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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)*
- Email correspondence between the editorial office and the authors*

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

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

obgyn@greenjournal.org.
Date: Mar 26, 2019
To: "Vrunda Bhavsar Desai"
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-269

RE: Manuscript Number ONG-19-269

Laparoscopic Hysterectomy Route, Resource Use, and Outcomes: Change after Power Morcellation Warning

Dear Dr. Desai:

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

REVIEWER COMMENTS:

Reviewer #1: This is a retrospective analysis of NSQIP data to look at the change in the utilization of LSH vs. TLH/LAVH after the FDA safety statement regarding power morcellation. The results and conclusions of this study were strengthened with the use of an interrupted time series approach that accounted for hysterectomy practice trends.

1. Line 119 - Did you consider excluding women having a hysterectomy as part of surgery for pelvic organ prolapse (POP)? These procedures increase operative time, RVUs and cost. I wonder if this would decrease total RVUs in the LSH group as sacrocolpopexy is often performed with an LSH for POP. If women had a CPT code for sacrocolpopexy were they included?

2. Line 164 - RVUs are driven by type of procedure (CPT code) and do not accurately reflect complexity. They are highly subjective and predisposed to significant external forces.

3. Line 308 - How was operative time defined? Was it time of closure of skin, etc. If concomitant procedures were performed how was this controlled for or identified?

4. Line 316 - Length of stay has also decreased because of hospitals utilizing ERAS protocols.

Reviewer #2: This is an interesting descriptive study from the large national NSQIP database examining hysterectomy trends, outcomes, and resource allocation with data from approximately 145,000 women before and after the morcellation warning from the FDA in 2014. Findings included a rise in all laparoscopic hysterectomies although there was a decrease in laparoscopic supracervical hysterectomies. There was a change in resource allocation; however, outcomes remained unchanged. After the warning, women undergoing laparoscopic supracervical hysterectomies were more likely to be undergoing prolapse surgery or to have more serious medical co-morbidities. Not being able to pull out robotic hysterectomy information separately is a big limitation of this study.

In the abstract, in line 67 - This sentence needs to be reworded in order to understand the meaning: "and slower reduction in use of inpatient hospitalization for TLH/LAVH".

The discussion should include more background and comments on supracervical hysterectomies to include other benefits of removing the cervix such as decreased risk of cervical cancer, no need for cervical cancer surveillance, and post-operative
bleeding. In addition, other purported benefits of supracervical hysterectomy are not evidenced based to include sexual function. The lower rate of supracervical hysterectomy found in your study might be more right-sized reserving this procedure for patients undergoing prolapse correction surgery and using the cervix as a barrier for the mesh as well as patients who need quicker procedures because of medical co-morbidities. It is also more likely that surgeons did supracervical hysterectomies because they took less time and require less laparoscopic skill.

While you hypothesized why you found an increased in hospitalization but a decrease in length of stay, it would also be nice for you to comment on what that means in terms of cost differential. If you are unable to comment, please state this as a limitation in your discussion regarding resource allocation.

Line 322, the word should be "voluntary" not "voluntarily"

Reviewer #3: This submission examines and reports on the change, utilization, resource use and outcomes for women undergoing laparoscopic hysterectomy before and after the April 2014 FDA warning regarding power morcellation using NSQIP data from 2012-16. The report appears well constructed and is well written. The fact that background trends are accounted for using an interrupted time series approach seems novel and valuable.

However, upon further reflection, it seems difficult to make that much of the data reported when the numbers of laparoscopic hysterectomies are viewed in isolation from the numbers of vaginal and abdominal procedures for benign indications performed during the same period. The authors seems to have access to the numbers for abdominal and vaginal routes of hysterectomy. I do not understand why they did not include theses and address them as well? With this in mind, other than the "interrupted time series" approach, it seems that there is limited new information here that has not already been reported in the articles the authors reference (ref 14-17).

Line 207-209: "Overall, our sample included 145,746 women who underwent benign hysterectomies in 2012-2016. Within this cohort, 83,440 underwent laparoscopic hysterectomy, including 10,340 women undergoing LSH and 73,000 women undergoing TLH/LAVH."
1/ Does this mean that 62306 underwent TAH (145K - 83K)?
2/ Consider adding percentages

In other words, Related to this, understanding how the rate of abdominal hysterectomy change using an interrupted time series analysis also seems important and relevant to the findings presented here.

Separately, the discussion should probably address previous reports about increased after the FDA warning for the sub-group of patients undergoing myomectomy: From https://www.medscape.com/viewarticle/895039

"Overall, major and minor complications remained stable before and after the FDA-issued warning. But among the subset of 25,571 women (33.9%) who underwent hysterectomy for uterine fibroids, major complications significantly increased after the FDA-issued warning from 1.9% to 2.4% (adjusted odds ratio [OR], 1.23; P = .02), and minor complications significantly increased from 2.7% to 3.3% (adjusted OR, 1.21; P = .01).

Further thoughts:
1/ The trend toward decreased SCH may be due partially to increased surgeon skill and expertise with TLH. TLH is a technically more difficult procedure. Even if a procedure was completed as a TLH, abdominal morcellation still may have occurred. In my own practice, I continue to perform abdominal morcellation for very large uteri after TLH. (I just switched to contained manual morcellation and stopped using power morcellators.
2/ While they commented on their limitations to include only voluntary NSQIP hospitals, it may have been interesting to see if there were trends between hospital type (i.e, academic, community, combination).

Minor point: Line 115-6: "To adequately capture secular trends in practice patterns and isolate changes induced by the FDA safety warning, our analysis included a broad time period from 2012 to 2016." I am not sure what is meant here. "Secular" to me simply means non-religious or non-spiritual. I suggest this be rephrased.

Thank you for the opportunity to review this submission.

Reviewer #4: Commend on a good manuscript.

Strength of the manuscript is that takes into account secular trends in adoption of laparoscopic hysterectomy (LH) by interrupted time series approach, and tries to break down LH into LSH versus TLH/LAVH.
Found no increase risk of 30-day surgical complications during study period.

There is STROBE checklist at the end of the manuscript. This does not seem to be mentioned in the manuscript.

Would like to see, or recommend considering, the following in the manuscript:

Does the transient decrease in overall rate of LH correspond to increase in TAH? While this might be presumed, would be good to confirm.

What might account for the shift of TLH/LAVH to LSH? Can uterine weight data be obtained? Are larger uteri removed by TAH, with smaller uteri converted from TLH/LAVH to LSH?

The reason for the ban is risk of malignancy found in the specimen. What were the rates of cancer - leiomyosarcoma or uterine cancer - by route?

Perhaps there should be some discussion that the risk to the patient of spreading cancer cells is not just from power morcellation, but should include all morcellation, including manual morcellation.

This was mentioned as a limitation of the study ie. the lack of data or information exactly on specimen removal, but at least might deserve mention a possible explanation for the transient decrease in the only temporary decline in rate of LH or a mention of area of future research...

Did surgeons just learn to switch from power to manual morcellation in a bag?

STATISTICAL EDITOR COMMENTS:

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

lines 63 and Table 2: The relationship is more nuanced. If the same metric were compared (post warning aOR, which is the same metric used to cited 0.49 (0.45-0.53) for LSH, then the change was NS: aOR = 1.01 (0.96-1.06). Should compare like with like in the sentence or elaborate on the description of what is being compared.

lines 70-71 and Table 4: Although it is reassuring that there were no statistical differences in rates or odds, the rates of complications were all relatively small and there was insufficient power, even given the large samples at hand, to generalize (with the usual criteria of power) the NS findings.

lines 66-69: For consistency and without loss of information to the reader, should round ORs and CIs to nearest .01.

Fig 1, A, B, C: Since the Tables reflect the trends of the two epochs, it would be informative to add to the legends for 1A, 1B and 1C to comment on the numerical and statistical differences at the end date (Q4 of 2016) between the observed vs hypothetical values based on extrapolating trends observed prior to FDA warning. That is, 1B is clearly different, but are the observed differences for the end date for 1A and 1C statistically different, or did they eventually to the prior trend?

