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:** Oct 30, 2020
**To:** "Sybil Sailofsky" [redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-20-2407

RE: Manuscript Number ONG-20-2407

Comparison of Surgical Outcomes Following Total Laparoscopic Hysterectomy (TLH) and Total Vaginal Hysterectomy (TVH) in Large Uteri

Dear Dr. Sailofsky:

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 Nov 20, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is a retrospective cohort study comparing outcomes after total vaginal hysterectomy and total laparoscopic hysterectomy using a national database. The study is well done and the manuscript is well written.

1. Introduction Lines 89-91, is there any more recent data here?
2. Methods: Line 143, what is meant by postoperative diagnosis code, please clarify.
3. Results: Out of 391,245 hysterectomies, only 1870 vaginal hysterectomies met inclusion criteria. Can you report out of all the hysterectomies, the frequency of type of hysterectomy so readers can get an idea of the proportion of the types of hysterectomy performed in this database?
4. Discussion: I would emphasize that you controlled for removal of tubes/ovaries when taking into account the effect of shorter operative time with vaginal hysterectomy on operative morbidity.
5. Discussion: I don't think surgeons choose not to perform vaginal hysterectomy on large uteri because they are afraid of complications necessarily, but rather they lack the experience. Each surgeon is going to do the type of hysterectomy that they are more comfortable performing. Unfortunately, this is a large determinant of route of hysterectomy which this study can't address as no surgeon characteristics were collected.

Reviewer #2:

Thank you for submitting your research to the Green Journal. Your manuscript, a TLH vs TVS NSQIP database study evaluating perioperative outcomes, is well written, well designed.

Abstract: no comments

Introduction:
1. lines 101-108: this analysis seems more appropriate for the discussion section

Methods: no comments

Results: no comments

Discussion/Conclusion
1. I question the operating time assertions that are made. Your data demonstrates that a) TLH is longer than TVH, b) once adjusting for confounders, difference in operative time washed out (i.e. explained by confounders), c) operating time was an independent predictor of morbidity, d) there was no difference in morbidity between the two groups. You then assert that because TVH is independently associated with an operating time of less than two hours, and operative time was an independent predictor of morbidity, therefore "the shorter surgical time afforded by TVH in this group of patients is associated with a lower risk of major morbidity". You provide this assertion despite the evidence in your study that a) adjusting for confounders washed out the difference in time between the two surgeries, and b) there was NO difference in major or minor morbidity between the groups. This assertion of protective effect of shorter operating time of TVH on morbidity is not supported by your own data, based on a combination of two unrelated/independent secondary endpoints that contradict the primary endpoints of the study. This just does not hold up to scrutiny. Please remove this assertion in both the discussion and the conclusion.

Table 1:
1. Many parentheses remain unidentified. For instance, race, non-white: 632 (33.8) - I assume 33.8 = mean, but this is not labeled anywhere in the table.

Table 2:
1. Again, numbers in parentheses remain unidentified.

Table 3:
1. again, numbers in parentheses remain unidentified.

Thank you once again for your submission

Reviewer #3:

The submitted study "Comparison of Surgical Outcomes Following Total Laparoscopic Hysterectomy (TLH) and Total Vaginal Hysterectomy (TVH) in Large Uteri" is a retrospective cohort study evaluating surgical outcomes between total laparoscopic hysterectomy (TLH) and total vaginal hysterectomy (TVH) with uterine weight (UW) > 250 grams

1. The authors do a nice job of laying out the advantages of both minimally invasive approaches in the introduction including the advantages of both and some common potential limitations. I appreciate that their introduction is logical, supported by high quality studies, and progresses to the objective, building on existing data.

2. The strength of the size of the comparative groups helps minimize some of the bias of only a relatively few individuals performing TVH's on large uteri. With TVH as a skill that is being less commonly performed, there are likely fewer and fewer surgeons performing TVH's on large uteri. Fortunately the comparative groups are large.

3. It's unclear on the surface why patients were excluded if they underwent a TLH, and then a vaginal procedure at the same time. Please help explain. Potentially due to operative time, but if this was so, were patient's operative times included if they underwent a TVH and colporrhaphy or other procedure? It seems in that case TVH would be falsely marked as longer than it actually is.

