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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)\*

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<sup>\*</sup>The corresponding author has opted to make this information publicly available.

**Date:** Nov 01, 2019

To: "Graham Chapman"

From: "The Green Journal" em@greenjournal.org

Subject: Your Submission ONG-19-1879

RE: Manuscript Number ONG-19-1879

Perioperative safety of surgery for pelvic organ prolapse in the elderly and frail

### Dear Dr. Chapman:

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 14 days from the date of this letter. If we have not heard from you by Nov 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

# **REVIEWER COMMENTS:**

Reviewer #1: This article addresses the important topic of perioperative complications in elderly and frail patients undergoing prolapse surgery. It uses the American College of Surgeons' NSQIP database over a 7 year period, stratifying patients by age into controls, the elderly, and the very elderly. This topic has high relevance given the high incidence of pelvic organ prolapse in the elderly and the increasing number of those patients who seek surgical treatment.

- 1. Abstract: Clearly describes the purpose and outcome of the study. Its content specifically and accurately reflects that of the article.
- 2. Introduction: Clearly introduces the objective of the study, which is to analyze the impact of aging and frailty on perioperative morbidity in the elderly patient undergoing prolapse surgery. This is presented against the background of existing data regarding prolapse surgery in the elderly, and the relative importance of specific conditions related to age, compared with age itself. The authors utilized a large surgical database in hopes that this would provide more useful information than existing trials which they state under-represent elderly patients.
- 3. Methods: The authors stratified age into three groups, and used a validated frailty index. Appropriate primary and secondary outcome measures were used.
- 4. Results: The results show a significantly higher risk of complications and mortality in the very elderly group compared with the elderly and non-elderly groups. As the authors note, these conclusions are limited by the retrospective nature of the study and the heterogeneity among groups.
- 5. Discussion: The authors' findings of higher surgical risk after prolapse surgery in the very elderly contrast with previous studies showing low rates of serious complications in this age group. Their discussion does not contain any comment or analysis of possible reasons for these discrepant findings. What are the reasons the authors believe their results are more accurate? In addition, a comparison of these findings to other studies examining the effect of old age on complications in other surgical subspecialties would help to put the author's results into a more general context.
- 6. Tables: Appropriate and reflect the study groups and outcomes clearly.
- 7. References: Appropriate.

#### Reviewer #2:

Overall: A national quality improvement project database was used to identify patients who underwent surgery for prolapse from 2010 to 2017. They compared a control group (45-64 years, index population) to those aged 65-79 (elderly) and  $\geq$ 80 (very elderly). The primary outcome was the composite rate of serious complications and mortality. The frailty rate was 7.2% in the index population, compared to 14.5% in the elderly and 16.8% in the very elderly. The composite rate of serious complications in the index population was 4.5%, compared to 4.7% in the elderly (p=0.4), and 9.0% in the very elderly (OR 2.1, 1.8-2.4, p<0.001). On multivariate logistic regression, the only age group independently associated with serious complications was the very elderly. Complications surrounding prolapse surgery increase substantially in the cohort of patients over the age of 80, independent of frailty and medical or surgical risk factors.

Disclosures: None to report.

Human subjects: IRB exemption from review.

### Abstract:

1. The abstract is well written and is representative of the article.

#### Introduction:

2. The purpose is clear and concise, the background is succinctly described.

#### Methods:

- 3. Methods are well described and the procedures used are presented in great detail.
- 4. Line 116: What are the 5 perioperative variables used to calculate the mFI-5?

### Results:

5. The data answered the study question.

#### Discussion

6. The discussion is well written, relevant and data support the conclusions

#### References:

7. The following reference may be of use:

You're How Old? Correlating Perioperative Complication Risk in Octogenarians Undergoing Colpocleisis for Pelvic Organ Prolapse.

Sifuentes R, Wolff BJ, Barnes HC, Wozniak A, Mueller ER, Pham TT.

Female Pelvic Med Reconstr Surg. 2019 Jul 24. doi: 10.1097/SPV.000000000000759. [Epub ahead of print]

PMID: 3135635

### Tables/Figures:

- 8. Consider adding the word "study" prior to the word "population" in the title of all 3 figures
- 9. Table 1: The totals for racial/ethnic group add up to less than 100% for all three study groups. Is this due to missing data?

