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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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RE: Manuscript Number ONG-19-1153

IMPACT OF GASTROINTESTINAL ADJUVANT CHEMOTHERAPY REGIMENS IN WOMEN WITH OVARIAN MUCINOUS CARCINOMA

Dear Dr. Frumovitz:

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 Sep 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is an intriguing well-written small study comparing the prognosis of patients with ovarian mucinous carcinoma who receive traditional gynecologic neoadjuvant chemotherapy to those who receive traditional gastrointestinal adjuvant chemotherapy. This data comes from GOG trial 241 that was closed secondary to lack of accrual.

The authors found improved survival in patients who received the gastrointestinal regimen. There is biologic plausibility given the similarity of ovarian mucinous carcinomas to primary gastrointestinal malignancies.

Although the authors acknowledge that using gastrointestinal regimens for this indication is off label, it is unclear whether the patients were informed and what the process was for this off-label use.

In addition to mentioning the role of expanding horizons and coupling with medical oncologists to think outside the box for the treatment of rare and resistant tumors, it seems prudent to mention precision medicine and the role of utilizing the specific chemotherapy to which the tumor responds regardless of traditional practice.

This study is very specific and relevant to gynecologic oncologists.

Reviewer #2: This is a very important research question in gynecologic oncology given the scarcity of treatment options for invasive mucinous carcinomas of the ovary. It was very disappointing that GOG-241 closed early due to low accrual, highlighting the difficulties associated with studying rare tumors, and therefore the subject matter of this manuscript is extremely important.

However, the issues with this particular study is that most patients who were treated had stage 1 disease. As a result, there were too few events both in recurrences and deaths (6 recurrences in the GI chemotherapy group vs 14 recurrences in the gynecologic chemotherapy group, and 3 deaths in the GI group vs 14 deaths in the gynecologic chemotherapy group).

The number of factors to be included in a multivariate analysis depends on the number of events in the smallest group, and usually each factor should be added based on the general rule of 10 events per factor. Therefore, it is difficult to make any meaningful conclusions based on this multivariate analysis, given the few events that occurred. Furthermore, the results of this multivariate analysis was not statistically significant.

Although it would take a lot of work and time, perhaps it would be worthwhile to combine data with other institutions in order to increase the numbers, and also to increase the number of events. Alternatively, one can wait until more time has passed.
pass to further recruit patients and have more events. If there were more patient with advanced stage disease, this would likely contribute to more events as well.

If this is not possible, then I would re-word the manuscript such that the multivariate analysis is not included, citing the few events as the reason that this could not be done. Also would emphasize that this is hypothesis-generating and interesting results in the univariate analysis.

I do think that this is a very interesting question, and it would be helpful to have some data disseminated that supports the used of a GI chemotherapeutic regimen for invasive mucinous adenocarcinomas of the ovary, but based on this particular manuscript, definitive conclusions cannot be made given the number of patients and few events, and the manuscript should therefore be worded as such.

Reviewer #3: I appreciated the introduction. I thought it was a well-written synopsis of the current landscape of the challenges with mucinous ovarian cancer, including its relative rarity, its misclassification and its treatment.

Misclassification of non-gynecologic tumors as gynecologic-origin tumors has been a persistent issue in prior studies examining mucinous-type tumors, can the authors discuss how they avoided this pitfall? The median number of cycles was 6. Would some of these patients be candidates for 3 cycles of chemotherapy (GOG157, Bell et al.)? And if so, was treatment different before and after 2006? What impact would an 'early stage, high risk' categorization and regimen have on outcomes and data analysis?

Considering the large percentage of stage I and II patients and the therefore expected associated high optimal tumor-debulking rate, as well as the very large confidence interval (1.64-164.44) for OS between 'optimal' and no gross residual, the few number of patients this is based on, do the authors feel this is a relevant metric to report in this trial based on the patients included, considering this concept has its origins and applicability in epithelial ovarian cancers, mostly serous histology and mostly advanced stage?

Can the authors comment more on the multivariate analysis PFS, moreso than the univariate, as this may be the most accurate marker of chemotherapy efficacy? Looking at table 4 the multivariate PFS with GI regimen versus GYN regimen appears to be 0.42 with a confidence interval crossing 1 and a P value of 0.15, making it not statistically significant. The multivariate OS with GI regimen appears however to be possibly favorably impacted (P value 0.06, a trend?). This begs the question of how a similar PFS could result in an improved OS?

