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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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Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

Date: Sep 09, 2022
To: "Kirsten Jorgensen" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-1412

RE: Manuscript Number ONG-22-1412

Disparities in Fertility-Sparing Treatment and Preservation after a Diagnosis of Cervical, Ovarian, or Endometrial Cancer: a Population-Based Study

Dear Dr. Jorgensen:

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 30, 2022, we will assume you wish to withdraw the manuscript from further consideration.

EDITOR COMMENTS:

You point out in Discussion that some of your findings are in contrast, but would be ideal to speculate as to why. Also, to speculate on why such a low rate of ART.

REVIEWER COMMENTS:

Reviewer #1: This is a retrospective, population-based cohort study using linked data from administrative healthcare databases in California to examine associations between the use of fertility-sparing interventions and assisted reproductive technology (ART) among women with a history of early stage cervical, uterine, or ovarian malignancies.

Overall, this is in interesting study that integrates unique administrative datasets in a manner that facilitates novel analyses. A significant limitation is that the most novel analysis—examining ART usage following early-stage gynecologic cancer diagnosis—is based on a very small number of cases, which may limit the robustness of conclusions. In addition, the finding that fertility-sparing treatment was more common among racial/ethnic minorities is contrary to large body of literature on disparities in cancer care and does not have a clear underlying cause, raising the possibility that this conclusion is an aberration resulting from errors in methodology or ascertainment. A more thorough discussion of that contextualizes this finding in the prior literature would strengthen the manuscript.

Although the large number of patients in this cohort is a strength of the study, the use of CCR data spanning 2000-2015 creates the potential for non-uniform ascertainment bias in the secondary outcome (ART utilization), due to changing demographics in California during these decades (https://www.ppic.org/publication/californias-population/). Non-Hispanic whites made up a larger proportion of the population in 2000 compared to 2015, meaning that white women in this cohort would tend to have a proportionally longer follow up time for ascertainment of ART usage relative to Hispanic women. The conclusions in the manuscript would be significantly strengthened if appropriate adjustments were made for demographic

changes over time.

Lines 92-99: Since prior surgical history is presumably unknown for women in this cohort, the exposure assessment may incorrectly classify some women as having fertility-sparing surgery if they had prior USO and/or hysterectomy. Is there an approach to estimate the degree to which misclassification may be present in the data? If not, this should be discussed as a limitation.

Line 175: Be consistent is use of "women" vs "patients" to describe cohort members.

Lines 189-190: Although efforts to protect confidentiality are commendable, many values not reported on the Tables can be ascertained with certainty by subtraction of other categories from the column total (see for example Martial Status in Table 1).

Line 191: Presumably some percentage of women with early-stage uterine cancer in this cohort failed hormonal-based management and require subsequent hysterectomy - are these women excluded by the study design? If not then this rate should be reported, as it may partially explain the relatively low rate of live birth observed in this group.

Lines 210-215: The section regarding sensitivity analyses should be significantly expanded so that the results can be better interpreted by a non-specialist without referring to the Appendix.

Lines 230-232, lines 235-237, lines 238-240: The findings in this manuscript differ from both naïve expectation and prior published results in several key areas. A more thorough discussion of methodological differences that may have accounted for these discrepancies seems warranted.

Table 1: I think the percentages should be column-based since this would allow easier assessment of variable distribution by exposure category. Also, were missing data categories included or excluded from tables used for statistical testing?

Reviewer #2: Review of Manuscript ONG-22-1412 "Disparities in fertility-sparing treatment and preservation after a diagnosis of cervical, ovarian or endometrial cancer: A population based study"

A retrospective cohort study that evaluates the utilization of fertility sparing surgery in young women with early stage cervical, uterine and ovarian cancer from the California Cancer Registry has been submitted. As noted by the authors, the study covers the years 2000-2015 and is generally robust in terms of available information. That being said, the authors do point out some of the potential challenges as it relates to full data availability which were outlined in the methods. Importantly, during the years chosen, several important oncologic changes occurred namely utilization of a new staging system for different cancers as well as increased knowledge about the potential acceptability as well as safety of trachelectomy in young women with cervical cancer. Importantly, the authors do not comment on these systematic changes and the potential impact on patient management. The define in lines 94-98 the procedures consistent with surgical fertility preservation. The majority of the included patients had either cervical or ovarian cancer. In addition, the authors have elected to use 45 as the upper limit of the study, and although women certainly may conceive at or after age 45, spontaneous conception is low and ART is likely to be needed. The authors have appropriately included a STROBE checklist. I have the following questions and comments.

Title - Consider noting this is from the California Cancer Registry

Précis - Consider use of "among" rather than "by"

Abstract - See methods for questions related to substages and histology of the different types of cancer.
Line 25 - minor point - You are describing women diagnosed with these specific gynecologic malignancies and not all gynecologic malignancies.

Line 29 - Another minor point, consider noting "Across all three cancer types…"

Line 33 - "This study demonstrates…"

Introduction - Line 43 - Definitive therapy is still consider the SOC for most so perhaps so additional verbiage like, "While definitive surgical resection including hysterectomy and BSO is indicated for many, fertility preserving surgery is a reasonable alternative…."

Methods -
Line 81 - Why did you select age 45 as the upper age cutoff? Why not age 40? How might inclusion of women ages 40-45 impact your results? Is information on permanent sterilization either tubal or partner vasectomy available in your database?

Line 82 - What staging criteria was used for endometrial cancer (1988 with Stages IA, IB and IC or 2009 with Stages IA

and IB)? How did you know that patients had Stage IB - presume based on imaging?

There are limited details about the tumors themselves to frame the application of these findings. From an oncologic standpoint and for all tumor types do you have information about the histology and/or grades of the tumor? I suspect that most women with ovarian cancer had germ cell or stromal tumors? Were certain histologies excluded from this analysis? For instance, women with a small cell cervical cancer should not be offered fertility preservation and thus excluded?

Line 111 - For women that received radiotherapy did they remain in the potential analysis re: various fertility outcomes? If so why since conception was likely not feasible?

Results - Line 154 - Did you consider evaluating outcomes based on time?

Discussion - Line 277 - What about availability of oncologic information (as noted above) as a limitation?

Tables - Table 1 - No real comments although for the Uterine cancer patients with Stage IB disease it seems like there should be about 267 patients among the 2 cells which could be similar to some of the provided cells for women having fertility preservation.

Table 2 - Are the 49 women with cervical cancer that received radiation in the various denominators for conception, ART, etc. as the receipt of radiation would have precluded their ability to conceive.

Table 3 - No comments

Figures - Figure 1 - No comments on the flow diagram.

Figures 2&3 - Cancer stage (last row) is unusual since you have included Stage IC for women with uterine and cervical cancer. A legend needs to be added noting that there were no women with Stage IC for these 2 tumor types and thus the comparison is Stage IB vs. IA.

Appendix - No comments.

Reviewer #3: In this manuscript, the authors evaluate fertility sparing treatment (defined as retention of 1 ovary and uterus) and ART in women with early stage cervical, endometrial, and ovarian cancer using linked data including the California Cancer Registry from 2000-2015. The data is robust with more than 1800 women identified and detailed outcome data available, and the statistical analyses straightforward. Constructive comments included below:

Introduction
Lines 53-56: although related, it is interesting to combine these aims as the outcomes (fertility sparing treatment and ART) are separate outcomes: knowing you have cancer and planning fertility sparing treatment, incidentally finding cancer after surgery which happened to be fertility sparing, and then downstream ART access following a cancer diagnosis. ART is not necessarily required in fertility preservation treatment and would be more necessary with only retention of the ovaries/uterus.

As an extension, a CKC/radical trachelectomy, IUD/oral progestins are intentional treatments with known cancer- whereas fertility sparing treatment in ovarian cancer may have a large percentage that were fertility sparing by accident (found on final path and ovary couldn't be saved at time of surgery). Unlikely to ever know the difference.

Similarly, although it makes sense somewhat to include cervical cancer with endometrial and ovarian, if a patient has early-stage disease (Stage IA/IB) and is pre-menopausal, standard of care for surgical treatment is optional removal of the ovaries, therefore is also fertility sparing (with possibility of IVF). There is data that also supports retention of ovaries in young endometrial cancer patients, which allows for IVF. Including these patients may reveal more about ART use.

Methods
-Lines 100-102, why not include superovulation, IUI as well?

-Line 104- why was age divided at 35?

-Line 108- why was the Yost SES index used?

Results
-What percentage were radical trachelectomy (technically more difficult and not offered by all physicians) versus CKC? The differences might disappear if separated given the resources needed to seek care from a provider that offers trachelectomy.

-It is difficult to interpret your data with missing numbers in each of the table- if the data is de-identified by virtue of being

in a database, why are they excluded?

-Why is the MV regression data for fertility sparing treatment presented as both a Table (3) and figure (3) whereas ART use is only presented as figure?

Discussion
Although there were no differences by insurance status, California in general has better insurance access (Medi-cal) than other areas of the country therefore this may be different in other areas of the U.S.

STATISTICAL EDITOR COMMENTS:

Table 1: The number of unknowns for Charlson comorbidity score in cervical CA group is similar to the number with score ≥ 1. This complicates the analysis and adjustment and deserves mention among limitations. Similar for unknown insurance status. For endometrial CA, the number unknown for cancer Stage represents a similar problem.

Table 3: Since CIs are included, there is no need to include column of p-values, so should be omitted. Should include column of unadjusted ORs with CIs to contrast with aORs. To be clear, all variables in table were included in the multivariable model and retained in the final model, correct?

Suggestion: Tables 1, 3 and Fig 1 have arranged the groups in order as cervical, endometrial, and then ovarian. Figs 2 and 3 has ordered them as endometrial, cervical and then ovarian. Suggest it would be better to have a consistent order throughout.

EDITORIAL OFFICE COMMENTS:

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. 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.

8. 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

9. 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.

10. 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.

Original Research: 300 words

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, 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.

13. 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.

14. 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.

15. 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.

16. 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.

17. Figures

Figure 1: Are any additional exclusion boxes needed?

Figures 2-3: Can be resubmitted as-is, unless changes have been requested by the Statistical Editor.

18. 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.

19. 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 https://wkauthorservices.editage.com/open-access/hybrid.html.

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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 30, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Deputy Editor, GYN

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if you have any questions.

September 29, 2022
MD Anderson Cancer Center
Houston, TX

Dear Dr. Wright and associate editors of Obstetrics and Gynecology,

We thank the editors for the opportunity to revise and resubmit our manuscript entitled, "Disparities in Fertility-Sparing Treatment and Preservation after a Diagnosis of Cervical, Ovarian, or Endometrial Cancer: a Population-Based Study" (Manuscript #ONG-22-1412). We greatly appreciate the comments made by each of the reviewers.

We have incorporated changes to our manuscript based on the feedback from the reviewers and believe the edits have substantially enhanced our manuscript and provided necessary additional information. The detailed responses to individual reviewer and editor comments are included below.

Thank you for consideration of our manuscript for publication, we look forward to hearing from you.

Sincerely,

Kirsten Jorgensen, MD
Dept. of Gynecologic Oncology and Reproductive Medicine
Dept. of Health Services Research
The University of Texas MD Anderson Cancer Center
1155 Pressler St., Houston, TX 77030-1362
[redacted]

EDITOR COMMENTS:

You point out in Discussion that some of your findings are in contrast, but would be ideal to speculate as to why. Also, to speculate on why such a low rate of ART.
We appreciate the editor's comment. The discussion has been edited to include our speculations as to why our conclusions differed from prior work (lines 573-704). Our findings of differences in fertility-sparing treatment by race and ethnicity may have been impacted by population differences in rates of hysterectomy (higher among non-White women), rates of germ cell and sex cords stromal tumors being higher among non-White women, and the significant proportion of our cohort that was diagnosed on the day of surgery (lines 632-640). We speculated our findings regarding insurance may have been due to an overall high rate of insurance among our population, as California in general is a highly insured state and the people included in our study had even higher rate of insurance. We added discussion about the low rate of ART (lines 669-671), likely related to follow-up time in the study, and the fact that the treatments for low-risk, early-stage cervical, endometrial, and ovarian cancer may variably impact fertility and may not require future ART use.

REVIEWER COMMENTS:

Reviewer #1: This is a retrospective, population-based cohort study using linked data from administrative healthcare databases in California to examine associations between the use of fertility-sparing interventions and assisted reproductive technology (ART) among women with a history of early stage cervical, uterine, or ovarian malignancies.

Overall, this is in interesting study that integrates unique administrative datasets in a manner that facilitates novel analyses. A significant limitation is that the most novel analysis—examining ART usage following early-stage gynecologic cancer diagnosis—is based on a very small number of cases, which may limit the robustness of

conclusions. In addition, the finding that fertility-sparing treatment was more common among racial/ethnic minorities is contrary to large body of literature on disparities in cancer care and does not have a clear underlying cause, raising the possibility that this conclusion is an aberration resulting from errors in methodology or ascertainment. A more thorough discussion of that contextualizes this finding in the prior literature would strengthen the manuscript.
We thank this reviewer for their comment. We have edited the discussion to contextualize our findings and have taken steps to limit errors in methodology leading to discrepant results. Notably, in response to this and other reviewer's comments, we re-analyzed our data after excluding high-risk histologies and these findings have been added to the manuscript.

Our findings of differences in fertility-sparing treatment by race and ethnicity may have been impacted by population differences in rates of hysterectomy (higher among non-White women), rates of germ cell and sex cords stromal tumors being higher among non-White women, and the significant proportion of our cohort that was diagnosed on the day of surgery (lines 632-640). We reviewed our data and found that within our cohort there were no racial or ethnic differences among those diagnosed on the same day as their treatment versus a different day, however, we acknowledge that the inclusion of same-day diagnoses may affect interpretation of our results.

Although the large number of patients in this cohort is a strength of the study, the use of CCR data spanning 2000-2015 creates the potential for non-uniform ascertainment bias in the secondary outcome (ART utilization), due to changing demographics in California during these decades (https://urldefense.com/v3/__https://www.ppic.org/publication/californias-population/__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi_A8N6RJw$). Non-Hispanic whites made up a larger proportion of the population in 2000 compared to 2015, meaning that white women in this cohort would tend to have a proportionally longer follow up time for ascertainment of ART usage relative to Hispanic women. The conclusions in the manuscript would be significantly strengthened if appropriate adjustments were made for demographic changes over time.
We appreciate this reviewer's comment regarding the possibility of demographic change during the study time period. We have added the year of diagnosis to our baseline characteristics and multivariate analysis. We reviewed our data and found a non-significant difference in the proportion of participants in the study by race and ethnicity over the study time period. We have added reference to this on lines 721-722 in the manuscript. We would be happy to include these data in the manuscript or in an appendix.

We acknowledge that there is a difference in the follow-up time for women diagnosed earlier in the study time than those later in the study time period. Due to this, we included diagnosis year on multivariate and univariate analysis. With regard to ART specifically, we discuss our findings may have been impacted by follow-up time, as we found a statistically significant difference between those diagnosed 2000-2007 and 2008-2015 (lines 669-674).

Lines 92-99: Since prior surgical history is presumably unknown for women in this cohort, the exposure assessment may incorrectly classify some women as having fertility-sparing surgery if they had prior USO and/or hysterectomy. Is there an approach to estimate the degree to which misclassification may be present in the data? If not, this should be discussed as a limitation.
We appreciate this comment and have edited our discussion to acknowledge the limitation of unknown prior surgical history (lines 632-635) and include acknowledgement of misclassification in the limitations (line 723). Based on rates of hysterectomy in the population for the ages of interest in our study, approximately 5 hysterectomies per 1000 people occur, thus we estimated a low rate of misclassification. Data on unilateral (salpingo-)oophorectomy are few, however, appear to follow similarly low rates in the age range of our cohort, suggesting minimal amount of misclassification.

Line 175: Be consistent is use of "women" vs "patients" to describe cohort members.
We have edited the manuscript and used "women" to refer to cohort members. We acknowledge that the use of "women" excludes possible transgender individuals, however, the dataset we used for this study only recognizes men and women, and data we had access to only included women.

Lines 189-190: Although efforts to protect confidentiality are commendable, many values not reported on the Tables

can be ascertained with certainty by subtraction of other categories from the column total (see for example Martial Status in Table 1).
We appreciate this reviewer's comment and have edited our tables. We have reviewed reporting standards for each of the datasets we utilized, and we believe we have hidden necessary cells. Those with unmasked values <11 have a calculated score less than that required to mask, according to California Cancer Registry rules. Scores are based on factors that would allow for recognition including sex, age, location, and other variables.

Line 191: Presumably some percentage of women with early-stage uterine cancer in this cohort failed hormonal-based management and require subsequent hysterectomy - are these women excluded by the study design? If not then this rate should be reported, as it may partially explain the relatively low rate of live birth observed in this group.
We appreciate this comment. Unfortunately, we do not have data for subsequent hysterectomies and agree that this may partially explain the low rate of live birth observed in this group. Additionally, we recognize that anyone treated with fertility-sparing surgery may have recurrence or ongoing disease. We included discussion regarding recurrence or ongoing disease contributing to the low number of births overall in lines 712-714.

Lines 210-215: The section regarding sensitivity analyses should be significantly expanded so that the results can be better interpreted by a non-specialist without referring to the Appendix.
We recognize the importance of explaining the sensitivity analysis and have included the citation for the initial paper describing the E-value (VanderWeele and Ding, 2017) and have clarified the language in our methods section (lines 259-265). In order to meet the word count and not distract significantly from the primary outcomes of the paper, we have included the results of the sensitivity analysis in Appendix 3. We would be happy to put this table in the main text but feel the pertinent take-away can be summarized with the sentences we have in the text (lines 566-569).

Lines 230-232, lines 235-237, lines 238-240: The findings in this manuscript differ from both naïve expectation and prior published results in several key areas. A more thorough discussion of methodological differences that may have accounted for these discrepancies seems warranted.
We appreciate this reviewer's comment and have revised our manuscript to include a thorough investigation by year and histology type, with subsequent revisions to the text. We have also completed additional analyses unreported in the manuscript to assess if results could be explained by women diagnosed on the same day as surgery versus those with a prior diagnosis and found that this could not explain the differences we found between race and ethnicity. Notably, we revised our initial cohort to exclude specific high-risk histologies and have included Appendix 2 to list the specific histology types that were included. After excluding high-risk histologies, we still found differences in fertility sparing treatment and ART use by race and ethnicity and other variables of interest.

We have provided hypotheses as to why our results were different. The discussion has been edited to include our speculations as to why our conclusions differed from prior work (lines 573-704). Our findings of differences in fertility-sparing treatment by race and ethnicity may have been impacted by population differences in rates of hysterectomy (higher among non-White women), rates of germ cell and sex cords stromal tumors being higher among non-White women, and the significant proportion of our cohort that was diagnosed on the day of surgery. We speculated our findings regarding insurance may have been due to an overall high rate of insurance among our population, as California in general is a highly insured state and the people included in our study had even higher rate of insurance (lines 641-647).

Table 1: I think the percentages should be column-based since this would allow easier assessment of variable distribution by exposure category. Also, were missing data categories included or excluded from tables used for statistical testing?
We thank this reviewer for their comment. We have maintained row-based percentages as the exposures are the sociodemographic or clinical variables and we want to facilitate comparisons between fertility-sparing and not-fertility sparing treatment. If the editors feel strongly the percentages should be column based, we would be happy to change them.

Missing data categories were excluded in the logistic regression analysis.

Reviewer #2: Review of Manuscript ONG-22-1412 "Disparities in fertility-sparing treatment and preservation after a diagnosis of cervical, ovarian or endometrial cancer: A population based study"

A retrospective cohort study that evaluates the utilization of fertility sparing surgery in young women with early stage cervical, uterine and ovarian cancer from the California Cancer Registry has been submitted. As noted by the authors, the study covers the years 2000-2015 and is generally robust in terms of available information. That being said, the authors do point out some of the potential challenges as it relates to full data availability which were outlined in the methods. Importantly, during the years chosen, several important oncologic changes occurred namely utilization of a new staging system for different cancers as well as increased knowledge about the potential acceptability as well as safety of trachelectomy in young women with cervical cancer. Importantly, the authors do not comment on these systematic changes and the potential impact on patient management.

The define in lines 94-98 the procedures consistent with surgical fertility preservation. The majority of the included patients had either cervical or ovarian cancer. In addition, the authors have elected to use 45 as the upper limit of the study, and although women certainly may conceive at or after age 45, spontaneous conception is low and ART is likely to be needed. The authors have appropriately included a STROBE checklist. I have the following questions and comments.

We thank this reviewer for their comments. We reviewed our data and have listed the stage criteria used for our dataset on lines 178-182. All stages were based on available information and American Joint Committee on Cancer staging was used, with specific editions mentioned in the text. We additionally included a review of histologies considered eligible for fertility-sparing procedures, and have revised the text, tables, and figures accordingly. We also included year of diagnosis in our analysis and found there were trends (such as more ART instances earlier in the dataset) that were significant. Additionally, we reviewed our data for rates of trachelectomy versus LEEP or cone and found that the rates did not differ significantly among different races and ethnicities (data not presented in the manuscript), thus, although we acknowledge that the type of procedure preferred by providers may have changed over the course of the study period, it does not appear to explain our results.

Title - Consider noting this is from the California Cancer Registry

We appreciate this comment. In order to stay within the word count suggested by the journal, we have retained our original title. Additionally, the study utilized 3 different databases, including the California Cancer Registry, and we have taken care to mention them in the abstract and main manuscript.

Précis - Consider use of "among" rather than "by"

We have edited the precis to reflect this comment.

Abstract - See methods for questions related to substages and histology of the different types of cancer.

We have edited the manuscript and feel it is stronger after exclusion of high-risk histologies that would not be eligible for fertility-sparing surgery. We have included a new appendix (Appendix 2) to list the histology types we included in our study.

Line 25 - minor point - You are describing women diagnosed with these specific gynecologic malignancies and not all gynecologic malignancies.

We have edited wherever possible to note it is only these three gynecologic malignancies, not all gynecologic malignancies (line 15, 27, 58, 80, 704).

Line 29 - Another minor point, consider noting "Across all three cancer types…"

We have edited this to more accurately reflect the results in our data (line 31-33).

Line 33 - "This study demonstrates…"

We have edited this (line 56).

Introduction - Line 43 - Definitive therapy is still consider the SOC for most so perhaps so additional verbiage like, "While definitive surgical resection including hysterectomy and BSO is indicated for many, fertility preserving surgery

is a reasonable alternative…."
We appreciate this comment and have edited the manuscript to reflect it (line 66-67).

Methods -
Line 81 - Why did you select age 45 as the upper age cutoff? Why not age 40? How might inclusion of women ages 40-45 impact your results? Is information on permanent sterilization either tubal or partner vasectomy available in your database?
The reviewer brings up an excellent point. We selected age 45 to be consistent with our, and others', prior studies. Forty is also a reasonable cutoff. Inclusion of those older than 40 may increase the number of those with non-iatrogenic causes of infertility thus artificially increasing the number who use assisted reproductive technology, or may sway a physician not to offer fertility preserving surgery, we felt it was important to include this age group both to be consistent and acknowledge that delay in childbearing is more common and this age group represents a growing percentage of people diagnosed with cancer who may considering childbearing.

The datasets used do not include information regarding tubal ligation status or vasectomy status of the partner. We included in our discussion the variable impact procedures may have on fertility (Lines 671-674) and acknowledge that we are limited by the data available.

Line 82 - What staging criteria was used for endometrial cancer (1988 with Stages IA, IB and IC or 2009 with Stages IA and IB)? How did you know that patients had Stage IB - presume based on imaging?
We thank the reviewer for this comment. We have edited the manuscript to reflect that staging was based on a combination of clinical and pathological stages, as defined by the AJCC and different editions were used for different diagnosis years (lines 178-180). Endometrial cancer was either stage IA or IB, there were no data for IC endometrial cancer stages in our data set, and for those diagnosed with IB it was likely presumptively by imaging, though we do not have detail on mode of staging. We have updated our tables to reflect that no endometrial cancer cases were diagnosed IC.

There are limited details about the tumors themselves to frame the application of these findings. From an oncologic standpoint and for all tumor types do you have information about the histology and/or grades of the tumor? I suspect that most women with ovarian cancer had germ cell or stromal tumors? Were certain histologies excluded from this analysis? For instance, women with a small cell cervical cancer should not be offered fertility preservation and thus excluded?
We appreciate this reviewer's comment and have edited our paper to address these concerns. The reviewer brought up an excellent point regarding histology. We reassessed our cohort and confirmed that only grade 1 endometrial cancer cases were included. We then assessed histology for all cancer types and excluded high-risk histologies that are contraindicated to offer fertility-preservation. We have added Appendix 2 to note the histology types that were included (for example, small cell cervical cancer was excluded from analysis). Additionally, for those with ovarian cancer, we stratified the histologies into germ cell, sex cord stromal, and epithelial. We included histology in our multivariable analysis (Table 3, Figure 2) and univariate analysis (Figure 3).

Line 111 - For women that received radiotherapy did they remain in the potential analysis re: various fertility outcomes? If so why since conception was likely not feasible?
We thank the reviewer for this comment and reassessed our data. We had not initially excluded women who received radiation from further analysis. On review of our data, no woman who received radiation had a live birth. Given the excellent point of the reviewer, we have removed these women from the analysis of live birth. We did not exclude those who had radiation from assessment for ART, as it is possible for a woman to be diagnosed, undergo fertility preservation via egg retrieval and subsequently receive radiation. We did, however, confirm that none of the women who received ART had radiation prior to the ART procedures. We have updated Figure 1 to reflect this exclusion and added it to lines 223-225.

Results - Line 154 - Did you consider evaluating outcomes based on time?
We thank this reviewer for their comment. We have added year of diagnosis to our analyses (multivariate and univariate). We additionally conducted analyses of the cohort over time, to ensure changes in the demographics of the

cohort remained constant throughout our study time period—specifically for the exposure of race/ethnicity. We found that the population in the California Cancer Registry had similar percentages of each racial/ethnic group during the study time period, despite changes in demographics of the overall California population during the same time period. .

Discussion - Line 277 - What about availability of oncologic information (as noted above) as a limitation?
The reviewer brings up an excellent point and we have edited the manuscript to include the histology, and year of diagnosis. We feel these edits have strengthened the study significantly. We have added to the discussion a limitation due to missing or unknown oncologic data (line 754-755). We reviewed our data to ensure that only grade 1 endometrial cancer was included (as guidelines recommend against fertility-sparing for grade 2 and 3) and have included this in the abstract and main text (lines 17, 156). We performed additional analyses of our data to investigate if the type of fertility-sparing procedure received (such as trachelectomy versus LEEP) differed among cervical cancer patients, and did not find significant results (this data was not included in the manuscript).

Tables - Table 1 - No real comments although for the Uterine cancer patients with Stage IB disease it seems like there should be about 267 patients among the 2 cells which could be similar to some of the provided cells for women having fertility preservation.
We thank the reviewer for their comment. Following exclusion of high-risk histologies, the numbers in the cells have slightly changed and this is updated in Table 1 and all additional tables and figures.

Table 2 - Are the 49 women with cervical cancer that received radiation in the various denominators for conception, ART, etc. as the receipt of radiation would have precluded their ability to conceive.
We thank the reviewer for this comment, and we have edited our analysis (multivariable and univariate analyses, as well as Figure 1) to reflect that radiation for cervical and ovarian cancer was an exclusion criterion for live birth. There were no endometrial cancer patients who received radiation after fertility-sparing treatment. For those who had radiation and ART, we confirmed that ART occurred prior to radiation. We did not assess for live births after ART in this study, thus a woman could have had ART and then radiation, and subsequently used a surrogate to have a biological child.

Table 3 - No comments
Figures - Figure 1 - No comments on the flow diagram.

Figures 2&3 - Cancer stage (last row) is unusual since you have included Stage IC for women with uterine and cervical cancer. A legend needs to be added noting that there were no women with Stage IC for these 2 tumor types and thus the comparison is Stage IB vs. IA.
We appreciate this comment and have clarified our tables. All tables and figures now have separate rows for IA, IB, IC and we have used “not applicable” to reflect that there were no women stage IC uterine or cervical cancer, and no women diagnosed with stage IB ovarian cancer included in our dataset.

Appendix - No comments.

Reviewer #3: In this manuscript, the authors evaluate fertility sparing treatment (defined as retention of 1 ovary and uterus) and ART in women with early stage cervical, endometrial, and ovarian cancer using linked data including the California Cancer Registry from 2000-2015. The data is robust with more than 1800 women identified and detailed outcome data available, and the statistical analyses straightforward. Constructive comments included below:

Introduction
Lines 53-56: although related, it is interesting to combine these aims as the outcomes (fertility sparing treatment and ART) are separate outcomes: knowing you have cancer and planning fertility sparing treatment, incidentally finding cancer after surgery which happened to be fertility sparing, and then downstream ART access following a cancer diagnosis. ART is not necessarily required in fertility preservation treatment and would be more necessary with only retention of the ovaries/uterus.
We appreciate the comments from this reviewer and recognize that these two outcomes are addressing different aspects of fertility preservation and treatment after a diagnosis of cancer. We decided to include both as we felt it would be interesting and important to acknowledge what disparities were similar and/or different between the two.

We have added statements to our discussion to address the possibility of incidental fertility-sparing treatment versus known cancer diagnoses followed by fertility-sparing surgery affecting our results (line 612-615). We reviewed our data and found no significant differences by race or ethnicity with respect to diagnoses on the day of surgery or prior to surgery. We noted this in lines 612-615 but did not include a table as to not overwhelm the reader with data. We would be happy to provide the data on the percentages of surgeries where the date of diagnosis and date of surgery are the same, however, it is possible the high percentage of diagnoses on the same day as surgery were due to administrative data entering of the dates versus truly when the cancer was diagnosed.

We also appreciate the comment regarding ART not being required, particularly for early stage cervical, endometrial, and ovarian cancer treatments. We have updated our discussion (line 646-649).

As an extension, a CKC/radical trachelectomy, IUD/oral progestins are intentional treatments with known cancer- whereas fertility sparing treatment in ovarian cancer may have a large percentage that were fertility sparing by accident (found on final path and ovary couldn't be saved at time of surgery). Unlikely to ever know the difference.
We appreciate this comment. We reviewed internally the percentages of cold knife cone vs LEEP vs trachelectomy to see if the disparities we saw in our data were modified by this breakdown and did not find a significant difference. Unfortunately, we don't have data on the breakdown of IUD versus oral progestins. We acknowledge in our discussion the possibility of incidental diagnoses of cancer at the time of surgery leading to the surgery being categorized as fertility-sparing versus a surgery that was specifically planned to be fertility-sparing (lines 612-615).

Similarly, although it makes sense somewhat to include cervical cancer with endometrial and ovarian, if a patient has early-stage disease (Stage IA/IB) and is pre-menopausal, standard of care for surgical treatment is optional removal of the ovaries, therefore is also fertility sparing (with possibility of IVF). There is data that also supports retention of ovaries in young endometrial cancer patients, which allows for IVF. Including these patients may reveal more about ART use.
We appreciate the comment by this reviewer and agree that a future analysis could be done to include those in whom the only uterus only is removed for endometrial or cervical cancer, however, we felt for this manuscript we would maintain the definition of fertility-sparing to include one ovary and the uterus at minimum after intervention. We chose this definition as a clear way to distinguish who should theoretically have retained fertility versus those who would not. We acknowledged that we do not have access to surgical history, therefore, even using our definition it is possible a woman had a prior hysterectomy or unilateral salpingo-oophorectomy and following the surgery registered in the California Cancer Registry would have been labeled as "fertility-sparing" but in actuality have been rendered infertile. An assessment of the overall rate of hysterectomy and limited prior studies of unilateral salpingo-oophorectomy suggests that the misclassification due to lack of surgical history in the dataset would be minimal (lines 607-610).

Methods
-Lines 100-102, why not include superovulation, IUI as well?
We thank the reviewer for this comment. According to the SART-CORS database, IUI is not considered ART, and superovulation or medication-assisted ovulation data are not collected. We agree that these are important treatments that may be utilized by cancer survivors, however unfortunately we lack the data to objectively report them.

-Line 104- why was age divided at 35?

We thank the reviewer for this comment. We divided at age 35 as it is noted in the literature to be the age of increased baseline fertility changes for women, and in obstetrics is the age after which a pregnancy is labeled "advanced maternal age" and is associated with increased risk. Additionally, prior studies have also used this cutoff and therefore we maintained it for consistency.

-Line 108- why was the Yost SES index used?
We acknowledge there are many ways to capture socioeconomic status, however, we were limited by the data available. In the California Cancer Registry, the Yost SES index is the most complete data available to describe socioeconomic status.

Results

-What percentage were radical trachelectomy (technically more difficult and not offered by all physicians) versus CKC? The differences might disappear if separated given the resources needed to seek care from a provider that offers trachelectomy.

We reviewed our data regarding percentages of LEEP/CKC vs Trachelectomy and found the majority of our cervical cancer patients received non-trachelectomy interventions. However, there was no statistically significant difference in receipt of LEEP/CKC vs trachelectomy by race (p=0.09). We did not include this data directly in the manuscript due to limited overall number of trachelectomies (94).

-It is difficult to interpret your data with missing numbers in each of the table- if the data is de-identified by virtue of being in a database, why are they excluded?

We appreciate this reviewer's comment and recognize the difficulty of interpretation with restricted cells. We have reviewed the policies of the CCR, SART-CORS, and OSHPD and have reported all possible cells and made note where cells were not reportable. Notably, the cells described as non-reportable are not missing data and were included in analyses to create Figures 2 and 3.

-Why is the MV regression data for fertility sparing treatment presented as both a Table (3) and figure (3) whereas ART use is only presented as figure?

We appreciate this distinction. Due to reporting guidelines, much of the table of the ART use would be unreportable due to low numbers, thus we felt the findings were best displayed in a figure. We would be happy to provide the table with restricted cells if the editors wish, however, we feel the table is of little value give the high percentage of unreportable cells. Conversely, we felt that there were sufficient number of instances of fertility-sparing treatment to merit publication of a table to better characterize the results displayed in the figure. Even with the higher number of instances we still had to restrict several cells due to reporting guidelines.

Discussion

Although there were no differences by insurance status, California in general has better insurance access (Medi-cal) than other areas of the country therefore this may be different in other areas of the U.S.

We appreciate the reviewer's comment. We reviewed the population in our dataset and agree that it overall represents a more highly insured population (likely reflective of California as a whole) and have acknowledged that in our discussion (lines 620-622).

STATISTICAL EDITOR COMMENTS:

Table 1: The number of unknowns for Charlson comorbidity score in cervical CA group is similar to the number with score ≥ 1. This complicates the analysis and adjustment and deserves mention among limitations. Similar for unknown insurance status. For endometrial CA, the number unknown for cancer Stage represents a similar problem.

We thank the statistical editor for their comment. Unfortunately, we are limited by the data available in our dataset and have acknowledged the limitation of missing data in our discussion (line 729-730).

Table 3: Since CIs are included, there is no need to include column of p-values, so should be omitted. Should include column of unadjusted ORs with CIs to contrast with aORs. To be clear, all variables in table were included in the multivariable model and retained in the final model, correct?

We thank the statistical editor for their comment and have omitted the columns of p-values from table 3. We have included a column of unadjusted ORs with CIs and have updated Table 3 to reflect this.

The variables in the multivariable model table were included in the analysis and this is clarified in the description below the table. Of note, histology was only included in the analysis for ovarian cancer, and this is described below the table.

Suggestion: Tables 1, 3 and Fig 1 have arranged the groups in order as cervical, endometrial, and then ovarian. Figs 2 and 3 has ordered them as endometrial, cervical, and then ovarian. Suggest it would be better to have a consistent order throughout.

We appreciate this suggestion and have changed our tables, figures, and appendices to be consistent throughout the manuscript.

EDITORIAL OFFICE COMMENTS:

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.
We acknowledge this and accept that this revision letter will be included in supplemental digital content.

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.**
We have added the funding information to the end of the abstract and the name of the IRB to the methods section.

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.
All co-authors will be made aware to complete this.

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.
We have included a sentence for the reason to assess race and ethnicity. The CCR collects race and ethnicity in a validated way. The data for race and ethnicity in the cohort included an “other/unknown” category. We have renamed this as “None of the above,” per journal policies, in Table 1. There was no distinction between “other” versus “unknown” in the dataset, but overall, the number of people represented in this category was <1% of the whole cohort, therefore, we feel it is not a high enough proportion to bias the analyses we present here.

Use "Black" and "White" (capitalized) when used to refer to racial categories.
We have edited the manuscript to reflect this.

List racial and ethnic categories in tables in alphabetic order. Do not use "Other" as a category; use "None of the above" instead.
We have edited the manuscript to reflect this.

Please refer to "Reporting Race and Ethnicity in Obstetrics & Gynecology" at https://urldefense.com/v3/__https://edmgr.ovid.com/ong/accounts/Race_and_Ethnicity.pdf__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi8UWr8RHA$.

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."
We have edited the manuscript to use person-first language wherever possible.

6. The journal follows ACOG's Statement of Policy on Inclusive Language (https://urldefense.com/v3/__https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi9OPfYcIQ$). 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."
We acknowledge the non-inclusiveness of database studies. We have chosen to report those in our study as “women” as that is the information available to us from the three datasets we used. We acknowledge the fact that this excludes how individuals may self-identify and hope to see databases changing in the future to be more inclusive.

7. 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://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi-BiIsQYg$ and the gynecology data definitions at https://urldefense.com/v3/__https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi_y_TmuFQ$. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.
We have reviewed our manuscript and used only standard definitions.

8. 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
We have reviewed our manuscript and the word count is 2934.

9. 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).**

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*** Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.**

We have confirmed the above acknowledgements and reporting guidelines. We have edited to report an updated gynecologic oncology fellows meeting where Dr. Kirsten Jorgensen is scheduled to present some of the results. We have edited the authors initials in the financial disclosure section.

10. 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.

The statements in the abstract are reflected in the body of the manuscript, tables, and figures.

In addition, the abstract length should follow journal guidelines. Please provide a word count.
Original Research: 300 words

We confirm that our abstract is within the guidelines. Word count: 300, including headings of each section.

11. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/abbreviations.pdf__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi_L9dy7aQ$. 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.

We have reviewed our manuscript and confirmed abbreviations. We use an abbreviation for assisted reproductive technology (ART) throughout this manuscript and feel that expansion of it for each instance it is used would detract from the readability of the manuscript. We would be happy to expand it if requested by the editors.

12. 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.

We have removed instances of the virgule symbol from our manuscript.

13. 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.

We have edited the manuscript to state “health care professional” where “provider” had been used previously.

14. 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.

We confirm that the effect size used in our abstract, manuscript and tables was an odds ratio (adjusted and unadjusted). We have removed p-values as per the statistical editor’s comments for multivariable analyses. We have left p-values in for the baseline characteristics table (Table 1).

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

We have standardized data to 2 decimal places for all confidence intervals and p-values.

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

All percentages have been edited to one decimal place.

15. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available at https://urldefense.com/v3/__http://edmgr.ovid.com/ong/accounts/table_checklist.pdf__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi-OVObTmw$.
We have reviewed the checklist and confirm that our tables conform to the journal style.

16. Please review examples of our current reference style at https://urldefense.com/v3/__https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf__;!!PfbeBCCAmug!nX6_T0iLV9P6Z41oW0vZjW657iiEK3uGTeAnSguBBFj_STfNKFDcVd9N1PGg5Wi4_2YJE2hWR2KiWi-TMjgp_w$. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.
We have reviewed the references and confirm they meet the journal reference style.

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.

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We confirm the reference are numbered in order of appearance.

17. Figures

Figure 1: Are any additional exclusion boxes needed?
We appreciate this comment and have edited Figure 1 to reflect exclusion of high-risk histologies, and for the analysis of live births: radiation and diagnosis after 2012.

Figures 2-3: Can be resubmitted as-is, unless changes have been requested by the Statistical Editor.
We have edited these to reflect the column ordering changes recommended by the statistical editor and to reflect our updated results after re-analysis using a baseline cohort that excludes high-risk histologies (a change made based on reviewer comments).

18. 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.
We have edited the supplemental files as such: Figure 1, Figure 2, Figure 3, Appendix 1, Appendix 2, and Appendix 3. References sited in the appendices are located in a separate reference per appendix, each beginning with reference number one (1).

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