OBSTETRICS & GYNECOLOGY

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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: Jun 18, 2019
To: "William D Winkelman" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-857

RE: Manuscript Number ONG-19-857

The impact of FDA statements about transvaginal mesh on routes of surgery for apical prolapse

Dear Dr. Winkelman:

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 Jul 09, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Precis: Following the safety communication about mesh, the proportion of apical procedures with abdominal colpopexy increased suggesting the transvaginal mesh was being replaced by transabdominal mesh.

Abstract: Objective - To assess the impact of the FDA safety communication on transvaginal mesh in 2011 and the reclassification of transvaginal mesh to a class 3 device in 2016 on national trends
Methods - retrospective cohort from 2008-2017 of apical prolapse repair as the primary or secondary procedure by CPT codes
Results - 36,463 eligible cases - transvaginal mesh decreased from 35% to 11% - after 2011 it decreased by 4.4% per quarter and abdominal colpopexy increased by 2.6% per quarter
There was no further significant change after the 2016 reclassification
Conclusions - There was a significant decrease in transvaginal mesh after the first communication in 2011 with abdominal colpopexy with transabdominal mesh having the greatest increase. The transvaginal procedures were replaced with transabdominal procedures after 2011 with no further change in 2016. The 2019 ban is expected to increase transabdominal colpopexy.

Introduction - prolapse repairs are introduced with the history of transvaginal mesh controversy
2016 - class 3 high risk reclassification and 2019 - halted sales of transvaginal mesh

Methods - retrospective cohort study of ACS NSQIP database - preoperative, intraoperative, and 30 day postoperative data on apical prolapse repair as primary or secondary procedure between 2008-2017 with primary outcome being surgery technique]
5 periods were evaluated based on FDA safety communications and reclassifications with a 12 month period after each
1) dates before 2011, 2) 12 months after 2011; 3) all cases after that until 2016: 4) the year after 2016 reclassification; 5) after 1 year from reclassification until 2017
statistical analysis - transvaginal mesh, intraperitoneal uterosacral ligament suspension, extraperitoneal sacrospinous legament suspension, or abdominal colpopexy

Results - 36,463 surgical cases with apical prolapse
2008 - 35% apical repaired with transvaginal mesh, by 2017 11% transvaginal mesh; extraperitoneal repairs increased from 16 to 20% and intraperitoneal increased 21 to 31%, abdominal colpopexy increased from 28-39%, and laparotomy decreased from 35 to 14%
1 year after the safety communication in 2011 transvaginal mesh decreased by 4.4% per quarter and then by 0.5% per quarter over the next 3 years.
The 2016 FDA reclassification did not affect intraperitoneal or extraperitoneal repair rate as they had decreasd in the years

prior to that.
Abdominal repairs incresed in the year after the FDA announcement vy 2.6% per quarter

Discussion - Transvaginal mesh use decreased after the FDA announcement in 2011 and all other approaches increased

This study shows an increase in transabdominal mesh as an alternative to transvaginal mesh. After 2016, there was no significant change in practice patterns indicating that opinion was well established. As the use of transvaginal mesh decreased, there is an increase in the 3 other times of repairs, and the biggest increase is expected in abdominal colpopexy.

Comments -

1. Line 163 - change is from class 2 to class 3

2. Verb tenses need to remain consistent throughout - particular attention to results

3. The main concern with this manuscript is that now, with transvaginal mesh being banned, it has less relevancy.

4. Perhaps the historical perspective of indicating that it may not affect practice all that significantly since the adjustments had already occurred would be useful.

5. Some more explanation should be given as to extraperitoneal and intraperitoneal technique should be given as to how it is done without mesh and without transabdominal approach to make clear to readers who don't do these procedures.

6. What is success of various repairs? Risk of recurrence?

7. What is complication risk?

8. Is this improving outcomes or is this ban eliminating option of transvaginal repair worsening outcomes because worse results with more risk?

9. More context would be useful to understand what this impact will be clinically.

Reviewer #2: This manuscript comes at a perfect time. With the FDA advisory and removal of all vaginal mesh less than a month ago this article needs to be published.

1. Intro: line 72: I would add reference to most recent FDA publication.

2. How behind is the data in the database? Is 2017 the most recent data available?

3. What statistical program was used for analysis. Please add

4. Very interesting that the 2016 advisory did not change but it probably was due to surgeons already deciding against mesh procedures. I agree that reclassifying the device probably did not add much.

Reviewer #3: Abbreviations used
ASC= Abdominal Sacrocolpopexy
TVM= Transvaginal Mesh
TAM= Transabdominal Mesh (synonymous with Total ASC)

Nice database review with a large number of cases accessed. Interesting topic as well. It would be of interest to surgeons in the US. The rise in RASC needs study.

