OBSTETRICS & GYNECOLOGY

**NOTICE:** This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

**Date:** Nov 01, 2019
**To:** "Alexander M Friedman" [redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-19-1834

RE: Manuscript Number ONG-19-1834

Use of Uterine Tamponade and Interventional Radiology Procedures

Dear Dr. Friedman:

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 14 days from the date of this letter. If we have not heard from you by Nov 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The authors reviewed an administrative dataset of 5 million deliveries between 2006 and 2014 to study the relationship between IR procedures (uterine artery embolization presumably), UT procedures (uterine balloon, presumably) and hysterectomy. They looked at the increase in procedures over time and in relation to hospital delivery volume. They also looked at SMM. Comments and questions follow.

1. General comment. Suggest replacing 'uterine tamponade' with 'intrauterine balloon' (or something like that). Similarly, suggest replacing 'interventional radiology procedures' with 'uterine artery embolization' (as there are many IR procedures).

2. Title. Might mention obstetrics (use of these procedures in obstetrics).

3. Abstract.
The abstract is a faithful representation of the manuscript. As some may read only the abstract, there are a couple things that might be explained more fully.
a. What is the Perspective database?
b. The objective is in lines 40-41, but everything in lines 44-49 is also listed as objectives. Would consider adding more information to the former and using the latter space to write about what you did. Would clarify that your morbidity composite did not include hysterectomy or transfusion.
c. Lines 63-65 and 68-70. Are the authors suggesting that UT and/or IR caused SMM? It will be important to avoid misinterpretation.

4. Introduction. This is a well-written overview of the sequelae of hemorrhage. Might include something about etiologies of increased hemorrhage, because treatment is tailored to them. In line 94, might define what makes PPH complicated.

5. Methods.
a. Lines 116-120. Please provide more information about the source of the data so that readers will have a better understanding of its potential utility.
b. Lines 122-125. Does the dataset provide information about whether medications were administered before or after devices were used, and when in the sequence hysterectomy and other outcomes such as ICU transfer or transfer to an outside hospital occurred?
c. Lines 129-137. Is the variable (or outcome) of uterotonic use being used to evaluate adequacy of care or to stratify etiology of hemorrhage?
d. Lines 138-145. The authors removed 2 SMM criteria removed from the composite. By doing so they created a new composite that includes morbidities as disparate as stroke and heart failure. Would refer to this as a morbidity composite

rather than SMM, to avoid confusion (because as presented, readers may miss a sentence and think that the authors are writing about transfusion and hysterectomy). Please report the individual components in addition to the study composite alone, because readers need to know what their patients are at risk for.
e. Lines 163-165. Would combine uterine atony and secondary postpartum hemorrhage, or explain the rationale for not doing so.

6. Results.
a. Lines 196-201. The authors report the overall number of UT and IR procedures, then the number of hysterectomies, and then the number (40%) of hysterectomies associated with diagnosis of uterine atony or delayed PPH. Suggest also reporting the N (%) of women with UT who required hysterectomy and the N (%) of women with IR who required hysterectomy - not as a function of the number of hysterectomies but as a function of the number of each procedure. This may be helpful information for counseling prior to procedures.
b. Lines 217-227. Did procedures increase because doctors are collectively becoming aware of the need for them, because of increasing availability in general, or because morbidity necessitating them increased? If the authors do not have the data to answer this question, would address in the discussion to avoid misinterpretation.
c. Lines 240-245. Please clarify SMM, as above.
d. Tables. Suggest moving the years of study data from tables 1 and 2 into a separate table that includes the N (%) with hysterectomy and other components of the morbidity composite, according to study procedure.
e. Figures. There are several figures with only a few bars each. This might be more easily be depicted as a couple of tables. The title of figure 3 should be revised if the authors are not certain that the embolization was performed prior to hysterectomy.

7. Discussion.
a. Lines 266-268. The authors write about hospital volume being a factor in use of IR procedures, whereas uterine tamponade was not. Would mention something about uterine artery embolization requiring an interventional radiologist (hospital volume might not be a factor after adjustment for this).
b. Lines 283-298. The authors report in lines 292-296 that they didn't know whether the uterine artery embolization procedures occurred after hysterectomy rather than before it (as a treatment for women with severe morbidity from ongoing bleeding rather than as a risk factor). Please explore this limitation more fully, as it is central to interpretation and application of the study findings. The last sentence of the abstract and the study conclusion are that women who need hysterectomy after uterine artery embolization are at particular risk, but the data did not actually show that.
c. Lines 302-305. As stated by the authors, recommendations came out after the study period that supported increased use of the study measures. As the authors found a significant change in practice over their 9-year study period, they might mention the limitation that the data they are presenting are already 5 years old (and may not reflect current prevalence).

Reviewer #2: Thank you for allowing me to review your manuscript. I find the manuscript to be well written. The work is original and clinically relevant. The objectives of the study are clearly stated and so is the methodology. The variables measured are appropriate to validated the purpose of the study. The tables and graphs are well done and accurately reflect the reported numbers/text. The discussion is extensive and objectively addresses the strengths and weaknesses of the study. The results are clearly explained and previous work is cited, and the findings of the study are placed in perspective. The results of this study are important and directly applicable to clinical practice. The main limitation of the study is the administrative database, as the authors mentioned in their discussion. However, the findings are definitely interesting, and clinically relevant. It would also have been clinically relevant to describe in detail the use of uterotonics, and any association with the need for subsequent use of UT, IR, hysterectomy. Transfusion is an important/significant metric and I think it should be displayed in the results.