4. In the use of the Clavien-Dindo Class for outcomes, while morbidity is listed, mortality needs to be included within the outcomes as well. It is zero for both groups, but unclear why only morbidity and not Clavien-Dindo Class V (mortality) is not included. The "cut point" of Clavien-Dindo Class that is also potentially the most interesting is class II, including transfusion rate and conversion from laparoscopic or vaginal approach to open, which other than major surgical injury is most likely to occur as an outcome.

5. Please address how patients are counted/discounted if the surgeon started with a minimally invasive approach for a large uterus (TVH or TLH) and then required conversion to an abdominal procedure and was thus counted by CPT as a TAH. If pulling charts by CPT code as you did, were these patients unintentionally excluded prior to your initial analysis? Most issues I have seen in practice and with colleagues have not been transfusion or injury issues, but required conversion to an open procedure to complete.

6. Under discussion limitations, it is good that you further address issues of vaginal access and descent and selection bias limitations in these situations. It is clear from the tone throughout the paper that the authors prefer TVH, but there are real limitations in patient selection that are included in multiple referenced ACOG, JMIG, and other best-practice algorithms that are lightly touched on here. It is a good addition of lines 264-266 to address who the specific cohort here actually represents. In the conclusion, please continue to provide the recommendation with this caveat, and try not to overreach to

a generalizable recommendation that anyone is equally a TLH and TVH candidate. There are also limitations in pain assessment or endometriosis diagnosis and treatment with TVH.

7. The timeframe of patient collection for this (2014-2018) spans the time when power morcellation was just being banned (April 2014 FDA statement) and new techniques were being developed and implemented. Was this addressed in potential time differences as a confounder with morcellation?

8. In the abstract conclusion lines 78-79, "TVH is not associated with an increased (need to add "composite") risk of major surgical morbidity or other adverse surgical outcomes." TVH is shown here to be statistically more likely to cause transfusion and intraoperative cystotomy.

9. The conclusion statement may benefit from some rewording. It states there is an association with operative time and TVH (though not statistically significant in adjusted OR) and then states because of this there may be a lower risk. The better statement would likely be something like: There is no statistical difference in operative time when adjusting for confounders between TLH and TVH for large uteri, and composite major morbidity (and mortality needs to be added from prior comment) are equivalent in this studied patient population. Uterine weight alone should not be a contraindication to a vaginal surgical approach to hysterectomy, and should be informed within the scope of best surgical approaches. TVH is a safe, effective option for many women with large uteri and consideration should be given to extending the uterine weight limits larger than the current recommendation of 12 weeks size (~280g).

10. In the flow sheet of figure 1, it shows that all "concomitant pelvic floor procedures" were excluded, though in materials and methods line 133-134 "any pelvic reconstructive procedure excepting those associated with a vaginal hysterectomy code" were excluded. Were A/P repair, suspension etc excluded completely, or included if it was at the time of TLH and kept if TVH performed? Please clarify.

STATISTICAL EDITOR COMMENTS:

Table 1: Need to stipulate that the format includes n(%) and include in footnote that the groups were matched on these characteristics.

Table 2: Again, need to include format of n(%) in Table or footnote. Lines 193-194, true, the median LOS was 1 day for each group, but there was a significant statistical difference by rank-sum test ($p < 0.001$).

Table 3: Again, need to specify format of n(%). There are some inconsistencies/typos and/or miscalculations in this Table vs text. For example, 23/3740 does not equal 0.3%, but rather 0.6% and 48/3740 does not equal 0.6%, but rather 1.3%. Assuming that the correct entries would be 0.3% and 0.6%, the counts would be 11 or 12 for the former and 22 or 23 for the latter. Need to enter the correct values in the Table and then verify the results of Fisher's test (line 163). Also, the comparison of transfusion rates yields Fisher's test $p = 0.06$, not .02, need to correct in Table and text. Also, need to tabulate the counts of composite for major complications (5.3% vs 4.3%), which from those %s and using Fisher's test has $p = 0.10$, not 0.31, so need to clarify. For the p-values for intraoperative cysto (0.8% vs 0.3%, $p = 0.01$) for intraop ureteral injury (0.6% vs 0.2%, $p = 0.02$), those values need clarification and verification of the p-values.

