NOTICE: This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-19-1156

Trends in Use and Effect on Survival of Simple Hysterectomy for Early-Stage Cervical Cancer

Dear Dr. Wright:

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 08, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a large study from the national cancer database registry looking at survival after simple or radical hysterectomy for early stage cervical cancer. Patients who had a radical hysterectomy for Stage 1B disease had decreased survival. This study was presented at SGO and two authors are conflicted.

Your introduction should include a brief mention of the staging process for cervical cancer and the difference between 1A2 and 1B1 tumors.

While you were able to classify type of institution where hysterectomy occurred, you do not mention that you were able to classify by surgeon type ie gyn oncologist or generalist. If not, this should also be mentioned as a weakness in your study. As you mention, it will be important to distinguish between minimally invasive and open hysterectomies for this outcome in the future.

Line 206 has a typo and includes a random "P".

I think you should adjust your conclusion to say caution should be exercised in doing a simple hysterectomy in women with 1B1 cervical cancer.

In figure 2, the survival curves should be labeled 1A2 and 1B1.

You must comment on your disparity findings and possible explanations in your discussion.

Reviewer #2: The manuscript entitled "Trends in Use and Effect on Survival of Simple Hysterectomy for Early-Stage Cervical Cancer" is an analysis of surgical approach to treatment of Stage IA2 and IB1 Cervical Cancer (≤ 2 cm) based on data from the National Cancer Database (NCDB). The objective is to evaluate the safety of simple hysterectomy for early stage cervical cancer, when compared to a radical approach. Key findings included a relatively high percentage of patients getting SH hysterectomy for stage IA2 (44.6%) and stage IB1 (35.3%) cervical cancer, with rates increasing over the time period evaluated. After propensity score weighting, which was used to reduce bias due to confounding variables, survival in patients undergoing SH for stage IA2 cervical cancer was not significantly different than those undergoing RH. However, for stage IB2 cervical, there was a 55% increased risk of death for those undergoing SH compared to RH.
1. Radical hysterectomy has been the recommended surgical treatment for most patients with early stage cervical cancer. However, there is significant morbidity associated with the procedure, and a relatively low risk of parametrial involvement, especially in small tumors <2cm. As such, many have been taking a more conservative surgical approach with SH with or without lymph node sampling for stage IA2 and IB1 cervical cancers, despite the lack of prospective randomized trials. Much of the available data is retrospective and from small institutional series. The current analysis provides a thorough analysis of 1530 women with stage IA2 and 3931 women with Stage IB1 cervical cancer. The percentage of women who received SH was surprisingly high in both cohorts, and increased over the analysis period of 2004 - 2015. Thus, the current manuscript is timely as it provides a retrospective analysis using a large database to provide guidance while we await results of several ongoing prospective trials evaluating this conservative surgical approach.

2. The methods of data collection are well described and thorough. Approach to analysis is well described and includes propensity score analysis to account for the impact of measured confounders on treatment approach. Please consider adding more discussion regarding the inverse probability of treatment weighted (IPTW) cohort, and how this adds to the analysis/findings. Would also consider adding more detail regarding known confounders in cervical cancer outcomes. The analysis is interesting and an opportunity for readers to learn more about this approach.

3. The current manuscript is significant for patients with early stage cervical cancer, many of whom are young and from disadvantaged socioeconomic backgrounds. The number of patients already being offered a more conservative surgical approach is strikingly high, given the lack of data from large prospective randomized trials. Please consider expanding/providing justification regarding statement: "It is unclear from our study why mortality was increased in women who should have been at very low risk." (line 285). Would also consider collecting patient education level likelihood of undergoing SH versus RH.

4. The manuscript is enjoyable and easy to read. It is well organized, length is appropriate, and abstracts, figures and tables provide value. This is a database analysis and the authors provide a thorough description of the weaknesses of such an analysis. References are complete. Few typographical errors include:
   a. Line 161 - comorbidity index ("index" is missing)
   b. Line 206 - delete capital P
   c. Table 3 - delete comma after Stage IA2 in column heading

Reviewer #3: This is a well written paper addressing an important and timely topic. My only suggestions are to address the "P" in line 206, page 8 and rewriting the full sentence beginning on line 296, page 12.

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

Tables 1, 2, 3: Need units for age.

Table 3: Should include columns of crude RRs to contrast with aRRs. The number of comparisons in this Table is large, but an inference threshold of .05 is used (95% CI). There is no adjustment for multiple hypothesis testing. Should use a stricter inference threshold (at minimum, 99% CIs) to avoid spurious associations. Also, many of the characteristics tested had an unfavorable number of adverse outcomes, compared to the use of 11 or more variables in the adjustment models, using the rule of 10 events per variable. This is especially an issue for many of the IA2 comparisons.

The high proportion of unknown entries for Grade makes interpretation/generalization of that portion of the analysis problematic (regarding the other, known Grades).

General: Need to state whether the survival and mortality were from all cause vs specifically related to cervical cancer.

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 Randi Zung and she will send it by email - rzung@greenjournal.org.***

- Please emphasize in the abstract that national guidelines do not support simple hysterectomy for 1B1 tumors to begin with and this data supports that.

- We prefer to avoid providing p-values only unless that is the only appropriate test of significance. Where appropriate in the abstract AND the text, please provide an effect size (such as an OR or RR) and 95% CI’s.

- I assume that it is not possible to indicate the type of specialty (Ob GYN vs Gyn Onc) of the surgeon in your database. This likely warrants being highlighted in your discussion.

- Please add a statement that emphasizes that there are no differences in these different outcomes for the IA2 patients.

- Would you consider making a comment about potential health disparities given a higher rate of SH for black v white women and higher death rates in the 1B group with SH? Perhaps to point out future area of research?

- Consider breaking this very large table down into 2 different tables, Demographic and Clinical.

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.

Any author agreement forms previously submitted will be superseded by the eCTA. During the resubmission process, you are welcome to remove these PDFs from EM. However, if you prefer, we can remove them for you after submission.

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. Please submit a completed STROBE checklist with your revision.

6. 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.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, tables, boxes, figure legends, and print appendixes) but exclude references.

8. 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).

9. 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:
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10. 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.

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"and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a
measurement.

12. Please review the journal’s Table Checklist to make sure that your tables conform to journal style. The Table Checklist

13. Figures 1 and 2 may be resubmitted as-is.

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information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can

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promptly.

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at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response
to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you
by Aug 08, 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

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