EDITOR COMMENTS:

1. Thank you for submitting this interesting work. Please specifically note the concerns of the statistical editor. It does appear that you have data available about abdominal procedures. Is there some reason you didn't include them to paint a broad picture of the practice of hysterectomy in this country? While I think it would add substantially to the strength of your paper, it is not a "deal breaker" if you choose not to include this. My preference is that you do so, however.

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.***

- The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances.
- "Utilization" isn't a sentient thing so it wouldn't experience anything. Perhaps "There was a transient reduction in the utilization of laparoscopic hysterectomy after...."

- aged 18 years or older

- Use commas throughout this list. You would be using semicolons if there list had complex elements in it.

- the virgules are fine here as they are part of your data set

- if she went to a different hospital, these would not be caught by NSQIP and that should be listed as limitation in discussion

- did you have any information on the specialty or sub-specialty of the surgeons? Can you describe the type of hospital (community? Academic? Tertiary? )

- unchanged from the post FDA warning rate of 4.7% or from 11.4%?

- I’ll be curious to see your speculation as to why this would be. It seems that large myomoatous uterus removal fell pre/post without ability to use power morcellation in these cases-as shown perhaps by your shift in indications for these. Do you think the time increased because of concomitant procedures for prolapse, etc or do you surmise some other reason?

- We do no allow authors to describe variables or outcomes in terms that imply a difference (such us of the terms “trend” or “tendency” or “marginally different”) unless there is a statistical difference. Please edit here and throughout.

- can you report any differences in the weight of uterus’s removed pre/post and by different methods?

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, as well as subsequent author queries. 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:

1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

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

4. Obstetrics & Gynecology follows the Good Publication Practice (GPP3)* guideline for manuscripts that report results that are supported or sponsored by pharmaceutical, medical device, diagnostics and biotechnology companies. The GPP3 is designed to help individuals and organization maintain ethical and transparent publication practices.

(1) Adherence to the GPP3 guideline should be noted in the cover letter.

(2) For publication purposes, the portions of particular importance to industry-sponsored research are below. In your cover letter, please indicate whether the following statements are true or false, and provide an explanation if necessary:
(2a) All authors had access to relevant aggregated study data and other information (for example, the study protocol) required to understand and report research findings.
(2b) All authors take responsibility for the way in which research findings are presented and published, were fully involved at all stages of publication and presentation development and are willing to take public responsibility for all aspects of the work.
(2c) The author list accurately reflects all substantial intellectual contributions to the research, data analyses, and publication or presentation development. Relevant contributions from persons who did not qualify as authors are disclosed in the acknowledgments.
(2d) The role of the sponsor in the design, execution, analysis, reporting, and funding (if applicable) of the research has been fully disclosed in all publications and presentations of the findings. Any involvement by persons or organizations with an interest (financial or nonfinancial) in the findings has also been disclosed.
(2e) All authors have disclosed any relationships or potential competing interests relating to the research and its publication or presentation.
The abstract should contain an additional heading, "Funding Source," and should provide an abbreviated listing of the funder(s).

In the manuscript, a new heading—"Role of the Funding Source"—should be inserted before the Methods and contain a detailed description of the sponsor's role as well as the following language:

"The authors had access to relevant aggregated study data and other information (such as study protocol, analytic plan and report, validated data table, and clinical study report) required to understand and report research findings. The authors take responsibility for the presentation and publication of the research findings, have been fully involved at all stages of publication and presentation development, and are willing to take public responsibility for all aspects of the work. All individuals included as authors and contributors who made substantial intellectual contributions to the research, data analysis, and publication or presentation development are listed appropriately. The role of the sponsor in the design, execution, analysis, reporting, and funding is fully disclosed. The authors' personal interests, financial or non-financial, relating to this research and its publication have been disclosed." Authors should only include the above statement if all of it is true, and they should attest to this in the cover letter (see #2, above).


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

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

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.
12. Please review the journal’s Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

13. 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.

14. 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.

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.

15. 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.

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

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Apr 16, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r) Please contact the publication office if you have any questions.
April 26, 2019

Nancy C. Chescheir, MD
Editor in Chief
Obstetrics & Gynecology

Dear Dr. Chescheir:

I am writing to resubmit our manuscript, “Laparoscopic Hysterectomy Route, Resource Use, and Outcomes: Change after Power Morcellation Warning,” for reconsideration for publication in *Obstetrics & Gynecology*.

As instructed, we have uploaded a track changes version of the revised manuscript, as well as a detailed response letter containing our point-by-point response to comments from reviewers and editors. Since the track changes function may affect page numbers, we also uploaded a clean version manuscript to make sure that all page numbers and paragraph numbers noted in our response letter are correctly reflected.

This study was approved by Yale University Human Investigation Committee and has IRB approval. Additionally, there was no commercial support for this work, I changed employment following completion of the data analysis and during the writing of the manuscript. I maintain an adjunct clinical appointment at Yale School of Medicine and can certify that CooperSurgical had no support of this work.

This manuscript is original work submitted solely to *Obstetrics & Gynecology* and not under consideration for publication elsewhere. All authors have approved of this submission and agree to not submit elsewhere until a final decision is made by the Editors of *Obstetrics & Gynecology*. I, the lead author, affirm 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. Thank you very much for considering our manuscript. We sincerely appreciate your time and look forward to your response.

Best Regards,

Vrunda Bhavsar Desai, MD
Adjunct Assistant Professor of Obstetrics, Gynecology and Reproductive Sciences
REVIEWER COMMENTS:

Reviewer #1:

This is a retrospective analysis of NSQIP data to look at the change in the utilization of LSH vs. TLH/LAVH after the FDA safety statement regarding power morcellation. The results and conclusions of this study were strengthened with the use of an interrupted time series approach that accounted for hysterectomy practice trends.

1. Line 119 - Did you consider excluding women having a hysterectomy as part of surgery for pelvic organ prolapse (POP)? These procedures increase operative time, RVUs and cost. I wonder if this would decrease total RVUs in the LSH group as sacrocolpopexy is often performed with an LSH for POP. If women had a CPT code for sacrocolpopexy were they included?

Response: We appreciate this comment. Since our research objective was to characterize the overall practice pattern of laparoscopic hysterectomy, we included hysterectomies performed laparoscopically for all benign indications. We did not exclude women who underwent a hysterectomy for pelvic organ prolapse or women who had a Current Procedural Terminology (CPT) code for sacrocolpopexy. Pelvic organ prolapse is among the most common reasons for hysterectomy and accounts for nearly 20% of laparoscopic hysterectomies nationwide (Desai et al. 2017; Jeppson et al. 2014). Hence these patients represent a substantial portion of the study population. Excluding them would preclude us from providing an accurate representation of the current practice of benign laparoscopic hysterectomy. Additionally, as noted in our Materials and Methods section (please see page 10 paragraph 3 in manuscript), all multivariable regression analyses in our study adjusted for patients’ diagnosis category (which includes pelvic organ prolapse). Hence our estimated effect of the U.S. Food and Drug Administration (FDA) safety warning of power morcellation on operative time and other resource use reflects the net effect independent of changes in patients’ surgical indications over time.

References:

2. Line 164 - RVUs are driven by type of procedure (CPT code) and do not accurately reflect complexity. They are highly subjective and predisposed to significant external forces.

Response: Thank you for this comment. We recognize that relative value units (RVUs) are tied to reimbursement and may be influenced by policy and other external factors. However, we would like to clarify that the specific RVU measure used in our analysis was the “work” RVU. Unlike the overall RVU used in reimbursement policies which additionally factors in practice expenses and medical liability insurance, the “work” component RVU intends to reflect the time and effort needed for a physician to perform the procedure and hence should reasonably capture the surgical complexity. This work RVU measure is one of the standard risk factors used in the validated American College of Surgeons National Surgical Quality Improvement Program (NSQIP) surgical risk calculator (Liu et al. 2016), and has been shown to be a strong predictor for surgical complications (Glasgow et al. 2014). Multiple prior studies evaluating outcomes of hysterectomies have used work RVU to account for differences in surgical complexity (Khavanin et al. 2013; Harris et al. 2016). Given these considerations, we have chosen to retain this measure in our analysis.

References:


3. Line 308 - How was operative time defined? Was it time of closer of skin, etc. If concomitant procedures were performed how was this controlled for or identified?

