

OBSTETRICS & GYNECOLOGY



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

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

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

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

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:

obgyn@greenjournal.org.

Date: Jun 25, 2019
To: "Hector Mendez-Figueroa" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-978

RE: Manuscript Number ONG-19-978

Hurricane Harvey: Peripartum Outcomes Before and After A Natural Weather Disaster

Dear Dr. Mendez-Figueroa:

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 Jul 16, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: In this manuscript, the authors compare composite maternal and neonatal outcomes among Texas women before and after Hurricane Harvey. The study relies on data collected in a large database maintained by Baylor University. Like other similar studies, the hurricane appears to have had a negative impact on clinical outcomes. I'm reminded of Sir Rutherford Hill's "rules of causation" that were used to establish the link between smoking and lung cancer. One of the rules was that the association had to make biologic sense. While the authors point out that a natural disaster could raise stress hormones among other things and this could cause wide-ranging effects on maternal and fetal physiology, there is not a good reason why women after the hurricane should be so different than those before it? Why should there be such a remarkable combination of risk-reducing factors (white, educated, insured, higher income, etc) among database enrollees after the hurricane? Is it possible that enrollment into the database (a voluntary exercise) after the hurricane was disfavored among women who would have otherwise "normalized" the study population to pre-hurricane characteristics? If this is the case, then why believe the clinical outcomes are so unique as they reflect an underlying bias as to who was enrolled into the database before and after the hurricane. Curiously, if Duff showed neural tube defects were more common among Floridian women after a past hurricane, and this (I think) 1st trimester event is "real," then why not look for the same association in this Texas population? In other words, the population shouldn't really matter if a sufficient disaster (and its secondary effects) induce the observed effects on women. In any case, I have the following specific questions and comments:

- 1) The author's affiliations are confusing - some are listed as "2" but there is not a "2" institution.
- 2) Line 66 - I am unclear what is being referred to as having a 19% decline in affected regions. Please clarify.
- 3) Line 90 - data are plural thus it should be written, "...these data were collected..."
- 4) Line 127 - non-eligible patients refers to those w/o a delivery date. This seems kind of odd for a database to be missing when a patient delivered. What happened? What is the missingness across all the variables across all the enrolled subjects?
- 5) The aOR for adverse outcomes per timeframe appears to show basically that over time most outcomes were getting better and then Harvey hits and things reverse OR...maybe bad outcomes cycle for diverse reasons and the hurricane had nothing to do with them?
- 6) I don't follow why the R2 is included in Figure 3. The trend line isn't necessary to show how the Aug 2017 date is linked to a departure from past performances. At best 80% of the variance in your data is unexplained by the featured trend line...not inspiring.

Overall, interesting study and for its kind its better but the sample makes me uncomfortable that features related to how/who enrolls into this database impacted the measured clinical outcomes.

Reviewer #2: Summary

This study examines the impact of peripartum outcomes after Hurricane Harvey, which occurred on August 25th, 2017. The data source for these analyses is a perinatal database of women delivering at a public and private clinic. This data source is maintained by Baylor College of Medicine. The study compared deliveries occurring after Hurricane Harvey (August 25th - June 2018, 280 days after Harvey) to deliveries occurring before Hurricane Harvey (August 2011-August 24th, 2017). The main outcomes were composite measures of maternal and neonatal morbidity, but individual components of these composite measures were also examined. Consistent with other studies of natural disaster, the authors conclude that the period after Hurricane Harvey had an increase in adverse outcomes, despite fewer at-risk baseline characteristics.

General comments

In general, the manuscript is well written with sufficient detail to follow the methods. A strength of this article is the well-maintained database of perinatal outcomes to examine these exposure periods. As with most ecological analyses, this could be further strengthened by having a comparable area in Texas that was not affected by Harvey, but that may not be practically feasible. The authors do provide comparisons over this time period and adjust for differences across groups; however, there are clear selection effects occurring before and after Harvey. This is likely due to out-migration from the area by lower socioeconomic status groups. I was also concerned by the exclusion criteria of limiting to only those with first birth if they had more than 1 birth during the comparison period. How might that differentially affect the two time periods? In addition, while the sample had fewer risk factors, the "exposed" group was older and may have contributed to the findings, depending on how age was handled in the adjustment. Finally, the mechanism for how a natural disaster may influence perinatal outcomes could be further elaborated in the Introduction. For example, stress may influence outcomes over a longer period of time, compared to lack of resources or ability to get to medical care. Presenting some information on these contextual factors for Houston (if available) in the introduction may also help in interpretation of findings. I have included detailed comments below.

Specific comments

Abstract

- 1* p. 3, line 27. Instead of saying "our perinatal database," be specific about what the database is and from where.
- 2* p.3, line 31. Instead of enrolled, do you mean delivered prior to August 25th, 2017?

