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:** Jul 25, 2019
**To:** "Joshua I Rosenbloom" [redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-19-1167

RE: Manuscript Number ONG-19-1167

Expectant management of hypertensive disorders of pregnancy and future cardiovascular morbidity

Dear Dr. Rosenbloom:

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 Aug 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a very interesting study of the risk of cardiovascular events later in life for mothers who had hypertensive disease in pregnancy, divided into delivery within 7 days and after 7 days. It uses a New York state database and some reasonable assumptions to define the patients who fit the criteria and to define the diagnosis to delivery interval. There is a trend identified suggesting an increased risk with a longer delay in delivery. It is a retrospective study.

I have some questions that may clarify and improve the utility of the paper:

1. The database needs to be defined better. Other than knowing it is a New York based database, I would like to know how long it has been running, how many patients are in it total, who gets entered into the database (are all deliveries required), why the years of 2005 to 2014 were picked out of the entire database (it may be all that is available, but we should know that), who sends in the data (hospital, individual provider, etc), and finally, has there been any verification of accuracy (audits for validity of the information)?

2. Is there any way to determine if this is an actual difference in rate of CV disease or a difference in timing? Do the patients who were delivered earlier eventually get the same rate of CV disease, just not as soon? It may be that the length of time available in the database doesn't allow for this kind of information, but if it has been running for a longer time, starting the analysis earlier than 2005 might give more information.

3. If you add the "no delivery date calculable" group into either group, does that change the outcome (will the 147 patients make the results less significant if they were all in one group or the other)?

4. Table 1 in the "severe preeclampsia" category looks unlikely to have $p=0.79$ with the percent difference and every other subgroup in that category at $p<0.001$. That's just looking at the numbers and not calculating the statistics, but it looks odd. You might re-verify the math.

5. Finally, as a proponent of useful papers, I would suggest a little speculation: If it were you or your spouse with preeclampsia without severe features at 35 weeks, given this (preliminary) information, would that sway you to deliver earlier than you might have before you had this information? In addition, what are your suggestions for types of testing and frequency of testing that should be done to watch for developing CV disease in these women?

Thank you for your work. Teasing information out of these large databases with the poor translation between ICD codes (9 or 10) and actual medical care is difficult and frustrating. Nice job getting what you did from this information.

Reviewer #2: Thank you for this article.

Specific comments:

Abstract: I would include one sentence mentioning the sensitivity analyses in he abstract, as that thought was in my mind as I read it and I would want to know they are there,

Methods:
Line 95: can you be more specific on what CV disease this is ( I am assuming not CHTN)

Can you include some data here on the reliability of this database in terms of accuracy of coding.

Results: overall well described.

Discussion: well described strengths and weaknesses.

Reviewer #3: This manuscript describes a retrospective cohort study that utilized a state inpatient database system to question whether a longer length of time between the diagnosis of a hypertensive disorder of pregnancy and delivery was associated with increased cardiovascular morbidity in the years after delivery. The median follow-up was 5 to 6 years. The primary outcome was a composite. The investigators found an adjusted hazard ratio of 1.45. A strength of the study was the large number of patients in the database.

1. How the diagnosis of chronic hypertension was managed appears a bit confusing. Patients with chronic hypertension only were excluded, as were those with chronic hypertension and a hypertensive disorder other than superimposed preeclampsia. Using this paradigm suggests that one could reliably distinguish between chronic hypertension and related disorders and chronic hypertension and superimposed preeclampsia - I am not so sure this is a reliable distinction. How many patients were excluded based on this distinction? Would it be possible to include/analyze such patients as a matter of scientific interest?

2. In line at 179, there is a < before the number 11 in two places. I think this is a typographical error.

3. As the authors note in the discussion, the issue of gestational age of delivery (and thus gestational age of onset hypertensive disease) would seem likely important. I am certain the authors have considered this from every angle, but I would ask whether such simple things as birthweight might be available? Perhaps the authors could add a sentence on page 15 as to what "further investigations that include gestational age" were not done because of the informational limitations.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 142-143: The follow-up for each cohort needs to be separately shown and if there was a difference in > 7 days vs ≤ 7 days, that needs to be explained. Also, were the loss to follow-up rates the same for both cohorts?

lines 197-201: Were all deaths included as events, or just those related to cardiovascular disease?