Response: Our study used the American College of Surgeons NSQIP participant use data file. Per the NSQIP operations manual, operative time is defined as time from incision to completion of all procedure related activities. There is no separation of times for concomitant procedures. When concomitant procedures are performed, their time is
included in the total operative time. We have revised our Materials and Methods section to clarify this definition of operative time. Specifically, we stated:

“For resource utilization, we evaluated each patient’s total operative time (defined as time from incision to completion of all procedure related activities in minutes), …”
(Please see page 8 paragraph 3 in manuscript.)

4. Line 316 - Length of stay has also decreased because of hospitals utilizing ERAS protocols.

Response: We appreciate this suggestion. The American College of Obstetricians and Gynecologists (ACOG) issued a Committee Opinion in 2018 encouraging the use of Enhanced Recovery After Surgery (ERAS) pathways and one major benefit of ERAS was shorter hospital stay. Although the ERAS protocols might not be widely used in gynecologic surgeries during our study period (2012-2016), some institutions might have adopted them early which could potentially confound the decreased length of stay in the post-warning period observed in our study. Unfortunately the NSQIP data does not contain information about use of ERAS precluding us from formally testing this hypothesis. In response to this comment, we revised our Discussion section to acknowledge this possible confounding factor. Specifically, we stated:

“Third, length of stay shortened among inpatient TLH procedures, which may reflect a shift of lower-risk patients from the outpatient to inpatient setting or potential confounding effect of Enhanced Recovery After Surgery protocols adopted in recent years.” (Please see page 16 paragraph 2 in manuscript.)

Reference:

Reviewer #2:

This is an interesting descriptive study from the large national NSQIP database examining hysterectomy trends, outcomes, and resource allocation with data from approximately 145,000 women before and after the morcellation warning from the FDA in 2014. Findings included a rise in all laparoscopic hysterectomies although there was a decrease in laparoscopic supracervical hysterectomies. There was a change in resource allocation; however, outcomes remained unchanged. After the warning, women undergoing laparoscopic supracervical hysterectomies were more likely to be undergoing prolapse surgery or to have more serious medical co-morbidities. Not being able to pull out robotic hysterectomy information separately is a big limitation of this study.

Response: We thank the reviewer for the thorough review. We recognize that not being able to separate robotic-assisted hysterectomy from other laparoscopic hysterectomy is a limitation. This is because the dataset used in our analysis relied on CPT codes to document procedures while there is not a dedicated CPT code to indicate robotic-assisted
hysterectomy. We have explicitly acknowledged this limitation in our Discussion section as follows:

“Finally, our classification of surgical routes relied on CPT codes which could not distinguish robotic-assisted versus conventional laparoscopic surgery.” (Please see page 17 paragraph 1 in manuscript.)

In the abstract, in line 67 - This sentence needs to be reworded in order to understand the meaning: "and slower reduction in use of inpatient hospitalization for TLH/LAVH".

Response: As suggested, we have revised this sentence to the following to help clarify its meaning:

“After the FDA warning, … the decreasing trend in the likelihood of inpatient stay for TLH was attenuated (OR for each calendar quarter elapsed=0.92 in pre-warning period, 95% CI: 0.91-0.93; and 0.97 in post-warning period, 95% CI: 0.97-0.98).” (Please see Abstract on page 4 in manuscript.)

The discussion should include more background and comments on supracervical hysterectomies to include other benefits of removing the cervix such as decreased risk of cervical cancer, no need for cervical cancer surveillance, and post-operative bleeding. In addition, other purported benefits of supracervical hysterectomy are not evidenced based to include sexual function. The lower rate of supracervical hysterectomy found in your study might be more right-sized reserving this procedure for patients undergoing prolapse correction surgery and using the cervix as a barrier for the mesh as well as patients who need quicker procedures because of medical co-morbidities. It is also more likely that surgeons did supracervical hysterectomies because they took less time and require less laparoscopic skill.

Response: We appreciate these suggestions and have revised our Discussion section to address these points. Specifically, we clarified the benefits of removing the cervix, noted lack of clinically significant advantage of supracervical (versus total) hysterectomy, and discussed the appropriateness of retaining supracervical hysterectomy for selected patients. However, we respectfully disagree with the statement that laparoscopic supracervical hysterectomy (LSH) takes less time or skill. Indeed, specimen removal following an LSH often extends the surgical time and requires specific skills (e.g., safe use of the power morcellator).

The revised text reads as follows: “Although reduced access to LSH may subject some patients to higher complication rates since LSH tends to have better outcomes than other hysterectomy approaches, this should be balanced against increased use of other laparoscopic routes, as well as improved safety for patients with occult uterine cancer and the benefits of removing the cervix (e.g., decreased risk for cervical stump bleeding and cervical cancer). In general, there is little evidence for clinically significant benefits of supracervical hysterectomy over total hysterectomy, and the lower rate of LSH in the post-warning period might reflect more appropriate practice of reserving this procedure
for selected conditions (e.g., prolapse correction).” (Please see page 15 paragraph 2 in manuscript.)

While you hypothesized why you found an increased in hospitalization but a decrease in length of stay, it would also be nice for you to comment on what that means in terms of cost differential. If you are unable to comment, please state this as a limitation in your discussion regarding resource allocation.

Response: Since the NSQIP data used in our analysis does not contain cost information, we were unable to evaluate changes in cost. We have revised our manuscript to acknowledge this as a study limitation. Specifically, we stated:

“The overall impact of these changes on costs of care could be substantial. Unfortunately, we do not have cost data to evaluate their financial impact, which warrants close attention in further research.” (Please see page 16 paragraph 2 in manuscript.)

Line 322, the word should be "voluntary" not "voluntarily"

Response: Thank you for noting this. We have changed this text to “voluntary”. Please see page 17 paragraph 1 in manuscript.

Reviewer #3:

This submission examines and reports on the change, utilization, resource use and outcomes for women undergoing laparoscopic hysterectomy before and after the April 2014 FDA warning regarding power morcellation using NSQIP data from 2012-16. The report appears well constructed and is well written. The fact that background trends are accounted for using an interrupted time series approach seems novel and valuable.

However, upon further reflection, it seems difficult to make that much of the data reported when the numbers of laparoscopic hysterectomies are viewed in isolation from the numbers of vaginal and abdominal procedures for benign indications performed during the same period. The authors seems to have access to the numbers for abdominal and vaginal routes of hysterectomy. I do not understand why they did not include these and address them as well? With this in mind, other than the "interrupted time series" approach, it seems that there is limited new information here that has not already been reported in the articles the authors reference (ref 14-17).

Response: We appreciate this comment, but would like to clarify that in addition to using a rigorous interrupted time series approach, we included a longer follow up period than those prior studies referenced in our manuscript. This enabled us to capture longer term impact of the FDA warning after surgeons had time to adopt and learn new specimen removal techniques. We demonstrated that the reduction in use of laparoscopic hysterectomy observed in previous studies only reflected a transient impact of the FDA warning, while use of laparoscopic hysterectomy recovered afterwards to a level similar
to its predicted use had there been no FDA warning. This is an important finding and uniquely extends our understanding about clinical response to the FDA warning.

With regard to our focus on laparoscopic hysterectomy, please note that the objective of our study was to closely examine practice patterns of laparoscopic hysterectomy since it is the one type of hysterectomy most affected by the FDA safety warning regarding power morcellation. Furthermore, there are many important questions that are unique to laparoscopic hysterectomy. For instance, the FDA warning might affect the various laparoscopic routes differently. It may influence LSH the most as cervical preservation in LSH commonly requires morcellation for specimen removal, whereas the cervix is removed in total laparoscopic hysterectomy (TLH) and laparoscopic-assisted vaginal hysterectomy (LAVH) allowing for specimen extraction vaginally. Meanwhile, due to differences in surgical approach, the various routes of laparoscopic hysterectomy need to adopt different specimen extraction techniques in order to avoid uncontained power morcellation. Yet there has been little data on route-specific practice changes and patient safety and resource use after these changes. Carefully addressing these questions takes rigorous and extensive analyses and interpretation. Therefore, our study has focused on assessing changes of the different surgical routes within laparoscopic hysterectomy.