Introduction

- 3* p.5, lines 61-70. Include more details on how Houston was affected specifically by these factors and if there was documentation of lower SES groups leaving the area. What about the role of stress? Is the main mechanism through disruption of health services? This may explain why you see less of an impact for those that say they were personally affected by Harvey, but more of an overall effect for all those who remained in the area. This could be further discussed in the Discussion section as well.
- 4* P.5, line 72. Other studies suffer from selection bias. This may also be the case here as well. This should be included in the Discussion. It may be that the effects would be even larger if the higher risk groups remained, but it should still be discussed.

Methods

- 5* P.7, lines 96-97. Instead of excluding women with two or more deliveries, you might consider a sensitivity analysis of within mother comparisons. Births within the same mother after vs. before Harvey. Sample size may be limited and there are limitations to within-mother analyses; however, it may lend further support to your argument. I also wonder how this criterion may be differentially applied across exposed and unexposed time periods. I would like to see parity separated into more categories than just nulliparous (yes/no), but rather categories that extend to 2+ or 3+.
- 6* P.7, lines 98-104. Was time since Harvey examined as a dose response? There is suggestion of this in the last line of the Results section. It is stated that results by trimester are not statistically different, but from what? Each other (i.e., effects were similar across trimester) or from the non-exposed period? I'm more interested in the magnitude of these relationships, as significance is affected by both magnitude and sample size - the latter of which is reduced with more categories. Consider presenting these findings as a supplement. No dose response may suggest that both lack of resources (short-term effect) and stress (longer-term effect) play a role.
- 7* P.8, lines 119-123. How was age handled in the adjustment? If only a binary variable, this may not be adjusting enough for age-effects. Consider more categories for parity in the adjustment as well. Why was insurance not adjusted for? You state that you adjusted for factors significant in univariate analyses. In general, more details on how the variables were handled/defined in the regression models are needed.

8* P.8, line 123. The results show sensitivity analyses by time periods and subgroup analyses. This needs to be described in the methods section not the results section. Why was the reference group switched for Figure 2 (exposed is now the reference)? This was confusing at first.

Results

9* p.8, line 134. What do you mean by "have private insurance enabling care outside of pregnancy..." ?

10* p.9, lines 148-163. Some of the description about what was done is in the results and needs to be moved to the methods section.

11* P.9, Figure 2. Why would one see the period of 2011-2012 have higher rates of maternal morbidity? It is interesting to see that this had an effect for maternal health but not neonatal health. What might explain this, was there something else happening around this time in the area or Texas more generally?

12* P.10, lines 166-167. Consider presenting the trimester results as a supplementary table.

Discussion

13* P.11, lines 199-205. Is it stress or disruption of resources/care? Some reference to stress should be included in the introduction. Also, contextualize your results within these different pathways. Stress would likely have a longer-term impact or have a critical window of exposure during pregnancy, whereas, resources may be a more immediate impact that would lessen further from the event. How do your findings fit in to the various mechanisms that may increase risk after a natural disaster?

14* P.11, lines 206-216. You should discuss the role of selection bias, which seems to be very clear from your comparison of descriptive characteristics before and after Harvey. How might this have impacted your findings?

Reviewer #3: This is a retrospective cohort study examining perinatal outcomes following Hurricane Harvey. The authors demonstrate an increase in adverse obstetric outcomes associated with the hurricane, consistent with prior, similar studies. While they do provide results from a larger cohort that previously published, it conforms what is known. They also do not distinguish between the effects of interrupted services versus physiologic stress or other factors that may explain these associations. So, while the data are copious, this manuscript does not further our understanding of the association between natural disasters and adverse outcomes. While such events are difficult to predict, understanding the causal link is necessary to mitigate the effects.

Specific comments -

1. There are methodological descriptions found in the results section (eg lines 161-163).
2. Please describe why the antecedent time range was chosen; the data are heavily weighted to prior to the event
3. Line 103- what constitutes "major?"
4. Figure 2 should be removed. It does not add to the manuscript and is distracting and potentially confusing, as it demonstrates there is a protective effect over time but does not include the hurricane's data and trend are better demonstrated with figure 3

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: The cohorts differ in many baseline characteristics. Should corroborate the adjustment model with analysis of those delivered after Harvey with matched controls prior to Harvey.
2. Table 2: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70 , which is violated in premature rupture of membranes and many other entries.
3. Table 3: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70 , which is violated in arterial cord blood < 7.1 and many other entries.
4. Table 4: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons

should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70 , which is violated in neonatal deaths and many other entries. Also, the last column has no p-value entries, so the column heading needs to be changed.

5. Fig 1: What does "duplicates N = 235" mean? If there are individuals who delivered more than once during the time of the study, then either only one of those deliveries should be randomly chosen for inclusion in the analysis, or an adjustment made in the analysis for repeated counts of an individual woman. That is, those are not independent events.

