OBSTETRICS & GYNECOLOGY

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

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

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

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

Date: Oct 25, 2019
To: "Tirsit Asfaw" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1579

RE: Manuscript Number ONG-19-1579

Long-term device outcomes of mesh implants in pelvic organ prolapse repairs

Dear Dr. Asfaw:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Nov 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This study extends the follow-up of the authors previously published work in 2015. The methods are sound and the data provided are timely and clinically relevant. Overall, I think this will be a valuable addition to the literature.

1 - Given the substantial overlap with the authors prior 2015 publication, the authors should be explicit in the Introduction and Discussion about the similarities and differences of this manuscript and this earlier paper.

2- Excluding sacrocolpopexies is a weakness of this study and should be acknowledged. With declining use and now regulatory removal of vaginal mesh, use of minimally invasive sacrocolpopexy has increased and population-based estimates of reintervention for this mesh-based procedure would be valuable. It would have been ideal if the authors had included sacrocolpopexies as a 3rd group in this analysis.

3- The authors have previously published data from this same dataset that reinterventions for mesh are highest when slings and vaginal mesh are used concurrently. Sling use was higher in the mesh than the non-mesh group in this study however, it is unclear to me if this was accounted for in the propensity analysis.

Reviewer #2: Chughtai and colleagues present a retrospective cohort study evaluating for long term safety measures and re-interventions after surgical correction of pelvic organ prolapse with and without vaginal mesh. I have the following questions/comments for the authors:

1- The abstract is succinct and clear. My only concern is that line 62-63 and lines 67-69 seem like the same result reported twice as the numbers are exactly the same. If these are 2 different results, please clarify further.

2- The data source, patient population, and outcome are well described. The statistical methods seem appropriate.

3- The results are clearly presented and the information intriguing with the provision of risk of intervention at 5 years being a useful figure for counseling.

4- Table 1. Consider the addition of p-values to show similarity between groups.

5- Paragraph starting at line 230: This paragraph is confusing. Starting at line 240 the argument progression goes astray. The narrative of the pharmaceutical companies being slow to act makes sense but then there are several statements that seem to be in support of the pros. Then the last sentence explains that it was lack of evidence against cons that forced the FDAs hand. Consider splitting this into two paragraphs to separate the arguments.

6- Figures are helpful and attractive.

Reviewer #3: Comments to Author:

1- This study is notably limited by the data set the authors used, but it does provide important information on rates of re-intervention for mesh on a larger number of women and over a longer period of time than previous studies have examined.

2- While the gynecologic community understands that there is a clear need for long term data on complications of mesh, the introduction could improve how it leads the reader to this conclusion. Both the introduction and discussion could benefit from improved organization and flow.

3- The data does not account for any surgeries performed prior to 2008, as mesh was not coded for at that time; however, this also prevents the authors from identifying whether a woman had previous POP surgery of any kind prior to 2008. Thus, when it is stated that a woman had a primary surgery with mesh after 2008, there is no way to verify if this is actually her 1st surgery versus her 2nd or 3rd surgery for POP, with the original surgery performed prior to 2008.

4- The results section lacks data that the data set can produce. Specifically, it would benefit the reader if the authors elaborated on reoperation rates for recurrent POP between mesh and non-mesh, not just reoperation rates for mesh complications. The authors also discuss in their methods that they have divided surgical centers into low, intermediate and high volume but then do not discuss this data or differentiate outcomes based on these volumes.

Abstract

5- Line 58: Were safety events really assessed? It seems only re-intervention was assessed. Safety such as peri-operative morbidity or specifics of mesh complications such as SBO, bladder erosion, etc., were not assessed and authors should consider removing.

Introduction:

6- The organization of the introduction needs to be improved to flow more coherently.

7- The last paragraph addresses the issue that previous mesh studies were RCTs at high volume institutions which limits applicability to communities. It would be interesting to see comments in the results and discussion sections on their results for rates of re-intervention based on hospital surgical volume.

Methods:
8- No issue with data source

Results:

9- Table 1 demonstrates that in the unmatched cohort, 55% of patients in non-mesh vs 72.3% of patients in mesh group underwent concurrent apical support. Good apical support is traditionally thought to help prevent recurrence of POP. It would be interesting to comment that despite more apical support procedures in mesh patients, there was still higher rate of repeat POP surgery overall.