We appreciate the reviewer’s suggestion to additionally examine abdominal and vaginal hysterectomy. However, in the process of revising our manuscript, we identified an article newly published this month that already assessed long term trend for abdominal and vaginal hysterectomies (Jorgensen et al. 2019). They reported that use of abdominal hysterectomy decreased one year after the FDA safety warning despite an initial increase. Meanwhile, use of vaginal hysterectomy generally decreased over time. Given this publication, we have chosen to continue focusing our manuscript on our original research question of detailing changes in laparoscopic hysterectomy. However, we will be happy to add an analysis on trend of abdominal and vaginal hysterectomy if the reviewer and the Editor prefer.

Despite some similarities, we would like to clarify several important distinctions between our study and the Jorgensen et al. (2019) article. First, substantively, we focused on evaluating changes in utilization rate, operative time, inpatient hospitalization, length of stay, and patient outcomes for each distinct laparoscopic route. This helped inform whether the new techniques adopted in different laparoscopic routes after the FDA warning might jeopardize patients’ safety or affect resource use. In contrast, the Jorgensen et al. (2019) article characterizes change in surgical outcomes for all hysterectomies combined (without distinguishing surgical route) which may mask important changes in specific routes. Second, methodologically, we measured a comprehensive set of patient clinical risk factors and all our analyses carefully adjusted for these risk factors. Hence our findings inform the net impact of the FDA warning independent of changes in patient characteristics over time. In contrast, the Jorgensen et al. (2019) article reported a descriptive analysis without risk adjustment. Therefore, we believe our study still makes a unique and important contribution to the field.

Reference:

Line 207-209: "Overall, our sample included 145,746 women who underwent benign hysterectomies in 2012-2016. Within this cohort, 83,440 underwent laparoscopic hysterectomy, including 10,340 women undergoing LSH and 73,000 women undergoing TLH/LAVH."

1/ Does this mean that 62306 underwent TAH (145K - 83K)?
2/ Consider adding percentages

Response: In response to this comment, we have revised the relevant text to clarify that the remaining patients underwent abdominal or vaginal hysterectomy. We also added the corresponding percentages as suggested. Specifically, we stated:

“Overall, our sample included 145,746 women who underwent benign hysterectomies in 2012-2016. Within this cohort, 83,340 (57.2%) underwent laparoscopic hysterectomy, including 10,340 women (7.1%) undergoing LSH and 73,000 women (50.1%) undergoing TLH. The remaining patients underwent abdominal (n=35,229, 24.2%) or vaginal (n=27,177, 18.6%) hysterectomy.” (Please see page 11 paragraph 4 – page 12 paragraph 1 in manuscript).

In other words, Related to this, understanding how the rate of abdominal hysterectomy change using an interrupted time series analysis also seems important and relevant to the findings presented here.

Response: Please see our detailed response to the first general comment by Reviewer #3 above. That comment raised a similar question regarding changes in abdominal hysterectomy.

Separately, the discussion should probably address previous reports about increased after the FDA warning for the sub-group of patients undergoing myomectomy: From https://nam05.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.medscape.com%2Fviewarticle%2F895039&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20cfa0e%7C7cd8cbeb21394df8b4114e3e87abeb5c%7c0%7c1%7c636892166163601097&amp;sd=5R3a%2FOBP6eMIS%2BmdkZSGUeoxMZ22KOe4gNYPXmATW4c%3D&amp;reserved=0
"Overall, major and minor complications remained stable before and after the FDA-issued warning. But among the subset of 25,571 women (33.9%) who underwent hysterectomy for uterine fibroids, major complications significantly increased after the FDA-issued warning from 1.9% to 2.4% (adjusted odds ratio [OR], 1.23; P = .02), and minor complications significantly increased from 2.7% to 3.3% (adjusted OR, 1.21; P = .01).

Response: This comment refers to the Multinu et al. (2018) study (which is already referenced in our manuscript) that reports no change in complication rates after the FDA warning in all hysterectomies overall, but a significant increase in complication rates for the subset of women undergoing hysterectomy for uterine fibroid. In response to this comment, we performed an additional analysis evaluating potential changes in surgical
outcomes for the subset of women in our sample who underwent a hysterectomy for uterine fibroid. We found no significant change in their surgical outcomes in the post-warning period. We have revised our Materials and Methods section and Results section to incorporate this analysis as follows:

“We also performed sensitivity analyses on surgical outcomes by focusing on … patients with a diagnosis of uterine fibroids.” (Please see page 11 paragraph 2 in manuscript.)

“Sensitivity analysis limiting to … patients with uterine fibroids showed similar results.” (Please see page 14 paragraph 3 in manuscript.)

Reference:

Further thoughts:
1/ The trend toward decreased SCH may be due partially to increased surgeon skill and expertise with TLH. TLH is a technically more difficult procedure. Even if a procedure was completed as a TLH, abdominal morcellation still may have occurred. In my own practice, I continue to perform abdominal morcellation for very large uteri after TLH. (I just switched to contained manual morcellation and stopped using power morcellators.

Response: We appreciate this comment. However, if there is a decreasing trend in use of supracervical hysterectomy due to improved surgeon skill and expertise with TLH over time, this effect should have been captured as a background trend in our interrupted time series analysis. Our finding of a significant reduction in use of LSH reflects practice change after accounting for any background trends. Therefore, we have chosen not to modify our manuscript in response to this point.

Regarding contained manual morcellation, we agree that it has been adopted by surgeons in clinical practice. Accordingly, we have noted the following in our Discussion section:

“Since the FDA cautioned against power morcellation, novel methods of specimen extraction (e.g., power morcellation within a specimen bag, contained manual morcellation, specimen removal via colpotomy) were adopted to enable completion of hysterectomy in a minimally invasive fashion.” (Please see page 15 paragraph 3 in manuscript.)

2/ While they commented on their limitations to include only voluntary NSQIP hospitals, it may have been interesting to see if there were trends between hospital type (i.e., academic, community, combination).

Response: We thank the review for this suggestion. Unfortunately the NSQIP data does not contain information about hospital characteristics. We have revised our Discussion section to acknowledge this limitation. Specifically, we stated:
“Additionally, as no surgeon or hospital characteristics are available in the data, we could not evaluate their potential role in modifying practice responses.” (Please see page 17 paragraph 1 in manuscript.)

Minor point: Line 115-6: "To adequately capture secular trends in practice patterns and isolate changes induced by the FDA safety warning, our analysis included a broad time period from 2012 to 2016." I am not sure what is meant here. "Secular" to me simply means non-religious or non-spiritual. I suggest this be rephrased.

Response: We have changed “secular trends” to “background trends” in this sentence to help clarify its meaning. In addition, we carefully edited our manuscript to consistently use “background trends” (and avoid using “secular”) throughout. Please see Abstract on page 4, page 6 paragraph 2, page 7 paragraph 3, and page 15 paragraph 2 in manuscript.

Thank you for the opportunity to review this submission.

Response: We thank the reviewer for the thorough review of our manuscript.

Reviewer #4:

Commend on a good manuscript.

Strength of the manuscript is that takes into account secular trends in adoption of laparoscopic hysterectomy (LH) by interrupted time series approach, and tries to break down LH into LSH versus TLH/LAVH.

Found no increase risk of 30-day surgical complications during study period.

Response: We thank the reviewer for the encouraging remarks.

There is STROBE checklist at the end of the manuscript. This does not seem to be mentioned in the manuscript.

Response: We appreciate this comment. Per journal submission instructions, we completed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist and included it as part of our submission packet. Since the STROBE checklist was intended for use in the review process, we did not include this information in our manuscript.

Would like to see, or recommend considering, the following in the manuscript:

Does the transient decrease in overall rate of LH correspond to increase in TAH? While this might be presumed, would be good to confirm.
Response: Please see our detailed response to the first general comment by Reviewer #3 above. That comment raised a similar question regarding changes in abdominal hysterectomy.

What might account for the shift of TLH/LAVH to LSH? Can uterine weight data be obtained? Are larger uteri removed by TAH, with smaller uteri converted from TLH/LAVH to LSH?