Reviewer #3: Well written manuscript that is easy to follow and read. I would appreciate more information about your modelling process - there are many ways to evaluate which variables are included in a final model. Could you perhaps include a supplemental table of all variables in the univariate model that you evaluated, and indicate which were kept and which were dropped and their associated ORs that lead you to include/exclude? Also - did your final multivariate logistic regression model include interaction terms? For example - did you explore if the NSQIP modified frailty index-5 score had different predictive abilities in the baseline, elderly and very elderly group? Given only one OR is provided, it seems like it was modelled as static across all 3 groups and I wonder if it's predictive ability in the very elderly group is being masked by not allowing it to "vary" across groups in your model. I'd like to see the stats reported on line 174 - 176 specified for elderly and very elderly separately.

Please report a goodness of fit measure for this model - such as ROC or Hosmer-Lemeshow.

I appreciate Table 2. Too often modelling papers focus on ORs, but I believe this will be the table that most clinicians find useful.

#### STATISTICAL EDITOR COMMENTS:

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

Table 1: Should statistically compare the elderly and very elderly cohorts vs the index age group for each of the characteristics cited. Should explain in Table footnote the distinction made between "Frailty index" and "Frail". Also, elsewhere in text frailty index is described as %, while in Table 1 it is a proportion. Should use one consistent format. Among the baseline differences, one that is both statistically and clinically important, would be the ASA class. Should elaborate that into proportion in Class 1, 2, 3, 4, besides aggregating classes 3 and 4.

Table 3: This appears to be composite rates for the serious complications cited in Table 2 and elsewhere. Should consistently format as "serious complication rates". These are apparently crude ORs, so should state in Table footnote. Since CIs are included, no need to include separate column for p-values, could be indicated by footnotes, if desired.

Table 4: Should include crude ORs in separate column and should indicate in footnote the variables included as adjustors in the final model. Again, the p-values are redundant, since CIs are included, but could list in footnote to Table if desired.

Fig 1: Very useful figure, but I do not see the light grey background in my version of the Figure. Might consider vertical lines to indicate the 3 age groups.

Fig 2: Again, I do not see any difference in background corresponding to the elderly or very elderly age groups. Should change the title to Composite serious complication rate. Again, might consider use of vertical lines to demarcate the 3 age cohorts.

Fig 3: Probably could be included as supplemental material.

Should also show the relationship of ASA vs age, perhaps as proportion in Class 3 or 4 vs age. Also, as sensitivity analysis, how did the analysis of serious complication rates change if one were to separately analyze women with Class 3 or 4, just as was done in Table 3. That is, were the higher serious complication rates in the very elderly also applicable when only Class 3 or 4 ASA were considered?

#### **EDITOR COMMENTS:**

### 1. Specific manuscript comments:

We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting.

## PRESENTATION OF STATS INFORMATION

P Values vs Effect Size and Confidence Intervals

While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

This is true for the abstract as well as the manuscript.

Please provide absolute values for variables, in addition to assessment of statistical significance.

We ask that you provide crude OR's followed by adjusted OR's for all variables.

Line 64: You don't tell us in the methods section how the "frailty index" is differentiated from "Being frail". As such, this sentence is unclear. This continues to line 65-66: What is the index population you are referring to here? It seems like you referring to the age reference—were frail-patients only taken from all of those age groups? I don't see how this comparison was made. It seems like you should control for age and then look at frail-patients only .

Line 74: add age 70 years. Same true for all age designations—need units (like on line 75).

Line 87: Define frailty.

- Line 101: Why was it exempt?
- Line 103: please say "from the years of 2010 to 2017" as "between" strictly means you excluded 2010 and 2017.
- Line 113: can you detail the mFI-5 in a box?
- Line 120-121: It seems this is how you defined "frail" vs Frailty index. Can you make this really clear how you used these terms?
- Line 123: Does the NSQIP report only complications in the immediate perioperative period or does it extend to sometime longer? Is it restricted to inpatient procedures or does it include ambulatory procedures?
- Table 4: I'm unclear what this regression is about. In footnote, please provide the variables in the analysis. Are these the aOR for the composite outcome?

Please address the comments by the statistical editor regarding adding an analysis looking at ASA categories to explore this measure as an association with safety outcomes for older women.

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

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

- 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, references, tables, boxes, figure legends, and print appendixes) but exclude references.
- 6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:
- \* All financial support of the study must be acknowledged.
- \* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- \* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
- \* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).
- 7. 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.

- 8. 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.
- 9. 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.
- 10. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

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

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

- 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.
- 12. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.
- 13. Figures 1–3: Please upload as high-res figure files (eps, tiff, jpeg, etc.) on Editorial Manager.
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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.

- 15. If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:
- \* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
  - \* A point-by-point response to each of the received comments in this letter.