Tables 1, 2 and lines 148-151: The cohorts were different in many characteristics at baseline. The outcome events were relatively infrequent (N = 216 vs N = 67). The adjusted hazards model adjusted for 16 covariates, which makes the model likely over fitted. Should use matching algorithm to corroborate that the difference is actually associated with difference in timing of HTN treatment, rather than simply reflecting differences at baseline. Given the sample sizes and the relatively large cohort of controls ( ≤ 7 days), that approach should be feasible.

Table 1: Need to enumerate all missing data.

Table 2: Need to include crude HR to contrast with aHR. need units for age (per year, per decade etc). The analysis by year is likely under powered, considering how the adverse events would be distributed into smaller subsets, particularly for the later years of entry and for some of the less frequent co-morbidities.

Fig 2: Needs a concise legend with explanation of the statistical difference. The y-axis should be re-labelled. Survival

analysis was the method used, but the proportions are not those who survived, but rather those who did have death or a cardiovascular readmission event.

EDITOR COMMENTS:

1. Thank you for this submission. As noted by the Statistical Editor, we have concerns about a few things and would like to see further explicated or analyzed:

A. Please provide the follow up time period for both groups, not just the overall group.

B. Please provide an analysis using matching for some of the variables that are quite different in your two groups (with and without hypertensive diseases of pregnancy). Consider age, race, multiple gestation, pre-existing hypertension and other differences noted in Table 1 We have concerns that these differences may be the explanation, or at least may dilute the effect of, the differences in outcomes in your groups. Given the at OR for some of your outcomes at the lower bound is close to 1, we would like to make sure that there is really a difference when controlling for these other differences.

2. 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.

3. 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.

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

4. 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.

5. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

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

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 limits for different article types are as follows: Original Research articles, 300 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. 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 via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

16. Figures 1–2: Please upload as a figure file on Editorial Manager.

17. 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/ifauth.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.

18. 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.

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 Aug 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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

Dear Dr. Chescheir:

Thank you very much for the opportunity to revise our manuscript. We have endeavored to address all of the comments and suggestions, especially the editorial comments and those of the statistical reviewer. We look forward to hearing from you.

We are pleased to "OPT IN" to having our response letter made publically available.

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.

Sincerely,
Joshua Rosenbloom

REVIEWER COMMENTS:

Reviewer #1: This is a very interesting study of the risk of cardiovascular events later in life for mothers who had hypertensive disease in pregnancy, divided into delivery within 7 days and after 7 days. It uses a New York state database and some reasonable assumptions to define the patients who fit the criteria and to define the diagnosis to delivery interval. There is a trend identified suggesting an increased risk with a longer delay in delivery. It is a retrospective study.

Response: We would like to thank the reviewer for the comments and the careful consideration of our manuscript.

I have some questions that may clarify and improve the utility of the paper:

1. The database needs to be defined better. Other than knowing it is a New York based database, I would like to know how long it has been running, how many patients are in it total, who gets entered into the database (are all deliveries required), why the years of 2005 to 2014 were picked out of the entire database (it may be all that is available, but we should know that), who sends in the data (hospital, individual provider, etc), and finally, has there been any verification of accuracy (audits for validity of the information)?

Response: Thank you for this important question. We have added the following to the manuscript: "The New York SID captures approximately 97% of all acute care hospital discharges in the state of New York from 1990-2016. Information in the database includes basic demographic data such as age, race, and payer, as well as *International Classification of Diseases, 9th Revision, Clinical modification* (ICD-9-CM) billing codes from the hospital discharge. Furthermore, ICD-9-CM procedure codes as well as the day of the hospitalization on which the procedure occurred are included. Data are collected at the state level and are sent to the Agency for Healthcare Research and Quality which cleans and restructures the data to a common format before providing it for analysis. The years 2005-2014 were chosen to include a period with adequate time for follow-up. We did not use data from 2015 and beyond due to the adoption of the ICD-10 coding system in that year."