Could the authors comment on time to recurrence? Looking at figure 1A and 1B, it appears the median time to recurrence for GI regimen is not reached at 10 years and for GYN regimen it may be closer to 4+ years. Is the early initial drop off seen from those patients with advanced stage disease in which a GI regimen is more effective? and the subsequent and persistent separation of curves the 'cures' of the early stage patients in whom the type of chemotherapy (or any chemotherapy at all for that matter) may be irrelevant?

What impact would a 'cross-over' in the event of recurrence either to a GI regimen from an initial GYN regimen or vice versa have on survival?

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: Although there were no statistically significant differences (other than proportion receiving Bevacizumab), the samples and subsets were modest in size and there was low power to discern whether the lack of difference could be generalized. For example, the 3x difference in rates of suboptimal tumor debulking (favoring the GI regimen cohort) was NS due to the low counts. Had the series been larger, with the same relative difference, that would have required adjustment or matching to resolve.

2. Table 3: Given the large number of comparisons, a stricter inference threshold should be applied to avoid spurious associations. Based on these data, that would negate the conclusions re: GI vs GYN chemo regimen type (for both overall survival and progression-free survival), suboptimal tumor debulking status (for overall survival). Also, due to lack of power, the NS findings cannot necessarily be generalized.

3. Table 3: There are relatively few adverse events for most of the row entries. One cannot with confidence corroborate whether the proportional hazards model assumptions were met.

4. Table 4, lines 175-178: The aHR of 0.17(95% CI .03-1.07) is NS, so there is no trend. The number of adverse events is too few to allow for adjustment with 4 variables. The adjustment model is likely over fitted.

5. Fig 1: Need to include a legend with concise explanation of the stats used. Appears to be log-rank.

ASSOCIATE EDITOR - GYN COMMENTS:
Please try to revise Abstract, Intro, etc to target the general OBGYN readership of green journal.

EDITORIAL OFFICE COMMENTS:

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2. 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.

3. 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.

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

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 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.

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

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. 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%).

14. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

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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 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 21 days from the date of this letter. If we have not heard from you by Sep 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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RE: Manuscript Number ONG-19-1153

RESPONSE TO REVIEWER COMMENTS:

Reviewer #1: This is an intriguing well-written small study comparing the prognosis of patients with ovarian mucinous carcinoma who receive traditional gyn neoadjuvant chemotherapy to those who receive traditional gi adjuvant chemotherapy. This data comes from GOG trial 241 that was closed secondary to lack of accrual.

The authors found improved survival in patients who received the gi regimen. There is biologic plausibility given the similarity of ovarian mucinous carcinomas to primary gi malignancies.

Although the authors acknowledge that using gi regimens for this indication is off label, it is unclear whether the patients were informed and what the process was for this off-label use.

RESPONSE: The text has been updated to include a sentence stating that patients were counseled about this off-label use during treatment discussions.

Lines 137-138: “Our clinical practice is to inform patients of this off-label use and to counsel them on the rationale for this recommendation at the time of treatment counseling.”

In addition to mentioning the role of expanding horizons and coupling with medical oncologists to think outside the box for the treatment of rare and resistant tumors, it seems prudent to mention precision medicine and the role of utilizing the specific chemotherapy to which the tumor responds regardless of traditional practice.

RESPONSE: This important point has been elaborated upon in our Discussion section.

Lines 278-284: “Additionally, patients with ovarian mucinous carcinoma may benefit from the growing evaluation of precision oncology. The molecular landscape is more similar to some gastrointestinal tumors, containing mutations in KRAS and BRAF with much high frequency than other histologic subtypes of ovarian carcinomas [24, 25]. Future studies of novel agents targeting these aberrations may have efficacy in patients with ovarian mucinous carcinoma, and basket trials combining gastrointestinal and ovarian mucinous carcinomas may be able to take advantage of their molecular similarities.”