6. Fig 2: I assume there were sufficient counts of maternal and neonatal morbidity to allow for adjustment with 7 variables, but should include the counts for these analyses as on-line material. Again, need to include the counts for individual time periods of group B strep and hypertension/pre-eclampsia and justify adjustment for 7 variables. Should clarify for reader that the vertical red line, the referent, is the time after Harvey.

7. Fig 3, lines 156-160: Unclear as to what stats test was used to evaluate the "statistically upward trend". In all 3 graphs, the upward trends appear to precede the 3rd quarter of 2017. Should use time series analysis and compare the slopes.

8. Also, need to include concise, descriptive legends to figures.

Associate Editor's Comments

Our enthusiasm for this manuscript is conditional on

- 1) A propensity score analysis and
- 2) A time series analysis

Our concern is that the differences you have shown may be due to residual confounding or may merely be reflective of a trend toward worse outcomes that was already underway before the hurricane.

That said, we are very happy that you sent this to us, and look forward to evaluating a revision.

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. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Any author agreement forms previously submitted will be superseded by the eCTA. During the resubmission process, you are welcome to remove these PDFs from EM. However, if you prefer, we can remove them for you after submission.

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained."

*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

4. In order for an administrative database study to be considered for publication in Obstetrics & Gynecology, the database used must be shown to be reliable and validated. In your response, please tell us who entered the data and how the accuracy of the database was validated. This same information should be included in the Materials and Methods section of the manuscript.

5. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and

not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at <http://ong.editorialmanager.com>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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 and gynecology data definitions at <https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, 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. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

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

10. 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.

11. 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.

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

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

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

If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at <http://ong.editorialmanager.com>. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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 Jul 16, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2018 IMPACT FACTOR: 4.965

2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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

Nancy C. Chescheir, M.D.
Editor-in-Chief
Obstetrics and Gynecology
409 12th Street, SW
Washington, DC 20024

Dear Dr. Chescheir:

Enclosed please find our revised article for consideration for publication *Obstetrics and Gynecology*, entitled "Hurricane Harvey: Peripartum Outcomes Before and After A Natural Weather Disaster".

We thank the reviewers and editors for their insightful and appropriate comments. In addressing their comments in a systematic fashion as outlined below, we believe that we have significantly strengthened both the merit and inherent readability of our manuscript. Our responses to each of the reviewer comments are highlighted below.

Should your editorial staff prefer further revisions of our manuscript, we would be happy to work with you to accomplish this. There exists no potential financial conflict of interest with any of the authors.

We thank you in advance for ongoing consideration of our work, and look forward to your response.

Sincerely,

Hector Mendez-Figueroa M.D., Corresponding author

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Reviewer Comment	Response
<p>Reviewer #1: Reviewer #1: In this manuscript, the authors compare composite maternal and neonatal outcomes among Texas women before and after Hurricane Harvey. The study relies on data collected in a large database maintained by Baylor University. Like other similar studies, the hurricane appears to have had a negative impact on clinical outcomes. I'm reminded of Sir Rutherford Hill's "rules of causation" that were used to establish the link between smoking and lung cancer. One of the rules was that the association had to make biologic sense. While the authors point out that a natural disaster could raise stress hormones among other things and this could cause wide-ranging effects on maternal and fetal physiology, there is not a good reason why women after the hurricane should be so different than those before it? Why should there be such a remarkable combination of risk-reducing factors (white, educated, insured, higher income, etc) among database enrollees after the hurricane?</p> <p>Is it possible that enrollment into the database (a voluntary exercise) after the hurricane was disfavored among women who would have otherwise "normalized" the study population to pre-hurricane characteristics? If this is the case, then why believe the clinical outcomes are so unique as they reflect an underlying bias as to who was enrolled into the database before and after the hurricane. Curiously, if Duff showed neural tube defects were more common among Floridian women after a past hurricane, and this (I think) 1st trimester event is "real," then why not look for the same association in this Texas population? In other words, the population shouldn't really matter if a sufficient disaster (and its secondary effects) induce the observed effects on women. In any case, I have the following specific questions and comments:</p> <p>Comments for the authors:</p> <ol style="list-style-type: none"> 1. The author's affiliations are confusing - some are listed as "2" but there is not a "2" institution. 2. Line 66 - I am unclear what is being referred to as having a 19% decline in affected regions. Please clarify. 3. Line 90 - data are plural thus it should be written, "...these data were collected..." 4. Line 127 - non-eligible patients refers to those w/o a delivery date. This seems kind of odd for a database to be missing when a patient delivered. What happened? What is the missingness across all the variables across all the enrolled subjects? 	<p><i>Overall.</i> We thank the Reviewer for their supportive comments, and thoughtful suggestions.</p> <p>We do wish to clarify three overall points.</p> <ol style="list-style-type: none"> 1. This study was actually conducted at the two obstetrical hospitals affiliated with Baylor College of Medicine. As noted in our revised manuscript, the rate of enrollment in our study remained unchanged over the entirety of the preceding and post-ceding Harvey interval. This is reflected in the manuscript – line 88-91: “This database and biorepository involves active approach and enrollment, and does not rely on volunteers to self-identify nor enter data. The rate of enrollment among qualified patients into the perinatal database did not change significantly throughout the study period, consent rates ranged from 86% in 2012 to 92% in 2018” 2. Our biologic plausibility is not limited to stress, and it is notable that our data pertaining to stress and perceived stress per se fails to support that plausibility in while. As made further evident in the revised manuscript, we consider other biologic factors including exposures to chemical and environmental pollutants (such as polycyclic aromatic hydrocarbons, or PAHs) which we have previously demonstrated to be linked in ambient form to several of our outcomes of interest (preterm birth and SGA). We have taken the opportunity to speculate on this biologic plausibility, but are cautious in doing so as this current study could neither support nor refute such a conclusion. 3. We certainly appreciate the work of Duff et al and their notable findings. The relationship with ONTD with first trimester exposure following Harvey was not the goal of the current manuscript, and would require a different dataset and approach since we enroll women in PeriBank at the time of delivery and would not be encoding in this dataset terminations of pregnancy that might be anticipated with the full spectrum of ONTDs. Rather, if that were the study we were conducting we would be more likely to utilize our statewide birth defects registry. This could certainly be a topic of future investigations.