Table 4: Need to include as a footnote which variables were retained in the final model for computation of the aORs. Also, would likely be of more clinical utility to index the change vs operating time to longer times (e.g., 10 minute intervals) and uterine weight to more than 1 gram increments. Also, are comorbidities indexed as any vs none or incremented by the number of comorbidities?

EDITORIAL OFFICE COMMENTS:

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

A. OPT-IN: Yes, please publish my point-by-point response letter.
B. OPT-OUT: No, please do not publish my point-by-point response letter.

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

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

3. 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. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

5. 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.

6. All submissions that are considered for potential publication are run through CrossCheck for originality. There are lines of text in the Abstract and Methods that match too closely to previously published works by Sheyn, Sailofsky, et al. Please be sure to cite all information and data used from previous papers.

7. 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 observational studies (ie, STROBE), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE). 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, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

8. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

9. 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.

10. 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).

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

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

12. 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.

13. The commercial name (with the generic name in parentheses) may be used once in the body of the manuscript. Use the generic name at each mention thereafter. Commercial names should not be used in the title, précis, or abstract.

14. 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.

15. 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%").

16. 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.

17. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital

object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

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

18. Figure 1: Please check initial n values (391,245-48,286=342,959). Please upload as a figure file on Editorial Manager.

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

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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.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors' comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Nov 20, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Associate Editor, Gynecology

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

[redacted]

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# Cover Letter

November 15, 2020

Re: Revision and resubmission of manuscript, "Comparison of Surgical Outcomes Following Total Laparoscopic Hysterectomy (TLH) and Total Vaginal Hysterectomy (TVH) in Large Uteri."

The Editors
*Obstetrics & Gynecology*
409 12th Street, SW
Washington, DC 20024-2188

Dear Editors,

We are submitting our revised manuscript with changes specifically addressing the reviewers' and editors' comments and critiques. As the lead author, I re-affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and any discrepancies from the study as planned have been explained. Further, we have followed the STROBE guidelines throughout. We are only submitting the manuscript to *Obstetrics & Gynecology* and will not submit to any other journal until a final decision is rendered. This abstract was presented at the 49th Annual AAGL Conference on 11/09/2020.

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REVIEWER COMMENTS:

Reviewer #1:

This is a retrospective cohort study comparing outcomes after total vaginal hysterectomy and total laparoscopic hysterectomy using a national database. The study is well done and the manuscript is well written.

1. Introduction Lines 89-91, is there any more recent data here?

***Additional citations are provided regarding residency surgical volume (Lines 93-98) however, since the majority of studies comparing TLH and TVH, particularly for large uteri, are retrospective, comparative outcome literature is limited to articles cited in this manuscript.***

2. Methods: Line 143, what is meant by postoperative diagnosis code, please clarify.

***This meant that should malignancy be diagnosed intra-operatively, and therefore added as a post-operative diagnosis in the operative report and coded as such, these surgeries were***

***excluded. In the event that this is referring to "postoperative diagnosis" with regard to propensity score matching, this was an editing error and has been deleted.***

3. Results: Out of 391,245 hysterectomies, only 1870 vaginal hysterectomies met inclusion criteria. Can you report out of all the hysterectomies, the frequency of type of hysterectomy so readers can get an idea of the proportion of the types of hysterectomy performed in this database?

***This was added to the results section, line 192-196.***

4. Discussion: I would emphasize that you controlled for removal of tubes/ovaries when taking into account the effect of shorter operative time with vaginal hysterectomy on operative morbidity.

***Added lines 273-275; This is an excellent point and we added this to the discussion. There may be some contribution to differences in operative time (as explained in the text).***

5. Discussion: I don't think surgeons choose not to perform vaginal hysterectomy on large uteri because they are afraid of complications necessarily, but rather they lack the experience. Each surgeon is going to do the type of hysterectomy that they are more comfortable performing. Unfortunately, this is a large determinant of route of hysterectomy which this study can't address as no surgeon characteristics were collected.

***This is also a great point and we have amended the discussion/conclusion to reflect this.***

Reviewer #2:

Thank you for submitting your research to the Green Journal. Your manuscript, a TLH vs TVS NSQIP database study evaluating perioperative outcomes, is well written, well designed.

