

OBSTETRICS & GYNECOLOGY



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.

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obgyn@greenjournal.org.

Date: Jan 31, 2019
To: "Jason D. Wright" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2426

RE: Manuscript Number ONG-18-2426

Application of Minimum-Volume Standards for Hospitals Treating Women with Ovarian 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 Feb 21, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a well-written, thoughtful paper that addresses an important area of health services delivery. This study presents a fair perspective of what is potentially lost (access to care in underserved areas) and what is gained (improved mortality at higher volume centers) from setting minimum volumes for treating women with ovarian cancer. Higher volume centers have lower observed to expected 60-day, 1-year, 2-year and 5-year mortality. However, this paper also showed that by setting minimum volume standards to hospital centers this can decrease accessibility to care for patients and may limit patients in underserved and rural areas. This is an important issue for the readers of the Green Journal to reflect upon as more health systems look to set minimum volume numbers for specific procedures and diseases such as the one addressed in this paper, ovarian cancer.

What is important about this study is that it provides quantitative data to implicitly held beliefs that higher surgical volumes lead to improved outcomes. The use of a national database to identify patient helps to capture a large proportion of the population. The multivariable models used appropriate variables for consideration and are presented in a way that is easy for the reader to understand. Modeling choices were reasonable and well thought out. The conclusion that limiting surgical volumes for treatment of ovarian cancer would result in restricted care at many hospitals is demonstrated by the data. While this does provide an access to care issues, the observed-expected mortality ratios provide an indication of quality of care that is tangible for readers. The use of administrative databases does provide some limitations and the study authors appropriately address these in the discussion portion of the paper.

Reviewer #2:

This is a retrospective study using the National Cancer Database to identify women with ovarian cancer between 2005 -2015. Estimates were made about the prior year's hospital surgical volume and categorical y classified into quartiles from low to high volume for comparison. Multivariable models were utilized to estimate observed to expected mortality at various points in time. Implementing minimum number restrictions were than modeled to assess impact on mortality and access to care. The authors should be applauded for addressing an issue that really needs to be defined across all specialties and procedures with specific outcomes. They address both disparities and access to care for a cancer where regionalization may not always be possible given the resources as modeled in the restriction data.

Abstract:

Line 51 The objectives should specify what is being modeled in terms of survival, hospital closure with implications for

access. This is described in the methods section however it is difficult to tease out until you read the manuscript.

Introduction:

Overall this is a very thorough review of the problem with supporting references. The purpose of this study is clearly outlined. My only comments related to some of the older citation are below.

Line 98 Explain the distinction between high volume hospitals and procedures. The reference #2 N Engl J Med 2002; 346:1128-37 is from the 90's and primary focused around cardiovascular procedures. The importance of the multidisciplinary high volume hospital care vs. high volume surgeon is going to vary by procedure, comorbidities and date, particularly when looking at 60 day mortality.

There should be further discussion of ovarian cancer surgical staging by surgeon type. Within this current National Cancer Data Base how many of these cases were done by Gyn/Onc vs. general surgery or general gynecology? Also given the references Gynecol Oncol 2010;118:262-7 has this changed over time. With relatively similar mortality rates across low and high volume hospitals in this study perhaps there is a difference in the type of surgeon and not the volume which is more important.

Materials and methods:

Line 170-173 Was there additional information on neoadjuvant, peritoneal chemo or adequate debulking at the time of initial surgery? These all could impact the O/E ratio. Adherence to standard of care guidelines has been directly shown to impact survival Gynecol Oncol. 2015 Dec; 139(3): 495-499

Results:

Table 1 The unknown stage of 31% and grade 40% at low volume hospitals vs. 14 % and 23% at high volume hospitals may significantly impact the regression analysis and impacted on adjusted O/E.

Figure 1 The trends suggest a greater impact and variability in the short term ie 60 days than long term. The figure and legend stands alone and is easy to understand. It looks like figure 2 restates the same thing and may be redundant. Explain how this adds to what is already presented.

Discussion:

Line 243 Discuss more about the NCD participation particularly on surgical teams, bebulking and changes in treatment over time. A low volume hospital with a high volume surgeon may be adequate and support the concern about establishing min. numbers by hospital. If this is not available a proxy could be both unknown grade and stage over time. It is listed in table 1 but not over time by volume. If there was a declining rate of unknown over time this may be due to improved surgeon volume adherence to guidelines even at low volume hospitals.

Line 289-293 This is a good clinical teaching point about O/E and prevention of one death per 297 patients Overall the limitations were addressed along with both the strengths and weaknesses.

Reviewer #3:

OVERALL: This is an original research study that uses the National Cancer Database to identify the number of hospitals that would be potentially affected by the implementation of minimum hospital volume standards for the care of ovarian cancer. It contributes to a growing body of literature that has shown improved surgical outcomes at high-volume hospitals and with high-volume surgeons. While more literature is supporting improved survival for ovarian cancer patients undergoing surgery at high volume centers, I was not able to identify any prior studies examining the impact of implementation of minimum-volume standards. Therefore, I believe that this manuscript is an important contribution to the field, as few before have looked at how these revelations about the impact of volume should impact our health care delivery. I do have some concerns about the statistical approach, especially given the noisiness of low-volume hospital data.

