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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.

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.
RE: Manuscript Number ONG-18-1154

Concomitant Hysterectomy Lowers the Rate of Repeat Surgery for All Pelvic Organ Prolapse Repair in a Cohort of Nearly 100,000 Women

Dear Dr. Dallas:

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 Aug 10, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Thank you for your submission. For the future of prolapse repair, it is very important to understand the risk factors of recurrent prolapse. As you stated, more patients are interested in uterine preservation. Being able to counsel patients regarding uterine preservation versus hysterectomy is an important as we move forward. I have included the following suggestions. I am most concerned about being clear regarding your cohort design.

Abstract
- Objective—revise "on a population level"
- Methods—State the study design—retrospective cohort study using the Office of Statewide Health Planning and Development
- Methods—How were the patients identified—using CPT codes?
- Results—I would recommend clarifying the percentages. 56% of the index prolapse repairs involved multiple compartments—are these the patients who also had a hysterectomy? 14% of all of the patients meeting inclusion criteria were mesh augmented?
- Results—The mean follow-up time seems very long. If the data are skewed, you may consider reporting this as a median instead.

How did you know that patients didn't have a prior repair? How did you know that patients didn't have a prior hysterectomy?—This question is addressed later in the methods section of the manuscript, but this could be more clear in the abstract

Comparing hysterectomy at time of prolapse repair versus hysteropexy or repair with uterine preservation (native tissue and mesh augmented repair) would better describe the approach. Or stating hysterectomy with prolapse repair versus uterus in situ with prolapse repair.

Methods
- State clearly the type of study design you are performing in the first sentence. Then move on to describe the OSHPD dataset
- Clarify what is submitted in the reports to OSHPD—just the codes? All notes? Complete health information?
- Throughout the paper, "data" is used as a singular noun but should be plural. Change to "data are"
- Define the "study period" more clearly in line 159—is this the time period of the dataset? Within 12 months of follow-up?
Results
- Describe the uterus in situ group like you did in lines 205-207. Percentage of patient with mesh augmented repair and concomitant incontinence procedure
- Line 231-233—These demographic factors describe race and not ethnicity (Hispanic vs Non-Hispanic)
- Increasing age was associated with an increased odds of requiring a repeat surgery—Can you elaborate on this? Was age categorical—patients in 20-40 years were more likely to require repeat surgery? Was age continuous in the modeling—so for each year increase in age, the risk for repeat increased by X?

Discussion
- Revise sentence 256-257: Modeling demonstrated that hysterectomy was associated with decreased risk of repeat surgery when adjusted and unadjusted. These results remained statistically significant

Reviewer #2:

Abstract - Objective - To evaluate the association between concomitant hysterectomy and the time of pelvic organ prolapse (POP) surgery with the risk of subsequent prolapse surgery.

Methods - Data from California OSHPD collected including patients undergoing anterior, apical, and posterior repair in California between 2005-2011 and the association with recurrent POP surgery.

Results - 93,831 women were included in the cohort - 45% of whom had concomitant hysterectomy. The need for recurrent surgery was lower if concomitant hysterectomy was performed (3 vs 4.4%). Hysterectomy decreases the risk of future surgery for recurrence in the anterior, posterior, and apical compartments. Hysterectomy also leads to an increased risk of peri-operative complications and longer hospital stay.

Conclusions - population based cohort - hysterectomy decreases risk of future surgery by 1/3 but this only amounts to a 1-3% difference in surgery. This needs to be weighed against the increased risk of peri operative morbidity.

Introduction - Discussion of nationwide impact of POP, with 30% suffering from recurrence after initial surgery. Risk of recurrence has been found to be related to preoperative stage of prolapse. The role of hysterectomy in recurrence is unclear, so this study evaluates the association between hysterectomy and POP with recurrence.

Methods - California OSHPD data from 2005-2011. This allowed identification of mesh use and concomitant incontinence procedure for POP repair. Secondary outcomes were perioperative complications.