10- Table 2 demonstrates that more patients with mesh underwent any type of re-intervention than in women without mesh (717 vs 992), which is worth noting. The way Table 2 is currently written appears that women in the non-mesh group had higher rates of re-operation for POP overall (71.6% vs 65.7%), when in fact more women with mesh underwent re-intervention for recurrent POP: 652 patients versus 513 patients, or 5.3% of all patients vs 4.2% of all patients. This supports that mesh actually may be inferior to native tissue repair in treatment of POP, which may be worth mentioning to bolster the argument against the use of transvaginal mesh.

11- Line 167: Patients with mesh were more likely to receive apical support but less likely to undergo concurrent hysterectomy. Also, women getting mesh were older with more co-morbidities. This makes me wonder if these women had undergone POP procedures previously that were not captured in the data window starting at 2008, which is a potential flaw in the study data and potentially worth noting in the discussion. Alternatively, the surgeries could have been performed by surgeons such as urologists, who do not typically perform hysterectomies and were some of the earliest adopters of mesh, as it allowed them to provide apical support without hysterectomy.

12- Line 178: Consider using "median time to re-intervention was 4.7 years" over "follow-up", as this is a more accurate statement.

13- The authors mention dividing surgical centers into low, intermediate, and high volume centers. This is included in Table 1 but is never mentioned again in article. Including in results would be very interesting, given that the authors'

introduction suggests that higher volume centers with mesh have fewer complications.

Discussion:

14- Line 199: It should be emphasized that not only are the authors' reoperation rates almost doubled compared to those published by the Cochrane review, but that this rate of mesh complication may actually be underestimated—the reason being that they are only capturing the women who underwent re-intervention and not any of the women who may have had mesh erosions and complications that were conservatively managed.

15- Line 201-202: This line was also used in the introduction and, again, it would be beneficial to support this statement with evidence in the discussion.

16- Line 207: I like that the author states that there is an accumulation of mesh erosions and re-interventions over 5 years but consider referring to one of the Kaplan Meier curves or give some numerical data to support this statement. This is a powerful statement but the way it is organized in this discussion lacks the "punch" or power that it could potentially have.

17- Line 213: Recommend including length of follow-up in Scottish study rather than stating "over the long term," especially since authors state their study has the longest follow-up in current literature.

18- Line 216 - 228 and Line 230 - 250 may be more powerful in the introduction. The introduction did not compel me to appreciate the objective of the study but placing more of this information in the beginning of the article would improve this.

19- Line 248: Based on the evidence in this paragraph, stating that the FDA decision was only "in part" justified feels timid. If the author wishes to not come off too opinionated, could state instead "The recent FDA decision in 2019 was based on lack of "reasonable assurance" from manufacturers on long-term safety and efficacy for POP" to remove opinion.

Conclusion:

20- Line 284-285 "there is still a large number of ongoing mesh exposures that did not decline over time leading to re-interventions" - I understand the desired point of this sentence but it is confusingly worded and does not deliver the impact that it could.

21- Line 289: "Information about treating surgeons on all patients" - I am having a hard time following what is meant by this last portion of the sentence. Please clarify.

Figures and Tables:

22- Please see comments on Table 2 in results section. Overall, tables and figures are well organized.

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: Many readers would not be familiar with comparison by "Diff". Should provide more detail in Table legend and also include the p-values for comparison by characteristics for the matched cohorts. Should also include and compare the median follow-up times for the matched and unmatched cohorts.

2. Table 2: Should statistically compare the complication rates, total and by subset for the matched cohorts.

3. Fig 2: Should include a concise description of the statistical comparison of the matched cohorts, either in figure itself or its legend.

4. General: This is a large sample, with long follow-up and careful analysis by matching. However, there are limitations to its interpretation/generalization. The results depend on ongoing surveillance within NY and on identification of potential confounders at baseline. If there were differential rates of follow-up or censoring of data for either cohort, then the results may be biased. Also, since there is apparently no information available re: the baseline severity of prolapse, smoking status, ASA class, the groups may not have been matched adequately by the variables at hand and subsequent risk of recurrence. Needs to include a more complete enumeration of limitations.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this

revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
A. OPT-IN: Yes, please publish my point-by-point response letter.
B. OPT-OUT: No, please do not publish my point-by-point response letter.