Response: The NSQIP data used in our analysis unfortunately does not contain direct measures about uterine weight. However, CPT codes for laparoscopic hysterectomies distinguish uterus ≤250 grams versus >250 grams. For instance, CPT code 58541 reflects “Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less”, while CPT code 58543 reflects “Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g”. Therefore, in response to this comment, we performed an additional analysis by categorizing patients’ uterine weight based on CPT codes. We found that among women who underwent an LSH, the proportion having a uterus greater than 250 grams decreased from 23.9% in the pre-warning period to 18.4% in post-warning period (p<0.001). For women who underwent other laparoscopic hysterectomies (TLH or LAVH), the proportion decreased from 18.1% in pre-warning period to 17.3% in post-warning period (p=0.007). These data suggest that women with larger uteri might have been shifted away from laparoscopic hysterectomy, especially LSH. We have updated our Table 1 to incorporate this information.

We also revised our multivariable regression analysis for operative time, likelihood of inpatient hospitalization, length of stay, and surgical outcomes to include this indicator of uterine weight as an additional risk factor. There is no meaningful change in our findings. All relevant results in Tables 3-4 and Appendix 3 have been updated accordingly, as well as Results section text (please see pages 12-14 in manuscript).

The reason for the ban is risk of malignancy found in the specimen. What were the rates of cancer - leiomyosarcoma or uterine cancer - by route?

Response: In a prior publication from our research team, we thoroughly examined the risk of occult uterine cancer in a large population-based sample of women undergoing hysterectomy for presumed benign indications (Desai et al. 2019). In that publication, we showed that 0.27% of the women undergoing LSH and 1.06% of the women undergoing TLH had unexpected uterine cancer (including all subtypes such as endometrial carcinoma, leiomyosarcoma, and other uterine sarcomas). We have revised our introduction section to incorporate this information. Specifically, we stated:

“Power morcellation may be used in laparoscopic hysterectomy to facilitate specimen removal where an electromechanical device cuts uterine tissue into smaller fragments. However, 0.27-1.06% of patients undergoing laparoscopic hysterectomy may have unexpected uterine cancer, while power morcellation could inadvertently disperse cancer cells into peritoneal cavity. Therefore, in April 2014, the U.S. Food and Drug
Administration (FDA) cautioned against uncontained power morcellation.” (Please see page 6 paragraph 1 in manuscript.)

Reference:

Perhaps there should be some discussion that the risk to the patient of spreading cancer cells is not just from power morcellation, but should include all morcellation, including manual morcellation.

Response: As suggested, we have revised our Discussion section to note the potential risk of spreading cancer cells associated with manual morcellation. Specifically, we stated:

“Moreover, possible spread of malignancy at the time of manual morcellation also warrants attention in future research.” (Please see page 16 paragraph 1 in manuscript.)

This was mentioned as a limitation of the study ie. the lack of data or information exactly on specimen removal, but at least might deserve mention a possible explanation for the transient decrease in the only temporary decline in rate of LH or a mention of area of future research...

Response: Regarding the temporary decline in use of laparoscopic hysterectomy, we provided the following possible explanation in our Discussion section:

“Similar to previous studies, we found a reduction in use of laparoscopic hysterectomy following the FDA warning. However, this reduction was transient. Utilization of laparoscopic hysterectomy recovered afterwards to a level similar to its predicted use had there been no FDA warning. This appeared to be due to increased use of TLH and LAVH where the uterine specimen can be removed vaginally either intact or after manual morcellation. … The transient reduction in use of laparoscopic hysterectomy was driven by decreased use of LSH.” (Please see page 15 paragraph 2 in manuscript.)

Did surgeons just learn to switch from power to manual morcellation in a bag?

Response: Since our data does not contain information on specific tissue extraction techniques, we could not determine whether the eventual increase in use of laparoscopic hysterectomy was due to a switch from power to manual morcellation in a bag. We have revised our Discussion section to acknowledge this as a study limitation. Specifically, we stated:

“…, we lacked information on specific tissue extraction techniques utilized in laparoscopic cases in our analysis. Hence, we could not compare techniques between the pre- and post-warning period ....” (Please see page 17 paragraph 1 in manuscript.)
STATISTICAL EDITOR COMMENTS:

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

lines 63 and Table 2: The relationship is more nuanced. If the same metric were compared (post warning aOR, which is the same metric used to cited 0.49 (0.45-0.53) for LSH, then the change was NS: aOR = 1.01 (0.96-1.06). Should compare like with like in the sentence or elaborate on the description of what is being compared.

Response: We appreciate this comment. In response, we have revised the relevant sentence to consistently report the post-warning adjusted odds ratio for LSH and TLH. Specifically, we stated the following:

“After adjusting for patient characteristics and background trends in practice, use of LSH was significantly lower in the post-warning than pre-warning period (odds ratio [OR]=0.49, 95% confidence interval [CI]: 0.45-0.53), while use of TLH was not affected (OR=1.01, 95% CI: 0.96-1.06).” (Please see Abstract on page 4 in manuscript.)

lines 70-71 and Table 4: Although it is reassuring that there were no statistical differences in rates or odds, the rates of complications were all relatively small and there was insufficient power, even given the large samples at hand, to generalize (with the usual criteria of power) the NS findings.

Response: We agree that since complications are rare, our sample size may not have adequate statistical power to detect small differences in complication rates between the pre- and post-warning period. Therefore, we have revised our discussion section to acknowledge this as a potential limitation. Specifically, we stated:

“However, since complications are rare in laparoscopic hysterectomy, even our large sample size might not have sufficient statistical power to detect small changes in patient outcomes. Efforts are needed to continue monitoring surgical outcomes in laparoscopic hysterectomy.” (Please see page 16 paragraph 1 in manuscript.)

lines 66-69: For consistency and without loss of information to the reader, should round ORs and CIs to nearest .01.

Response: Because some estimated ORs and the lower or upper limit of the CIs would show identical values if rounded to two decimal places, our initial manuscript retained three decimal places in some cases to help clarify the difference in value. In response to this comment, we have consistently revised our manuscript throughout to round all ORs and CIs to the nearest 0.01. Please see Abstract on page 4 and Results section on pages 12-14 in manuscript. In addition, because some of the rounded CIs take a value of 1.00, which could hinder interpretation of statistical significance, we used bold font in Tables 2-4 to indicate statistically significant estimates.
Fig 1, A, B, C: Since the Tables reflect the trends of the two epochs, it would be informative to add to the legends for 1A, 1B and 1C to comment on the numerical and statistical differences at the end date (Q4 of 2016) between the observed vs hypothetical values based on extrapolating trends observed prior to FDA warning. That is, 1B is clearly different, but are the observed differences for the end date for 1A and 1C statistically different, or did they eventually to the prior trend?

Response: As suggested, we have revised Figure 1 legends to report numerical and statistical differences at the 4th quarter of 2016 between the two scenarios: predicted utilization rate of each laparoscopic route after accounting for the effect of the FDA warning versus hypothetical utilization rate based on extrapolating the trends observed prior to FDA warning. Specifically, we stated:

"After adjusting for patient characteristics, the estimated utilization rates in the 4th quarter of 2016 with versus without the safety warning are: 60.2% versus 61.3% (p=0.41) for all laparoscopic hysterectomy, 4.4% versus 7.2% (p<0.001) for LSH, and 54.7% versus 53.5% (p=0.40) for TLH (including LAVH)." (Please see Figure 1 legends on page 31 in manuscript.)

EDITOR COMMENTS:

1. Thank you for submitting this interesting work. Please specifically note the concerns of the statistical editor. It does appear that you have data available about abdominal procedures. Is there some reason you didn't include them to paint a broad picture of the practice of hysterectomy in this country? While I think it would add substantially to the strength of your paper, it is not a "deal breaker" if you choose not to include this. My preference is that you do so, however.

Response: We thank the Editor for considering our manuscript. We have carefully revised our paper to address all comments from reviewers and the statistical editor. Please see our point-to-point responses above.

