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

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

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Date: Sep 02, 2022
To: "Mary Shea O'Brien" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-1380

RE: Manuscript Number ONG-22-1380

Post-operative complications of appendectomy in benign gynecologic surgery: A National Surgical Quality Improvement Program analysis

Dear Dr. O'Brien:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, STATISTICAL EDITOR COMMENTS (if applicable), and EDITORIAL OFFICE COMMENTS below. Your manuscript will be returned to you if a point-by-point response to each of these sections is not included.

The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your submission will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Sep 23, 2022, we will assume you wish to withdraw the manuscript from further consideration.

EDITOR COMMENTS:

In addition to responding to the excellent reviews below, I would recommend controlling for the indication of the procedure in the analyses if possible.

REVIEWER COMMENTS:

Reviewer #1: Review of Manuscript ONG-22-1380 "Post-operative complications of appendectomy in benign gynecologic surgery: A National Surgical Quality Improvement Program analysis"

A manuscript that evaluates the potential impact of presumed elective appendectomy performed at the time of benign laparoscopic Gyn surgery and utilizing data from the ACS NSQIP database has been submitted. The authors created 2 groups of patients those with and without an appendectomy who underwent surgery from 2010-2020. As noted, several appropriate exclusion criteria including the need/performance of a laparotomy, the potential or confirmed presence of malignancy as well as performance of a urogynecologic procedure that may have been associated with mesh placement were applied. Ultimately there were 1815 women undergoing an appendectomy which were initially compared to a group of 245,885 without an appendectomy before propensity weighting resulted in a matched sample size group of 1815. I have the following questions and comments.

Title - Consider using acronym in the title. Also note in the title this is laparoscopic surgical procedures.

Précis - Add laparoscopy to your precis please. Also consider (if space allows) that this was not urogynecologic surgery.

Introduction - Line 72 and 80 - Is there a difference between an "elective" and an "incidental" appendectomy. Consider using only one of these terms.

Methods - I presume you were not able to assess traditional laparoscopy as compared to robotics? How might this have impacted your findings?

Line 99 - Were all urogynecologic procedures excluded or just those with an increased risk of needing/receiving mesh?

Line 116 - Were emergency cases included/excluded?

Line 120 - Consider noting this is a composite endpoint of all the listed complications as compared between the 2 groups.

Line 123 - Should be Fisher's exact test.

Line 125 - Consider listing the variables from Table 1 here used in the propensity matching. Also operative time and LOS was not listed in Table 1.

Results -
Line 134 - Should this be "imbalance?"

Lines 137, 144, 146, etc. - While noting that the differences were $P < 0.01$ is correct, in table 2 you note that the differences were < 0.001. Please confirm which is correct and depict in the same fashion.

Line 165 - Consider noting at least the N and % for those with endometriosis here.

Discussion - Line 206 - Would operative note review have provided information that could have changed your assertion of whether the appendectomy was indicated or elective?

Tables - Tables - No comments

Figures -
Figure 1 - No comments

Figure 2 - Can you see if the final "s" from endometriosis fits on the same line?

Reviewer #2: Excellent use of the ACS NSQIP data base. It adds to the long standing debate on risk and benefits of incidental appendectomy. Further information on surgical technique may have added to the article overall.

Reviewer #3: The authors have written an interesting article on complications associated with appendectomy performed at the time of benign laparoscopic gynecologic surgery. They used the NSQIP database for this retrospective study. They found increased complication rate of 8.6% for patients undergoing concomitant appendectomy compared to 5.6% for patients who did not undergo appendectomy. The manuscript is overall well written, and the authors do address the limitations associated with this research project. I have several questions for the authors.

1. Were all of these surgeries performed by general gynecologists- or could specialists such as gynecologic oncologists be the surgeons?

2. Who performed the appendectomies in this study? I think it would be helpful to know if they were done by general surgeons or gynecologists- and if type of surgeon is at all associated with complications.

3. In figure 2- I think it would be helpful to know the indications for surgery in the control group as well (at least in the propensity score matched patients)- to see if there are differences in indications for surgery that are associated with these findings.

4. Were patients who had contaminated cases included? For example- someone presents with signs of peritonitis with unclear etiology and undergoes diagnostic laparoscopy by gyn- and not felt to be PID but purulence encountered- so appendectomy performed.