2. Is there any way to determine if this is an actual difference in rate of CV disease or a difference in timing? Do the patients who were delivered earlier eventually get the same rate of CV disease, just not as soon? It may be that the length of time available in the database doesn't allow for this kind of information, but if it has been running for a longer time, starting the analysis earlier than 2005 might give more information.

Response: Thank you for this question. We agree that by using survival analysis and proportional hazards we are limited to commenting on the timing of onset of CV disease. However, in order to answer the question of what the overall rates of CV disease are regardless of timing we would need to ensure that all patients had equal follow-up time. However this would limit our ability to use the dataset to its fullest extent. For instance if stopped after 5 years from delivery for each patient e would be unable to capture relevant events that occurred later. We do agree that including a longer follow-up time would be optimal but unfortunately the data from prior to 2005 is not available at our institution (each institution purchases the data from the Agency for Healthcare Quality and Research for use).

3. If you add the "no delivery date calculable" group into either group, does that change the outcome (will the 147 patients make the results less significant if they were all in one group or the other)?

Response: Thank you for this question. We ran these additional analyses as suggested and the results were not materially altered. We have added this to the manuscript.

4. Table 1 in the "severe preeclampsia" category looks unlikely to have $p=0.79$ with the percent difference and every other subgroup in that category at $p<0.001$. That's just looking at the numbers and not calculating the statistics, but it looks odd. You might re-verify the math.

Response: Thank you for this question- we repeated the relevant analysis and the p-value is correct. In this section of the table logistic regression was used to compare the relationship between the categories of hypertensive disorder (with gestational hypertension as the referent) and the time to delivery. The proportion of patients with severe preeclampsia who delivered in ≤7 days is very similar to the proportion of patients with gestational hypertension who delivered ≤7 days, which explains this insignificant p-value. However, for example, the proportion of patients with mild preeclampsia who delivered within 7 days is different than the proportion of patients with gestational hypertension who delivered within 7 days.

5. Finally, as a proponent of useful papers, I would suggest a little speculation: If it were you or your spouse with preeclampsia without severe features at 35 weeks, given this (preliminary) information, would that sway you to deliver earlier than you might have before you had this information? In addition, what are your suggestions for types of testing and frequency of testing that should be done to watch for developing CV disease in these women?

Response: Thank you for this provocative question. Although we are hesitant to speculate too much, the last paragraph of the manuscript does address some of these issues. The question of what kind of follow-up testing and frequency these patients should have is very important and there is insufficient evidence to answer this question.

Thank you for your work. Teasing information out of these large databases with the poor translation between ICD codes (9 or 10) and actual medical care is difficult and frustrating. Nice job getting what you did from this information.

Response: Thank you. We appreciate this comment.

Reviewer #2: Thank you for this article.

Specific comments:

Abstract: I would include one sentence mentioning the sensitivity analyses in the abstract, as that thought was in my mind as I read it and I would want to know they are there,

Response: Thank you, we have added a sentence regarding sensitivity analyses to the abstract.

Methods:
Line 95: can you be more specific on what CV disease this is ( I am assuming not CHTN)

Response: Thank you for this question. We have added that CV disease in pregnancy includes, for example, coronary artery disease, valvular disease and pre-existing cardiomyopathy. CHTN is not included as "cardiovascular disease in pregnancy"

Can you include some data here on the reliability of this database in terms of accuracy of coding.

Response: Thank you for this question. ICD-9 coding has been tested and validated for critical variables in this analysis including induction of labor, cesarean delivery, and preterm delivery. We have included this in the manuscript in the section on "strengths" in the Discussion.

Results: overall well described.

Response: Thank you for this comment.

Discussion: well described strengths and weaknesses.

Response: Thank you for this comment.

Reviewer #3: This manuscript describes a retrospective cohort study that utilized a state inpatient database system to question whether a longer length of time between the diagnosis of a hypertensive disorder of pregnancy and delivery was associated with increased cardiovascular morbidity in the years after delivery. The median follow-up was 5 to 6 years. The primary outcome was a composite. The investigators found an adjusted hazard ratio of 1.45. A strength of the study was the large number of patients in the database.