Regarding whether to include abdominal hysterectomy, Reviewer #3 raised a similar question in his/her first general comment. As detailed in our response there, the objective of our study was to closely examine practice patterns of laparoscopic hysterectomy since it is the one type of hysterectomy most affected by the FDA safety warning regarding power morcellation. Furthermore, there are many important questions that are unique to laparoscopic hysterectomy. For instance, the FDA warning might affect the various laparoscopic routes differently. It may influence LSH the most as cervical preservation in LSH commonly requires morcellation for specimen removal, whereas the cervix is removed in TLH and LAVH allowing for specimen extraction vaginally. Meanwhile, due to differences in surgical approach, the various routes of laparoscopic hysterectomy need to adopt different specimen extraction techniques in order to avoid uncontained power morcellation. Yet there has been little data on route-specific practice changes and patient
safety and resource use after these changes. Carefully addressing these questions takes rigorous and extensive analyses and interpretation. Therefore, our study has focused on assessing laparoscopic hysterectomies.

We appreciate the suggestion to additionally examine abdominal hysterectomy. However, in the process of revising our manuscript, we identified an article newly published this month that already assessed long term trend for abdominal hysterectomies (Jorgensen et al. 2019). They reported that use of abdominal hysterectomy decreased one year after the FDA safety warning despite an initial increase. Given this publication, we have chosen to continue focusing our manuscript on our original research question of detailing changes in laparoscopic hysterectomy. However, we will be happy to add an analysis on trend of abdominal hysterectomy if the reviewer and the Editor prefer.

Despite some similarities, we would like to clarify several important distinctions between our study and the Jorgensen et al. (2019) article. First, substantively, we focused on evaluating changes in utilization rate, operative time, inpatient hospitalization, length of stay, and patient outcomes for each distinct laparoscopic route. This helped inform whether the new techniques adopted in different laparoscopic routes after the FDA warning might jeopardize patients’ safety or affect resource use. In contrast, the Jorgensen et al. (2019) article characterizes change in surgical outcomes for all hysterectomies combined (without distinguishing surgical route) which may mask important changes in specific routes. Second, methodologically, we measured a comprehensive set of patient clinical risk factors and all our analyses carefully adjusted for these risk factors. Hence our findings inform the net impact of the FDA warning independent of changes in patient characteristics over time. In contrast, the Jorgensen et al. (2019) article reported a descriptive analysis without risk adjustment. Therefore, we believe our study still makes a unique and important contribution to the field.

Reference:

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.***

Response: We thank the Editor for the detailed review of our manuscript. We have reviewed and addressed all comments in the notated PDF file. These comments and our point-to-point responses are listed below.
Response: Thank you for noting this. In response, we have revised the relevant text to the following to avoid using the virgule symbol:

“We measured use of laparoscopic supracervical hysterectomy (LSH) versus total laparoscopic hysterectomy (TLH, including laparoscopic-assisted vaginal hysterectomy) in these patients …” (Please see Abstract on page 4 in manuscript.)

In addition, we have thoroughly reviewed our manuscript (including tables and figures) and rephrased all relevant text to avoid using the virgule symbol as suggested.

"Utilization" isn't a sentient thing so it wouldn't experience anything. Perhaps "There was a transient reduction in the utilization of laparoscopic hysterectomy after..." 

Response: In response to this comment and to stay within the word limit, we have revised the relevant text to the following:

“Despite a transient reduction after the FDA warning, utilization of laparoscopic hysterectomy increased in the long run.” (Please see Abstract on page 5 in manuscript.)

- aged 18 years or older

Response: We have changed “age 18 or older” to “aged 18 years or older” as suggested. Please see page 7 paragraph 3.

- Use commas throughout this list. You would be using semicolons if there list had complex elements in it.

Response: We have revised this sentence to consistently use commas throughout the list. Please see page 7 paragraph 3.

- the virgules are fine here as they are part of your data set

Response: We appreciate this clarification. In response, we have retained the virgules in similar situations when specifying variable values from the dataset.

- if she went to a different hospital, these would not be caught by NSQIP and that should be listed as limitation in discussion

Response: Collection of outcomes data in the NSQIP program was performed by a surgical clinical reviewer at each participating hospital using medical chart reviews and “if necessary, letters or phone calls to patients” (please see: https://www.facs.org/quality-programs/acs-nsqip/joinnow/inclexcl). Therefore, its readmission information is not limited to the index hospital. Per the NSQIP operations manual, its readmission variable
included both readmissions to the same hospital and readmissions to a different hospital. Therefore, we did not make changes to our manuscript.

- did you have any information on the specialty or sub-specialty of the surgeons? Can you describe the type of hospital (community? Academic? Tertiary?)

Response: Our analysis used the NSQIP main participant use data file which does not contain information on surgeon or hospital characteristics. We have revised our Discussion section to acknowledge this as a study limitation. Specifically, we stated:

“Additionally, as no surgeon or hospital characteristics are available in the data, we could not evaluate their potential role in modifying practice responses.” (Please see page 17 paragraph 1 in manuscript.)

- unchanged from the post FDA warning rate of 4.7% or from 11.4%?

Response: We have revised the structure of the relevant sentences to help clarify this interpretation. The revised text states:

“This was followed by an abrupt reduction to 4.7% in the second quarter of 2014 when the FDA warning was released (adjusted OR = 0.49, 95% CI: 0.45, 0.53, for utilization of LSH in the post-warning versus pre-warning period) which remained stable afterwards (adjusted OR for post-warning trend = 0.99, 95% CI: 0.98, 1.00).” (Please see page 13 paragraph 2 in manuscript.)

- I'll be curious to see your speculation as to why this would be. It seems that large myomatus uterus removal fell pre/post without ability to use power morcellation in these cases-as shown perhaps by your shift in indications for these. Do you think the time increased because of concomitant procedures for prolapse, etc or do you surmise some other reason?

Response: This comment refers to the increased operative time for LSH in the post-warning period. Since our analysis already adjusted for patients’ diagnosis category (e.g., uterine fibroids, pelvic organ prolapse) and surgical complexity (as approximated by total work RVU of all concomitant procedures), we postulate that the longer operative time of LSH was due to more complex specimen removal techniques adopted after the FDA warning. This is consistent with findings from other studies in the literature (Siedhoff et al. 2017). Therefore, we stated the following in our Discussion section:

“…operative time of LSH was longer after the FDA warning, and a previously decreasing trend in operative time for TLH leveled off in the post-warning period. This is likely due to the use of new tissue removal techniques, which requires surgeons’ adaption and may add complexity and prolong surgical time.” (Please see page 16 paragraph 2 in manuscript.)

Reference:

- We do no allow authors to describe variables or outcomes in terms that imply a difference (such us of the terms “trend” or “tendency” or “marginally different”) unless there is a statistical difference. Please edit here and throughout.

Response: In response to this comment, we have removed the relevant sentence. Please see page 14 paragraph 1 in manuscript. We have also reviewed the manuscript throughout to make sure there is no statement regarding non-significant findings.

- can you report any differences in the weight of uterus's removed pre/post and by different methods?

Response: As noted in our response to an earlier comment by Reviewer #4, we performed an additional analysis regarding uterine weight. Specifically, we categorized patients’ uterine weight based on CPT codes which distinguishes whether a hysterectomy was performed for uterus ≤250 grams versus >250 grams. Among women who underwent an LSH, the proportion having a uterus greater than 250 grams decreased from 23.9% in the pre-warning period to 18.4% in post-warning period (p<0.001). For women who underwent other laparoscopic hysterectomies (TLH or LAVH), the proportion decreased from 18.1% in pre-warning period to 17.3% in post-warning period (p=0.007). We have revised our Table 1 and relevant text in Results section to incorporate this information. Please see page 12 paragraph 2 in manuscript.

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, as well as subsequent author queries. 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:

1. **OPT-IN:** Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. **OPT-OUT:** No, please do not publish my response letter and subsequent email correspondence related to author queries.

Response: We fully support the journal’s effort to increase transparency around the peer review process. We would like to OPT-IN and have our response letter and subsequent email correspondence related to author queries published.

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.

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

Response: Thank you very much for the instructions. We will go through the eCTA process and make sure that all co-authors electronically sign the eCTA.

4. Obstetrics & Gynecology follows the Good Publication Practice (GPP3)* guideline for manuscripts that report results that are supported or sponsored by pharmaceutical, medical device, diagnostics and biotechnology companies. The GPP3 is designed to help individuals and organization maintain ethical and transparent publication practices.