5. Are prophylactic antibiotics recommended for laparoscopic appendectomy? Are you able to get info from this database whether pts received prophylactic antibiotics? If prophylactic antibiotics are not recommended currently- perhaps this intervention could help lower the complication rate.

6. If available, would be helpful to know the pathology for the appendix specimens.

STATISTICAL EDITOR COMMENTS:

Abstract: Should include concise description of matching, at least in terms of 1:1 match and caliper width used.

lines 124-129, Table 1: There are several details missing that should be specified in Methods. Clearly, there was a 1:1 match and all Appendectomy cases in the original cohort were matched to a control case. What caliper width was used? Was the algorithm for a match "greedy" or "optimal"? Rather than comparing pre and post matching in terms of p-values for the appendectomy vs no appendectomy groups, should show the SMD before and after and show that the caliper width criteria were all met.

Table 2: Many of the adverse outcomes were infrequent and there was little stats power to discern a difference, so most of those with NS findings are not generalizable. To name a few, wound disruption, PE, stroke, etc. Need to include this among the limitations of the study.

EDITORIAL OFFICE COMMENTS:

General: Please see the Instructions for Authors to review if your submission is currently submitted under the correct article type. Quality improvement submissions are usually considered under the Clinical Practice and Quality article type.

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, describe the reasons that race and ethnicity were assessed in the Methods section and/or in table footnotes. Race and ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories.

List racial and ethnic categories in tables in alphabetic order. Do not use "Other" as a category; use "None of the above" instead.

Please refer to "Reporting Race and Ethnicity in Obstetrics & Gynecology" at https://edmgr.ovid.com/ong/accounts/Race_and_Ethnicity.pdf.

5. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "People with disabilities" or "women with disabilities" instead of "disabled people" or "disabled women"; "patients with HIV" or "women with HIV" instead of "HIV-positive patients" or "HIV-positive women"; and "people who are blind" or "women who are blind" instead of "blind people" or "blind women."

6. The journal follows ACOG's Statement of Policy on Inclusive Language (https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language). When possible, please avoid using gendered descriptors in your manuscript. Instead of "women" and "females," consider using the following: "individuals;"

"patients;" "participants;" "people" (not "persons"); "women and transgender men;" "women and gender-expansive patients;" or "women and all those seeking gynecologic care."

7. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines:

SQUIRE 2.0 for quality improvement studies

Include the appropriate checklist for your manuscript type upon submission, if applicable, and indicate in your cover letter which guideline you have followed. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at www.equator-network.org/.

8. 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 data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

9. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Original Research: 3,000 words or Clinical Practice and Quality: 3,000 words

10. For your title, please note the following style points and make edits as needed:
* Do not structure the title as a declarative statement or a question.
* Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles.
* Abbreviations, jargon, trade names, formulas, and obsolete terminology should not be used.
* Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," "A Systematic Review," or "A Cost-Effectiveness Analysis" as appropriate, in the subtitle. If your manuscript is not one of these four types, do not specify the type of manuscript in the title.

11. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

* 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 or indicate whether the meeting was held virtually).
* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."
* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

12. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make 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 manuscript.

In addition, the abstract length should follow journal guidelines. Please provide a word count.

Clinical Practice and Quality: 300 words or Original Research: 300 words

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, except with ratios. 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. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

16. 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.

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

Express all percentages to one decimal place (for example, 11.1%"). Do not use whole numbers for percentages.

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

18. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the formal reference list. Please cite them on the line in parentheses.

If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Please make sure your references are numbered in order of appearance in the text.

19. Figures: Please upload as figure files on Editorial Manager.

20. Each supplemental file in your manuscript should be named an "Appendix," numbered, and ordered in the way they are first cited in the text. Do not order and number supplemental tables, figures, and text separately. References cited in appendixes should be added to a separate References list in the appendixes file.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded as a Microsoft Word document. Your revision's cover letter should include a point-by-point response to each of the received comments in this letter. Do not omit your responses to the EDITOR COMMENTS (if applicable), the REVIEWER COMMENTS, the STATISTICAL EDITOR COMMENTS (if applicable), or the EDITORIAL OFFICE COMMENTS.

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

Again, your manuscript will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Sep 23, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Shannon K. Laughlin-Tommaso, MD, MPH
Associate Editor, Gynecology

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.