Results - cohort of 93,831 with follow up for 1500 d, 44% had a single compartment repair, 56% had multi compartment repair, 45% hysterectomy, 14% mesh, 48.9% concurrent incontinence procedure.
3.8% had recurrent POP with mean repeat surgery at 1.9yrs. Repeat surgery if hysterectomy vs no hysterectomy - 3% vs 4.4%
secondary outcome - increased complications regardless of compartment of repair, hysterectomy leads to decreased risk of future surgery for recurrence in all comparisons.
White women and increasing age are associated with repeat risk of recurrence while mesh decreases risk of recurrence 36% of patients with hysterectomy had no POP uterine pathology and had a decrease risk of recurrence. If these patients are excluded, there is still a decreased risk of recurrence in patients with hysterectomy - 3.3% vs 4%.

Discussion - hysterectomy leads to a decrease in subsequent prolapse surgery which persists when control for demographics and regardless of compartment. However, the decrease risk of repeat surgery translates to a 1-3% difference in risk of repeat surgery limited by lack of information on surgery and type of surgery

Conclusions - Concomitant hysterectomy at time of POP surgery leads to a difference in repeat surgery but at the risk of increased perioperative morbidity

While it is unfortunate that this does not include specific details about type of surgery or type of surgeon, it is still a good paper with a large volume and important findings. There is a decreased recurrence prolapse, but definitely at an expense of increased complications so treatment needs to be individualized.

I would like to see some breakdown based on CPT codes of types of surgery - vaginal only, inclusion of abdominal - open or laparoscopic - or some sort of comparison by surgical type because an anterior repair is quite different from an abdominal sacrocolpopexy and it is difficult to compare the risk of recurrence between these procedures. Some information as to distribution of types of surgeries by codes would be helpful if it is possible to include - was their an equivalent distribution of approaches between the groups? Or are the hysterectomy procedures much more significant repair procedures as opposed to vaginal approaches only and therefore this could explain increase risk of recurrence in group without a hysterectomy. This would be then related to surgical approach rather than performance of hysterectomy, so some information based on procedure is needed.
Reviewer #3:

The authors have addressed most of the reviewers concerns.

This portion of the abstract conclusion should be changed because "approximately one-third" is misleading "a decreased risk of future surgery for prolapse recurrence by approximately one-third which translates to a modest 1-3% difference in risk."

It should be revised to say "a decreased risk of future surgery for prolapse recurrence by 1-3%"

EDITORS NOTE

Please make sure you expunge "Causal language" from your paper, including the title. Your paper can address associations, but not causation. Thanks. NC

STATISTICAL EDITOR COMMENTS:

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

lines 77-78: While it is an excellent point to contrast the decreased risk of future surgery for prolapse in terms of both relative and absolute risk, it would be an additional point of interest to include a concise summary of the relevant increases in absolute risk for transfusion, hemorrhage, LOS etc. This would help to achieve the goal of informing women re: risks and benefits of POP surgery.

lines 181, 339: As the Authors rightly state in title (lines 8-9) and in Abstract (lines 50, 66, 76), the study design allows for concluding associations and although used in common parlance in modelling terminology, the word "predict" should be avoided, lest the reader misinterpret the findings.

Methods, Tables 1-3: This is a very large study and the sample sizes are more than adequate for multivariate logistic adjustment. However, I would encourage, though not require, that the Authors consider supplementing their analysis with propensity matching. The cohorts were clearly different in multiple baseline characteristics, some of which (age, race, payer, comorbidities, index surgery) may be related to the primary and secondary outcomes. A matching algorithm could confirm the difference in subsequent surgery rates and difference in morbidity rates and strengthen their arguments.

EDITOR COMMENTS:

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

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

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. Each author on this manuscript must submit a completed copy of our revised author agreement form (updated in the August 2014 issue). Please note:
   a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.
   b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment
to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

- Substantial contributions to the conception or design of the work;
- OR
- the acquisition, analysis, or interpretation of data for the work;
- AND
- Drafting the work or revising it critically for important intellectual content;
- AND
- Final approval of the version to be published;
- AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The author agreement form is available online at http://edmgr.ovid.com/ong/accounts/agreementform.pdf. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained."

*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

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

6. All 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 web site 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.

7. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

8. 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 appendices).

Please limit your Introduction to 250 words and your Discussion to 750 words.

9. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).

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

11. 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, written in the present tense and stating 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."