<p>5. The aOR for adverse outcomes per timeframe appears to show basically that over time most outcomes were getting better and then Harvey hits and things reverse OR...maybe bad outcomes cycle for diverse reasons and the hurricane had nothing to do with them?</p> <p>6. I don't follow why the R2 is included in Figure 3. The trend line isn't necessary to show how the Aug 2017 date is linked to a departure from past performances. At best 80% of the variance in your data is unexplained by the featured trend line...not inspiring. Overall, interesting study and for its kind its better but the sample makes me uncomfortable that features related to how/who enrolls into this database impacted the measured clinical outcomes.</p>	<p><i>Specific Responses:</i></p> <p>1. We thank reviewer 1 for their attention to detail. We have corrected.</p> <p>2. We thank reviewer 1 for their attention to detail. We have corrected, and it now reads “retrospective analyses of U.S. birth records revealed a 19% decline in births among women in.....”</p> <p>3. We thank reviewer 1 for their attention to detail. We have corrected, and it now reads “these data were collected”</p> <p>4. There were several reasons why patients were missing delivery dates. Some were due to coding error while others were unknown. In our analyses, we exclude all patients missing this variable as part and parcel to our data cleaning. The “missingness” of each variable is diminished in our database as a result of uniform abstraction and entry by trained research personnel and with routine and scheduled audits and adjudication.</p> <p>5 & 6. We thank the reviewer for these two related comments. We have followed the additional suggestions of the other reviewers and editors, and conducted both a propensity analysis and a time to event analysis. We demonstrate that the increased trend in adverse outcomes is preserved (Table 3 and 4). We have also removed Figure 3 from the manuscript and replaced it with a new time trend analysis in Figure 3 and 4.</p>
<p>Reviewer #2: This study examines the impact of peripartum outcomes after Hurricane Harvey, which occurred on August 25th, 2017. The data source for these analyses is a perinatal database of women delivering at a public and private clinic. This data source is maintained by Baylor College of Medicine. The study compared deliveries occurring after Hurricane Harvey (August 25th - June 2018, 280 days after Harvey) to deliveries occurring before Hurricane Harvey (August 2011-August 24th, 2017). The main outcomes were composite measures of maternal and neonatal morbidity, but individual components of these composite measures were also examined. Consistent with other studies of natural disaster, the authors conclude that the period after Hurricane Harvey had an increase in adverse outcomes, despite fewer at-risk baseline characteristics.</p> <p>General comments</p> <p>In general, the manuscript is well written with sufficient detail to follow the methods. A strength of this article is the well-</p>	<p><i>Overall.</i> We similarly thank Reviewer 2 for their positive comments and kind suggestions.</p> <p>As with the first reviewer, we have taken these general comments to heart. We have:</p> <p>1. Better emphasized in the revised manuscript that stress in and of itself is highly unlikely to explain our observations; thus, our speculation on environmental chemicals and exposures and supporting cited references for this speculation. We have added the following sentences:</p> <p>” However, stress alone is unlikely to explain all observations noted in this report. Perinatal outcomes may be affected by increased levels of chemical and environmental pollutants (both ambient and soil or water-based) resulting from a hurricane’s widespread flooding and wind damage. Levels of polycyclic aromatic hydrocarbons such as benzo[a]pyrene, benzo[b]fluorene and</p>