A few important comments and smaller watch-outs:

Your conclusion "suggests" causality which was not modeled in the study. Your quote "decrease in TVM RESULTED in an increase in TAM" is problematic as worded. Time relationships are notorious for resulting in spurious relationships based on unmeasured variables that impact the relationship to make it appear linear. This is esp true in time relationship studies utilizing databases which have no opportunity to model or test the hypothesis. The main unmeasured variable here is that you looked at the 36,463 patients who were known to have apical procedures. During the study period, there were likely >300,000 prolapse procedures that did not include apical suspension. During this same time period, the dramatic rise in Robotic ASC likely caused a large number of patients who previously underwent no apical procedure to now include one in the form of an RASC. This may/could be a larger factor in the rise of the ASC total. The other omitted variable bias (moderating variable) is that it is also known that in an unknown percentage of doctor practices, TVM was converted to Intra/extraperitoneal Colpopexy and at the same time doctors who previously only performed Intra/extraperitoneal Colpopexy learned to perform RASC. This could result in an unchanged number of native tissue colpopexies but for two conflicting reasons.

The answer is to tone down language that suggests causality and more strongly acknowledge the potential for omitted variable bias. As listed above there are at least 2 other factors that could reasonably contribute to (or cause) the rise in ASC

The second conclusion that is not studied in this data is the "expectation" that this rise will continue. The robotic variable makes that unknown. We see in new technology introduction a hype cycle where use is maximized followed by a cooling off period with decreased use. It is unstudied as to what the trend would be after your study period and it is just as likely that RASC could have experienced a cooling off period during 2017-2020. I don't know that to occur, it just illustrates that your conclusions should stick to what data is looked at. I would have no problem if you downgraded that from "expectation" to some sort of speculation of possible futures.

I would like to offer an opinion on your secondary objectives. (line 219-230) Personally this is the most clinically relevant observation that can be directly evaluated by a look at 36,463 cases. The absence of clinically meaningful differences in postoperative complications stratified by surgical approach is well supported by your data and is of great impact, given the dire expectations of mesh use purported elsewhere. This could be considered in the results section and even the conclusion. It is of more interest and more directly supported by data than the other conclusions.

Line details:

1. line75-77 needs a reference and would benefit from a quote. I would not paraphrase what the FDA said about ASC. It needs to quote what they did say specifically.

2. line 66 and others: "mesh is intended to provide permanent solution. I would alter that to permanent "or improved durability". Improved durability is a more accurate representation of the intention of mesh rather than permanent solution.

3. line 142 Typo that won't get caught by editor. you called it inter peritoneal when you meant intra/extra peritoneal

STATISTICAL EDITOR'S COMMENTS:

1. lines 138-139: The chi-square test does not specifically identify one procedure as showing significance, but rather the distribution of all procedures was not random. If specific pairwise comparisons are cited in text, they need pairwise stats testing.

2. lines 148-149, Table 3: Again, this stats test was not for that specific surgery, need a pairwise test.

3. Table 1: Should statistically compare the patient characteristics in the various time epochs. Were they comparable in age, race/ethnicity or co-morbidities?

4. Tables 1, 2, 3: Should make clear in footnotes to the table what the p-value signifies. Is it comparison across all times or surgical approaches for deviation from random variation, or specific comparison of two time points or vaginal mesh vs a specific other surgery?

5. Fig 1: The lines do not represent "predicted" values, but rather, the data are fitted to a linear regression for each time epoch. Do the Authors have an explanation for the sudden change in vaginal mesh and abd colpopexy procedures in the 2009-2010 time period? This appears to be just prior to the FDA statement and furthermore it calls into question the use of a linear summary of that period, since it consisted of two proportions with a sudden jump, not a gradual change.

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.

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.

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. 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.

5. 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, tables, boxes, figure legends, and print appendixes) but exclude references.

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

7. 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."

8. 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.

9. 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.

10. 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.

11. 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.

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Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

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If you choose to revise your manuscript, please submit your revision 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 Jul 09, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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

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

William Winkelman, MD, FACOG
Clinical Fellow
Mount Auburn Hospital

June 18, 2019

Dr. Chescheir:

Thank you for the opportunity to revise our paper for reconsideration for publication in Obstetrics & Gynecology. In response to the reviewers' comments we have made the following revisions.