September 10, 2022

Re: ONG-22-1380, resubmission of manuscript "Post-operative complications of appendectomy in benign gynecologic surgery: A National Surgical Quality Improvement Program analysis"

Dear Editors,

Thank you for the opportunity to revise our manuscript, *Post-operative complications of appendectomy in benign gynecologic surgery: A National Surgical Quality Improvement Program analysis.* We appreciate the careful review and constructive suggestions.
Following this letter are the editor and reviewer comments with our responses in italics, including how and where the text was modified. Changes made in the manuscript are marked using track changes. This revision has been developed in consultation with all coauthors, and each author has given approval to the final form of this revision.
Since submission, the abstract for this manuscript has been accepted as a virtual poster presentation at the 51st AAGL Global Congress of Minimally Invasive Gynecology to be held in December 2022 in Aurora, CO. We have updated our title page to reflect this change.

Sincerely,

M. Shea O'Brien, MD

EDITOR COMMENTS:

In addition to responding to the excellent reviews below, I would recommend controlling for the indication of the procedure in the analyses if possible.

Thank you for your comments. Unfortunately, the NSQIP database does not include indication for procedure. It does include post-operative diagnoses, which were used to exclude specific patients from the population cohort (See lines 73-78).

REVIEWER COMMENTS:

Reviewer #1:

Review of Manuscript ONG-22-1380 "Post-operative complications of appendectomy in benign gynecologic surgery: A National Surgical Quality Improvement Program analysis"

A manuscript that evaluates the potential impact of presumed elective appendectomy performed at the time of benign laparoscopic Gyn surgery and utilizing data from the ACS NSQIP database has been submitted. The authors created 2 groups of patients those with and without an appendectomy who underwent surgery from 2010-2020. As noted, several appropriate exclusion criteria including the need/performance of a laparotomy, the potential or confirmed presence of malignancy as well as performance of a urogynecologic procedure that may have been associated with mesh placement were applied. Ultimately there were 1815 women undergoing an appendectomy which were initially compared to a group of 245,885 without an appendectomy before propensity weighting resulted in a matched sample size group of 1815. I have the following questions and comments.

Title - Consider using acronym in the title. Also note in the title this is laparoscopic surgical procedures.

Thank you for your comment. We have adjusted the title, as suggested. It now reads "Post-operative complications of appendectomy in benign gynecologic laparoscopic surgery: a NSQIP analysis".

Précis - Add laparoscopy to your precis please. Also consider (if space allows) that this was not urogynecologic surgery.

Thank you for your suggestion. We have added laparoscopic surgery to the précis. The precis now reads "Concomitant appendectomy in benign gynecologic laparoscopic surgery is associated with increased risk of post-operative complications. "

Introduction - Line 72 and 80 - Is there a difference between an "elective" and an "incidental" appendectomy. Consider using only one of these terms.

Thank you for your comment. We have removed both terms and replaced with concomitant appendectomy to maintain consistency throughout the manuscript. Line 39-42 now reads "However, the practice of ***concomitant*** *appendectomy at the time of a benign gynecologic procedure remains controversial, and many gynecologic surgeons do not perform appendectomy due to the concern for increased risks of infection, ileus, blood loss, operating time, and morbidity." And line 47-49 reads "In a general surgery population undergoing* ***concomitant*** *appendectomy during open abdominal and trauma surgeries, appendectomy was associated with increased risk of post-operative wound complications and sepsis."*

Methods - I presume you were not able to assess traditional laparoscopy as compared to robotics? How might this have impacted your findings?

Thank you for your comment. We used the overall participant use files for our analysis which do not contain robotic surgery as a variable separate from laparoscopic surgery, unlike certain procedure targeted subsets of NSQIP that do report this data.

However, a recent systematic review looking at robotic vs laparoscopic surgery for endometriosis found no difference in intraoperative complications (Restaino S, Mereu L, Finelli A, Spina MR, Marini G, Catena U, Turco LC, Moroni R, Milani M, Cela V, Scambia G, Fanfani F. Robotic surgery vs laparoscopic surgery in patients with diagnosis of endometriosis: a systematic review and meta-analysis. J Robot Surg. 2020 Oct;14(5):687-694. doi: 10.1007/s11701-020-01061-y. Epub 2020 Mar 7. PMID: 32146573.)