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

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

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

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

5. 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.

6. 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.

7. 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).

8. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

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

10. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies

between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

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

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

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

13. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

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

15. The Journal's Production Editor has the following queries about the figures in your manuscript:

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

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

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

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

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

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each

author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Nov 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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

_____

[redacted]

November 13th, 2019

Dear Editor,

Thank you for your review and request for revisions of our manuscript entitled “Long-term device outcomes of mesh implants in pelvic organ prolapse repairs” in *Obstetrics & Gynecology*. We have addressed the comments provided by the reviewers below. Thank you again and we look forward to a positive outcome.

Sincerely,

Bilal Chughtai, MD
Assistant Professor of Urology
Assistant Professor of Urology in Obstetrics and Gynecology

Weill Cornell Medicine
Department of Urology
Department of Obstetrics and Gynecology
[redacted]

[redacted]

Reviewer #1

1 - Given the substantial overlap with the authors prior 2015 publication, the authors should be explicit in the Introduction and Discussion about the similarities and differences of this manuscript and this earlier paper.

Thank you for your comment. We have revised the introduction to highlight that this is a long-term study versus our earlier study which only had 12 month follow up.

Please see page 5 line 114.

2- Excluding sacrocolpopexies is a weakness of this study and should be acknowledged. With declining use and now regulatory removal of vaginal mesh, use of minimally invasive sacrocolpopexy has increased and population-based estimates of reintervention for this mesh-based procedure would be valuable. It would have been ideal if the authors had included sacrocolpopexies as a 3rd group in this analysis.

Thank you for your comment. We agree that sacrocolpopexies are a very important cohort to study, ultimately the cohort who undergo sacrocolpopexies likely have larger degree of prolapse and may have different set of complications compared to those undergoing transvaginal repairs. Therefore, we decided against including them in this study. We have added this to the limitation section and will pursue this for future studies.

Please see page 14 line 317.

3- The authors have previously published data from this same dataset that reinterventions for mesh are highest when slings and vaginal mesh are used concurrently. Sling use was higher in the mesh than the non-mesh group in this study however, it is unclear to me if this was accounted for in the propensity analysis.

Thank you for your question. Concurrent sling procedure was included as one of the matching variables in propensity score. We have clarified this in the methods section.

Please see page 7 line 165.

Reviewer #2

1- The abstract is succinct and clear. My only concern is that line 62-63 and lines 67-69 seem like the same result reported twice as the numbers are exactly the same. If these are 2 different results, please clarify further.

Thank you for your comment. The abstract was revised to correct this. The duplicative lines 67-69 were removed.

Please see page 2 line 66.

2- The data source, patient population, and outcome are well described. The statistical methods seem appropriate.

Thank you for your comment.

3- The results are clearly presented and the information intriguing with the provision of risk of intervention at 5 years being a useful figure for counseling.

Thank you for your comment.

4- Table 1. Consider the addition of p-values to show similarity between groups.

Thank you for your comment. We understand that p-values are easier to interpret. However, p-values can be misleading in the comparison in our study as we have a relatively large sample size and significance can be due to larger sample size.

Therefore, we decided to show both p value and standardized differences. The reason to show standardized difference is that there is a recommended threshold below which (<0.1) covariate balance is considered achieved. We have also clarified this in the methods and in the footnote of the table.

Please see page 8 line 170 and Table 1.

5- Paragraph starting at line 230: This paragraph is confusing. Starting at line 240 the argument progression goes astray. The narrative of the pharmaceutical companies being slow to act makes sense but then there are several statements that seem to be in support of the pros. Then the last sentence explains that it was lack of evidence against cons that forced the FDAs hand. Consider splitting this into two paragraphs to separate the arguments.

Thank you for your comment. We have revised this section to two paragraphs to make language clearer.

Please see page 13 lines 273 and 285.

6- Figures are helpful and attractive.

Thank you for your comment.