maintained database of perinatal outcomes to examine these exposure periods. As with most ecological analyses, this could be further strengthened by having a comparable area in Texas that was not affected by Harvey, but that may not be practically feasible. The authors do provide comparisons over this time period and adjust for differences across groups; however, there are clear selection effects occurring before and after Harvey. This is likely due to out-migration from the area by lower socioeconomic status groups. I was also concerned by the exclusion criteria of limiting to only those with first birth if they had more than 1 birth during the comparison period. How might that differentially affect the two time periods? In addition, while the sample had fewer risk factors, the "exposed" group was older and may have contributed to the findings, depending on how age was handled in the adjustment. Finally, the mechanism for how a natural disaster may influence perinatal outcomes could be further elaborated in the Introduction. For example, stress may influence outcomes over a longer period of time, compared to lack of resources or ability to get to medical care. Presenting some information on these contextual factors for Houston (if available) in the introduction may also help in interpretation of findings. I have included detailed comments below.

Abstract

1* p. 3, line 27. Instead of saying "our perinatal database," be specific about what the database is and from where.

2* p.3, line 31. Instead of enrolled, do you mean delivered prior to August 25th, 2017?

Introduction

3* p.5, lines 61-70. Include more details on how Houston was affected specifically by these factors and if there was documentation of lower SES groups leaving the area. What about the role of stress? Is the main mechanism through disruption of health services? This may explain why you see less of an impact for those that say they were personally affected by Harvey, but more of an overall effect for all those who remained in the area. This could be further discussed in the Discussion section as well.

4* P.5, line 72. Other studies suffer from selection bias. This may also be the case here as well. This should be included in the Discussion. It may be that the effects would be even larger if the higher risk groups remained, but it should still be discussed.

Methods

5* P.7, lines 96-97. Instead of excluding women with two or more deliveries, you might consider a sensitivity analysis of within mother comparisons. Births within the same mother after vs. before Harvey. Sample size may be limited and there are limitations to within-mother analyses; however, it may lend further support to your argument. I also wonder how this

dibenz[a,h]anthracene have been found to be higher in placental tissue among preterm deliveries compared to term deliveries in women living close to Superfund sites in Harris County, Texas²⁴. Changes within epigenetic markers linked to fetoplacental development have been observed in placental tissue of women exposed to environmental pollutants such as polybrominated diphenyl ethers²⁵. Exposure to air pollution has been linked to an increased risk of preterm birth among residents of Harris County²⁶. Regardless of the potential causal driving factors, which we can only speculate on with our current analysis, it is of note that our observed impact was significant in time series analysis among gravidae of lower socioeconomic strata. Given associations between socioeconomic status and both stress and environmental exposures, we speculate that our observations are consistent with the notion that perinatal morbidity in association with natural disasters may be another example of health disparities and is worthy of future focused study and investigations."

2. Our adjusted variables followed basic statistical methodologic approaches, whereby we adjusted for those found in univariate analyses to differ. This indeed included maternal age. A more detailed description of how confounders were handled is included in the methods section.

3. We added a sub-analysis of subjects with more than one pregnancy in the database, particularly those with one pregnancy before and one after Hurricane Harvey. The following sentence was added to the manuscript: "Finally, matched pair analysis conducted on gravidae in our database with one recorded and abstracted delivery before and one after August 25, 2017 (n=810 subjects) revealed no significant changes in the rate of composite neonatal morbidity, group B Streptococcus colonization intrapartum and hypertensive disorders of pregnancy. However, the rate of composite maternal morbidity was noted to be significantly higher prior to the storm, 11.7% vs. 6.9%, $p < 0.01$; this is consistent with generalized trends when comparing primiparous and multiparous gravidae."

Specific Responses:

1. We thank Reviewer 2 for the helpful suggestion. We have revised to now reads "Using an

<p>criterion may be differentially applied across exposed and unexposed time periods. I would like to see parity separated into more categories than just nulliparous (yes/no), but rather categories that extend to 2+ or 3+.</p> <p>6* P.7, lines 98-104. Was time since Harvey examined as a dose response? There is suggestion of this in the last line of the Results section. It is stated that results by trimester are not statistically different, but from what? Each other (i.e., effects were similar across trimester) or from the non-exposed period? I'm more interested in the magnitude of these relationships, as significance is affected by both magnitude and sample size - the latter of which is reduced with more categories. Consider presenting these findings as a supplement. No dose response may suggest that both lack of resources (short-term effect) and stress (longer-term effect) play a role.</p> <p>7* P.8, lines 119-123. How was age handled in the adjustment? If only a binary variable, this may not be adjusting enough for age-effects. Consider more categories for parity in the adjustment as well. Why was insurance not adjusted for? You state that you adjusted for factors significant in univariate analyses. In general, more details on how the variables were handled/defined in the regression models are needed.</p> <p>8* P.8, line 123. The results show sensitivity analyses by time periods and subgroup analyses. This needs to be described in the methods section not the results section. Why was the reference group switched for Figure 2 (exposed is now the reference)? This was confusing at first.</p> <p>Results</p> <p>9* p.8, line 134. What do you mean by "have private insurance enabling care outside of pregnancy..." ?</p> <p>10* p.9, lines 148-163. Some of the description about what was done is in the results and needs to be moved to the methods section.</p> <p>11* P.9, Figure 2. Why would one see the period of 2011-2012 have higher rates of maternal morbidity? It is interesting to see that this had an effect for maternal health but not neonatal health. What might explain this, was there something else happening around this time in the area or Texas more generally?</p> <p>12* P.10, lines 166-167. Consider presenting the trimester results as a supplementary table.</p> <p>Discussion</p> <p>13* P.11, lines 199-205. Is it stress or disruption of resources/care? Some reference to stress should be included in the introduction. Also, contextualize your results within these different pathways. Stress would likely have a longer-term impact</p>	<p>institutional perinatal database inclusive of deliveries from two large hospitals in Houston, Texas,,..."</p> <p>2. We thank Reviewer 2 for the helpful suggestion. We have revised to now reads "All women enrolled delivered prior to August 25th, 2017 were the reference group."</p> <p>3. Reviewer 2 raises a very interesting question and point. In order to answer this question, we have adjusted the time trend analysis of CMM by socioeconomic status and have shown that the increase in rate was observed among women in lower socioeconomic status (Figure 4). This is interesting and significantly strengthens both our observations and their implications, suggesting that lower SES renders susceptibility while higher SES buffers against the impact of Hurricane Harvey. This suggests that we cannot attribute our observations to either loss of lower SES from our region and shows that our findings are not confounded by SES. Rather, they suggest the unique susceptibility of women of lower SES. We thank the second reviewer for prompting us to dig into this deeper and enabling us to make some interesting and novel observations.</p> <p>4. We thank Reviewer 2 for the helpful suggestion. We have revised to now read: "Given the significant difference in baseline demographics between the groups, unintentional selection bias due to migration out of the hurricane's affected area is a possibility. However, based on our time trend analyses which demonstrated that significance was retained among gravidae of lower socioeconomic status, it is more likely that socioeconomic strata experience distinct susceptibility and resilience to natural disasters. Specifically, in the case of Hurricane Harvey, our data demonstrate vulnerability of women of lower socioeconomic status as they experienced a significant higher rate of composite maternal morbidity which was not observed among higher socioeconomic strata over the same comparative interval. Whether this is due to an association with a yet unidentified individual, community-based, or environmental protective or mitigating factor cannot be determined by the current analysis. As noted above, this may be partially attributable to health disparities, specifically social and environmental justice disparities."</p>
--	---

or have a critical window of exposure during pregnancy, whereas, resources may be a more immediate impact that would lessen further from the event. How do your findings fit in to the various mechanisms that may increase risk after a natural disaster?

14* P.11, lines 206-216. You should discuss the role of section bias, which seems to be very clear from your comparison of descriptive characteristics before and after Harvey. How might this have impacted your findings?

5. We thank Reviewer 2 for their very insightful and helpful analytic suggestions, all of which we have now systematically performed. We have added a subgroup analysis of women with more than one delivery – one pre and one post-hurricane. Although parity may be a confounder, the direction of results is unlikely to change as evidenced by the lack of discrepancy between crude and adjusted ORs. Moreover, we are concerned for over-stratification by parity, which itself retains significant collinearity.

6. We thank Reviewer 2 for the insightful suggestion. We have added a time trend analysis and were both enthused and intrigued with the results. As shown in our revised manuscript, the time trend analyses revealed that exposure to Hurricane Harvey was associated with an upward and significant trend in CMM but not CNM (Figure 3). This further supports our findings in our subgroup and sensitivity analyses. We have also added additional information regarding effect by trimester: “Outcomes following the Hurricane were also similar across all trimesters of pregnancy. (Supplemental table).”

7. We thank Reviewer 2 for the helpful suggestion. We have followed these suggestions and revised to now reads: “Analysis was corrected for possible confounders identified on univariate analysis: maternal age (<20, 20-34, ≥35 years), maternal race and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), maternal education (less than high school, high school or higher), marital status (married, not married), nulliparity (no, yes), body mass index (<18.5 to 24.9 kg/m², BMI 25 to 29.9 kg/m² and ≥ 30.0 kg/m²), Household income (less than \$34,999, \$35,000-\$74,999 and \$75,000 and above), and method of payment (private, federal/state and none).”

8. We thank Reviewer 2 for the helpful suggestion. All descriptions were moved to the methods section. We have also added footnotes to the figure 2 to further clarify the analysis.