Reviewer #3: This is a retrospective analysis of large administrative database looking at trends of use of uterine tamponade, interventional radiology procedures, and peripartum hysterectomy. The objective of the paper is "[t]o characterize use of and outcomes with" these procedures. While this paper describes trends, the outcomes reported do not provide meaningful insight into the utility of these procedures. The authors demonstrate an increase of in these procedures over the 8 year period included. They demonstrate an increase in severe maternal mortality in those cases in which additional procedures were used as opposed to those cases where it they were not. However, there is no demonstration that the increase in use of these procedures improved patient outcomes. After reviewing this manuscript, I was left wondering how I would apply this information to clinical practice.

Additionally, I had some specific thoughts:

Precis: no mention of outcomes related to morbidity; this would be more relevant

Methods: discuss the validity of these data, or administrative data in general

Methods: provide some justification for why factors such as geographic region were considered? what is the colinearity with the urban/rural distinction? what about suburban settings?

Discussion, line 290-291; discuss the way in which misclassification would affect the results

Discussion, line 292; that no direct record review was performed in implied by the use of deidentified administrative data. This is not a second limitation. A more thoughtful discussion of beneifts and limitations would strengthen this manuscript.

Supplemental material: Please provide the information in the supplemental table 1 in the body of the main paper -- the presentation of statistical significance is not appropriate for a supplement.

STATISTICAL EDITOR COMMENTS:

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

lines 195-200: Should provide a flow diagram indicating how many procedures were included in each subset for the final analysis.

lines 205-209: The stats test used (chi-square) tests whether the allocation of data vs quintile was random, it does not show that one quintile was significantly higher or lower than another. The wording should be changed to reflect that, unless the Authors want to include stats that specifically test each quintile vs a referent (which would require a stricter inference threshold than $p < .05$).

lines 210-215: No stats were included in Table 1, so if those are being cited, should expand the Table to include stats comparisons of the columns. If the analysis refers to Table 2, should clarify.

lines 218-227 and Fig 1A-1D: Should either indicate in figures or in supplemental material, then counts for the number of numerator events in each histogram. Should also include error bars for the point estimates.

lines 228-233 and Fig 2A-2B: Same comment as re: Fig 1. Should clarify that the designation of most common, or lowest common etc are nominal, not by specific stats test, since the stats test was for overall differences, not specific pairwise comparisons.

lines 233-237 and Fig 3: Same comment as re: Fig 1. Again should clarify that the comparisons cited are for overall trend, not for specific pairwise testing.

lines 240-245 and Table 2: Should include in footnote to Table the variables retained in the final model as adjustors. Also, need to justify for all subsets that the counts of adverse outcomes justifies multivariable adjustment (ie, should have at a ratio of > 10:1 for counts vs number of adjustors). lines 240-245: The comparison is for all 3 categories, not specifically for UT vs no or IR vs no. If those are deemed important, should specifically test.

lines 246-250: Need to provide stats testing for each pairwise comparison, of re-word the results.

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

***The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.***

- We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting.

- In methods of manuscript, please explain what a "repeat cross sectional study" is.

- Please share a description of this data base in the abstract.

- PRESENTATION OF STATS INFORMATION: P Values vs Effect Size and Confidence Intervals
While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, 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.

This is true for the abstract as well as the manuscript.

Please provide absolute values for variables, in addition to assessment of statistical significance.

We ask that you provide crude OR's followed by adjusted OR's for all variables.

- This is unclear to me from the abstract. Please tell us in methods the years used in the analysis and what you seem to have done which is to look at two 3-year epochs (2006-8 and 2012-14) and compared them.

- Since your analysis ended in 2014, you can't really imply in the conclusion that that "they are being increasingly common". You can only state that they increased between the 2 epochs you studied. In fact, almost as much time as passed from the beginning of epoch 2 (2012) to now (7 years) as from beginning of epoch 1 and 2 (6 years). As far as association of increased SMM in women w/ hysterectomy after IR or UT, please write this to be clear that its not possible to report if this is because women who were sicker BEFORE the interventions were the ones at higher risk of SMM so that the less invasive procedures were tried first. As written, the implications are that the interventions (UT, IR) are the association.

- please indicate if Bakri is a brand name.

- It seems important as well to discuss that decision making about when to try less invasive procedures vs going directly to hysterecomy cannot be gleaned from the administrative data base. Patients who are less stable (more sick) may be treated w/ less invasive procedures first, or vice versa, so maternal status as well as availability of IR procedures, etc may be important.

- Please confirm that this preceded the switch to ICD-10 which I thought occurred in 2014.

- bed number? bed volume? Bed size makes me think of twin, double, queen....

- was Tricare considered "other"?

- please tell us how you grouped the years. In the abstract, you provide data on 2006-8 and 2012-14. Later in the manuscript, you include another epoch. This all needs to be explained.

- Avoid starting a sentence w/ a numeral. Either spell it out or edit sentence to not start w/ a number).

- This should be noted in the discussion as a weakness. Your data suggests that about 60% of delivery hospitalization hysterectomies were done for reasons other than hemorrhage. Given that accreta spectrum, dysplasia, cancer would be the other major groups of hysterectomies and those don't make up close to 60% of hysterectomies in this setting, there must be some coding problems identifying atony and peripartum hysterectomy.

- Please make the 3rd primary objective information a new paragraph.

- We don't allow "in press" references. Your paper will need to be held until this paper publishes. Please adjust your references to include it as a numbered ref. with place holders for issue number, page number, etc.

- add error bars to your graphs

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. Please submit a completed STROBE checklist with your revision.

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 short title of no more than 45 characters, including spaces, for use as a running foot.

10. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word 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 1-4 may be resubmitted as-is.

Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

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 14 days from the date of this letter. If we have not heard from you by Nov 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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