INTRODUCTION: The introduction does an excellent job of providing background and a framework for the paper's main question.

-The authors refer to literature examining the performance of high-volume surgeons and high-volume hospitals. In gynecologic oncology, has the literature focused more on hospitals or surgeons?

-Is volume also associated with chemotherapy and radiation outcomes?

-Lines 105-107: For what procedures have minimum procedural volumes been proposed? Any gynecologic procedures or any directly related to ovarian cancer care?

-Lines 108-109: What data are there for minimum-volume standards? Or is it purely theoretical?

-The suggestion of limiting care to high-volume centers does make me think about transplant centers, cardiac care, and stroke care. While perhaps not purely surgical, it might be worth reviewing data for minimum volume cutoffs in other fields of medicine.

-Lines 114-115: It is not clear to me that the study actually achieves the objective specified here. While it does identify a percent of hospitals and patients who may be affected by minimum volume standards, I do not think that it actually achieves either of these goals. The objective is better stated in the abstract as predicting the impact of the standards, as the effect on outcomes is outside the scope of this study.

METHODS:

-Are the hospitals included in the NCDB and CoC-affiliated hospitals representative of hospitals nationally? Are there certain criteria (e.g. volume, services provided, etc.) a hospital must meet to be affiliated with the CoC?

-Line 132: How are the authors defining "treated"? I assumed that they mean at least 1 patient who underwent surgical treatment for ovarian cancer, but that is not actually specified. To be included, were patients required to be diagnosed and treated at the same hospital?

-Is there any data about the type of providers at the hospitals (i.e. gynecologic oncologists, surgical oncologists, etc.)?

-Line 166: Does the time period start at diagnosis or initiation of treatment?

-I am concerned about how low volume the low volume hospitals are and how that affects the results. While the O/E ratio of mortality does allow the authors to compare the observed versus expected mortality for a hospital, these small numbers would still make the estimates unreliable for low-volume hospitals. This could make some hospitals seem better due to chance rather than because they are actually better. This is an issue that is well documented in the literature (e.g. Dimick et al. Ranking hospitals on surgical mortality: the importance of reliability adjustment. Health Serv Res. 2010; 45(6 Pt1):1614-29). Other authors have approached this problem by using shrinkage estimation techniques that adjust the performance estimates of low-volume hospitals away from extremes.

RESULTS:

-Line 200: As above, I would clarify exactly what the inclusion criteria are in the Methods, as well as how the authors are defining treatment.

-Line 201-203: Are these cutoffs similar to what has been seen in the prior literature?

-I am surprised that patients receiving care at low volume hospitals are more likely to residents of urban areas. How do the data define metropolitan versus urban? I would think that patients in urban areas would be more likely to be closer to high-volume hospitals.

-I would include more some comments about the characteristics of low versus high volume hospitals, similar to how the authors commented on patients receiving care at low versus high volume hospitals.

-Line 228-229: As above, I do not quite believe the O/E mortality ratio for the low volume hospitals

-Line 234-236: Again, these are very noisy estimates, and I do not think that this is actually true.

DISCUSSION:

-Lines 252-253: I do not see where this is noted.

-Line 268: I assume the authors meant <4 .

-Line 300: This argument for why the authors focused on mortality and not morbidity or perioperative complications is not clear to me. I do not think that the "We therefore believe..." sentence logically follows the prior sentences.

-Line 303: Perhaps adding a "Fourth" before "We examined the association..." would help the logical flow of this paragraph.

-Line 306: It is not clear to me from this paragraph how examining short and long term outcomes mitigates the impact of patients receiving numerous therapies. Could the authors please clarify?

Reviewer #4: The authors used the well described and utilized NCDB to attempt to elucidate the link between "high volume" centers and ovarian cancer mortality to model the effects of using case volume to set restrictions on which hospital could provide care.

The authors well recognize the extreme limitation on the data/conclusions that can be drawn and outline them well in the discussion, my concern is always that no one reads any of the details but simply reads the abstract and conclusions. I would suggest that the conclusion should focus more on the fact that using a simple metric like surgical volume alone CANNOT predict outcomes for patients and should not be a basis for decisions about care

1. While I understand statistically why the authors chose to use cut points of 1 or two cases, that would the EXTREMELY low surgical volume centers and even using up to 4 would eliminate 35% of the hospitals but less than 8% of the patients. There is so much more to survival than surgery in ovarian cancer and it becomes impossible to factor in the other issues (where did they get their chemo, what type of physician provided their care both for surgery and for subsequent chemotherapy/treatment). None of this can be modeled in these data.