As such, we would not expect our findings to change if surgery was completed via robotic instead of laparoscopic route. We have edited lines 63-65 in methods to read "Each case included in the analysis had at least one Current Procedural Terminology (CPT) code listed representing a laparoscopic surgery ***which could include traditional laparoscopy or surgery with robotic assistance****."*

Line 99 - Were all urogynecologic procedures excluded or just those with an increased risk of needing/receiving mesh?

Thank you for your question. The urogynecologic CPT codes that were excluded were vaginal suspensory procedures and urinary incontinence procedure, as these procedures may require usage of mesh. We have listed the excluded codes in the Appendix. We have added a reference to our appendix within the manuscript on lines 65-68. "Patients were excluded if they had any CPT

code indicative of an open abdominal surgery, bowel resection, or urogynecology procedure where there was potential for utilization of mesh (Appendix).”

Line 116 - Were emergency cases included/excluded?

Thank you for your question. Our initial analysis did not review whether cases were emergency or not but we have included this in further analysis. We found 3% of appendectomy cases versus 6% of without appendectomy cases were emergent. We have added this data to Table 1 and Line 109-110 “Patients who underwent surgery without appendectomy were more likely to have emergency surgery (Table 1).” We have also included this variable in our propensity matching which is noted on Lines 94-95 “Surgical characteristics used were year of surgery, number of CPT codes, and emergency surgery.”.

Line 120 - Consider noting this is a composite endpoint of all the listed complications as compared between the 2 groups.

Thank you for your comment. This edit has been made and line 87-88 now reads “The primary outcome was a composite of post-operative complications compared between the two groups.”

Line 123 - Should be Fisher's exact test.

Thank you for your comment. This has been corrected.

Line 125 - Consider listing the variables from Table 1 here used in the propensity matching. Also operative time and LOS was not listed in Table 1.

Thank you for that observation. This has been added on line 92-95 and it reads "Demographic information utilized for propensity matching included age, race, BMI, presence of medical co-morbidities, and ASA class. Surgical characteristics used were year of surgery, number of CPT codes, and emergency surgery."

As you noted, the operative time and length of stay are reported in table 2, not table 1 and this statement has been removed.

Results -

Line 134 - Should this be "imbalance?"

Thank you for catching this typo. It has been corrected.

Lines 137, 144, 146, etc. - While noting that the differences were $P < 0.01$ is correct, in table 2 you note that the differences were < 0.001. Please confirm which is correct and depict in the same fashion.

Thank you for your comment. The table lists the correct values ($p<0.001$) and the text has been altered to match.

Line 165 - Consider noting at least the N and % for those with endometriosis here.

Thank you for your comment. The percentage and total number of patients with the most common diagnoses has been added in the text. Line 136-140 now reads "The most common post-operative diagnoses by ICD-9 or ICD-10 codes in patients undergoing concomitant appendectomy were endometriosis (32%, n=561); adnexal pathology including ovarian cysts

and benign neoplasms (18%, n=314); uterine pathology, most commonly fibroids (15%, n=270), and abdominal or pelvic pain (15%, n=268).

Discussion – Line 206 – Would operative note review have provided information that could have changed your assertion of whether the appendectomy was indicated or elective?

Thank you for this comment. Unfortunately, with database studies, we are limited by information provided. We agree that having the ability to review operative findings, pathology, or use of intra-operative antibiotic prophylaxis would all have provided very useful information, specifically on whether the appendectomy was "indicated" or "elective". We have edited line 179-183 to read "There may be contributing factors that are not captured by database including the patient' hemodynamic status pre-operatively, use or appropriate antibiotic prophylaxis, intra-operative findings, surgical strategy, difficulty of surgery secondary to factors such as severe endometriosis or intra-abdominal adhesions, and surgeon experience level among a list of many other factors."

Tables - Tables - No comments

Figures -

Figure 1 - No comments

Thank you

Figure 2 - Can you see if the final "s" from endometriosis fits on the same line?

Thank you for your comment. This has been corrected.

Reviewer #2:

Excellent use of the ACS NSQIP database. It adds to the long-standing debate on risk and benefits of incidental appendectomy. Further information on surgical technique may have added to the article overall.