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

Again, your paper will be maintained in active status for 14 days from the date of this letter. If we have not heard from you by Nov 15, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD Editor-in-Chief

2018 IMPACT FACTOR: 4.965

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

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

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November 15, 2019 Dr. Nancy C. Chescheir Editor-in-Chief *Obstetrics and Gynecology* RE: Manuscript Number ONG-19-1879

Dear Dr. Chescheir,

Please find the attached revised manuscript for our original research article entitled "Perioperative safety of surgery for pelvic organ prolapse in the elderly and frail" for your review. We have read the instructions for authors. Additionally, below you will find our point-by-point responses to the reviewer and editor comments.

We are grateful for the opportunity to submit our revised work, and thank you for your consideration.

Sincerely,

Graham C. Chapman, M.D.



# **REVIEWER COMMENTS:**

Reviewer #1: This article addresses the important topic of perioperative complications in elderly and frail patients undergoing prolapse surgery. It uses the American College of Surgeons' NSQIP database over a 7 year period, stratifying patients by age into controls, the elderly, and the very elderly. This topic has high relevance given the high incidence of pelvic organ prolapse in the elderly and the increasing number of those patients who seek surgical treatment.

- 1. Abstract: Clearly describes the purpose and outcome of the study. Its content specifically and accurately reflects that of the article.
- 2. Introduction: Clearly introduces the objective of the study, which is to analyze the impact of aging and frailty on perioperative morbidity in the elderly patient undergoing prolapse surgery. This is presented against the background of existing data regarding prolapse surgery in the elderly, and the relative importance of specific conditions related to age, compared with age itself. The authors utilized a large surgical database in hopes that this would provide more useful information than existing trials which they state under-represent elderly patients.
- 3. Methods: The authors stratified age into three groups, and used a validated frailty index. Appropriate primary and secondary outcome measures were used.
- 4. Results: The results show a significantly higher risk of complications and mortality in the very elderly group compared with the elderly and non-elderly groups. As the authors note, these conclusions are limited by the retrospective nature of the study and the heterogeneity among groups.
- 5. Discussion: The authors' findings of higher surgical risk after prolapse surgery in the very elderly contrast with previous studies showing low rates of serious complications in this age group. Their discussion does not contain any comment or analysis of possible reasons for these discrepant findings. What are the reasons the authors believe their results are more accurate? In addition, a comparison of these findings to other studies examining the effect of old age on complications in other surgical subspecialties would help to put the author's results into a more general context.
- -We added a paragraph to the discussion to more thoroughly compare and contrast our results to prior studies in prolapse surgery as well as in other surgical fields. Lines 211-224.
- 6. Tables: Appropriate and reflect the study groups and outcomes clearly.
- 7. References: Appropriate.

Reviewer #2:

Overall: A national quality improvement project database was used to identify patients who underwent surgery for prolapse from 2010 to 2017. They compared a control group (45-64 years, index population) to those aged 65-79 (elderly) and  $\geq$ 80 (very elderly). The primary outcome was the composite rate of serious complications and mortality. The frailty rate was 7.2% in the index population, compared to 14.5% in the elderly and 16.8% in the very elderly. The composite rate of serious complications in the index population was 4.5%, compared to 4.7% in the elderly (p=0.4), and 9.0% in the very elderly (OR 2.1, 1.8-2.4, p<0.001). On multivariate logistic regression, the only age group independently associated with serious complications was the very elderly. Complications surrounding prolapse surgery increase substantially in the cohort of patients over the age of 80, independent of frailty and medical or surgical risk factors.

Disclosures: None to report.

Human subjects: IRB exemption from review.

#### Abstract:

1. The abstract is well written and is representative of the article.

#### Introduction:

2. The purpose is clear and concise, the background is succinctly described.

## Methods:

- 3. Methods are well described and the procedures used are presented in great detail.
- 4. Line 116: What are the 5 perioperative variables used to calculate the mFI-5?
- -The 5 characteristics used in the mFI-5 are functional status, diabetes mellitus, hypertension requiring medication, heart failure, and chronic obstructive pulmonary disease. The mFI-5 is now described in lines 114-125 and is depicted in a new table (Table 1).

# Results:

5. The data answered the study question.

# Discussion:

6. The discussion is well written, relevant and data support the conclusions

### References:

7. The following reference may be of use:

You're How Old? Correlating Perioperative Complication Risk in Octogenarians Undergoing Colpocleisis for Pelvic Organ Prolapse.

Sifuentes R, Wolff BJ, Barnes HC, Wozniak A, Mueller ER, Pham TT.

Female Pelvic Med Reconstr Surg. 2019 Jul 24. doi: 10.1097/SPV.000000000000759. [Epub ahead of print] PMID: 3135635

-We appreciate this suggested reference and have incorporated it into the manuscript (line 88).