Reviewer 1:

- Line 163 - change is from class 2 to class 3
    - We have corrected the typo to clarify that the change was form class II to class III device

- Verb tenses need to remain consistent throughout - particular attention to results
    - We have made revisions throughout the manuscript to maintain consistent verb use

- The main concern with this manuscript is that now, with transvaginal mesh being banned, it has less relevancy.
    - We appreciate the comment. We feel that this study remains relevant as it may provide insight to the future direction of pelvic reconstructive surgery. Additionally, while transvaginal mesh kits have been withdrawn from the market in the United States, it is still available in other countries and this study may provide insight into trends on a global scale.

- Perhaps the historical perspective of indicating that it may not affect practice all that significantly since the adjustments had already occurred would be useful.
    - Again, we appreciate the comment and agree, that this does provide important historical perspective. We hope that this study provides not only perspective on the use of transvaginal mesh but may provide a framework for understanding practice trends should the FDA make statements about the safety of transabdominal mesh, midurethral slings or other medical devices.

- Some more explanation should be given as to extraperitoneal and intraperitoneal technique should be given as to how it is done without mesh and without transabdominal approach to make clear to readers who don't do these procedures.
    - We have added a few sentences, lines 99-106 clarifying the types of procedures performed. "These procedures were classified into four major categories: intraperitoneal colpopexy procedures such as a uterosacral ligament suspension in which the vaginal apex is suspended to the as a uterosacral ligament bilaterally without the use of mesh; extraperitoneal colpopexy procedures such as a sacrospinous ligament suspensions in which the vaginal apex is suspended to the sacrospinous ligament without the use of mesh; abdominal colpopexy procedures in which transabdominal mesh is used to suspend the vaginal apex to the anterior longitudinal ligament of the sacrum; transvaginal mesh procedures in which mesh is used transvaginally to support the vaginal apex." We have included two references about extraperitoneal and

intraperitoneal colpopexy procedures. We feel that additional explanations of the procedure fall beyond the scope of this manuscript

- American Urogynecologic Society (AUGS) also publishes general fact sheets that are publicly available and provide general overview of the four procedure types included in this study https://www.augs.org/patient-fact-sheets//. The International Urogynecologic Association (IUGA) similarly publishes leaflets that provide a good introduction to the main apical prolapse surgeries in urogynecology https://www.yourpelvicfloor.org/leaflets/

- What is success of various repairs? Risk of recurrence?

  Thank you for this questions. Success rates of apical prolapse procedures can be complex and depend on both subjective and objective definitions of success and the duration of follow up. There are no clear established values and a brief mention of success rates would over simplify a complicated topic. I would recommend readers refer to a general review article of the topic. An excellent option is below. We have added this citation to the manuscript and a brief statement about recurrence rates (line 75)

  - Kenton, Kimberly (2019). Pelvic organ prolapse in women: surgical repair of apical prolapse (uterine or vaginal vault prolapse). Brubaker, Linda (Ed.), *UpToDate*. Retrieved June 17, 2017, from https://www.uptodate.com/contents/pelvic-organ-prolapse-in-women-surgical-repair-of-apical-prolapse-uterine-or-vaginal-vault-prolapse

- What is complication risk?
  - Overall apical prolapse surgeries are safe procedure. In this cohort of patients we found an overall mortality rate of 4.7 per 10,000 and no different between surgical approaches. We have added a sentence to the results section discussing mortality in the postoperative period (lines 163-164). Complications assessed in this study are listed in table 3 and include surgical site infections, VTE, sepsis, stroke, CVA, MI, death, PE, Renal insufficiency, renal failure, 30 day reoperation, postoperative urinary tract infection, pulmonary embolism.

- Is this improving outcomes or is this ban eliminating option of transvaginal repair worsening outcomes because worse results with more risk?
  - We think this is an interesting point and we think that there are arguments on both sides. There are many who believe that the withdrawal of transvaginal mesh limits options for women, while others believe that the risks of transvaginal mesh outweigh the benefit. We feel that assessing the value of transvaginal mesh for prolapse repair is beyond the scope of this manuscript. We have however added a sentence to the discussion in lines 244 “There are some who believe that the withdrawal of transvaginal mesh limits treatment options for women, while others believe it provided added protections for women.”

- More context would be useful to understand what this impact will be clinically.
  - The results of this study may not be meaningful in the care for an individual patient but may provide insight into larger trends that we might expect in the surgical treatment of apical prolapse.

Reviewer #2:

- Intro: line 72: I would add reference to most recent FDA publication.

- We have added the following reference “Urogynecologic Surgical Mesh Implants. U.S. Food and Drug Association. https://www.fda.gov/medical-devices/implants-and-prosthetics/urogynecologic-surgical-mesh-implants. Published 2019.”