12. 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. Please provide a word count.

13. 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.

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

15. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

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

17. Please revise the following figure:

Figure 1: Please upload high res version of these graphs (eps, tiff, jpeg). Items pasted into Word often lose resolution and appear poorly in print.

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.
Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

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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, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

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 Aug 10, 2018, 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

If you would like your personal information to be removed from the database, please contact the publication office.
July 23, 2018

Re: “Association Between Concomitant Hysterectomy and Repeat Surgery for Pelvic Organ Prolapse Repair in a Cohort of Nearly 100,000 Women”

Dear Editors of Obstetrics and Gynecology,

Thank you for the opportunity to submit revisions for our work “Association Between Concomitant Hysterectomy and Repeat Surgery for Pelvic Organ Prolapse Repair in a Cohort of Nearly 100,000 Women.” Please see responses to reviewers document below and the attached tracked changes document.

The lead author, Dr. Lisa Rogo-Gupta*, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

This research work is IRB exempt, see our institutions guidelines:

http://researchcompliance.stanford.edu/hs/new/resources/faqs/index.html#application

The following activities are not considered to involve human subject(s):

- Private data or specimens were not collected specifically for the currently proposed research through an intervention or interaction with living individuals AND the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement).

https://www.oshpd.ca.gov/HID/Data_Request_Center/IPA.html

This study was approved by the California Protection of Human Subjects (CPHS). OSHPD ID 2110818-01

Sincerely,

Lisa Rogo-Gupta, MD

*The manuscript’s guarantor
Response to Reviewers

Reviewer #1
Thank you for your submission. For the future of prolapse repair, it is very important to understand the risk factors of recurrent prolapse. As you stated, more patients are interested in uterine preservation. Being able to counsel patients regarding uterine preservation versus hysterectomy is an important as we move forward. I have included the following suggestions. I am most concerned about being clear regarding your cohort design.

Abstract
1. Objective—revise on a population level
   a. Line 51 has been revised to read “in a large population based cohort.”
2. Methods—State the study design—retrospective cohort study using the Office of Statewide Health Planning and Development
   a. Line 54 has been revised to read “Data from the Office of Statewide Health Planning and Development (OSHPD) for the state of California was used in this retrospective cohort study…”
3. Methods—How were the patients identified—using CPT codes?
   a. Lines 55-58 read “… to identify all women who underwent… using CPT and ICD-9 procedure codes.”
4. Results—I would recommend clarifying the percentages. 56% of the index prolapse repairs involved multiple compartments—are these the patients who also had a hysterectomy? 14% of all of the patients meeting inclusion criteria were mesh augmented?
   a. Line 64 was revised to read “Of index repairs, 48% involved multiple prolapse compartments and 14.0% were mesh augmented.”
5. Results—The mean follow-up time seems very long. If the data are skewed, you may consider reporting this as a median instead.
   a. Line 66-67 now includes the mean and median follow up time.
6. How did you know that patients didn’t have a prior repair? How did you know that patients didn’t have a prior hysterectomy?—This question is addressed later in the methods section of the manuscript, but this could be more clear in the abstract
   a. Line 58-59 was clarified to read “Women with a diagnosis code indicating prior hysterectomy were excluded, and the first prolapse surgery during the study period was considered the index repair.”
7. Comparing hysterectomy at time of prolapse repair versus hysteropexy or repair with uterine preservation (native tissue and mesh augmented repair) would better describe the approach. Or stating hysterectomy with prolapse repair versus uterus in situ with prolapse repair.
   a. Line 61-63 was added to include the suggested statement “We compared reoperation rates for POP surgery with hysterectomy versus POP surgery with uterine preservation or other method of apical suspension.”

Methods
8. State clearly the type of study design you are performing in the first sentence. Then move on to describe the OSHPD dataset
   a. Beginning with line 182, the first sentence includes the statement “retrospective cohort study” and the second sentence begins the explanation for the OSHPD dataset as recommended.
9. Clarify what is submitted in the reports to OSHPD—just the codes? All notes? Complete health information?
   a. Lines 186-211 include information and references regarding the dataset.

10. Throughout the paper, "data" is used as a singular noun but should be plural. Change to "data are"
   a. The suggested changes were made throughout the paper.