Abstract: no comments

Introduction:
1. lines 101-108: this analysis seems more appropriate for the discussion section
***We appreciate the Reviewer's comments, however, we feel that this portion of the introduction provides important background for the necessity of this study and we respectfully would like to have it remain in this position. If the editors feel it is important to position these statements in the discussion, we would be happy to do so.***

Methods: no comments

Results: no comments

Discussion/Conclusion
1. I question the operating time assertions that are made. Your data demonstrates that a) TLH is longer than TVH, b) once adjusting for confounders, difference in operative time washed out (i.e. explained by confounders), c) operating time was an independent predictor of morbidity, d) there was no difference in morbidity between the two groups. You then assert that because TVH is independently associated with an operating time of less than two hours, and operative time was an independent predictor of morbidity, therefore "the shorter surgical time afforded by TVH in this group of patients is associated with a lower risk of major morbidity". You provide this assertion despite the evidence in your study that a) adjusting for confounders washed out the difference in time between the two surgeries, and b) there was NO difference in major or minor morbidity between the groups. This assertion of protective effect of shorter operating time of TVH on morbidity is not supported by
your own data, based on a combination of two unrelated/independent secondary endpoints that contradict the primary endpoints of the study. This just does not hold up to scrutiny. Please remove this assertion in both the discussion and the conclusion.

***We have clarified this portion of the discussion and the conclusion. After adjusting for confounders using logistic regression we found that the route of surgery was not independently associated with an increased risk of major morbidity, however, longer operating times were associated with major morbidity independent of surgical route. We also found on logistic regression that the vaginal route is associated with shorter operating time, even after adjusting for variables that may increase operating time for laparoscopy including uterine weight, adnexal procedures and lysis of adhesions. Thus TVH may be associated with less morbidity compared to TLH by virtue of the vaginal approach being associated with shorter operating time. We hope that this provides more clarity to our discussion.***

Table 1:
1. Many parentheses remain unidentified. For instance, race, non-white: 632 (33.8) - I assume 33.8 = mean, but this is not labeled anywhere in the table.

Table 2:
1. Again, numbers in parentheses remain unidentified.

Table 3:
1. again, numbers in parentheses remain unidentified.

***We have clarified the notations for the tables, thank you for pointing this out and we apologize for the oversight***

Thank you once again for your submission

Reviewer #3:

The submitted study "Comparison of Surgical Outcomes Following Total Laparoscopic Hysterectomy (TLH) and Total Vaginal Hysterectomy (TVH) in Large Uteri" is a retrospective cohort study evaluating surgical outcomes between total laparoscopic hysterectomy (TLH) and total vaginal hysterectomy (TVH) with uterine weight (UW) > 250 grams

1. The authors do a nice job of laying out the advantages of both minimally invasive approaches in the introduction including the advantages of both and some common potential limitations. I appreciate that their introduction is logical, supported by high quality studies, and progresses to the objective, building on existing data.
***We appreciate this comment. Thank you.***

2. The strength of the size of the comparative groups helps minimize some of the bias of only a relatively few individuals performing TVH's on large uteri. With TVH as a skill that is being less commonly performed, there are likely fewer and fewer surgeons performing TVH's on large uteri. Fortunately the comparative groups are large.

***We appreciate this comment. Thank you.***

3. It's unclear on the surface why patients were excluded if they underwent a TLH, and then a vaginal procedure at the same time. Please help explain. Potentially due to operative time, but if this was so, were patient's operative times included if they underwent a TVH and colporrhaphy or other procedure? It seems in that case TVH would be falsely marked as longer than it actually is.

***We excluded any procedure that contained additional CPT except those listed for hysterectomy and cystoscopy (52000). What we were referring to with the statement that any additional procedure with an additional pelvic reconstructive CPT code was excluded other than hysterectomy, were hysterectomy codes 58267 and 58270 which include in their description enterocele repair, most likely referring to a McCall's culdoplasty. This was better clarified in the methodology to make it clear that only surgeries which included only hysterectomy codes and no other extraneous CPT codes.***

4. In the use of the Clavien-Dindo Class for outcomes, while morbidity is listed, mortality needs to be included within the outcomes as well. It is zero for both groups, but unclear why only morbidity and not Clavien-Dindo Class V (mortality) is not included. The "cut point" of Clavien-Dindo Class that is also potentially the most interesting is class II, including transfusion rate and conversion from laparoscopic or vaginal approach to open, which other than major surgical injury is most likely to occur as an outcome.