Tables/Figures:

- 8. Consider adding the word "study" prior to the word "population" in the title of all 3 figures
- -This change has been made.
- 9. Table 1: The totals for racial/ethnic group add up to less than 100% for all three study groups. Is this due to missing data?
- -For racial/ethnic group, in addition to the variables listed in this table, the database also lists "race unknown" and "other race". We did not include these variables in this table. Additionally, some patients in the database had two ethnicities, such as Caucasian and Hispanic, thus the numbers do not add up to 100%.

Reviewer #3: Well written manuscript that is easy to follow and read. I would appreciate more information about your modelling process - there are many ways to evaluate which variables are included in a final model. Could you perhaps include a supplemental table of all variables in the univariate model that you evaluated, and indicate which were kept and which were dropped and their associated ORs that lead you to include/exclude?

-Our model was created by considering all variables that were statistically significant on univariate logistic regression with p<0.05, followed by stepwise backward multivariate logistic regression, eventually including only variables that retained statistical significance with P<0.05 after this process in our final model. The only exception was the "Elderly" age group, which was not statistically significantly associated with the outcome, but was nonetheless included in the final model. We added a supplemental table including all variables evaluated on univariate regression and indicated which were kept for stepwise backward variable elimination as well as those included in the final model.

Also - did your final multivariate logistic regression model include interaction terms? For example - did you explore if the NSQIP modified frailty index-5 score had different predictive abilities in the baseline, elderly and very elderly group? Given only one OR is provided, it seems like it was modelled as static across all 3 groups and I wonder if it's predictive ability in the very elderly group is being masked by not allowing it to "vary" across groups in your model.

-We appreciate this suggestion, and in response we performed a stratified analysis using interaction terms between the mFI-5 score and the age groups. A significant interaction was found between the mFI-5 score and the Elderly age group, but not the very elderly age group. This is discussed in lines 186-190 in the results and 270-279 in the discussion.

I'd like to see the stats reported on line 174 - 176 specified for elderly and very elderly separately.

-The statistics for impact of mFI-5 is now reported separately in the elderly and very elderly using the interaction terms as stated in the prior comment.

Please report a goodness of fit measure for this model - such as ROC or Hosmer-Lemeshow.

-The AUC-ROC is 0.6402 and is now reported on line 184.

I appreciate Table 2. Too often modelling papers focus on ORs, but I believe this will be the table that most clinicians find useful.

# STATISTICAL EDITOR COMMENTS:

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

Table 1: Should statistically compare the elderly and very elderly cohorts vs the index age group for each of the characteristics cited.

-Of note, this is now Table 2. Columns were added including the p-value for the comparison between the elderly/very elderly cohorts versus the index group. P-values were used in this situation, as opposed to OR(95%CI), to minimize text in this large table.

Should explain in Table footnote the distinction made between "Frailty index" and "Frail".

-This was clarified in the variable column, variables are now named: "mFI-5 score" and "frail (mFI-5 score ≥ 0.4)".

Also, elsewhere in text frailty index is described as %, while in Table 1 it is a proportion. Should use one consistent format.

-We appreciate this comment. We opted to use and report the frailty index (mFI-5) both as its raw score (a proportion) as well as as a dichotomous variable (frail versus not frail, with frailty being considered as mFI-5 score ≥ 4). The mFI-5 has been used each way in prior literature. If this is deemed to be unclear or unnecessarily complicated, we can simplify and only use the mFI-5 score, as this seems to be more significantly associated with the outcome. We attempted to clarify our use of the frailty index in lines 114-125 in the methods section.

Among the baseline differences, one that is both statistically and clinically important, would be the ASA class. Should elaborate that into proportion in Class 1, 2, 3, 4, besides aggregating classes 3 and 4.

-This change was made to Table 2, ASA classes 1-4 are now separately listed.

Table 3: This appears to be composite rates for the serious complications cited in Table 2 and elsewhere. Should consistently format as "serious complication rates". These are apparently crude ORs, so should state in Table footnote. Since CIs are included, no need to include separate column for p-values, could be indicated by footnotes, if desired.

-Changes were made to consistently format as "serious complications". Changes were made to the table title and footnote. This is now Table 4.

Table 4: Should include crude ORs in separate column and should indicate in footnote the variables included as adjustors in the final model Again, the p-values are redundant, since CIs are included, but could list in footnote to Table if desired.

-This is now table 5. These changes were made. All variables used in the final model are now included in the table. Crude odds ratios were added. All variables included in the model were noted in the footnote, and the p-value column was removed.