11. Define the "study period" more clearly in line 159—is this the time period of the dataset? Within 12 months of follow-up?
   a. A sentence was added to clarify the difference between the study period versus the follow-up time. (Line 117)

Results

12. Describe the uterus in situ group like you did in lines 205-207. Percentage of patient with mesh augmented repair and concomitant incontinence procedure
   a. Lines were added to describe this group as requested “There were differences... more common in the hystero-preservation group.” (Paragraph beginning at line 212).

13. Line 231-233—These demographic factors describe race and not ethnicity (Hispanic vs Non-Hispanic)
   a. The terminology was chosen (“race/ethnicity”) to reflect the categories included in the section. Races include Black, Asian, White, while Hispanic is considered an ethnic determination. We will defer to the Editor for the use of these terms in this Journal for consistency

14. Increasing age was associated with an increased odds of requiring a repeat surgery—Can you elaborate on this? Was age categorical—patients in 20-40 years were more likely to require repeat surgery? Was age continuous in the modeling—so for each year increase in age, the risk for repeat increased by X?
   a. Age was modeled as a continuous variable so for each year increase in age, the risk for repeat surgery increased by the stated amount (see Table 3).

Discussion

15. Revise sentence 256-257: Modeling demonstrated that hysterectomy was associated with decreased risk of repeat surgery when adjusted and unadjusted. These results remained statistically significant
   a. This section of the discussion was revised (Line 241).

Reviewer #2

Abstract - Objective - To evaluate the association between concomitant hysterectomy and the time of pelvic organ prolapse (POP) surgery with the risk of subsequent prolapse surgery.
Methods - Data from California OSHPD collected including patients undergoing anterior, apical, and posterior repair in California between 2005-2011 and the association with recurrent POP surgery.
Results - 93,831 women were included in the cohort - 45% of whom had concomitant hysterectomy. The need for recurrent surgery was lower if concomitant hysterectomy was performed (3 vs 4.4%). Hysterectomy decreases the risk of future surgery for recurrence in the anterior, posterior, and apical compartments. Hysterectomy also leads to an increased risk of peri-operative complications and longer hospital stay.
Conclusions - population based cohort - hysterectomy decreases risk of future surgery by 1/3 but this only amounts to a 1-3% difference in surgery. This needs to be weighed against the increased risk of peri operative morbidity.

Introduction - Discussion of nationwide impact of POP, with 30% suffering from recurrence after initial surgery. Risk of recurrence has been found to be related to preoperative stage of prolapse. The role of hysterectomy in recurrence is unclear, so this study evaluates the association between hysterectomy and
POP with recurrence.

Methods - California OSHPD data from 2005-2011. This allowed identification of mesh use and concomitant incontinence procedure for POP repair. Secondary outcomes were perioperative complications.

Results - cohort of 93,831 with follow up for 1500 d, 44% had a single compartment repair, 56% had multi compartment repair, 45% hysterectomy, 14% mesh, 48.9% concurrent incontinence procedure. 3.8% had recurrent POP with mean repeat surgery at 1.9yrs. Repeat surgery if hysterectomy vs no hysterectomy - 3% vs 4.4% secondary outcome - increased complications regardless of compartment of repair, hysterectomy leads to decreased risk of future surgery for recurrence in all comparisons. White women and increasing age are associated with repeat risk of recurrence while mesh decreases risk of recurrence. 36% of patients with hysterectomy had no POP uterine pathology and had a decrease risk of recurrence. If these patients are excluded, there is still a decreased risk of recurrence in patients with hysterectomy - 3.3% vs 4%.

Discussion - hysterectomy leads to a decrease in subsequent prolapse surgery which persists when control for demographics and regardless of compartment. However, the decrease risk of repeat surgery translates to a 1-3% difference in risk of repeat surgery. limited by lack of information on surgery and type of surgery

Conclusions - Concomitant hysterectomy at time of POP surgery leads to a difference in repeat surgery but at the risk of increased perioperative morbidity

While it is unfortunate that this does not include specific details about type of surgery or type of surgeon, it is still a good paper with a large volume and important findings. There is a decreased recurrence prolapse, but definitely at an expense of increased complications so treatment needs to be individualized.