2. There is a chance that some of these low volume surgical hospitals may have GYN Oncs or specialized folks coming in to help the areas with surgery and may explain better outcome group or that these cases were not thought to be cancer and so were essentially the better types of ovarian cancer (some of this was likely accounted for in the multivariate). Just no way to know and I don't know if there is any way (and perhaps the authors did this) that the "high performers" and "low performers" can be compared stratified by volume to see if there are any other characteristics (physician types, hospital size, location, patient characteristics etc) that could explain the differences

3. The authors spell out the differences for hospitals with cases of 1 or 3 or 5 in the results and in Table 3 but in looking at the figures (Figure 2 really shows the spread of results), it appears that to consistently be under one--the surgical volumes need to be MUCH higher (40-50) but really no mention in the text about what the best O/E ratios would be based on the volume (or I missed it?). For the readers, it might be good to add volumes of 10 or 20 to the Table 3 data just for easy visual reference in addition to the figures.

4. In the abstract and the discussion, likely needs more emphasis that there is not one simple measure (e.g. number of cases) that can predict outcomes and that no matter the volume, a significant number of hospitals do better and others do worse than expected but the trend is for better outcomes with higher volume.

STATISTICAL EDITOR COMMENTS:

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

Table 2: Suggest stating in simpler terms how tractable the lower volume hospitals were. That is, how much turnover would there be from year to year in identifying at years' end, those with volumes of 1, 2, 3 etc?

Fig 2: Although this contains useful information, it is probably difficult to read. Suggest moving it to on-line material and either including along the x-axes of Fig 1 the number of hospitals at each increment. Alternatively, could include a Table giving number of patients and hospitals at each hospital volume increment, along with the corresponding O/E ratio.

It might be of interest to speculate more, given hypothetical thresholds of 1, 2, 3, 5 or 10 as the prior year volume, how many 60 day, 1, 2 or 5 year mortalities (both % changes and predicted counts) would change if all patients at the low volume hospitals were instead treated at the higher volume hospitals and assuming that the lower O/E would be transferable to those patients. Realizing that is an assumption subject to future review. This idea was stated well on lines 289-293, I think it could be developed more fully and perhaps expanded into a table or other format.

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.

- The objective for the abstract should be a simple "to" statement without background.

- 2017?

- In both the abstract and the paper, please provide absolute numbers as well as which ever effect size you are reporting +

Confidence intervals. P values may be omitted for space concerns. By absolute values, I mean something like xx (outcome in exposed)/yy(outcome in unexposed) (zz%) (Effect size= ; 95% CI=.) An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4)

- increasing--was this a threshold--above vs below the threshold, or was there a continuum?
Is 2 better than 1 for instance? Can you make this clearer?

- in your paper, you use cut points of 1, 3 and 5 but not 2. They don't have to be same in the abstract and paper, but I'm not sure there is a good reason to make them different, either.

- I'm sure this is statistically correct, but how could a hospital with a treatment volume of 1 have more than 1 death observed?

- Go ahead and spell out NCDB and CoC throughout.

- you included the Deyo score but from this list starting on line 124, it doesn't seem that the diagnoses needed to complete the Deyo score would be available.

- The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances. O/E is fine.

- Did you combine these two factors into one "SES" variable?

- Please provide this classification system either in the Supplemental Digital content or in a box.

- on line 132 you state that the primary focus was on outcomes in 1 year; here you give several primary outcomes. This seems to be in conflict.

- does this mean that on average, all hospitals who treat more than 1 patient would have an O/E above 1? How could that be? Shouldn't the expected rate be the "average"?

- Given that you showed that women in the lower volume hospitals were older, had more co-morbidities and more likely to have Stage 4 Ovarian cancer than those in higher volume sites, isn't some of these disparities to be expected? Can you look at the outcomes for low volume patients with more surgically-favorable patients in the prior year vs less so? Maybe to try to avoid limiting access altogether, the strategy would be to encourage docs and patients in the face of poor surgical risks to go to a higher volume hospital but tolerate (?) low volume centers with better risk candidates?

- you showed less of an effect on O/E

- by process measures do you mean national guidelines? I think of process measures in terms of outcomes in QI studies

- earlier you said primary focus was 1 year survival. Please clarify. Is it worth suggesting some other solutions? Gyn Onc docs operating in smaller hospitals with generalist there? (recognizing that there are some problems with that as well)--so decentralization of the doc and hospital. Please consider Tom Rigg's suggestion for alternate way to present your data.

2. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

3. 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. 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 for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. 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 <http://ong.editorialmanager.com>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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 26 typed, double-spaced pages (6,500 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.

8. Title - The Editors would like to suggest, "Potential Consequences of Minimum-Volume Standards for Hospitals Treating Women with Ovarian Cancer."

9. 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).

10. 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.

11. 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.

12. 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.

13. 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.

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

15. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at <http://links.lww.com/LWW-ES/A48>. The cost for publishing an article as open access can be found at <http://edmgr.ovid.com/acd/accounts/ifaauth.htm>.

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.

16. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at <http://ong.editorialmanager.com>. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Feb 21, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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

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