Thank you for your comments. We agree, and unfortunately are limited by the data available in the NSQIP database which does not record intraoperative findings or details regarding technique. We have edited our limitations line 179-183 to read "There may be contributing factors that are not captured by database including the patient' hemodynamic status pre-operatively, use or appropriate antibiotic prophylaxis, intra-operative findings, surgical strategy, difficulty of surgery secondary to factors such as severe endometriosis or intra-abdominal adhesions, and surgeon experience level among a list of many other factors."

Reviewer #3:

The authors have written an interesting article on complications associated with appendectomy performed at the time of benign laparoscopic gynecologic surgery. They used the NSQIP database for this retrospective study. They found increased complication rate of 8.6% for patients undergoing concomitant appendectomy compared to 5.6% for patients who did not undergo appendectomy. The manuscript is overall well written, and the authors do address the limitations associated with this research project. I have several questions for the authors.

1. Were all of these surgeries performed by general gynecologists - or could specialists such as gynecologic oncologists be the surgeons?

Thank you for your question. Unfortunately, NSQIP does not report break down of surgical specialties but rather reports general specialties like Gynecology, Urology, Obstetrics or General Surgery. We limited surgeries to those performed by Gynecology, but cannot comment on additional training (MIGS, FPMRS, GYN Oncology) of the operating surgeon.

2. Who performed the appendectomies in this study? I think it would be helpful to know if they were done by general surgeons or gynecologists- and if type of surgeon is at all associated with complications.

Thank you for your question. We limited the study to Gynecology only as the primary specialty (Figure 1) but are unable to comment if the appendectomy was performed by a General Surgeon since NSQIP only reports the primary surgical specialty.

3. In figure 2- I think it would be helpful to know the indications for surgery in the control group as well (at least in the propensity score matched patients)- to see if there are differences in indications for surgery that are associated with these findings.

Thank you for your comment. Unfortunately, the NSQIP database does not include indication for procedure. It does include post-operative diagnoses, which were used to exclude specific patients from the population cohort (See lines 74-76).

4. Were patients who had contaminated cases included? For example- someone presents with signs of peritonitis with unclear etiology and undergoes diagnostic laparoscopy by gyn- and not felt to be PID but purulence encountered- so appendectomy performed.

Thank you for your questions. Our initial analysis did not further analyze by wound classification. However, we are now excluding "dirty or infected" wound cases (Lines 74-76), and we have added wound classification to Table 2. Patients undergoing appendectomy were more likely to have "contaminated" wound classification. This finding has been added to Line 133-135 "Wound classification was statistically significant in both the overall and propensity-weighted analysis with the appendectomy group more likely to be classified as class 3 or "contaminated" (6% vs 2%, p<0.001)(Table 2)."

Excluding "dirty or infected" wounds affected our overall analysis. The overall complication rate remained increased in the appendectomy group in both the overall and propensity-matched analysis. Rates of sepsis were increased in the appendectomy group in the overall analysis, but were not significant in the propensity-matched analysis. These findings are discussed on lines 152-164, which reads, "Existing literature is inconsistent, with some studies highlighting the safety of concomitant appendectomy and others demonstrating increased rates of post-operative infection.9,10 While we did not find statistically significant differences in deep surgical site infections, organ space infections, or sepsis, we found an increase in superficial surgical site infections. Surgical wound classification has been validated as a predictor of surgical site infections.13 However, surgical wound classification, specifically for appendectomy, is subject to a wide range of interpretation, and there are often discrepancies in the wound classification based on who reports the data – surgeon versus operating room nurse.14,15 A concomitant

appendectomy is often categorized as "clean contaminated" as the gastrointestinal tract is entered in a controlled manner, however it may be categorized as "contaminated" if there is presumed surrounding non-purulent inflammation. The increased number of cases in the "contaminated" wound classification may have contributed to the increased rates of sepsis in the overall cohort or increased rates of superficial surgical site infections in the propensity-weighted analysis."

5. Are prophylactic antibiotics recommended for laparoscopic appendectomy? Are you able to get info from this database whether pts received prophylactic antibiotics? If prophylactic antibiotics are not recommended currently- perhaps this intervention could help lower the complication rate.

Thank you for your question. Antibiotic prophylaxis is recommended for appendectomy – Cefoxitin or Cefotetan. The NSQIP database does not capture granular data on whether antibiotics were administered and which antibiotics were given.