1. I would like to see some breakdown based on CPT codes of types of surgery - vaginal only, inclusion of abdominal - open or laparoscopic - or some sort of comparison by surgical type because an anterior repair is quite different from an abdominal sacrocolpopexy and it is difficult to compare the risk of recurrence between these procedures. Some information as to distribution of types of surgeries by codes would be helpful if it is possible to include - was their an equivalent distribution of approaches between the groups? Or are the hysterectomy procedures much more significant repair procedures as opposed to vaginal approaches only and therefore this could explain increase risk of recurrence in group without a hysterectomy. This would be then related to surgical approach rather than performance of hysterectomy, so some information based on procedure is needed.

   a. We appreciate the comment from the reviewer. We attempt to address this within the context of known limitations in prolapse procedure codes in a few ways. First, in Table 2 we included the number of procedures for each compartment as well as multiple compartment repairs as we agree repair of multiple compartments suggests more ‘significant’ repair. Second, we included the procedure codes so readers could be reminded of the limitation of these codes. For example, "hysterectomy with cystocele" does not indicate approach (vaginal or abdominal). If requested by the editor we could include number of repairs by individual codes. Third, we performed a sensitivity analysis by excluding all hysterectomies we could identify as an abdominal approach (13,730). These remaining 28,610 patients who presumably had hysterectomy and POP repair by a vaginal approach were then compared to the overall uterine-sparing group. Even with this adjustment, our results and conclusions are unchanged with the repeat surgery rates greater in the uterine preservation group than the hysterectomy group.
(4.4% versus 3.0, respectively, p<0.001). Details of this sensitivity analysis was added to our methods, results, and conclusions sections.

Reviewer #3
The authors have addressed most of the reviewers concerns.
1. This portion of the abstract conclusion should be changed because "approximately one-third" is misleading "a decreased risk of future surgery for prolapse recurrence by approximately one-third which translates to a modest 1-3% difference in risk." It should be revised to say "a decreased risk of future surgery for prolapse recurrence by 1-3%".
   a. The conclusion section of the abstract was changed accordingly. The related sentence in the conclusion section of the manuscript was also revised.

EDITOR’S NOTE
1. Please make sure you expunge "Causal language" from your paper, including the title. Your paper can address associations, but not causation. Thanks. NC
   a. We have reviewed the manuscript and have made efforts to include recommended language. To begin, the title states the association (though the linked title in the submission is the original, it is changed in the document).

STATISTICAL EDITOR COMMENTS
1. The Statistical Editor makes the following points that need to be addressed: Lines 77-78: While it is an excellent point to contrast the decreased risk of future surgery for prolapse in terms of both relative and absolute risk, it would be an additional point of interest to include a concise summary of the relevant increases in absolute risk for transfusion, hemorrhage, LOS etc. This would help to achieve the goal of informing women re: risks and benefits of POP surgery.
   a. This information has been added to Table 1
2. Lines 181, 339: As the Authors rightly state in title (lines 8-9) and in Abstract (lines 50, 66, 76), the study design allows for concluding associations and although used in common parlance in modelling terminology, the word "predict" should be avoided, lest the reader misinterpret the findings.
   a. We appreciate the comment and have removed the word “predict”.
3. Methods, Tables 1-3: This is a very large study and the sample sizes are more than adequate for multivariate logistic adjustment. However, I would encourage, though not require, that the Authors consider supplementing their analysis with propensity matching. The cohorts were clearly different in multiple baseline characteristics, some of which (age, race, payer, comorbidities, index surgery) may be related to the primary and secondary outcomes. A matching algorithm could confirm the difference in subsequent surgery rates and difference in morbidity rates and strengthen their arguments.
   a. We have included the encouraged propensity matching analysis to the manuscript.