Fig 1: Very useful figure, but I do not see the light grey background in my version of the Figure. Might consider vertical lines to indicate the 3 age groups.

-If the grey background does not show up in the higher quality images that are now submitted, we will add vertical lines to delineate the 3 age groups.

Fig 2: Again, I do not see any difference in background corresponding to the elderly or very elderly age groups. Should change the title to Composite serious complication rate. Again, might consider use of vertical lines to demarcate the 3 age cohorts.

-Title changed to composite serious complication rate. See above regarding vertical lines.

Fig 3: Probably could be included as supplemental material.

-This was kept as Figure 4 as an attempt to highlight the increase in the very elderly of some of the most severe individual complications and mortality.

Should also show the relationship of ASA vs age, perhaps as proportion in Class 3 or 4 vs age.

-The relationship of ASA class 3 or 4 vs age is now depicted in a new figure, figure 2.

Also, as sensitivity analysis, how did the analysis of serious complication rates change if one were to separately analyze women with Class 3 or 4, just as was done in Table 3. That is, were the higher serious complication rates in the very elderly also applicable when only Class 3 or 4 ASA were considered?

-We appreciate this suggestion. This sensitivity analysis was completed and added to the manuscript (lines 174-177). In patients with ASA class 3 and 4 only, similar trends of higher complications rates in the very elderly are seen.

# **EDITOR COMMENTS:**

1. Specific manuscript comments:

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better context than citing P values alone.

This is true for the abstract as well as the manuscript.

-We made changes throughout the abstract and manuscript to use odds ratio with confidence intervals as opposed to p-values whenever possible. Table 2 does primarily use p-values to minimize text as it is a large table.

Please provide absolute values for variables, in addition to assessment of statistical significance.

-Table 2 is now complete with absolute values of all variables and assessment of statistical significance.

We ask that you provide crude OR's followed by adjusted OR's for all variables.

-We added crude odds ratio's in addition to the adjusted odds ratios in the multivariable logistic regression, now in Table 5.

Line 64: You don't tell us in the methods section how the "frailty index" is differentiated from "Being frail". As such, this sentence is unclear. This continues to line 65-66: What is the index population you are referring to here? It seems like you referring to the age reference—were frail-patients only taken from all of those age groups? I don't see how this comparison was made. It seems like you should control for age and then look at frail-patients only.

-We attempted to clarify this issue. The abstract now only mentions the frailty index. The mFI-5 index as well as the differentiation of the mFI-5 score versus "being frail" are now explained in lines 114-125.

Line 74: add age 70 years. Same true for all age designations—need units (like on line 75).

-This change was made throughout the manuscript.

Line 87: Define frailty.

-This was added to lines 88-89 of the manuscript.

Line 101: Why was it exempt?

-Our IRB deemed thus study exempt from review as it fell under "45CFR46.101(b)(4); Research involving the collection or study of existing data, documents, records, pathological

specimens, or diagnostic specimens." The study involved the analysis of preexisting deidentified data.

Line 103: please say "from the years of 2010 to 2017" as "between" strictly means you excluded 2010 and 2017.

-This change was made, now on line 104.

Line 113: can you detail the mFI-5 in a box?

-We detailed the mFI-5 in what is now Table 1.

Line 120-121: It seems this is how you defined "frail" vs Frailty index. Can you make this really clear how you used these terms?

-We used the mFI-5 score as a continuous variable, and we used "being frail" as a dichotomous variable defined by a mFI-5 score ≥0.4. We attempted to clarify this issue in lines 114-125.

Line 123: Does the NSQIP report only complications in the immediate perioperative period or does it extend to sometime longer? Is it restricted to inpatient procedures or does it include ambulatory procedures?

-NSQIP reports complications for the first 30 days after surgery. This is now stated on line 112. The database includes both inpatient and outpatient procedures.

Table 4: I'm unclear what this regression is about. In footnote, please provide the variables in the analysis. Are these the aOR for the composite outcome?

-This is the multivariate logistic regression for the composite outcome of all serious complications. We attempted to clarify. All variables included in the model are now seen in the updated table (now Table 5). Crude odds ratios were added. All variables that were considered in the stepwise backward logistic regression are now listed in the footnote.

Please address the comments by the statistical editor regarding adding an analysis looking at ASA categories to explore this measure as an association with safety outcomes for older women.

-Per these comments we performed an additional sensitivity analysis including only patients with ASA class 3 and above, and found similar trends of low complication rates in the index and elderly populations compared to higher rates of complications in the very elderly. Lines 174-177.

- 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. 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:
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