6. If available, would be helpful to know the pathology for the appendix specimens.

Thank you for your comment. We agree that pathology would provide very useful information but are unfortunately limited by the data available in NSQIP.

STATISTICAL EDITOR COMMENTS:

Abstract: Should include concise description of matching, at least in terms of 1:1 match and caliper width used.

Thank you for your comment. A statement on the propensity matching has been added to the abstract on Lines 16-20. It now reads, "A matched cohort was created by computing propensity scores, and outcomes were again compared between groups. All appendectomy patients were 1:1 matched to a unique without appendectomy patient using a greedy matching based on the propensity score calculated from demographic and surgical characteristics."

Lines 124-129, Table 1: There are several details missing that should be specified in Methods. Clearly, there was a 1:1 match and all Appendectomy cases in the original cohort were matched to a control case. What caliper width was used? Was the algorithm for a match "greedy" or "optimal"? Rather than comparing pre and post matching in terms of p-values for the appendectomy vs no appendectomy groups, should show the SMD before and after and show that the caliper width criteria were all met.

We performed a 1:1 match using the "nearest" option in the R package matchit to perform a greedy matching on the propensity score. The propensity scores were estimated from the twang package using a gradient boosting approach. We did not require any fixed caliper value and let the algorithm find the closest remaining control patient for treated (appendectomy patient), we note that 2.3% of matched pairs have propensity scores more than 0.01 units apart. While we agree that SMD are slightly more meaningful to evaluate matching, we have made the choice to continue to report means/proportions/p-values since the majority of readers will be more familiar with this. We note that prior to matching many features/variable levels have high SMD (variables with |SMD|>0.1 include year, age, Hispanic race, White race, normal BMI, obese BMI, severe obesity, hypertension, emergency surgery, and number of CPT codes). After matching all SMDs are less than 0.1 in absolute value (max is 0.057). Language in the methods

section has been modified to clarify some of these details. Please see lines 95-99 "All appendectomy patients were 1:1 matched to a unique patient without appendectomy using a greedy matching based on the propensity score estimated using a gradient boosting approach. Matching was confirmed by evaluating the standardized mean difference between the appendectomy and without appendectomy groups and confirming these quantities to be less than 0.1" as well as references 11 and 12.

Table 2: Many of the adverse outcomes were infrequent and there was little stats power to discern a difference, so most of those with NS findings are not generalizable. To name a few, wound disruption, PE, stroke, etc. Need to include this among the limitations of the study.
Thank you for your comment. We agree that many of the individual complications are so rare as to have low power to detect differences and have added the following to our limitations on Lines 184-186: "Despite using a large database of surgeries for analysis, many post-operative complications such as wound disruption and stroke are quite rare, and we have low power to detect differences in our matched cohort."

EDITORIAL OFFICE COMMENTS:

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* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).

* Name the IRB or Ethics Committee institution in the Methods section (if applicable).

* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

We have added the information regarding IRB exempt status to methods (Line 58-60) "This study was deemed exempt by the Institutional Review Board (Protocol Number 21.0759) at University of Louisville."

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MDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=mHgXrVkC9H29yjylXf9ec4%2FAk9ENOGYWBuWmcndM7XI%3D&reserved=0.

Thank you. Race was reported as a demographic variable captured in NSQIP. Above recommendations for reporting have been followed.

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qzjjt4kFP7CJ3jUbTncCo5nf6ZnrEn8%3D&reserved=0.

None of these checklists are applicable to this database study.

8. 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 data definitions at https://nam11.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-obstetrics-data-definitions&data=05%7C01%7Cshea.obrien%40louisville.edu%7Ce02476f501a84094e35408da8cfb5bf2%7Cdd246e4a54344e158ae391ad9797b209%7C0%7C0%7C637977309216494059%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=uZ8ocF3sBEIp7Xrqi9vlUHyFxvi4LwUfgQsgUH7yzDQ%3D&reserved=0 and the gynecology data definitions at https://nam11.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-gynecology-data-definitions&data=05%7C01%7Cshea.obrien%40louisville.edu%7Ce02476f501a84094e35408da8cfb5bf2%7Cdd246e4a54344e158ae391ad9797b209%7C0%7C0%7C637977309216494059%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=R0sfsgibu8lo7utFVk7IqHupRgnWEe%2FB9ilaep4hpXQ%3D&reserved=0. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

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