- How behind is the data in the database? Is 2017 the most recent data available?
  - The most recent Participant Use Data File (PFU) is from 2017 and has been included in this study. The data from 2018 is not yet available.

- What statistical program was used for analysis. Please add
  - The majority statistical analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC) and the interrupted time-series analyses were performed in STATA 12 (StataCorp LP, College Station, TX).This has been added to the methods.

Reviewer #3:

- Your conclusion "suggests" causality which was not modeled in the study. Your quote "decrease in TVM RESULTED in an increase in TAM" is problematic as worded. Time relationships are notorious for resulting in spurious relationships based on unmeasured variables that impact the relationship to make it appear linear. This is esp true in time relationship studies utilizing databases which have no opportunity to model or test the hypothesis. The main unmeasured variable here is that you looked at the 36,463 patients who were known to have apical procedures. During the study period, there were likely >300,000 prolapse procedures that did not include apical suspension. During this same time period, the dramatic rise in Robotic ASC likely caused a large number of patients who previously underwent no apical procedure to now include one in the form of an RASC. This may/could be a larger factor in the rise of the ASC total. The other omitted variable bias (moderating variable) is that it is also known that in an unknown percentage of doctor practices, TVM was converted to Intra/extraperitoneal Colpopexy and at the same time doctors who previously only performed Intra/extraperitoneal Colpopexy learned to perform RASC. This could result in an unchanged number of native tissue colpopexies but for two conflicting reasons. The answer is to tone down language that suggests causality and more strongly acknowledge the potential for omitted variable bias. As listed above there are at least 2 other factors that could reasonably contribute to (or cause) the rise in ASC
  - This is an excellent point and we agree that this study does not intend to determine causality. We have revised our conclusions to better reflect the findings of the study and have elaborated on some of the potential reasons why there was a concurrent rise in abdominal sacrocolpopexy
  - We have added additional detail to the limitations of the study on lines 250-253: “It is possible that some of the trends seen in abdominal sacrocolpopexy are driven by national trends in robotic surgery. Surgeons who previously only performed intraperitoneal or extraperitoneal colpopexy procedures, with the aid of the robot, were now able to perform a laparoscopic abdominal sacrocolpopexy.”

- The second conclusion that is not studied in this data is the "expectation" that this rise will continue. The robotic variable makes that unknown. We see in new technology introduction a hype cycle where use is maximized followed by a cooling off period with decreased use. It is unstudied as to what the trend would be after your study period and it is just as likely that RASC could have experienced a cooling off period during 2017-2020. I don't know that to occur, it just

illustrates that your conclusions should stick to what data is looked at. I would have no problem if you downgraded that from "expectation" to some sort of speculation of possible futures.
    - We again thank the reviewer for an excellent point. We have modified the language so that our statement expresses speculation rather than expectation

- I would like to offer an opinion on your secondary objectives. (line 219-230) Personally this is the most clinically relevant observation that can be directly evaluated by a look at 36,463 cases. The absence of clinically meaningful differences in postoperative complications stratified by surgical approach is well supported by your data and is of great impact, given the dire expectations of mesh use purported elsewhere. This could be considered in the results section and even the conclusion. It is of more interest and more directly supported by data than the other conclusions.
    - We have further emphasized this point in the manuscript and have added a statement in the abstract, methods and results section discussing postoperative complication risks.
    - Lines 52-53 “There were no clinically meaningful differences in postoperative complications when stratified by surgical approach”
    - Lines 61-64: “Given similar rates of complications between the different surgical approaches, the authors do not expect there to be clinically meaningful changes in perioperative complications for patients undergoing apical reconstructive surgery”
    - Lines 257-259: “Moreover, given similar rates of complications between the different surgical approaches, the authors do not expect there to be clinically meaningful changes in perioperative complications for patients undergoing apical reconstructive surgery”

- Line 75-77 needs a reference and would benefit from a quote. I would not paraphrase what the FDA said about ASC. It needs to quote what they did say specifically
    - We have included the exact phrasing in the FDA statement about ASC and MUS

- Line 66 and others: "mesh is intended to provide permanent solution. I would alter that to permanent "or improved durability". Improved durability is a more accurate representation of the intention of mesh rather than permanent solution.
    - We have made the correction from permanent to “more durable”

- Line 142 Typo that won't get caught by editor. you called it inter peritoneal when you meant intra/extra peritoneal
    - Again, thank you for noticing the typo. We have made the correction and checked the remainder of the document to insure that there weren’t other similar errors elsewhere in the text.

