig 3A are fractions or MMR**
Response: *This has been addressed in the Figure 3 legend. The numbers in Figure 3 are cause-specific maternal mortality rates expressed per 1,000,000 live births. Also, the sentence in the manuscript has been revised from*
"The large fraction of cases ...."
to
"The high rates of maternal death with non-informative and less informative causes of death such as....."

Comment 44): **Line 244: obstetric embolism - I see blood clot and amniotic embolism on Fig 3B - which one? Both?**
Response: *This has been clarified in the text*
Page 9
"Figure 3A shows maternal deaths in 2018 by cause-of-death category: less informative categories, namely, 'Other specified pregnancy-related conditions' (ICD-10 O268) and 'Other maternal diseases not elsewhere classified' (ICD-10 O99) were responsible for a substantial fraction of maternal deaths, whereas hypertensive disorders, circulatory system diseases and amniotic fluid and blood clot embolism were the most frequent clearly specified causes (Figures 3A and 3B)."
.

Comment 45): **Line 254: more likely reflects increases in these conditions and in pregnancies among women with CNS/mental disorders, no?**
Response: *Yes, it could reflect increases in the listed conditions or increases in pregnancies among women with these conditions, etc. The sentence has been edited.*

Page 12
"The increases in maternal deaths from chronic hypertension, genitourinary tract infection, diabetes mellitus, malnutrition, liver disorders, mental and CNS disorders and diseases of the respiratory system could represent true increases in these conditions, increases in maternal deaths from these conditions or an increase in misclassification of non-maternal deaths from these conditions."

Comment 46): Line 260: Are there any examples of the impact of these ACOG/state based maternal mortality review efforts? The example of the UK is nice, but a US example would be helpful.

Response: *Work done by the Maternal Mortality Review Committees has appeared in the literature. An example, a report based on the findings of 9 state maternal mortality review committees, has now been cited in connection with issues related to identifying preventable factors.*

Page 11
"Reports from such Maternal Mortality Review Committees show that approximately half of all pregnancy-related deaths were caused by hemorrhage, cardiovascular and coronary conditions, cardiomyopathy, and infection, and that more than 60 percent of pregnancy-related deaths were preventable [34]. Patient-related factors such as a lack of knowledge about warning signs (38%), health care provider-related issues including misdiagnosis (34%) and system-related factors, such as a lack of coordination between providers (22%), were the most commonly identified contributors to pregnancy-related deaths [34].

34. Building U.S. Capacity to Review and Prevent Maternal Deaths. Report from nine maternal mortality review committees. Available at (http://reviewtoaction.org/ Report_from_Nine_MMRCs).

Comment 47): Line 267: Please elaborate on the impact of mental health issues and discontinuation of prenatal care and maternal mortality. Is the reader to assume that mental health issues leads to stopping prenatal care which leads to maternal mortality?

Response: *The MBRACE report provides details about the lack of receipt of antenatal care among the women who died. Among the women who received antenatal care (before death), only 30% received the recommended level of antenatal care. However, we have deleted the reference to antenatal care as the example regarding recognition of cardiovascular disease should suffice to illustrate the point being made. The sentence now reads*

Page 10
"Some of the recent caveats emerging from the Confidential Enquiry into Maternal Deaths in the United Kingdom are notable [35], including the need for heightened awareness of cardio-vascular diseases among women with chest pain, orthopnea or persistent tachycardia, and the unexpected number of deaths due to undiagnosed aortic dissection [35]."

Comment 48): Line 271: social determinants: this needs to be included in the abstract. Cite data from the US in this section in additional to general statements from WHO and Marmot?