9. We thank Reviewer 2 for the helpful suggestion. This phrase was meant to highlight the fact that several federal and state funding sources do not offer coverage to women after 6 weeks postpartum and therefore lack adequate medical care in between or after pregnancies. It now reads “have insurance enabling medical care outside of

	<p>pregnancy and the 6 week post partum interval.”</p> <p>10. We thank Reviewer 2 for the helpful suggestion. All descriptions were moved to the methods section.</p> <p>11. We thank Reviewer 2 for the comment. That particular question is outside the scope of the current study. Additionally, with the new sample size the difference in maternal morbidity is no longer statistically significant. This is now reflected in the revised manuscript.</p> <p>12. We thank Reviewer 2 for the helpful suggestion. We have revised and the data is included as Supplemental table.</p> <p>13. We thank Reviewer 2 for the helpful suggestion. We have revised and added additional information to the discussion as noted above with our response to reviewer #1. We have notably included our broader and speculative biologic plausibility beyond the proverbial “stress in pregnancy” considerations.</p> <p>14. We thank Reviewer 2 for the helpful suggestion. As detailed previously, we have now included a time trend analysis evaluating several socioeconomic parameters. We have appropriately revised to now read: “Given the significant difference in baseline demographics between the groups, unintentional selection bias due to migration out of the hurricane’s affected area is a possibility. However, based on our time trend analyses which demonstrated that significance was retained among gravidae of lower socioeconomic status, it is more likely that socioeconomic strata experience distinct susceptibility and resilience to natural disasters. Specifically, in the case of Hurricane Harvey, are data demonstrate vulnerability of women of lower socioeconomic status as they experienced a significant higher rate of composite maternal morbidity which was not observed among higher socioeconomic strata over the same comparative interval. Whether this is due to an association with a yet unidentified individual, community-based, or environmental protective or mitigating factor cannot be determined by the current analysis.”</p>
<p>Reviewer #3: This is a retrospective cohort study examining perinatal outcomes following Hurricane Harvey. The authors demonstrate an increase in adverse obstetric outcomes associated with the hurricane, consistent with prior, similar studies. While they do provide results from a larger cohort that previously published, it conforms what is known. They also do not</p>	<p><i>Overall.</i> We thank Reviewer 3 for their thoughtful comments. We have revised and have notably included our broader and speculative biologic plausibility beyond the proverbial “stress in pregnancy” considerations. We have emphasized further in our manuscript the distinctions in findings</p>

distinguish between the effects of interrupted services versus physiologic stress or other factors that may explain these associations. So, while the data are copious, this manuscript does not further our understanding of the association between natural disasters and adverse outcomes. While such events are difficult to predict, understanding the causal link is necessary to mitigate the effects.

Specific comments -

1. There are methodological descriptions found in the results section (eg lines 161-163).
2. Please describe why the antecedent time range was chosen; the data are heavily weighted to prior to the event
3. Line 103- what constitutes "major?"
4. Figure 2 should be removed. It does not add to the manuscript and is distracting and potentially confusing, as it demonstrates there is a protective effect over time but does not include the hurricane's data and trend are better demonstrated with figure 3

between our study and other, much smaller and not population based, studies.

We do wish to note that in contrast to Hurricane Katrina, for example, services in our institution were not interrupted and prenatal visits including entry to care by gestational age are coded and known. As with all database analyses, causal links are neither the goal nor aim. Rather sound observational data which spur future hypothesis-driven and causal analyses are our goal. We are enthused by our sensitivity and time series analyses in this regard.

Response to specific comments:

1. We thank Reviewer 3 for this comment, all descriptions were moved to the methods section
2. We thank Reviewer 3 for this insightful question. Although this approach produced uneven comparison groups, the time range was chosen to allow for historical trends to be assessed and evaluated. This is appropriate in a cohort design, since our "exposure" was Hurricane Harvey and equivalent "exposure" measures would be the same weeks of August-September of preceding years. This approach allows for an appropriately comprehensive assessment of the baseline population and allows us to estimate the change in rates of certain outcomes in significant association with Hurricane Harvey, and not other coincident recurrent events in those same exposure weeks on an annual preceding basis.

Had we alternately used a select group of women (case-control design) we would have risked trend selection bias on our part. In order to make this more transparent to the reader, the following was added to the manuscript:

"This reference group was chosen to allow for a more comprehensive view of the baseline study population and to illustrate an estimate in the change in rates of certain outcomes over time, treating Hurricane Harvey as the exposure of interest."

3. We thank Reviewer 3 for this insightful question. We have revised to now read: "Although the Gulf Coast of Texas is constantly at risk of tropical storms and disturbances, no major hurricane (category 3 or higher) affected the area from 2011 to 2017".