EDITOR COMMENTS:
1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor’s specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter. ***The notated PDF is uploaded to this submission’s record in Editorial Manager. If you cannot locate the file, contact Katie McDermott and she will send it by email – kmcdermott@greenjournal.org.***
a. Editor comment 1: When you write that a study occurred between date 1 and date 2, it literally excludes those boundary dates. For instance, “This study was performed between Feb 2018 and Jan 2019” would mean it was performed from March.
   a. **We have corrected this language.**

b. Editor comment 2: The Journal style does not include the use of the virgule (/) except in numeric expressions. Please edit here and in all instances.
   a. **We have corrected this language.**

c. Editor comment 3: In the abstract, please provide absolute numbers as well as which ever effect size you are reporting + Confidence intervals. P values may be omitted for space concerns. By absolute values, I mean something like xx (outcome in exposed)/yy(outcome in unexposed) (zz%) (Effect size= ; 95% CI= ) An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4)
   a. **We have revised this in the abstract and have removed the p values for space**

d. Editor comment 4: see reviewer #3 comments regarding this statement.
   a. The conclusion has been revised

e. Editor comment 5: This is a very well written introduction. You clearly outline the literature gaps, clinical relevance, objectives and hypothesis. Thanks!
   a. Thank you for the positive feedback!

f. Editor comment 6: For data presented in the text, please provide the raw numbers as well as data such as percentages, effect size (OR, RR, etc) as appropriate and 95% CI’s.
   a. **We have corrected this language.**

g. Editor comment 7: 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)
   a. Thank you for the reference and we have added this to our limitations section.
   We also reviewed the language in the conclusion and overall manuscript to make sure we are not being perceived as overstating our findings. Our intended purpose is to state the results in the setting of the limitations of epidemiologic research. Given this particular question cannot be answered using a randomized controlled trial (of hysterectomy versus uterine preservation), we are limited in the possible study design options for projects geared towards gaining a better understanding this issue (as presented in the introduction).

h. Editor comment 8: are all of these findings statistically significant? If not, please avoid describing them as showing a difference.
   a. **We have corrected this language.**

i. Editor comment 9: I do think that reporting a propensity analysis would make your findings potentially stronger, as recommended by the statistical editor. If it merely supports your findings, you could include it in supplemental digital content and reference it in the results section. Otherwise, you could report in your results section as well.
   a. **We have included the encouraged propensity matching analysis to the 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.

3. Each author on this manuscript must submit a completed copy of our revised author agreement form (updated in the August 2014 issue). Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

* Substantial contributions to the conception or design of the work;
OR
the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
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The author agreement form is available online at http://edmgr.ovid.com/ong/accounts/agreementform.pdf. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript’s lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript’s guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

a. The requested statement was added to the cover letter on Page 1 of this document.
5. In order for an administrative database study to be considered for publication in Obstetrics & Gynecology, the database used must be shown to be reliable and validated. In your response, please tell us who entered the data and how the accuracy of the database was validated. This same information should be included in the Materials and Methods section of the manuscript.
   a. This information was added to the methods section of the manuscript.

6. 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 web site 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.
   a.

This research work is IRB exempt, see our institutions guidelines:

http://researchcompliance.stanford.edu/hs/new/resources/faqs/index.html#application

The following activities are not considered to involve human subject(s):

- Private data or specimens were not collected specifically for the currently proposed research through an intervention or interaction with living individuals AND the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement).

https://www.oshpd.ca.gov/HID/Data_Request_Center/IPA.html

This study was approved by the California Protection of Human Subjects (CPHS). OSHPD ID 2110818-01

This information was added to the cover letter and methods

7. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.
8. 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 appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

a. Word Count: 3105 (Manuscript) 404 (Abstract). The addition of the requested information by the reviewers (complications and their RR and CI, additional details in the methods section) has expanded the word count of our abstract. Here is a new abstract that is 249 words, please review for adequate content. Given the responses as above to the requests for additional content, we chose to provide an alternative abstract here for review by the editor and can replace the abstract in the manuscript file if deemed adequate to address the abovementioned concerns.

**Objectives:** To evaluate the association of hysterectomy at the time of Pelvic Organ Prolapse (POP) repair risk of subsequent POP surgery.

**Methods:** Data from the California Office of Statewide Health Planning and Development were used in this retrospective cohort study to identify all women who underwent an anterior, apical, posterior or multiple compartment POP repair at non-federal hospitals between January 1, 2005- December 31, 2011 using CPT and ICD-9 codes. Women with a code indicating prior hysterectomy were excluded, and the first POP surgery during the study period was considered the index repair. Demographic and surgical characteristics were explored for associations with the primary outcome. Reoperation after POP surgery with hysterectomy was compared to reoperation after other apical suspension.