Response: Thank you for this comment.

1. How the diagnosis of chronic hypertension was managed appears a bit confusing. Patients with chronic hypertension only were excluded, as were those with chronic hypertension and a hypertensive disorder other than superimposed preeclampsia. Using this paradigm suggests that one could reliably distinguish between chronic hypertension and related disorders and chronic hypertension and superimposed preeclampsia - I am not so sure this is a reliable distinction. How many patients were excluded based on this distinction? Would it be possible to include/analyze such patients as a matter of scientific interest?

Response: Thank you for this question. We excluded 183 patients who had a diagnosis of chronic hypertension as well as a hypertensive disorder of pregnancy other than superimposed preeclampsia. We did this as a conservative approach to ensure that only patients with a clearly documented hypertensive disorder of pregnancy were included. (The method is similar to that used in Jarvie JL, Metz TD, Davis MB, Ehrig JC, Kao DP. Short-term risk of cardiovascular readmission following a hypertensive disorder of pregnancy. Heart. 2018 Jul;104(14):1187-1194.) However, to address the reviewer's question we repeated the analysis including these patients. The results were unaltered, and we have added this to the manuscript.

2. In line at 179, there is a < before the number 11 in two places. I think this is a typographical error.
Response: Thank you for this comment. Due to restrictions on presentation of results from HCUP data, any counts <11 are reported as "<11" to preserve patient privacy. We have ensured this is stated in the Methods to avoid any confusion.

3. As the authors note in the discussion, the issue of gestational age of delivery (and thus gestational age of onset hypertensive disease) would seem likely important. I am certain the authors have considered this from every angle, but I would ask whether such simple things as birthweight might be available? Perhaps the authors could add a sentence on page 15 as to what "further investigations that include gestational age" were not done because of the informational limitations.

Response: Thank you for this question. Unfortunately there is no linkage between the maternal and neonatal chart, so birthweight data are not available. The only data on gestational age that is available is the ICD-9 code for preterm delivery, and we have only included patients with this code. ICD-10 coding does include gestational age in the maternal record, so we anticipate that future analyses in this dataset could have more detailed data on gestational age available. We have included the sentence that "We limited this analysis to only preterm deliveries to ensure roughly comparable gestational ages, but further investigations that include gestational age will be important for determining if our findings are due primarily to the early-onset of the hypertensive disorders or to the duration of expectant management regardless of gestational age of exposure."

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 142-143: The follow-up for each cohort needs to be separately shown and if there was a difference in > 7 days vs ≤ 7 days, that needs to be explained. Also, were the loss to follow-up rates the same for both cohorts?

Response: Thank you for this question. The median follow-up period for the 0-7 days group was 5.2 years (interquartile range 3.0, 7.8), and the median follow-up period for the >7 days group was similar at 5.2 years (interquartile range 3.0, 7.5). This is an administrative database of hospital discharges, there is no specific loss to follow-up that is calculable. The primary reason for loss to follow-up is moving from the state of New York, since the database captures approximately 97% of hospital discharges in the state.

lines 197-201: Were all deaths included as events, or just those related to cardiovascular disease?

Response: Thank you for this question- all deaths were included.

Tables 1, 2 and lines 148-151: The cohorts were different in many characteristics at baseline. The outcome events were relatively infrequent (N = 216 vs N = 67). The adjusted hazards model adjusted for 16 covariates, which makes the model likely over fitted. Should use matching algorithm to corroborate that the difference is actually associated with difference in timing of HTN treatment, rather than simply reflecting differences at baseline. Given the sample sizes and the relatively large cohort of controls ( ≤ 7 days), that approach should be feasible.

Response: Thank you for this important suggestion. To address this, we performed propensity score matching with a 3:1 match and then repeated the analysis. The results from this analysis were very similar to the adjusted analysis presented in the manuscript. We have added the details of the methods and results of this propensity score analysis to the manuscript.