4. In deference to the comments by the other 2 reviewers and the editor, we have retained Figure 2

	but revised as noted above. We have replaced figure 3 as noted above.
<p>STATISTICAL EDITOR'S COMMENTS:</p> <p>1. Table 1: The cohorts differ in many baseline characteristics. Should corroborate the adjustment model with analysis of those delivered after Harvey with matched controls prior to Harvey.</p> <p>2. Table 2: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70, which is violated in premature rupture of membranes and many other entries.</p> <p>3. Table 3: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70, which is violated in arterial cord blood < 7.1 and many other entries.</p> <p>4. Table 4: Should include another column of crude ORs with CIs to contrast with aORs. Many of the row comparisons should not include aORs, due to low counts of adverse outcomes. There were 7 variables used as adjustors, so the minimum count of adverse outcomes should be ≥ 70, which is violated in neonatal deaths and many other entries. Also, the last column has no p-value entries, so the column heading needs to be changed.</p> <p>5. Fig 1: What does "duplicates N = 235" mean? If there are individuals who delivered more than once during the time of the study, then either only one of those deliveries should be randomly chosen for inclusion in the analysis, or an adjustment made in the analysis for repeated counts of an individual woman. That is, those are not independent events.</p> <p>6. Fig 2: I assume there were sufficient counts of maternal and neonatal morbidity to allow for adjustment with 7 variables, but should include the counts for these analyses as on-line material. Again, need to include the counts for individual time periods of group B strep and hypertension/pre-eclampsia and justify adjustment for 7 variables. Should clarify for reader that the vertical red line, the referent, is the time after Harvey.</p> <p>7. Fig 3, lines 156-160: Unclear as to what stats test was used to evaluate the "statistically upward trend". In all 3 graphs, the upward trends appear to precede the 3rd quarter of 2017. Should use time series analysis and compare the slopes.</p> <p>8. Also, need to include concise, descriptive legends to figures.</p>	<p><i>Response to Statistical Editor</i></p> <p>1. We thank the statistical editor for their thoughts and guidance. We have done so, and we have added this information to the methods section of the manuscript. We are highly enthused with our resultant observations and findings and are incredibly grateful for the suggestions to do so.</p> <p>We have conducted a matched pair analysis on women with one pregnancy before and one after Hurricane Harvey. The following sentence was added to the manuscript: "Finally, matched pair analysis conducted on gravidae in our database with one recorded and abstracted delivery before and one after August 25, 2017 (n=810 subjects) revealed no significant changes in the rate of composite neonatal morbidity, group B Streptococcus colonization intrapartum and hypertensive disorders of pregnancy. However, the rate of composite maternal morbidity was noted to be significantly higher prior to the storm, 11.7% vs. 6.9%, $p < 0.01$; this is consistent with generalized trends when comparing primiparous and multiparous gravidae."</p> <p>2. We thank the editor for their thoughts and guidance. We have done so and have included all changes in the updated tables.</p> <p>3. We thank the editor for their thoughts and guidance. We have done so and have included all changes in the updated tables.</p> <p>4. We thank the editor for their thoughts and guidance. We have done so and have included all changes in the updated tables.</p> <p>5. We thank the editor for this comment. The figure has been corrected to state that "women with >1 delivery." We have also clarified that we randomly chose one delivery in women with >1 delivery in our database. In other words, we have multiple gravidae who have delivered more than one baby in our population-based database, and we included only one delivery at random to avoid confounding by repeat measures. In the process of doing so, we ultimately removed approximately 2500 events. We have uniformly corrected the manuscript and tables to reflect the correct sample size with the updated analysis. No changes were noted in the direction of association or in the significant differences</p>

Associate Editor's Comments

Our enthusiasm for this manuscript is conditional on

1) A propensity score analysis and

2) A time series analysis

Our concern is that the differences you have shown may be due to residual confounding or may merely be reflective of a trend toward worse outcomes that was already underway before the hurricane. That said, we are very happy that you sent this to us, and look forward to evaluating a revision.

previously reported.

6. We thank the editor for their thoughts and guidance. We have added the count for each adverse outcome to the figure. We have also added clarification of the meaning of the vertical red line.

7. We thank the editor for bringing our error to our attention, and have now corrected. Figure 3 was replaced and a time series analysis has now been reported.

8. Thank you for this point. Indeed, we have now done so.

Response to Associate Editor

We concur with this concern and have significantly revised our manuscript to include not only a propensity score analysis and a time series analysis, but also a time series analysis corrected for socioeconomic status. This led to a further strengthening of the significance, novelty, and likely clinical importance of our findings. We can now state with much greater confidence that our observations were not, in fact, merely a trend toward worse outcomes that was already underway. Rather, the combination of our matched-pair analysis, time series, and propensity score analyses suggest that Hurricane Harvey was a disruptive exposure which is associated with worse composite outcomes in gravidae of lower socioeconomic strata. The specificity and significance of these findings not only have strengthened our confidence in our conclusions but have hopefully laid a methodologic framework for other investigative teams to follow in their future analyses. We thank the thoughtful editors and reviewers of the Green Journal in partnering with us to do so.