Reviewer #2: This is a very important research question in gynecologic oncology given the scarcity of treatment options for invasive mucinous carcinomas of the ovary. It was very disappointing that GOG-241 closed early due to low accrual, highlighting the difficulties associated with studying rare tumors, and therefore the subject matter of this manuscript is extremely important.

However, the issues with this particular study is that most patients who were treated had stage 1
disease. As a result, there were too few events both in recurrences and deaths (6 recurrences in
the GI chemotherapy grp vs 14 recurrences in the gynecologic chemotherapy group, and 3 deaths
in the GI group vs 14 deaths in the gynecologic chemotherapy group). The number of factors to
be included in a multivariate analysis depends on the number of events in the smallest group, and
usually each factor should be added based on the general rule of 10 events per factor. Therefore,
it is difficult to make any meaningful conclusions based on this multivariate analysis, given the
few events that occurred. Furthermore, the results of this multivariate analysis was not
statistically significant.

RESPONSE: Thank you for these valid points. We have decided to remove the multivariable
analysis from this manuscript for the above reasons.

Although it would take a lot of work and time, perhaps it would be worthwhile to combine data
with other institutions in order to increase the numbers, and also to increase the number of
events. Alternatively, one can wait until more time has passed to further recruit patients and have
more events. If there were more patient with advanced stage disease, this would likely contribute
to more events as well.

If this is not possible, then I would re-word the manuscript such that the multivariate analysis is
not included, citing the few events as the reason that this could not be done. Also would
emphasize that this is hypothesis-generating and interesting results in the univariate analysis.

RESPONSE: Thank you for this important point. Given the rarity of this tumor type and the
amount of time required to generate even this small number of events, we believe it would be too
difficult to await more events or add enough institutions to the dataset in order to significantly
increase the power of the study. We do agree that the few number of events makes a
multivariable analysis problematic, and have removed the multivariable analyses text and Table
from the manuscript.

I do think that this is a very interesting question, and it would be helpful to have some data
disseminated that supports the used of a GI chemotherapeutic regimen for
invasive mucinous adenocarcinomas of the ovary, but based on this particular manuscript,
definitive conclusions cannot be made given the number of patients and few events, and the
manuscript should therefore be worded as such.

Reviewer #3: I appreciated the introduction. I thought it was a well-written synopsis of the
current landscape of the challenges with mucinous ovarian cancer, including its relative rarity, its
misclassification and its treatment.

Misclassification of non-gynecologic tumors as gynecologic-origin tumors has been a persistent
issue in prior studies examining mucinous-type tumors, can the authors discuss how they avoided
this pitfall?
RESPONSE: We have updated the language in our Methods section to provide further detail about the process used to evaluate mucinous tumors and determine the primary site of origin.

Lines 121-127: “All pathology material was reviewed by gynecologic pathologists. A rigorous macroscopic and microscopic examination was performed to confirm an ovarian primary. If necessary, ancillary tests such as immunohistochemical stains and in situ hybridization for high risk human papillomavirus were obtained. A thorough clinical correlation (re-review of clinical findings, personal history, imaging studies and endoscopic examination) was obtained in those cases where the pathology examination could not determine with certainty an ovarian origin.”

The median number of cycles was 6. Would some of these patients be candidates for 3 cycles of chemotherapy (GOG157, Bell et al.)? And if so, was treatment different before and after 2006? What impact would an 'early stage, high risk' categorization and regimen have on outcomes and data analysis?

RESPONSE: The practice at our institution has largely been to treat patients with 6 cycles of adjuvant chemotherapy. However, we did do a statistical analysis comparing the number of cycles received before and after 2006, and found that the average number was 6 for both groups. A sentence was added in the Results section to note these findings. (Lines 188-190)

Considering the large percentage of stage I and II patients and the therefore expected associated high optimal tumor-debulking rate, as well as the very large confidence interval (1.64-164.44) for OS between 'optimal' and no gross residual, the few number of patients this is based on, do the authors feel this is a relevant metric to report in this trial based on the patients included, considering this concept has its origins and applicability in epithelial ovarian cancers, mostly serous histology and mostly advanced stage?