(1) Adherence to the GPP3 guideline should be noted in the cover letter.

(2) For publication purposes, the portions of particular importance to industry-sponsored research are below. In your cover letter, please indicate whether the following statements are true or false, and provide an explanation if necessary:
(2a) All authors had access to relevant aggregated study data and other information (for example, the study protocol) required to understand and report research findings.
(2b) All authors take responsibility for the way in which research findings are presented and published, were fully involved at all stages of publication and presentation development and are willing to take public responsibility for all aspects of the work.
(2c) The author list accurately reflects all substantial intellectual contributions to the research, data analyses, and publication or presentation development. Relevant contributions from persons who did not qualify as authors are disclosed in the acknowledgments.
(2d) The role of the sponsor in the design, execution, analysis, reporting, and funding (if applicable) of the research has been fully disclosed in all publications and presentations of the findings. Any involvement by persons or organizations with an interest (financial or nonfinancial) in the findings has also been disclosed.
(2e) All authors have disclosed any relationships or potential competing interests relating to the research and its publication or presentation.

(3) The abstract should contain an additional heading, "Funding Source," and should provide an abbreviated listing of the funder(s).

(4) In the manuscript, a new heading—"Role of the Funding Source"—should be inserted before the Methods and contain a detailed description of the sponsor's role as well as the following language:
"The authors had access to relevant aggregated study data and other information (such as study protocol, analytic plan and report, validated data table, and clinical study report) required to understand and report research findings. The authors take responsibility for the presentation and publication of the research findings, have been fully involved at all stages of publication and
presentation development, and are willing to take public responsibility for all aspects of the work. All individuals included as authors and contributors who made substantial intellectual contributions to the research, data analysis, and publication or presentation development are listed appropriately. The role of the sponsor in the design, execution, analysis, reporting, and funding is fully disclosed. The authors' personal interests, financial or non-financial, relating to this research and its publication have been disclosed." Authors should only include the above statement if all of it is true, and they should attest to this in the cover letter (see #2, above).


Response: These requirements are not applicable since our study is not supported or sponsored by pharmaceutical, medical device, diagnostics and biotechnology companies.

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.

Response: In response to this instruction, we have revised our Materials and Methods section to state that this study was approved by Yale University Human Investigation Committee. Please see page 8 paragraph 1 in manuscript. This information is also noted in our cover letter.

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://nam05.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2FAbout-ACOG%2FACOG-Departments%2FPatient-Safety-and-Quality-Improvement%2FReVITALize&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20cfa0e%7Cdd8cbdeb21394df8864114e3e87abe6c%7C0%7C1%7C63689216136301097&amp;reserved=0. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.
Response: Thank you for providing the links to these guidelines. We have reviewed the standard obstetric and gynecology data definitions available at these sources, and made sure that our manuscript is consistent with these revitalize definitions.

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.

Response: We thank the Editor for these guidelines and have carefully revised our manuscript to meet these requirements. Our manuscript now has 5,493 words (excluding acknowledgements and 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).

Response: We confirm that our manuscript is in compliance with these guidelines regarding Acknowledgments.

We would like to disclose that we have submitted an abstract based on this study to the American College of Surgeons Quality and Safety Conference in Washington, DC (July 19–22). However, because the abstract is still under review, it is unclear whether the study will be presented at this conference. Therefore, we did not include information about this potential presentation in the current manuscript. We will keep the journal informed if the abstract is accepted for presentation.

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

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

Response: As suggested, we have carefully reviewed our Abstract to ensure consistency in content between the Abstract and the manuscript. In addition, we confirm that our Abstract includes a clear conclusion statement and we have provided the word count for the Abstract as instructed. The abstract currently contains 300 words. Please see pages 4-5 in manuscript.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://nam05.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fabbreviations.pdf&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20cfa0e%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C636892166163601097&amp;sd=V8rcnxvKRP08%2FkO5gjkz9Nr1C7TK%2FpdMgp%2Fu2CISU%3D&amp;reserved=0. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

Response: We have verified that our manuscript title and précis conform to the guidelines for abbreviations. We also confirm that any acronyms used in the manuscript are spelled out the first time they are used.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

Response: Thank you for noting this. We have thoroughly reviewed our manuscript (including tables and figures) and rephrased all relevant text to avoid using the virgule symbol except when referring to data values.

12. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: https://nam05.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Ftable_checklist.pdf&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20cfa0e%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C636892166163601097&amp;sd=BTB0zc7gon0Ts8LFckcOH867Kx0GcKs07%2BahOMI3rzA%3D&amp;reserved=0.

Response: Thank you for providing the guidelines for Tables. We have reviewed these guidelines and updated the previous superscript symbols in Tables 1-4 to the accepted format (e.g., *, †). We recognize that the guidelines recommend using a hyphen between the two numbers in a confidence interval; however, because some estimates in our tables reflect negative values, we have used a comma to separate the two numbers in confidence intervals to avoid confusion.

13. 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 (i.e., 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 (e.g., Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://nam05.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2FClinical-Guidance-and-Publications%2FSearch-Clinical-Guidance&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20efa0e%7Cdd8cbebb21394df8b4114e3e87aeb5c%7C0%7C1%7C636892166163601097&amp;amp;data=3JjP1mraQQce4KTBfcpn8oc3vV3hXY1pYbc4DtDdkE%3D&amp;amp;reserved=0.

Response: We have reviewed the relevant ACOG documents and made sure that all references cited in our manuscript reflect the latest version and are still current and available.

14. 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.

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 (e.g., STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Response: Figures 1A-1C were created in Microsoft Excel. As requested, we have uploaded the corresponding original Excel files.

15. 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 https://nam05.safelinks.protection.outlook.com/?url=http%3A%2F%2Flinks.lww.com%2FLWW-ES%2FA48&amp;amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708db20efa0e%7Cdd8cbebb21394df8b4114e3e87aeb5c%7C0%7C1%7C636892166163601097&amp;amp;data=fNfL0%2FFF1f4tdVr1c6k5IpxZNL0ceq8I3lyIzck%3D&amp;amp;reserved=0. The cost for publishing an article as open access can be found at https://nam05.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Facd%2Faccounts%2Fifauth.htm&amp;amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708db20efa0e%7Cdd8cbebb21394df8b4114e3e87aeb5c%7C0%7C1%7C636892166163601097&amp;amp;data=Vaeg8m5jZklfGaupw4BG2efx0L5f5gSel0NZpdXj%2F0%3D&amp;amp;reserved=0.
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.

Response: Thank you for this information. We will keep an eye out for future emails about publication route and will make sure to respond promptly.

16. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at https://nam05.safelinks.protection.outlook.com/?url=http%3A%2F%2Fong.editorialmanager.com&amp;data=02%7C01%7Cvrunda.desai%40yale.edu%7C655c0c08322e40a9202708d6b20cfa0e%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C636892166163611102&amp;data=6Pd2Wvr7gwZoUteDFp6O4XpyvIlpRKxqXF5%2Bd2pTz29o%3D&amp;reserved=0. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word. If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Response: Thank you and we greatly appreciate the opportunity to revise and resubmit our manuscript. We have developed this document with point-by-point responses to each of the comments from reviewers and the Editor as instructed. All co-authors have reviewed and approved of this resubmission.
Hi Randi,

Here is the updated manuscript addressing your questions. Additionally we recently were invited to present our work at the ACS-NSQIP conference so we have added this as well. Please let us know if we can be of any additional assistance. thanks

Vrunda

Vrunda B. Desai MD
Adjunct Assistant Professor
Yale School of Medicine
Department of Obstetrics, Gynecology and Reproductive Sciences

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From: Randi Zung <RZung@greenjournal.org>
Sent: Monday, May 6, 2019 1:13 PM
To: Desai, Vrunda
Subject: Your Revised Manuscript 19-269R1

Dear Dr. Desai:

Your revised manuscript is being reviewed by the Editors. Before a final decision can be made, we need you to address the following queries. Please make the requested changes to the latest version of your manuscript that is attached to this email. **Please track your changes and leave the ones made by the Editorial Office.** Please also note your responses to the author queries in your email message back to me.

1. General: The Editor has made edits to the manuscript using track changes. Please review them to make sure they are correct.