Reviewer #3

1- This study is notably limited by the data set the authors used, but it does provide important information on rates of re-intervention for mesh on a larger number of women and over a longer period of time than previous studies have examined.

Thank you for your comment. We agree despite the limitations of the dataset, this study provides insight into the long term outcomes of mesh for POP.

2- While the gynecologic community understands that there is a clear need for long term data on complications of mesh, the introduction could improve how it leads the reader to this conclusion. Both the introduction and discussion could benefit from improved organization and flow.

Thank you for your comment. Both the introduction and discussion have been revised for better flow and organization.

Please see Introduction on page 4 line 80 and Discussion on page 11 line 226.

3- The data does not account for any surgeries performed prior to 2008, as mesh was not coded for at that time; however, this also prevents the authors from identifying whether a woman had previous POP surgery of any kind prior to 2008. Thus, when it is stated that a woman had a primary surgery with mesh after 2008, there is no way to verify if this is actually her 1st surgery versus her 2nd or 3rd surgery for POP, with the original surgery performed prior to 2008.

There were no mesh-specific procedure codes prior to 2008. However, general prolapse repair codes already existed. Therefore, we excluded all patients with any POP code prior to 2008 to the first year of the data set 1995. This would likely ensure that this was the first POP operation for almost all patients in the study. We have revised our methods section to make this clear.

Please see page 6 line 140.

4- The results section lacks data that the data set can produce. Specifically, it would benefit the reader if the authors elaborated on reoperation rates for recurrent POP between mesh and non-mesh, not just reoperation rates for mesh complications. The authors also discuss in their methods that they have divided surgical centers into low, intermediate and high volume but then do not discuss this data or differentiate outcomes based on these volumes.

Thank you for your suggestion. We have revised analysis shown in Table 2. Table 2 now presents estimated risks of reintervention associated with each diagnosis at 5 years. We have also added subgroup analysis by hospital volume group. The higher risk of reoperation associated with POP repair using mesh was shown to be consistent in all volume groups. This has been added to the results section.

Please see page 10 line 210 and Table 2.

Abstract

5- Line 58: Were safety events really assessed? It seems only re-intervention was assessed. Safety such as peri-operative morbidity or specifics of mesh complications such as SBO, bladder erosion, etc., were not assessed and authors should consider removing.

Thank you for your question. We have assessed post-operative complications in our previous study and reported relevant outcomes. The current study mainly focuses on the longer-term outcomes. Because procedure codes for reoperations were not specific to whether it was removal or revision, we are not able to report mesh removal separately. We have added this to the limitation section.

Please see page 14 line 305.

Previous study: Chughtai B, Mao J, Buck J, Kaplan S, Sedrakyan A. Use and risks of surgical mesh for pelvic organ prolapse surgery in women in New York state: population based cohort study. BMJ. 2015;350:h2685.

Introduction:

6- The organization of the introduction needs to be improved to flow more coherently.

Thank you for your comment. The introduction has been revised for better flow and organization.

Please see page 4 line 81.

7- The last paragraph addresses the issue that previous mesh studies were RCTs at high volume institutions which limits applicability to communities. It would be interesting to see comments in the results and discussion sections on their results for rates of re-intervention based on hospital surgical volume.

We agree this would have been interesting data, but unfortunately, this dataset does not provide information about the training or experience of the implanting surgeon. This was made clearer in the limitation section.

Please see page 14 line 312.

Methods:
8- No issue with data source

Results:

9- Table 1 demonstrates that in the unmatched cohort, 55% of patients in non-mesh vs 72.3% of patients in mesh group underwent concurrent apical support. Good apical support is traditionally thought to help prevent recurrence of POP. It would be interesting to comment that despite more apical procedures in mesh patients, there was still higher rate of repeat POP surgery overall.

Thank you for your comment. We have included this observation and have added it to the discussion.

Please see page 11 line 246.

10- Table 2 demonstrates that more patients with mesh underwent any type of re-intervention than in women without mesh (717 vs 992), which is worth noting. The way Table 2 is currently written appears that women in the non-mesh group had higher rates of re-operation for POP overall (71.6% vs 65.7%), when in fact more women with mesh underwent re-intervention for recurrent POP: 652 patients versus 513 patients, or 5.3% of all patients vs 4.2% of all patients. This supports that mesh actually may be inferior to native tissue repair intreatment of POP, which may be worth mentioning to bolster the argument against the use of transvaginal mesh.

We have revised analysis shown in Table 2. Table 2 now presents estimated risks of reintervention associated with each diagnosis at 5 years, with statistical comparison. We have highlighted the higher reintervention rate in the discussion.

Please see page 11 line 246 and Table 2.

11- Line 167: Patients with mesh were more likely to receive apical support but less likely to undergo concurrent hysterectomy. Also, women getting mesh were older with more co-morbidities. This makes me wonder if these women had undergone POP procedures previously that were not captured in the data window starting at 2008, which is a potential flaw in the study data and potentially worth noting in the discussion. Alternatively, the surgeries could have been performed by surgeons such as urologists, who do not typically perform hysterectomies and were some of the earlier adopters of mesh, as it allowed them to provide paical support without hysterectomy.

Thank you for your reseponse. We excluded all patients with any POP code prior to 2008 to the first year of the data set which is 1995, which reduce any contamination of previous procedures in both groups. As for differentiating between urologist and gynecologists, unfortunately this is a limitation of the dataset and has been added to the limitation section.

Please see page 14 line 304.

12- Line 178: Consider using "median time to re-intervention was 4.7 years" over "follow-up", as this is a more accurate statement.

We are reporting the median time of patients being followed up after the initial POP repair. We have clarified this as: “The median length of follow-up after the index procedure was 4.7 years.”

Please see page 9 line 199.

13- The authors mention dividing surgical centers into low, intermediate, and high volume centers. This is included in Table 1 but is never mentioned again in article. Including in results would be very interesting, given that the authors' introduction suggests that higher volume centers with mesh have fewer complications.

Given that this study focuses on the comparison between POP repair with and without mesh, we have also added subgroup analysis by hospital volume group. The higher risk of reoperation associated with POP repair using mesh was shown to be consistent in all volume groups. This has been added to the results section.

Please see page 10 line 210.

Discussion:

14- Line 199: It should be emphasized that not only are the authors' reoperation rates almost doubled compared to those published by the Cochrane review, but that this rate of mesh complication may actually be underestimated—the reason being that they are only capturing the women who underwent re-intervention and not any of the women who may have had mesh erosions and complications that were conservatively managed.

Thank you, this has been revised to include the following. “This rate of mesh complication may actually be underestimated given that only women who underwent re-intervention are captured and not any of the women who had mesh erosions and complications that were conservatively managed in the office setting.”

Please see page 11 line 237.

15- Line 201-202: This line was also used in the introduction and, again, it would be beneficial to support this statement with evidence in the discussion.

Thank you for your comments, we have revised this to include a reference to the Cochrane review, which states, “We evaluated 37 randomised controlled trials (4023 women) comparing transvaginal grafts versus traditional native tissue repair for repairing vaginal prolapse.”

Please see page 11 line 233.

Reference: Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD012079. DOI: 10.1002/14651858.CD012079

16- Line 207: I like that the author states that there is an accumulation of mesh erosions and re-interventions over 5 years but consider referring to one of the Kaplan Meier curves or give some numerical data to support this statement. This is a powerful statement but the way it is organized in this discussion lacks the "punch" or power that it could potentially have.

Thank you, we have revised this sentence, “There is a continuous accumulation of mesh erosions and almost a 40% higher risk of reinterventions in patients receiving a mesh implant at a median follow up of 5 years.”

Please see page 11 line 244.

17- Line 213: Recommend including length of follow-up in Scottish study rather than stating "over the long term," especially since authors state their study has the longest follow-up in current literature.

Thank you for your comment. The sentence was revised to, “A Scottish study found that anterior and posterior compartment prolapse mesh procedures had significantly higher complication rates than non-mesh procedures over a median follow up of 5 years.”

Please see page 12 line 254.

18- Line 216 - 228 and Line 230 - 250 may be more powerful in the introduction. The introduction did not compel me to appreciate the objective of the study but placing more of this information in the beginning of the article would improve this.

Thank you for your comment. We have revised our introduction to include this information to improve flow, organization, and the impact of the introduction.

Please see page 4 line 81.

19- Line 248: Based on the evidence in this paragraph, stating that the FDA decision was only "in part" justified feels timid. If the author wishes to not come off too opinionated, could state instead "The recent FDA decision in 2019 was based on lack of "reasonable assurance" from manufacturers on long-term safety and efficacy for POP" to remove opinion.

Thank you for your comment. This line has been revised to “The most recent FDA decision in 2019 was justified based on lack of manufacturers providing “reasonable assurance” of the long-term safety and effectiveness for POP.”

Please see page 13 line 281.

Conclusion:

20- Line 284-285 "there is still a large number of ongoing mesh exposures that did not decline over time leading to re-interventions" - I understand the desired point of this sentence but it is confusingly worded and does not deliver the impact that it could.

Thank you for your comment. The sentence has been revised to, " The risk of mesh complications did not diminsh over time and these women warrant close follow up."

Please see page 16 line 342.

21- Line 289: "Information about treating surgeons on all patients" - I am having a hard time following what is meant by this last portion of the sentence. Please clarify.

Thank you for your comment. The sentence was corrected to read, "Registries should include comprehensive information about the nature and burden of POP recurrence, different types of re-treatment, patient-reported outcomes, and information about treating surgeons."

Please see page 16 line 345.

Figures and Tables:

22- Please see comments on Table 2 in results section. Overall, tables and figures are well organized.

Thank you for your comment. We have revised Table 2 accordingly.

STATISTICAL EDITOR'S COMMENTS:
1. Table 1: Many readers would not be familiar with comparison by "Diff". Should provide more detail in Table legend and also include the p-values for comparison by characteristics for the matched cohorts. Should also include and compare the median follow-up times for the matched and unmatched cohorts.

Thank you for your question. We understand that p-values are easier to interpret. However, p-values can be misleading in the comparison in our study as we have a relatively large sample size and significance can be due to larger sample size.

Therefore, we decided to show both p value and standardized. The reason to show standardized difference is that there is a recommended threshold below which (<0.1) covariate balance is considered achieved. We have also clarified this in the methods and in the footnote of the table.

2. Table 2: Should statistically compare the complication rates, total and by subset for the matched cohorts.

Thank you for your comment. We have revised analysis shown in Table 2. Table 2 now presents estimated risks of reintervention associated with each diagnosis at 5 years, with statistical comparison.

3. Fig 2: Should include a concise description of the statistical comparison of the matched cohorts, either in figure itself or its legend.

Thank you for your comment. We have now included this comparison on Table 2.

4. General: This is a large sample, with long follow-up and careful analysis by matching. However, there are limitations to its interpretation/generalization. The results depend on ongoing surveillance within NY and on identification of potential confounders at baseline. If there were differential rates of follow-up or censoring of data for either cohort, then the results may be biased. Also, since there is apparently no information available re: the baseline severity of prolapse, smoking status, ASA class, the groups may not have been matched adequately by the variables at hand and subsequent risk of recurrence. Needs to include a more complete enumeration of limitations.

Thank you for your comment. We have included these in the limitations.

EDITORIAL OFFICE COMMENTS

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

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

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

Thank you, the co-authors will be completing the questions of the eCTA.

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

Thank you for your comment. Data are submitted by healthcare facilities to New York State. The state conducts periodic audits to ensure data reliability and validity. We have included this in the methods section.

Please see page 6 line 125.

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

STROBE guideline was followed and the checklist is submitted.

5. 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.

The standard data definitions have been used when appropriate.

6. 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.

The length restrictions were followed.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

All financial support of the study has been acknowledged. Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, have been disclosed in the acknowledgments.

8. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

Please see page 2 line 49.

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

Please see page 2 line 50.

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

Please see page 2 line 53.

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

Standard abbreviations and acronyms were used.

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

The virgule symbosl have been removed from the text.

See page 7 line 151.

13. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

Please see Tables 1 and 2.

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

Please see Table 2.

15. The Journal's Production Editor has the following queries about the figures in your manuscript:

"Figure 1: Please upload a higher resolution version of this figure and add tick marks along the x-axis”

Thank you for your instruction. We have included a higher resolution version of Figure 1, with tick marks added.