Statistical Editor Comments

- Lines 138-139: The chi-square test does not specifically identify one procedure as showing significance, but rather the distribution of all procedures was not random. If specific pairwise comparisons are cited in text, they need pairwise stats testing.
    - We agree with this point and have tried to clarify in the manuscript so that the results we are describing are consistent with the statistical approach we used in the analysis. We have adjusted the sentence in 160 to “there was a significant difference in the proportion of apical procedures performed by each surgical approach for each time period”

- Lines 148-149, Table 3: Again, this stats test was not for that specific surgery, need a pairwise test.
    - We have similarly clarified lines 171-172 to reflect the fact that we performed a chi-square test. The revised sentence states “The operative time for transvaginal mesh was different between surgical approaches (p=0.001)”

- Table 1: Should statistically compare the patient characteristics in the various time epochs. Were they comparable in age, race/ethnicity or co-morbidities?
    - We appreciate the reviewer’s request. The interest in statistical differences of data presented in Table 1 seems to stem from the concern that differences in these populations could confound our results; yet, it has been shown that using statistical criteria to determine whether a characteristic is a confounder can lead to bias (Hernan et al. 2002). Instead, prior knowledge of the subject matter and biology should be used to determine potential confounders. The Strengthening the Reporting of Observations Studies in Epidemiology (STROBE) guidelines are widely considered as best practice recommendations. These guidelines state that “Inferential measures, such as standard errors and confidence intervals, should not be used to describe the variability of characteristics, and significance tests should be avoided in descriptive tables. Also, p values are not an appropriate criterion for selecting which confounders to adjust for in analysis; even small differences in a confounder that has a strong effect on the outcome can be important.” Despite the above, we will defer to the editor and add the p values if requested to do so.

    - Hernan MA, Hernandez-Diaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounder evaluation: an application to birth defects epidemiology. Am J Epidemiol. 2002 Jan 15;155(2):176-84.

    - Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007 Nov;18(6):805-35.

- Tables 1, 2, 3: Should make clear in footnotes to the table what the p-value signifies. Is it comparison across all times or surgical approaches for deviation from random variation, or specific comparison of two time points or vaginal mesh vs a specific other surgery?
    - We have added a footnote explaining the p values used in table 2 and 3

- Fig 1: The lines do not represent "predicted" values, but rather, the data are fitted to a linear regression for each time epoch. Do the Authors have an explanation for the sudden change in vaginal mesh and abd colpopexy procedures in the 2009-2010 time period? This appears to be just prior to the FDA statement and furthermore it calls into question the use of a linear summary of that period, since it consisted of two proportions with a sudden jump, not a gradual change.

- This is an excellent point. Transvaginal mesh kits were first introduced to the US in 2005 and we could speculate that the low rate of use is because it was a relatively novel device. Transvaginal mesh was heavily marketed and promoted by medical device companies however and this could explain the significant uptake in utilization in 2010. Unfortunately, we do not have the data to support this; therefore, we feel that speculation such as this falls beyond the scope of the manuscript however.
- We would also point to the following reference for additional information about predicted values in an interrupted time series analysis
    - Linden A. Conducting interrupted time-series analysis for single- and multiple-group comparisons. The Stata Journal. Volume 15 Number 2: pp. 480-500

Editorial Office Comments:

- 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:
    - OPT-IN: Yes, please publish my point-by-point response letter.

- 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.
    - In the method section we discuss the NISQIP database and the included citations discuss the data collection process and validation.
    - Lines 94-99: "This is a retrospective cohort study of surgical cases from The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database, which is a nationally validated, multicenter database initially developed to measure and improve surgical outcomes across specialties. There are over 700 hospitals that participate in the ACS NSQIP database including both community and academic hospitals. Preoperative, intraoperative and 30-day postoperative data is abstracted by trained personnel. [9] Data collection methods of the ASC NSQIP have been described in detail previously [10,11]

- 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, tables, boxes, figure legends, and print appendixes) but exclude references.
    - The word count is for the manuscript is 3838 and 18 pages excluding references.

- Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.
    - A running title is included on the cover letter and is 44 characters "FDA, transvaginal mesh and trends in apical surgery"

- 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."
    - We have revised the precis based on some of the other reviewers and it is 20 words and on lines 31-32 “Following the safety communication about transvaginal mesh in 2011, there was a significant increase in the use of transabdominal mesh for apical prolapse”

- 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.
    - We have updated the abstract based on the reviewers suggestions

- 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.
    - The word count of the abstract is 292

- 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.
    - We have corrected our manuscript title and have replaced “FDA” with “U.S. Food and Drug Administration”
    - We have also revised the tables and replaced abbreviations where appropriate

We hope these changes meet with your approval and look forward to hearing back from you.

Sincerely,
William Winkelman