***We have amended the methods and results section to reflect that we did include analysis of mortality, but that the mortality rate was 0 in both groups. We also agree with the reviewer that the most interesting outcomes are the ones that happen most often, i.e. transfusion, and we did perform separate logistic regression analyses for these. Unfortunately, because there is no way to firmly distinguish cases that were planned abdominal hysterectomies from those***

***that were converted from a minimally invasive approach, however, studies for both TLH and TVH for large uteri have suggested that this is not a common occurrence.***

5. Please address how patients are counted/discounted if the surgeon started with a minimally invasive approach for a large uterus (TVH or TLH) and then required conversion to an abdominal procedure and was thus counted by CPT as a TAH. If pulling charts by CPT code as you did, were these patients unintentionally excluded prior to your initial analysis? Most issues I have seen in practice and with colleagues have not been transfusion or injury issues, but required conversion to an open procedure to complete.

***Please see response to point #4. Unfortunately, it was not possible to discern whether cases were started as a TLH or TVH, and then converted to open (TAH). Those cases would have only been coded as a TAH, and therefore were excluded. The discussion on limitations was broadened to reflect this, lines: 289-293***

6. Under discussion limitations, it is good that you further address issues of vaginal access and descent and selection bias limitations in these situations. It is clear from the tone throughout the paper that the authors prefer TVH, but there are real limitations in patient selection that are included in multiple referenced ACOG, JMIG, and other best-practice algorithms that are lightly touched on here. It is a good addition of lines 264-266 to address who the specific cohort here actually represents. In the conclusion, please continue to provide the recommendation with this caveat, and try not to overreach to a generalizable recommendation that anyone is equally a TLH and TVH candidate. There are also limitations in pain assessment or endometriosis diagnosis and treatment with TVH.

***We agree with the reviewer and have amended the conclusion to better reflect the findings.***

7. The timeframe of patient collection for this (2014-2018) spans the time when power morcellation was just being banned (April 2014 FDA statement) and new techniques were being developed and implemented. Was this addressed in potential time differences as a confounder with morcellation?

***We were not able to evaluate whether power-morcellation or vaginal/mini-laparotomy morcellation was performed, however, in the case of power-morcellation for TLH , we would expect a shorter operating time; and if cold-knife morcellation was attempted for TLH, it would be expected that a similar amount of time/effort would be required to morcellate the uterus at the time of TVH as TLH, we have added this to the discussion as well.***

8. In the abstract conclusion lines 78-79, "TVH is not associated with an increased (need to add "composite") risk of major surgical morbidity or other adverse surgical outcomes." TVH is shown here to be statistically more likely to cause transfusion and intraoperative cystotomy.

***This was corrected.***

9. The conclusion statement may benefit from some rewording. It states there is an association with operative time and TVH (though not statistically significant in adjusted OR) and then states

because of this there may be a lower risk. The better statement would likely be something like: There is no statistical difference in operative time when adjusting for confounders between TLH and TVH for large uteri, and composite major morbidity (and mortality needs to be added from prior comment) are equivalent in this studied patient population. Uterine weight alone should not be a contraindication to a vaginal surgical approach to hysterectomy, and should be informed within the scope of best surgical approaches. TVH is a safe, effective option for many women with large uteri and consideration should be given to extending the uterine weight limits larger than the current recommendation of 12 weeks size (~280g).

***We agree with the reviewer and have amended the conclusion to better reflect this. We appreciate the suggestion for textual changes.***

10. In the flow sheet of figure 1, it shows that all "concomitant pelvic floor procedures" were excluded, though in materials and methods line 133-134 "any pelvic reconstructive procedure excepting those associated with a vaginal hysterectomy code" were excluded. Were A/P repair, suspension etc excluded completely, or included if it was at the time of TLH and kept if TVH performed? Please clarify.

***This was clarified, please see response to point #3. Only hysterectomy codes were included, that is 2 codes for hysterectomy also include enterocele repair; but separate codes such as for AP repair, apical suspension were excluded.***

STATISTICAL EDITOR COMMENTS:

Table 1: Need to stipulate that the format includes n(%) and include in footnote that the groups were matched on these characteristics.

***This was corrected***

Table 2: Again, need to include format of n(%) in Table or footnote. Lines 193-194, true, the median LOS was 1 day for each group, but there was a significant statistical difference by rank-sum test ($p < 0.001$).

***The notation was corrected. We have edited the results section regarding this table, 210-211.***

Table 3: Again, need to specify format of n(%). There are some inconsistencies/typos and/or miscalculations in this Table vs text. For example, 23/3740 does not equal 0.3%, but rather 0.6% and 48/3740 does not equal 0.6%, but rather 1.3%. Assuming that the correct entries would be 0.3% and 0.6%, the counts would be 11 or 12 for the former and 22 or 23 for the latter. Need to enter the correct values in the Table and then verify the results of Fisher's test (line 163). Also, the comparison of transfusion rates yields Fisher's test $p = 0.06$, not .02, need to correct in Table and text. Also, need to tabulate the counts of composite for major complications (5.3% vs 4.3%), which from those %s and using Fisher's test has $p = 0.10$, not 0.31, so need to clarify. For

the p-values for intraoperative cysto (0.8% vs 0.3%, p =0.01) for intraop ureteral injury (0.6% vs 0.2%, p = 0.02), those values need clarification and verification of the p-values.

***We apologize for the errors found the in tables, we believe these happened because of using a prior manuscripts table as a template. These were corrected, and all tables and models were re-ran to identify any more mistakes. There were no further mistakes identified, other than those that were corrected in the table. And appropriate corresponding changes were made in the manuscript. The conclusions did not change, only the value of the p-values. We utilized as primary outcome the occurrence of* any *complication, thus the sum total of the complications for each group would be greater than the number of patients experiencing any complication; to check this we did identify 198 patients who had TLH and 81 who underwent TLH who had at least one major complication. Additionally, to compare the difference between groups we used Wilcoxon rank-sum, which might account for the difference in results. If you believe the Fisher's exact test is more appropriate here, we would be happy to utilize it, and confirm that the p-value with the Fisher's test is = 0.10***

Table 4: Need to include as a footnote which variables were retained in the final model for computation of the aORs. Also, would likely be of more clinical utility to index the change vs operating time to longer times (e.g., 10 minute intervals) and uterine weight to more than 1 gram increments. Also, are comorbidities indexed as any vs none or incremented by the number of comorbidities?

***A footnote was added to table 4. We have changed the intervals for operating time to 10 minutes and uterine weight was converted to increments of 25 grams. The logistic model was re-run and corrections were made to the table, the impact of these changes, were minor on other variables as expected. The comorbidities are indexed as incremental, this was clarified in the methods section.***

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

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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.

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4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

***The following text was added to the methodology: NSQIP also collects data regarding sex, race and ethnicity; these are reported by the patient and recorded in the medical record. The reason for this type of data is primarily for demonstrating that the NSQIP sample is representative of the national population. We chose to include race and ethnicity in this study to determine if racial and ethnic disparities contribute to differences in outcome between TVH and TLH for large uteri.***

5. 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.

***The following text is included in the manuscript: The NSQIP database procures data on over 150 perioperative variables, including preoperative comorbidities, intraoperative variables, and 30-day mortality and morbidity outcomes for multiple surgeries. Data from over 600 participating hospitals are collected by certified Surgical Clinical Reviewers and data quality is maintained by standardizing training of all reviewers as well as intermittent inter-rater reliability audits of participating sites. Data from each site is obtained from medical chart review as well as direct contact with patients. NSQIP reports a 95% success rate in capturing outcomes on all cases within the database. The database uses Current Procedural Terminology (CPT™) to determine all procedures.***

6. All submissions that are considered for potential publication are run through CrossCheck for originality. There are  lines of text in the Abstract and Methods that match too closely to previously published works by Sheyn, Sailofsky, et al. Please be sure to cite all information and data used from previous papers.

***The similarities are likely in the methodology section due to description of the NSQIP data collection methodology. We chose to include this information even though it has been previously published as many readers may not be familiar with NSQIP and may not take the time to review prior cited manuscripts with regard to data collection. If the editors wish for us to remove this text we would be happy to do so.***

7. 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 observational studies (ie, STROBE), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE). 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, RECORD,
CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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8. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data

definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

***No issue with reVITALize definitions***

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***This research is 19 typed, double-spaced pages (3032 words).***

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* 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).

***As stated on the title page, this abstract was presented at the 49th Annual AAGL Conference on 11/09/2020.***

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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%").

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