RESPONSE: This is an important point, and it is true that the importance of tumor debulking status in mucinous ovarian cancer is less well understood. However, as oncologists often extrapolate cytoreduction status to mucinous ovarian cancer patients in practice, we believe that the readers of the journal may be interested to know that there were no differences between the two groups. But we acknowledge the limited conclusions that can be drawn from these specific data regarding debulking status for the reasons noted.

Can the authors comment more on the multivariate analysis PFS, more so than the univariate, as this may be the most accurate marker of chemotherapy efficacy? Looking at table 4 the multivariate PFS with GI regimen versus GYN regimen appears to be 0.42 with a confidence interval crossing 1 and a P value of 0.15, making it not statistically significant. The multivariate OS with GI regimen appears however to be possibly favorably impacted (P value 0.06, a trend?). This begs the question of how a similar PFS could result in an improved OS?

RESPONSE: As discussed by Reviewer #2 above, we have removed the multivariable model and its associated discussion from the manuscript.
Could the authors comment on time to recurrence? Looking at figure 1A and 1B, it appears the median time to recurrence for GI regimen is not reached at 10 years and for GYN regimen it may be closer to 4+ years. Is the early initial drop off seen from those patients with advanced stage disease in which a GI regimen is more effective? and the subsequent and persistent separation of curves the 'cures' of the early stage patients in whom the type of chemotherapy (or any chemotherapy at all for that matter) may be irrelevant?

**RESPONSE:** This is an interesting point. Although the number of patients in our study with late stage disease is limited, the numbers of patients with Stage III/IV disease were balanced between the GI and GYN chemotherapy groups. From a statistical standpoint, we believe the persistent separation of the curves actually denotes a true impact of chemotherapy, as the curves might actually converge over time if there was truly no difference between the two groups.

What impact would a 'cross-over' in the event of recurrence either to a GI regimen from an initial GYN regimen or vice versa have on survival?

**RESPONSE:** This is a very important question, and one which our data does not answer. We have limited data about which regimens patients received in third line and beyond treatments and the subgroup of patients with recurrence is smaller which makes comparisons difficult. For patients who have information regarding second line therapy, the majority of patients received a regimen similar to the first regimen that was given; i.e., most patients who received a GYN regimen initially subsequently received a GYN regimen (n=9/10), and those who received a GI regimen initially subsequent received a GI regimen (n=3/5). However, these numbers are small and thus no real conclusions can be drawn. We have added a sentence to the Discussion under “limitations” acknowledging this point.

Lines 257-260: “Fourth, this study only evaluated chemotherapy regimens that were administered for first line treatment, and thus no conclusions can be made about the utility of chemotherapy choice at recurrence or the impact of treatment crossover.”

**STATISTICAL EDITOR'S COMMENTS:**

1. Table 1: Although there were no statistically significant differences (other than proportion receiving Bevacizumab), the samples and subsets were modest in size and there was low power to discern whether the lack of difference could be generalized. For example, the 3x difference in rates of suboptimal tumor debulking (favoring the GI regimen cohort) was NS due to the low counts. Had the series been larger, with the same relative difference that would have required adjustment or matching to resolve.

**RESPONSE:** This is an important point, and we have added a sentence to the Discussion section under out limitations addressing the modest sample size and limited power. We have made a note.
in the text that our analyses were exploratory, and adjusted our Methods section to note the exploratory nature as well and thus we used the less conservative p-value cut-off of $p < 0.05$.

Lines 260-264: “Last, our study sample was still modest overall, and thus there may not have been enough power to detect differences in some of our analyses. We also had a small number of events, likely because of the large number of patients with stage I disease. For this reason, our univariable survival analyses were exploratory in nature and were not adjusted for multiple comparisons.”

2. Table 3: Given the large number of comparisons, a stricter inference threshold should be applied to avoid spurious associations. Based on these data, that would negate the conclusions re: GI vs GYN chemo regimen type (for both overall survival and progression-free survival), suboptimal tumor debulking status (for overall survival). Also, due to lack of power, the NS findings cannot necessarily be generalized.

**RESPONSE**: We have made a note in the text that our analyses were exploratory, and adjusted our Methods section to note the exploratory nature as well and thus we used the less conservative p-value cut-off of $p < 0.05$. We also changed “no significant differences” to “insufficient evidence of any differences” in the first paragraph of our Discussion.