Table 1: Need to enumerate all missing data.
Response: Thank you for this important question. We have added to the table enumeration of missing data on race. There were no other demographic data missing (payer, year of delivery). Specifically, payer is very rarely missing in the overall dataset due to reimbursement issues. Patients with missing age were excluded from the overall dataset and the number of these patients is not available. For the "clinical" data, the data are based on ICD-9 codes.

Table 2: Need to include crude HR to contrast with aHR. need units for age (per year, per decade etc). The analysis by year is likely under powered, considering how the adverse events would be distributed into smaller subsets, particularly for the later years of entry and for some of the less frequent co-morbidities.

Response: Thank you for this question. We have added the crude HR to the table. We have added the units for age. We agree the analysis by year may be underpowered- we included year in the adjusted model to account for any secular trends.

Fig 2: Needs a concise legend with explanation of the statistical difference. The y-axis should be re-labelled. Survival analysis was the method used, but the proportions are not those who survived, but rather those who did have death or a cardiovascular readmission event.

Response: Thank you, we have added this legend and changed the y-axis.

EDITOR COMMENTS:

1. Thank you for this submission. As noted by the Statistical Editor, we have concerns about a few things and would like to see further explicated or analyzed:

A. Please provide the follow up time period for both groups, not just the overall group.
Response: Thank you, we have added this to the manuscript.

B. Please provide an analysis using matching for some of the variables that are quite different in your two groups (with and without hypertensive diseases of pregnancy). Consider age, race, multiple gestation, pre-existing hypertension and other differences noted in Table 1 We have concerns that these differences may be the explanation, or at least may dilute the effect of, the differences in outcomes in your groups. Given the at OR for some of your outcomes at the lower bound is close to 1, we would like to make sure that there is really a difference when controlling for these other differences.

Response: Thank you for these important comments. We have completed a propensity score matched analysis and have added this to the manuscript.

**Date:** Sep 03, 2019
**To:** "Joshua I Rosenbloom"[redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-19-1167R1

RE: Manuscript Number ONG-19-1167R1

Expectant management of hypertensive disorders of pregnancy and future cardiovascular morbidity

Dear Dr. Rosenbloom:

Your revised manuscript has been reviewed by the Statistical Editor. There are some additional comments that the journal would like you to address prior to considering your revision further.

The Statistical Editor makes the following points that need to be addressed:

I thank the Authors for including the propensity score analysis, I believe it strengthens their conclusions about this data set. However, I would like to see more detail regarding that analysis in the main text.

Specifically, the matching of 2836 of the patients in the >7 day group vs the 3:1 control group should be included in Table form. That could be included as on-line material, showing the residual differences after matching and their significance/non-significance.

Also, the results of that matching process, in terms of HRs, should be shown in Table form contrasted with the adjusted HRs performed on the complete cohorts. That Table is important enough to include in the main text. That Table could either be a separate Table, or included as an additional column in Table 2, which now contrasts crude and adjusted HRs.

***

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.

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 7 days from the date of this letter. If we have not heard from you by Sep 10, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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

September 5, 2019

Dear Dr. Chescheir:

Thank you for the opportunity to further revise our manuscript for your consideration.

We confirm that we have read the instructions for authors.

Response to Statistical Editor:

We thank the Statistical Editor for the thoughtful comments.

Comment: I thank the Authors for including the propensity score analysis, I believe it strengthens their conclusions about this data set. However, I would like to see more detail regarding that analysis in the main text.
-Thank you for this comment. We have addressed the points below to include the requested information.

Specifically, the matching of 2836 of the patients in the >7 day group vs the 3:1 control group should be included in Table form. That could be included as on-line material, showing the residual differences after matching and their significance/non-significance.
-Thank you, we have added this to the supplemental appendix as supplemental table 2.

Also, the results of that matching process, in terms of HRs, should be shown in Table form contrasted with the adjusted HRs performed on the complete cohorts. That Table is important enough to include in the main text. That Table could either be a separate Table, or included as an additional column in Table 2, which now contrasts crude and adjusted HRs.
-Thank you, we have added this information as an additional column in table 2 in the main text.

Sincerely,
Joshua Rosenbloom