2. Precis: Please note the Editor’s suggested rephrasing of this sentence. If you approve, please edit your Abstract-Conclusion to that it is similarly stated. Please also note that the Editors have requested that you remove all causal language. Your study’s findings should be framed as “associations” throughout. See Line 259 as an example.
3. Line 61 (and elsewhere): For all instances where you describe “benign hysterectomies” please change to “hysterectomy for benign indications”. The hysterectomy itself is neither benign nor malignant.

4. Line 73 (Abstract-Results and Results section): Please note that effect sizes (RR, OR) within the zone of potential bias should be noted as weak. Those effect sizes in the zone of potential interest should be emphasized. (Ref: False alarms and pseudo-epidemics. The limitations of observational epidemiology. Grimes DA, Schulz KF. Ob Gyn 2012;120:920-7)

While this is an increase, it is no more than 3%. Do you really think it is worth calling it an increase? Particularly in light of the Grimes/Shulz article? Would you consider adding something like...use of laparoscopic hysterectomy did not change by a clinically relevant degree?

5. Line 242: Perhaps a 3% increase year over year is a rapid increase compared to a 1% increase prior to the FDA warning, which is what I think you are pointing out here. However, I’ve read this a couple of times to understand this as your meaning. As this type of research method is rather unique for us, can you provide some explanatory comment in this section. Something inserted before “by the fourth quarter...”. Perhaps something like: “In other words, prior to the FDA warning, the rates of laparoscopic hysterectomy increased every quarter by about 1%. Following the decline immediately after the warning, the rate of increase was actually higher, at about 3% each quarter.”

6. Line 259: Here, as in elsewhere, please edit for causal language. See my suggested edit in first line of paragraph above

To facilitate the review process, we would appreciate receiving a response within 48 hours.

Best,
Randi Zung

Randi Zung (Ms.)
Editorial Administrator | Obstetrics & Gynecology
The American College of Obstetricians and Gynecologists
409 12th Street, SW
Washington, DC 20024-2188
http://www.greenjournal.org
1. General: The Editor has made edits to the manuscript using track changes. Please review them to make sure they are correct.

Response: We thank the Editor for the detailed edits to the manuscript. We have carefully reviewed all suggested changes and made some minor additional revisions to make sure the content is correct.

2. Precis: Please note the Editor’s suggested rephrasing of this sentence. If you approve, please edit your Abstract-Conclusion to that it is similarly stated. Please also note that the Editors have requested that you remove all causal language. Your study’s findings should be framed as “associations” throughout. See Line 259 as an example.

Response: We appreciate the rephrased précis. We slightly modified the statement to the following to help ensure accuracy: “Rates of laparoscopic supracervical hysterectomy fell in association with power morcellation safety warnings; rates of other laparoscopic hysterectomies continued to rise without changes in patient outcomes.” (Please see page 4 in manuscript.)

In addition, as suggested, we have rephrased the conclusion section in Abstract to use similar language (please see page 6 in manuscript). We also carefully revised the manuscript throughout to avoid using causal language (please see page 5 Abstract, page 11 paragraph 2, page 12 paragraph 1, page 14 paragraphs 1-2 and 4, page 18 paragraph 2, and the title of Tables 2-4 in manuscript).

3. Line 61 (and elsewhere): For all instances where you describe “benign hysterectomies” please change to “hysterectomy for benign indications”. The hysterectomy itself is neither benign nor malignant.

Response: As suggested, we have revised the manuscript throughout to use “hysterectomy for benign indications”. Please see revised text on page 5 Abstract, page 9 paragraph 2, page 11 paragraph 2, page 12 paragraph 3, and page 13 paragraph 2, as well as Table 2 footnote and Figure 1 legend.

4. Line 73 (Abstract-Results and Results section): Please note that effect sizes (RR, OR) within the zone of potential bias should be noted as weak. Those effect sizes in the zone of potential interest should be emphasized. (Ref: False alarms and pseudo-epidemics. The limitations of observational epidemiology. Grimes DA, Schulz KF. Ob Gyn 2012;120:920-7)

While this is an increase, it is no more than 3%. Do you really think it is worth calling it an increase? Particularly in light of the Grimes/Shulz article? Would you consider adding something like...use of laparoscopic hysterectomy did not change by a clinically relevant degree?

Response: We appreciate this comment, and understand the concern that some statistically significant findings may not be clinically meaningful and weak associations in observational studies may be subject to potential biases. However, we would like to
clarify that the 3% increase in utilization found in our study was associated with one
calendar quarter elapsed, which is actually substantial when the cumulative change in
utilization over the entire post-warning period (11 calendar quarters) is considered.
Indeed, as detailed in the manuscript (please see page 13 paragraph 2), this rate of
quarterly increase translated to a change in utilization of laparoscopic hysterectomy from
54.0% of all hysterectomies in the second quarter of 2014 (when the FDA warning was
first released) to 60.2% of all hysterectomies by the fourth quarter of 2016. We
considered this effect size clinically important and therefore would prefer to keep the
relevant text in the Abstract and Results section.

This is also related to the Editor’s comment #5 below. We have included an additional
statement suggested by the Editor, i.e., “In other words, prior to the FDA warning, the
rate of laparoscopic hysterectomy increased every quarter by about 1%. Following an
initial decline after the warning, the rate of laparoscopic hysterectomy actually increased
more rapidly afterwards, at about 3% each quarter.” This helps clarify the interpretation
of this effect size as well.

5. Line 242: Perhaps a 3% increase year over year is a rapid increase compared to a 1%
increase prior to the FDA warning, which is what I think you are pointing out here. However,
I’ve read this a couple of times to understand this as your meaning. As this type of research
method is rather unique for us, can you provide some explanatory comment in this
section. Something inserted before “by the fourth quarter...”. Perhaps something like: “In other
words, prior to the FDA warning, the rates of laparoscopic hysterectomy increased every
quarter by about 1%. Following the decline immediately after the warning, the rate of increase
was actually higher, at about 3% each quarter.”

Response: We appreciate the opportunity to clarify this finding. In response, we have
inserted the suggested statement in the specified paragraph: “In other words, prior to the
FDA warning, the rate of laparoscopic hysterectomy increased every quarter by about
1%. Following an initial decline after the warning, the rate of laparoscopic hysterectomy actually increased more rapidly afterwards, at about 3% each quarter.” (Please see page
13 paragraph 2 in manuscript.)

6. Line 259: Here, as in elsewhere, please edit for causal language. See my suggested edit in
first line of paragraph above

Response: In response to this comment, we have revised this sentence to the following:
“The FDA warning was not associated with significant changes in the level or trend of
utilization for TLH.” (Please see page 14 paragraph 2 in manuscript.)

In addition, we have carefully revised our manuscript throughout to avoid using causal
languages. Please see page 5 Abstract, page 11 paragraph 2, page 12 paragraph 1, page
14 paragraphs 1 and 4, page 18 paragraph 2, and the title of Tables 2-4 in manuscript.
Here it is, attached.

Hi Denise,

Can we request the following changes:

1. In Figure B, the vertical dashed line marking the second calendar quarter in 2014 was missing.
2. A few places in the Figure legend needs to be corrected. Please see attached. let us know if we can be of additional assistance.

Thanks,

Vrunda

Vrunda B. Desai MD
Adjunct Assistant Professor
From: Denise Shields <DShields@greenjournal.org>
Sent: Monday, May 13, 2019 11:40 AM
To: Desai, Vrunda
Subject: figure in your Green Journal manuscript (18-269R1)

Re: “Laparoscopic Hysterectomy Route, Resource Use, and Outcomes: Change After Power Morcellation Warning”

Dear Dr. Desai,

Your figure have been edited and are attached for your review. Please review the attachments CAREFULLY for any mistakes.

PLEASE NOTE: Any changes to the figures must be made now. Changes made at later stages are expensive and time-consuming and may result in the delay of your article’s publication.

To avoid a delay, I would appreciate a reply no later than Wednesday, 5/13. Thank you for your help.

Best,
Denise

Denise Shields
Senior Manuscript Editor
Obstetrics & Gynecology
www.greenjournal.org

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<19-269R1 (05-15-19 v4).pdf>