**Results:** Of the 93,831 women included, 42,340 (45.1%) underwent hysterectomy with index repair. Forty-eight percent of index repairs involved multiple compartments, 14.0% included mesh, and 48.9% included an incontinence procedure. Mean follow up time was 1,485 days (median 1,500 days). The rate of additional POP surgery after hysterectomy was lower than after surgery without hysterectomy 3.0% vs. 4.4% (RR 0.67; 95% CI 0.62-0.71). Hysterectomy was associated with a decreased risk of future surgery for anterior (OR=0.71, 95% CI 0.64-0.78), apical (OR=0.76, 95% CI 0.70-0.84), and posterior POP (OR=0.69, 95% CI 0.65-0.75) and increased perioperative complications.

**Conclusions and Relevance:** Hysterectomy at the time of POP repair is associated with a decreased risk of future POP surgery by 1-3% and is independently associated with higher perioperative morbidity in a large population-based cohort.

b. Discussion: 710. Similarly, in earlier revision requests we have been asked to include additional information and limitations. We met the recommend word count here, please provide feedback if the editor feels any essential information has been eliminated.

9. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).

a. This information is provided.

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

a. **Short Title: Hysterectomy and Repeat Prolapse Repair**

11. 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, written in the present tense and stating 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."

a. **Precis:** Hysterectomy at the time of prolapse repair is associated with a 1-3% decreased risk of future prolapse surgery.

12. 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. Please provide a word count.

a. Please see above word counts for abstract and manuscript

13. Only standard abbreviations and acronyms are allowed. A selected list is available online at [http://edmgr.ovid.com/ong/accounts/abbreviations.pdf](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.

a. This has been reviewed.

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

a. This virgule symbol has been eliminated.

15. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

a. Please see above, the discussion section has been shortened as requested.
16. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

17. Please revise the following figure:

Figure 1: Please upload high res version of these graphs (eps, tiff, jpeg). Items pasted into Word often lose resolution and appear poorly in print.
   a. This was completed

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.

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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.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

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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, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

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 Aug 10, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology
Hello Denise-

Please see responses below:

1. AQ: List each author’s name as first name, last name, degrees. **Done in manuscript attachment**
2. AQ: Please provide an Author Agreement form from Dr. Syan with a signature (the form is blank in the signature section). **Please see attached**
3. AQ: Please provide a completed STROBE checklist. The checklist is available at [http://ong.editorialmanager.com](http://ong.editorialmanager.com). **Please see attached**
4. (Abstract Results, line 71) AQ: These data are in Table 3 as ORs and CIs, but where are the percentages? They should be found somewhere other than the abstract. **Please see Table 1**

Regards,
Lisa Rogo-Gupta

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On Wed, Aug 1, 2018 at 8:40 AM, KAI Dallas wrote:

Get [Outlook for iOS](https://www.outlook.com/ios.html)

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From: Denise Shields <dshields@greenjournal.org>
Sent: Wednesday, August 1, 2018 5:55 AM
To: 
Subject: your revised Green Journal manuscript (18-1154)

Dear Dr. Dallas,

Your revised manuscript, “Association Between Concomitant Hysterectomy and Repeat Surgery for Pelvic Organ Prolapse Repair in a Cohort of Nearly 100,000 Women” is being reviewed by the editors. Please address the following queries in the margin of the attached version of your manuscript.

1. AQ: List each author’s name as first name, last name, degrees.
2. AQ: Please provide an Author Agreement form from Dr. Syan with a signature (the form is blank in the signature section).
3. AQ: Please provide a completed STROBE checklist. The checklist is available at http://ong.editorialmanager.com.
4. (Abstract Results, line 71) AQ: These data are in Table 3 as ORs and CIs, but where are the percentages? They should be found somewhere other than the abstract.

In order to keep your manuscript moving through our process, please respond within 48 hours.

Regards,

Denise Shields
Senior Manuscript Editor

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Lisa
This looks perfect. Thank you!

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