3. Table 3: There are relatively few adverse events for most of the row entries. One cannot with confidence corroborate whether the proportional hazards model assumptions were met.

**RESPONSE**: As above, we have changed the wording to reflect an exploratory approach. We have also changed the wording in the Discussion section.

4. Table 4, lines 175-178: The aHR of 0.17(95% CI .03-1.07) is NS, so there is no trend. The number of adverse events is too few to allow for adjustment with 4 variables. The adjustment model is likely over fitted.

**RESPONSE**: Based on this and the above discussions, we have removed the multivariable model from the manuscript as well as the associated text.

5. Fig 1: Need to include a legend with concise explanation of the stats used. Appears to be log-rank.

**RESPONSE**: The title and legend of Figure 1 has been updated to include this information.

**ASSOCIATE EDITOR - GYN COMMENTS:**

Please try to revise Abstract, Intro, etc to target the general OBGYN readership of green journal.
**RESPONSE:** We updated the abstract to include the fact that ovarian mucinous cancers are diagnosed in young women at an early stage, as this is a demographic that a general OBGYN is more likely to manage first. We updated the Introduction of manuscript to include a paragraph to elaborate on this point, and highlight the collaborative roles general OBGYN physicians and gynecologic oncology physicians often play in managing these patients.

Lines 70-81: “Given the high frequency of localized disease at the time of diagnosis, it is not uncommon for these mucinous tumors to be initially found and resected by benign gynecologists. Once identified, these patients are subsequently referred to gynecologic oncologists, and a discussion between the patient and her physician is then had about the utility of a second surgical procedure for complete oncologic staging. Retrospective data suggest that the rates of lymph node metastases are extremely low in ovarian mucinous carcinoma, and lymphadenectomy is often omitted from staging procedures in this histologic subtype [6, 7]. National Comprehensive Cancer Network guidelines currently do not recommend adjuvant chemotherapy in patients with FIGO stage IA or IB disease, but include consideration of adjuvant chemotherapy in FIGO stage IC disease (preoperative or intraoperative rupture, or positive cytology in pelvic washings) [8]. Thus, the importance of pelvic washings at the time of initial surgical removal of these pelvic masses should be emphasized.”

**EDITORIAL OFFICE COMMENTS:**

1. 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.

**RESPONSE:** OPT-IN: Yes, please publish my point-by-point response letter.

2. 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.
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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.

**RESPONSE:** This has been added.

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

**RESPONSE:** We have edited the test in the Methods section to reflect this quality assurance process.

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](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.

**RESPONSE:** The STROBE checklist has been included and annotated as “Comments” with the responses.
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.

**RESPONSE:** We have reviewed the reVITALize definitions. Our manuscript with the reVITALize definitions listed.

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, references, tables, boxes, figure legends, and print appendixes) but exclude references.

**RESPONSE:** This has been confirmed.

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).

**RESPONSE:** This has been updated appropriately.

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

**RESPONSE:** This has been modified in the text to comply with the text constraints.
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.

**RESPONSE:** This has been reviewed. Word count for the abstract is now 300.

11. Only standard abbreviations and acronyms are allowed. A selected list is available online at [http://edmgr.ovid.com/ong/accounts/abbreviations.pdf](http://edmgr.ovid.com/ong/accounts/abbreviations.pdf). Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

**RESPONSE:** We have edited our text to comply with these guidelines.

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.

**RESPONSE:** The manuscript (Abstract and Methods) has been modified to remove the wording “and/or”.

13. 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.

**RESPONSE:** We have removed the p-values from Tables 2 and 3. We have also used effect size and confidence intervals where possible throughout the text, and removed the p-values.

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.

**RESPONSE:** For this analysis, we did not think that the NNTb or the NNTh would provide any additional information. We also did not perform any cost analyses.
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").

RESPONSE: We have standardized the data throughout the text to avoid more than 3 decimal places and 1 decimal place for p-values and percentages, respectively.

14. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

RESPONSE: The Discussion section has been updated to remove the statement about it being the largest retrospective study to date.

15. 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.

RESPONSE: The guidelines have been reviewed and the tables have been updated accordingly.

16. 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/ifauth.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.

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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 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 21 days from the date of this letter. If we have not heard from you by Sep 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology