OBSTETRICS & GYNECOLOGY

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

Date: Dec 08, 2021
To: "Shannon K Rush" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-2117

RE: Manuscript Number ONG-21-2117

Sixty-five Revisited: A Revised Markov Model Evaluating Oophorectomy at the Time of Benign Hysterectomy

Dear Dr. Rush:

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).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

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 Dec 29, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

An elegantly written paper on an important surgical decision. I have no significant criticisms of the work.

Reviewer #2:

This manuscript reflects the author's work to update the model described by Parker et al. in 2005 that assessed the optimal time for BSO at the time of the benign hysterectomy.

This paper is well-written work and thought-provoking. The research aimed to recreate the original model with more accurate and updated cardiovascular risk, ultimately changing the age of opportunistic BSO.

Since this article has the potential of shaping and guiding future recommendations for opportunistic BSO at the time of benign hysterectomy, I would encourage the author to describe such effects on bone health, mood disorders, and cognitive function. Oophorectomy before age 45 is a well-known risk factor for osteoporosis. Likewise, the neuroprotective effects of estrogen have been shown with the decrease of cognitive function following surgery. The Mayo Clinic Cohort Study of Oophorectomy and Aging found that women who underwent premenopausal bilateral oophorectomy were found to have an increased risk of developing de novo depressive symptoms and de novo anxiety symptoms. While this conditions might be not be the focus of author's study, it is worthwhile mention the limitations of the manuscript findings on such important conditions.

I agree with the author's conclusion the primary consideration favoring prophylactic bilateral oophorectomy is the lack of practical screening tools for ovarian cancer. Prophylactic bilateral oophorectomy could decrease the risk significantly while no effective and affordable early ovarian cancer screening tool is available. Said that, a shared decision about prophylactic BSO with the patient considering the available data should take place, and a statement in the discussion section about this good practice would be most welcomed.

In the spirit of advancing further care to minority groups, the authors should comment in the discussion session if the study's findings would also apply to other racial groups or if this would also constitute a limitation of its findings.

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This is a Markov model evaluating the risks/benefits of oophorectomy at the time of hysterectomy. The manuscript is well written.
1. Introduction: Line 36 is unclear, are you stating that 32% of women over the age of 50 have undergone hysterectomy in the US? That seems high.
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3. Methods: Line 91-93, can you explain more why death from hip fracture was NOT included? And why not hip fracture itself? That is a very morbid event. Please explain better why morbidity risks or incidence of disease was not included for all the outcomes.
4. Discussion: The discussion of strengths and limitations is balanced.

STATISTICS EDITOR COMMENTS:

Lines 122-125 and supplement, pg 14: The description in Methods of main text of the procedure for constructing hazard rate ratios in 1 yr increments from the data referenced is too sparse. Should explicitly state that the references cited did not provide HR estimates at 1yr increment and it was assumed that the HRs would conform to a quadratic function. The data provided actually conforms more to a step function, since only increments of age categories above and below age 50 are given. Should show (at least in supplemental), the analysis based on a step function, rather than as a continuous, monotone, quadratic function.

In an editorial (Menopause, Vol 25 (5), p 480) to reference # 15, several rebuttals are given to the analysis of ref # 15, including citing the CARDIA and SWAN studies. Should include more analysis of references in the discussion which counter the conclusions of the simulations.

Tables 1, 2: The HR ratios for mortality mostly include 1.00, so they plausibly show no difference in mortality. To then use the point estimates and their ranges in simulations seems based on a dubious interpretation of the data.

Table 3: Need to make clearer for the reader that the entries represent probabilities, expressed as %s, of being alive at age 80 years. Should also explain in footnote what is meant by the emboldened entries. I presume that they are significantly different from the other rows in the same age cohort. Should also indicate what is meant by "before 50" and "after 50". I believe from Methods that this meant from ages 45 and 50, respectively.

Fig 2: Should restructure the figure. Panels for death rates by breast ca, colorectal ca, lung ca and stroke should all have the same y-axis scale and should be aligned in rows. The death rate by CHD and survival should both have the same y-axis scale and be aligned side by side or possibly on the same graph.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased 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.

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:
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* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
* 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).
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3. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Methods section of the body text, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in 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), observational studies using ICD-10 data (ie, RECORD), 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, RECORD, 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 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.

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 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, 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).
* 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]."

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

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

11. 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.

12. 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.

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%").

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In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. 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.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

16. When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

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Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

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

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* 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. Do not omit your responses to the Editorial Office or Editors' comments.

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 Dec 29, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Deputy Editor, Gynecology

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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REVIEWER COMMENTS:

Reviewer #1:
An elegantly written paper on an important surgical decision. I have no significant criticisms of the work.
Thank you very much!

Reviewer #2:
This manuscript reflects the author's work to update the model described by Parker et al. in 2005 that assessed the optimal time for BSO at the time of the benign hysterectomy.
This paper is well-written work and thought-provoking. The research aimed to recreate the original model with more accurate and updated cardiovascular risk, ultimately changing the age of opportunistic BSO.
Since this article has the potential of shaping and guiding future recommendations for opportunistic BSO at the time of benign hysterectomy, I would encourage the author to describe such effects on bone health, mood disorders, and cognitive function. Oophorectomy before age 45 is a well-known risk factor for osteoporosis. Likewise, the neuroprotective effects of estrogen have been shown with the decrease of cognitive function following surgery. The Mayo Clinic Cohort Study of Oophorectomy and Aging found that women who underwent premenopausal bilateral oophorectomy were found to have an increased risk of developing de novo depressive symptoms and de novo anxiety symptoms. While this conditions might be not be the focus of author's study, it is worthwhile mention the limitations of the manuscript findings on such important conditions.
We agree that while this is not the focus of the paper, we should address some of the morbidity and quality of life impacts of BSO prior to age 50. Please see lines 361-364 for this discussion.

I agree with the author's conclusion the primary consideration favoring prophylactic bilateral oophorectomy is the lack of practical screening tools for ovarian cancer. Prophylactic bilateral oophorectomy could decrease the risk significantly while no effective and affordable early ovarian cancer screening tool is available. Said that, a shared decision about prophylactic BSO with the patient considering the available data should take place, and a statement in the discussion section about this good practice would be most welcomed.
We agree and have lines 365-369 that tried to reflect that point.

In the spirit of advancing further care to minority groups, the authors should comment in the discussion session if the study's findings would also apply to other racial groups or if this would also constitute a limitation of its findings.
We wholeheartedly agree. See our addition of this point to the discussion in lines 357-359.

Reviewer #3:
This is a Markov model evaluating the risks/benefits of oophorectomy at the time of hysterectomy. The manuscript is well written.
1. Introduction: Line 36 is unclear, are you stating that 32% of women over the age of 50 have undergone hysterectomy in the US? That seems high. It may seem high but that was what was reported as of 2018 in the National Health Interview Survey.
2. Introduction: Line 49-51, can you clarify more how the cardiovascular risk was overestimated? What do you mean? Perhaps the first paragraph of the results should go here. We made this clearer in the introduction, please see lines 92-97 for details.
3. Methods: Line 91-93, can you explain more why death from hip fracture was NOT included? And why not hip fracture itself? That is a very morbid event. Please explain better why morbidity risks or

incidence of disease was not included for all the outcomes. We added more information on excluding hip fracture, see lines 138-142. We specifically focused on mortality, as the main reason to complete this work was to challenge the original Markov model, which has been practice changing. We state this in the methods now more clearly in lines 143-146. We also discuss the lack of calculation of morbidity risk as a limitation of our model in the discussion in lines 361-364.
4. Discussion: The discussion of strengths and limitations is balanced.

STATISTICS EDITOR COMMENTS:
Lines 122-125 and supplement, pg 14: The description in Methods of main text of the procedure for constructing hazard rate ratios in 1 yr increments from the data referenced is too sparse. Should explicitly state that the references cited did not provide HR estimates at 1yr increment and it was assumed that the HRs would conform to a quadratic function. The data provided actually conforms more to a step function, since only increments of age categories above and below age 50 are given. Should show (at least in supplemental), the analysis based on a step function, rather than as a continuous, monotone, quadratic function.
Regarding the 1yr hazard increment calculation, the approach taken aims to be maximally flexible with respect to population-level changes in hazard, while still anchoring to the published 5yr rates. We add a supplemental Figure (*Control Figure 2, Appendix*) performed by taking a step-function hazard and by using only previously confirmed effects on hazard (see below). We added a discussion of this to the manuscript as well, see lines 173-180.

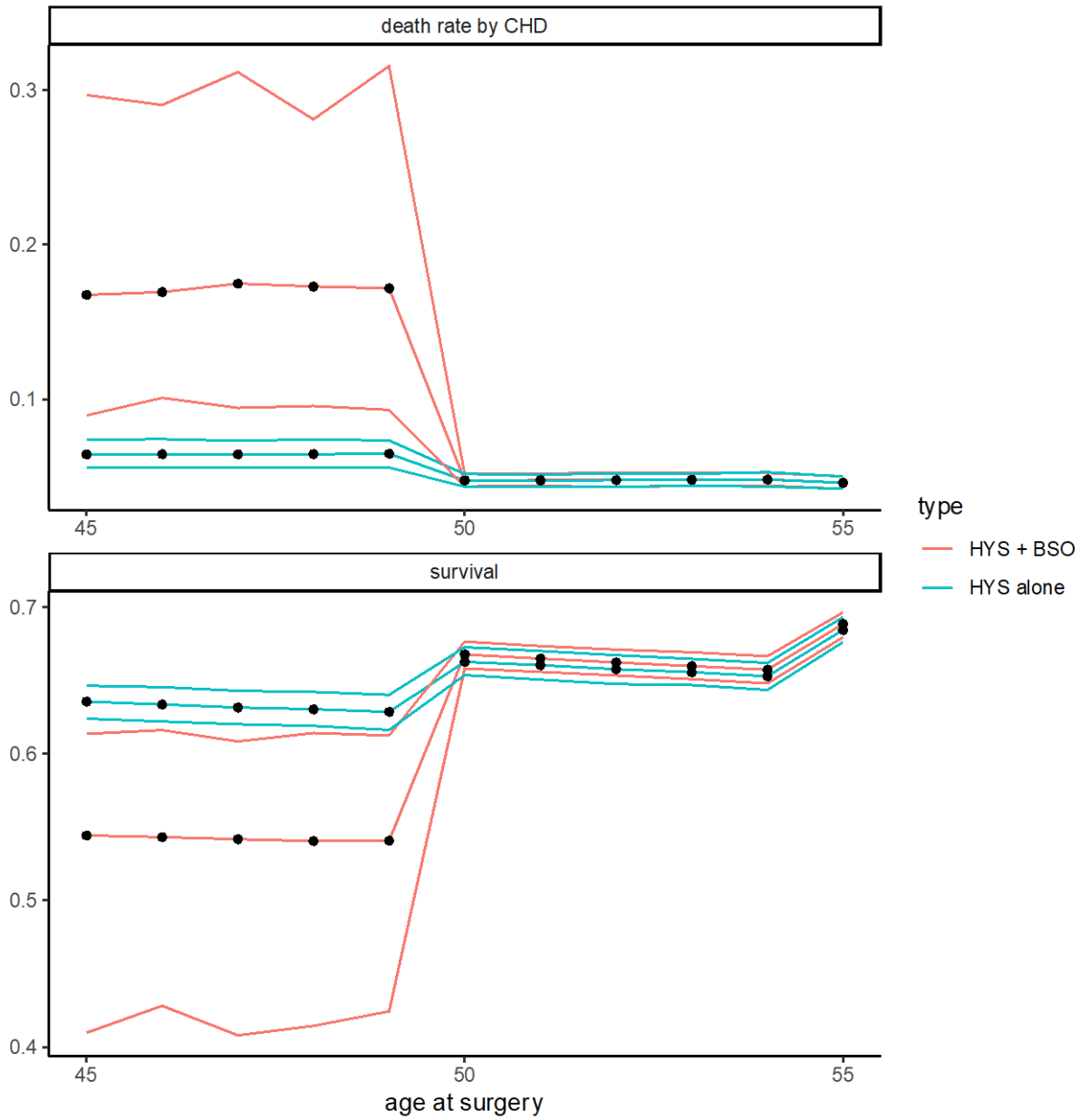

Figure 1: Results of a supporting control computation for comparison analogous to Fig 2 (main), but in which we have removed any factors for which prior work does not establish a nonsignificant hazard ratio, and we have assumed a step-function hazard ratio across the age-50 threshold. [Included as Control Figure 2, Appendix]

In an editorial (Menopause, Vol 25 (5), p 480) to reference # 15, several rebuttals are given to the analysis of ref # 15, including citing the CARDIA and SWAN studies. Should include more analysis of references in the discussion which counter the conclusions of the simulations.

The Laughlin-Tommaso paper addresses a population who all underwent hysterectomy with ovarian conservation. No one in this study underwent BSO. We utilized this reference to understand what effect hysterectomy alone would have on the mortality risks under study. The CARDIA study argues that hysterectomy was not associated with increases in CVD risk factors after menopause or surgery. The Swan study argued the same point, that hysterectomy status with and without oophorectomy did not significantly impact development of CVD risk factors as compared to women undergoing natural

menopause. Neither report on CVD incidence before and after surgery, however. They also both agree with the L-T paper that those who undergo HYS with or without BSO have higher rates of CVD risk factors in the pre-surgery period. I added these points to the discussion, see lines 302-315.

Tables 1, 2: The HR ratios for mortality mostly include 1.00, so they plausibly show no difference in mortality. To then use the point estimates and their ranges in simulations seems based on a dubious interpretation of the data.

The reviewer is correct that in using all available published summaries of hazard ratios, we include some non-significant (NS) effects. We emphasize that additional, supporting calculations were performed by eliminating all such NS effects, see lines 255-258. These control calculations led to the same conclusion about the effect of surgical timing on survival rates at age 80, though they came with narrower confidence limits. For our topline approach we favor reporting the more inclusive calculation because the Bayesian confidence intervals are thereby more reliable (not "dubious"!); dropping NS effects in a prediction context is arguably inferior because it fails to incorporate known levels of uncertainty in potentially relevant hazard ratios [e.g., Draper, 1995, *J. Roy. Statist. Soc. B*, 57:45-97, https://doi.org/10.1111/j.2517-6161.1995.tb02015.x; Hoetting et al. 1999, *Statist. Sci.* 14(4): 382-417. DOI: 10.1214/ss/1009212519]. By dropping the NS effects, our predictive calculation would be assuming that we are confident that said factors do not affect survival; this is different from what the published record shows on NS effects, which is simply that we are not confident that these factors do affect survival. Fortunately, these statistical gymnastics do not materially affect the finding about when surgical intervention has a differential effect on age-80 survival. We also add a discussion of this point in the Appendix where hazard ratios are first introduced.

Table 3: Need to make clearer for the reader that the entries represent probabilities, expressed as %s, of being alive at age 80 years. Should also explain in footnote what is meant by the emboldened entries. I presume that they are significantly different from the other rows in the same age cohort. Should also indicate what is meant by "before 50" and "after 50". I believe from Methods that this meant from ages 45 and 50, respectively.

Thank you, we added clear headings.

Fig 2: Should restructure the figure. Panels for death rates by breast ca, colorectal ca, lung ca and stroke should all have the same y-axis scale and should be aligned in rows. The death rate by CHD and survival should both have the same y-axis scale and be aligned side by side or possibly on the same graph.

We have made the suggested edits, see new figure 2.

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* Include your title page information in the main manuscript file. The title page should appear as the

first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors). Done!

* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript. No funding source was reported as there was none.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable). Not applicable.
* Name the IRB or Ethics Committee institution in the Methods section (if applicable). No IRB was needed for this project, as it was a model based on previously published data.
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context. We have included the locations of the studies utilized in our model.

3. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page. We will send this back as quickly as possible! No disclosures to report.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Methods section of the body text, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.
This is not applicable.

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This is not applicable.

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 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.
This is duly noted; we have reviewed the definitions and use language that is concordant with this.

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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. Not applicable.
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This paper has previously been presented at two conferences. I list them here as well as on the title page.
Previously presented at The Society for Academic Specialists in General Obstetrics and Gynecology Annual Meeting, October 2020, held virtually due to COVID-19.

Also presented at the first annual Heartland Association for Gynecologic Oncology Meeting, virtual presentation on September 11, 2020.
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Thank you for this reminder. Our word count is 275.

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We have reviewed this document and our manuscript is in line with recommendations. We also reviewed to ensure there were no abbreviations in the title or precis. Those that are used are spelled out the first time they appear.

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We removed the one use of provider and replaced with physicians.

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We have reported our findings as percentages or proportions with Bayesian confidence intervals.

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.
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We have formatted our tables accordingly.

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We have reviewed our references to ensure they are in the correct format.

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Thank you for these reminders – we have submitted the original figures as advised.

17. 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 revised the manuscript to refer to the appendix rather than supplement.

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