Response: *The Abstract has been edited to include a sentence on social determinants and 2 references have been added that address these issues.*

Page 3

"However, in 2018, non-Hispanic Blacks had a 2.5-fold higher maternal mortality rate compared with non-Hispanic Whites. This underscores the need for public health initiatives to address the social determinants of health, in addition to improving health care services."
Page 13
"Racial disparities in MMRs reflect many factors arising from racism [38] including closely connected social determinants of health such as income, social status, education, access to health care, housing, the physical environment, social supports, health behaviors, and culture [12,38-41].
References added
12. Collier AY, Molina RL. Maternal Mortality in the United States: Updates on Trends, Causes, and Solutions. Neoreviews 2019;20:e561-e574.
38. Noursi S, Saluja B, Richey L. Using the Ecological Systems Theory to Understand Black/ White Disparities in Maternal Morbidity and Mortality in the United States. J Racial Ethn Health Disparities. 2020 Jul 27. doi: 10.1007/s40615-020-00825-4.

Comment 49): Line 272: Can change to race differences or the differences between black and white, but "racial black white" is confusing
Response: *This sentence has been edited.*
Page 13
"The racial difference in maternal mortality in the United States is an indicator of longstanding health disparities: non-Hispanic Black women experienced a 2.5-fold higher maternal death rate than non-Hispanic White women in 2018 [8]."

Comment 50): Line 276: #33 is not in reference list
Response: *This has been corrected (reference number 32 appeared twice in the previous version of the manuscript).*

Comment 51): Line 278: Does "exceeded" here refer to the 5 fold higher death rate in England vs the 2.5 fold higher death rate in the US? Please be explicit
Response: *This sentence has been edited.*
Page 13
"These comparative statistics highlight the role of non-medical determinants of maternal mortality: the difference in MMRs among Black vs White women in England exceeded that in the United States despite the National Health Service in England providing free, high-quality medical care to all."

Comment 52): Line 280: cite for "factors arising from racism"
Response: *A reference (#38) has been added.*

53)   Line 286-295:
Comment a. The discussion of racial disparities feels tacked on and not well developed.
Response: *The discussion on racial disparities has been carefully considered, although it is brief. We have made changes in response to specific comments.*
Page 14
"Racial and ethnic disparities in MMRs need to be addressed on an urgent basis through broad-based public health initiatives. Although the etiologic role of the social determinants of

maternal death has been recognized for decades, the relative impact of these factors appears to be increasing [37]. Vulnerable segments of the population, especially non-Hispanic Black women, need to be supported through comprehensive and sustained public health programs that address preconceptional health and chronic conditions (at the individual level), implicit racial bias among health care providers (at the interpersonal level), quality of care in hospitals predominantly serving non-Hispanic Black women (at the community level) and paid parental leave and extended health insurance (at the societal level) [38]. Such initiatives are also required to support vulnerable women and address social determinants of health across the entire population. This need is highlighted by the distribution of maternal deaths in 2018: 287, 205 and 105 deaths occurred among non-Hispanic White, non-Hispanic Black and Hispanic women, respectively [8]."

Comment b. **31% of maternal deaths are to Blacks. So a larger proportion of maternal deaths are to white women as you state (44%) - but what is the distribution in the population? Among reproductive age women? Among pregnant women? That is, are Black women 31% of the population or are they disproportionately represented among maternal deaths? This is a tone deaf statement at best.**

Response: *Yes, we are aware of the distinction between numbers of maternal deaths and rates of maternal death. We provide rates of maternal mortality by race/ethnicity in 2018 under the section 'Current status' on pages 8-9. Non-Hispanic White women had an MMR of 14.7 per 100,000 live births compared with non-Hispanic black women who had an MMR of 37.1 per 100,000 live births. The section on 'Social determinants of health' starts out with a statement that maternal mortality rates were 2.5-fold higher among non-Hispanic Blacks compared with non-Hispanic Whites. This section also discusses causes of racial disparities and the myriad factors arising from racism that contribute to poorer outcomes among non-Hispanic Black women. We have reworked the argument to make these points clearer. On page 14, we continue the discussion on social determinants of health by providing the absolute numbers of maternal deaths among non-Hispanic White women, non-Hispanic Black women and Hispanic women. In our humble opinion, public health interventions should extend to preventing all avoidable maternal deaths in the population. Our statement/argument is not tone deaf – it is a nuanced statement/argument with a population and public health basis. Note that we are referring to all vulnerable women in the population and about public health initiatives targeting and addressing social determinants of health.*

Page 13-14
"Racial disparities in MMRs reflect many factors arising from racism [38] including closely connected social determinants of health such as income, social status, education, access to health care, housing, the physical environment, social supports, health behaviours, and culture [12,38-41]. The strong correlations and synergism between these factors ensures that vulnerable populations experience disproportionately high risks of outcomes such as maternal death.

Racial and ethnic disparities in MMRs need to be addressed on an urgent basis through broad-based public health initiatives. Although the etiologic role of the social determinants of maternal death has been recognized for decades, the relative impact of these factors appears to be increasing [37]. Vulnerable segments of the population, especially non-Hispanic Black women, need to be supported through comprehensive and sustained public health programs that address preconceptional health and chronic conditions (at the individual level), implicit racial

bias among health care providers (at the interpersonal level), quality of care in hospitals predominantly serving non-Hispanic Black women (at the community level) and paid parental leave and extended health insurance (at the societal level) [38]. Such initiatives are also required to support vulnerable women and address social determinants of health across the entire population. This need is highlighted by the distribution of maternal deaths in 2018: 287, 205 and 105 deaths occurred among non-Hispanic White, non-Hispanic Black and Hispanic women, respectively [8]."

Comment c. Please review and incorporate US literature - I'm intrigued by all the UK data. It is good data, but this is about US maternal mortality rates.
<u>Response:</u> *This has been addressed and US literature has been incorporated.*
Page 13-14
"Vulnerable segments of the population, especially non-Hispanic Black women, need to be supported through comprehensive and sustained public health programs that address preconceptional health and chronic conditions (at the individual level), implicit racial bias among health care providers (at the interpersonal level), quality of care in hospitals predominantly serving non-Hispanic Black women (at the community level) and paid parental leave and extended health insurance (at the societal level) [38].

Comment 54): Line 291-295: What should be the takeaway from this statement? That both race and SES status impact maternal mortality and health? I think some discussion of how race and SES are correlated / interact might be helpful here?
<u>Response:</u> *The relationship between race and SES is complex. These factors are also closely intertwined with other factors such as education, access to health care, housing, the physical environment, social supports, health behaviors, and culture. This has been addressed in the paragraph on page 13*
"Racial disparities in MMRs reflect many factors arising from racism [38] including closely connected social determinants of health such as income, social status, education, access to health care, housing, the physical environment, social supports, health behaviours, and culture [12,38-41]. The strong correlations and synergism between these factors ensure that vulnerable populations experience disproportionately high risks of outcomes such as maternal death."

Comment 55): Conclusion: This appears to just be the intro/abstract repeated. What is the reader to take away from this article? <u>Comment 56):</u>
<u>Comment 57):</u> Line 304: The methods to improve maternal mortality surveillance can be reiterated here in more detail as a specific call to action. 1) review committees 2)physicians education 3) pregnancy checkboxes with better data / more detail. In addition, the specific action items related to SDH and methods to address broader issues of maternal mortality should be spelled out: 1) investment in racial disparities 2)equitable access to healthcare (whatever other ideas are thought to be helpful) <u>Comment 58):</u>
<u>Response:</u> *The Conclusion section has been revised and addresses the above points.*
Page 14
"Seminal studies by the NCHS show that the recently documented temporal increases in MMRs in the United States were an artefact of changes in maternal mortality surveillance. Specific causes of maternal death which were not impacted by surveillance changes, such as preeclampsia-eclampsia showed substantial temporal declines. Although the pregnancy

checkbox improved the capture of maternal deaths, continued misclassification of non-maternal deaths, and the proliferation of non-informative causes of death have to be minimized by refining checkbox use, improving death certification processes and requiring the use of specific non-pregnancy chapter ICD-10 codes in conjunction with pregnancy checkbox use.

Strengthening routine maternal death reviews at the hospital, state and national level can lead to more informed and optimized obstetric practice. Diverse public health initiatives targeting the social determinants of health, and addressing individual-level, interpersonal, community and societal risk factors for maternal death are required for reducing racial disparities. Although the state of maternal health in the United States is not as dire as portrayed until recently, there is substantial scope for preventing avoidable maternal death."

Comment 59): Figure 1:
a. Was ICD-10 adopted on death certificates in 1999? It was not widely adopted in the US until later.
Response: *At issue is the coding of underlying cause of death information for maternal deaths. The Centers for Disease Control and Prevention/NCHS adopted ICD-10 coding in 1999 for all deaths in the United States. Please see <u>https://wonder.cdc.gov/wonder/help/ucd.html</u> which states that*
"Causes of death are classified in accordance with the International Classification of Disease. Deaths for 1979-98 are classified using the Ninth Revision (ICD-9). Deaths for 1999 and beyond are classified using the Tenth Revision (ICD-10)."

Comment b.: Why does panel A start at 1993 and panel B at 1999?
Response: *This Figure is sourced from our previously publication showing increasing adoption of the pregnancy checkbox by different states. Panel A provides the extended secular trend that highlights both the relatively small change which occurred with the adoption of ICD-10 in 1999 and the larger change associated with staggered introduction of the pregnancy checkbox by different states. Panel B, on the other hand, focuses on the components of the trend in maternal deaths rates following introduction of the pregnancy checkbox and shows that the temporal increases were entirely due to late maternal deaths and some specific less informative ICD-10 codes.*

<u>**Comment c.:**</u> **Could A & B be presented in 1 figure? 3 classifications, 1993-2014, with arrows for checkbox implementation? Not clear to me why this needs 2 figures.**
Response: *As mentioned above these Figure 1A and Figure 1Bs address different issues. The introduction of the pregnancy checkbox was responsible for several changes including, among others, an increase in the identification of maternal deaths and also large increases in the identification of maternal deaths from less informative causes. This presents a real and significant problem with surveillance that needs to be addressed if cause-of-death information is to be useful clinically and for prevention.*

<u>**Comment 60):**</u> **Figure 2:**
a. Why per million here? Or is that a typo of 100,000 on the Y axis?
Response: *As mentioned previously, overall maternal mortality rates are presented per 100,000 live births, while cause-specific maternal mortality rates, which are typically an order of magnitude smaller, are presented per 1,000,000 live births.*

Comment b.:   Make the Y axis the same for all panels?

Response: *The Y-axis has been tailored to highlight the pattern with regard to the specific causes of death presented in each panel. Thus, Panel A contrasts the temporal pattern of death rates from hypertensive disorders including preeclampsia, chronic hypertension and gestational hypertension. The intention is not to compare these rates with death rates in Panels B and C. Using the same scale for the 3 Y-axes would be appropriate if cross panel comparisons were required but would reduce the clarity of temporal patterns for less common causes of death.*

Comments c.: Panel A: I wonder if women with pre-eclampsia have HTN and is gets diagnosed earlier now? Thus the switch we see of eclampsia going down and HTN going up?

Response: *This is possible and but is not likely to have made a significant impact on overall rates of preeclampsia and chronic hypertension in pregnancy. There have been several publications on secular trends in preeclampsia rates in the literature which show temporal trends in preeclampsia are very different from the temporal trend seen in deaths from preeclampsia. For example, a study examining rates in the US showed that hospitalizations for preeclampsia increased, while deaths from preeclampsia in hospital decreased substantially in recent years (Lee JH, et al. Hawaii J Health Soc Welf. 2019. PMID: 31463474). Similarly, as mentioned in the manuscript, the increase in chronic hypertension in pregnancy that is documented in the literature is far smaller than the increase in death rates from chronic hypertension in pregnancy observed in this study. We are confident that the explanation provided in the manuscript, regarding misclassification of non-maternal deaths from hypertension, is the correct reason for the large temporal increase in maternal deaths from chronic hypertension.*

Comment 61): Figure 3:
a. Panel A: very hard to read and interpret. Not clear if the numbers are ratios per 100,000 or proportions (pie chart). In general, avoid pie charts. Use a stacked bar instead? Clarify if these are MMR per cause or proportions of deaths.

Response: *We rarely use pie charts but they are most appropriate in this context in order to show that depiction is all inclusive (the pie represents all causes of maternal death). We have clarified in the legend that the numbers in the pie chart refers to cause-specific maternal death rates per million live births. The Figure 3 legend now reads*
"Maternal deaths within International Classification of Diseases (ICD-10) cause-of-death categories, United States, 2018. Panel A shows maternal mortality rates (per million live births) within each ICD-10 cause-of-death category (all O chapter codes except those for late maternal death included) and Panel B shows cause-specific maternal mortality rates (per million live births) for specific causes of death of obstetric interest. Numbers in the pie chart (panel A) represent cause-specific maternal mortality rates per million livebirths. The components of the pie are mutually exclusive and all inclusive, and sum to an overall maternal mortality rate of 17.4 per 100,000 live births.

Comment b. Panel A: Is there any insight into what types of conditions are "puerperal complications"? It seems like things could be classified in a number of these categories, what are examples of cases for some of these. An appendix with exemplar cases would be very helpful to gain insight into the discrepancies related to coding.

Response: *As indicated in Panel A, puerperal complication are included in ICD-10 codes O85-O92. Causes of death under the 'Puerperal complications' category which show a temporal change during the study period are listed in Table 2 including*
  Obstetric embolism (O88)
      Amniotic fluid embolism (O881)
 Anesthesia complications in the puerperium (O89)
 Puerperal complications NEC (O90)
 Other complications NEC (O908)
 A full listing of the causes of death under the 'Puerperal complications' category is provided in Appendix Table 2.

Comment c.: **Panel B: are these the same data as in Table 2? Why per 1 million births? Ectopic pregnancy is not on Table 2 - I got confused.**
Response: *The information in Panel B is not the same as the information in Table 2. Panel B includes rates of selected causes of maternal death for 2018, while Table 2 presents rates of cause-specific maternal death and includes all maternal deaths from causes of death deemed not to have been affected by the pregnancy checkbox and which showed a significant temporal change over the study period. As previously mentioned, overall maternal mortality is presented per 100,000 live births while maternal mortality due to specific causes (which is much lower in frequency i.e., <1 per 100,000 live births) is expressed per 1,000,000 live births.*
Table 2 provides a list of maternal deaths from conditions deemed not to have been affected by the pregnancy checkbox and which showed a significant temporal change over the study period. Ectopic pregnancy satisfied the former criterion but not the latter. As mentioned in the manuscript, Appendix Table 2 includes maternal deaths from all conditions deemed not to have been affected by the pregnancy checkbox irrespective of whether they showed a significant temporal change over the study period. Ectopic pregnancy is listed in Appendix Table 2 and the subcategories of tubal ectopic pregnancy and ectopic pregnancy unspecified are also listed.

Comment d.: **Panel B: Are the components of mental /CNS disorders inclusive of suicide? I think this was referenced earlier in the paper, but again, what Is an example of the disease states included here?**
Reference: *As mentioned on page 6, deaths from suicide (and those from unintentional injury, drug overdose, homicide and unknown causes) are not categorized as maternal deaths by the NCHS and the WHO (maternal deaths by definition includes only those deaths that are from "any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes"). Thus, suicides are categorized as incidental deaths by the NCHS and fall into the non-maternal death category. There is some difference of opinion on this issue internationally and the Confidential Enquiry into Maternal Deaths in the UK classifies suicide as a direct cause of maternal death.*
Mental and CNS disorder complications in pregnancy, childbirth and the puerperium (ICD-10 O993) is a less informative code that includes a heterogeneous group of conditions which remain unspecified. This again highlights our recommendation for requiring the use of non-pregnancy chapter (psychiatric) codes so that relevant detail regarding the cause of death becomes available in cases where these non-informative or less informative codes are used.

Reviewer #3:

Comment: **The authors present a reasonable review of causes of maternal mortality in the US. While I appreciate the work here, much of what is being presented is not novel and is well known. The database used has been used in many works on the causes of maternal mortality. Additionally, health care disparities are well known to be determinants of poor outcomes in pregnant women.**

Response: *Broad aspects of the work presented here are well known. However, there are several crucial aspects of the Commentary that are original or less well understood. For instance, the literature does not appear to appreciate the seminal nature of in the recent NCHS reports which show that there was no recent temporal increase in maternal mortality in the United States in recent years. Further, there has not been an assessment of maternal mortality from an obstetric and public health standpoint (after accounting for surveillance bias). Finally, our findings reveal continued misclassification of non-maternal deaths as maternal deaths and we offer a few suggestions for addressing these problems.*

EDITORIAL OFFICE COMMENTS:

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

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.
Response: *All authors are aware that they should confirm that disclosures in their eCTA forms are disclosed on the manuscript title page.*

3. 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.
Response: *I have reviewed the DUA and confirm that the manuscript abides by the terms of the DUA (Note: our paper does not present subnational estimates).*

4. 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.
Response: *The race and ethnicity information in this manuscript was based on the classification of race and ethnicity made in the NCHS data source. This is mentioned in the study Methods section in the Appendix.*

5. If 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.
Response: *The ICD codes used are those available on the CDC Wonder website. The ICD-10 codes used are specified in the manuscript, Tables, Figures and Appendices.*

b. Use both the diagnosis and procedure codes.
Response: *Cause of death information in the Death files of the NCHS is based solely on ICD-10 diagnosis codes.*

c. Verify the selected codes apply for all years of the study.
Response: *Confirmed (per the list of ICD-10 codes in the CDC Wonder website).*

d. Conduct sensitivity analyses using definitions based on alternative codes.
Response: *Not applicable.*

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.
Response: *Not applicable as only ICD-10 codes used.*

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.
Response: *Title does not include database, geographic region or dates. Geographic region and dates mentioned in 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.
Response: *Not applicable (no linkage, or algorithms were used).*

6. **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.**
Response: *Definitions accessed and there was no problem with use of reVITALize definitions.*

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.
Response: *We have attempted to shorten the manuscript to the best of our ability, while also addressing Reviewer 2s requests for explanation and clarification. The manuscript is a little over slightly over 3000 words..*

8. 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).

Response: *This has been done.*

9. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.
Response: *The short tile for the manuscript is "Maternal mortality in the United States".*

10. 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 Current Commentary articles is 250 words. Please provide a word count.
Response: *The Abstract is consistent with the manuscript, it has a clear conclusion statement based on the manuscript and has been carefully checked. A word count for the Abstract has been provided (250 words).*

11. 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.
Response: *Abbreviations and acronyms are spelled out the first time they are used.*

12. 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.
Response: *The virgule symbol has not been used.*

13. 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%").
Response: *These rules have been followed where appropriate.*

14. 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.**
Response: *Table checklist style has been reviewed.*

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Response: *Reference style has been followed.*

**16. Figures 1-2: Okay.
Figure 3: Please add color to A.
Please cite figures in order in the manuscript, this includes A and B labels.**
Response: *Figure 3 has been redone in Color and Figures are cited in the manuscript in the
order to which they are referred.*

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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.
<u>Response:</u> *Figures also provided in Excel.*

17. 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.
<u>Response:</u> *This has been done.*

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Response: *Noted.*

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