Date: Oct 10, 2018
To: "Ana Isabel Tergas" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1662

RE: Manuscript Number ONG-18-1662

Cancer Prevention Strategies for Women

Dear Dr. Tergas:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Oct 26, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: In this review, the authors comprehensively summarize a number of factors contributing to cancer risk in the average woman, and should be commended for a thorough review.

Major Suggestions:

1. The authors briefly mention in the section on smoking cessation that behavioral therapy is effective, but only elaborate on the pharmacologic treatments. Would include a sentence or two on the most effective behavioral approaches.

2. Are there any data that quantitate the effects of bariatric surgery on cancer risk reduction? If so, would include those.

3. Would include as a general statement in the section on coffee - though it seems obvious - that consumption of high calorie, sugar-loaded coffee drinks may mitigate any beneficial effects (i.e. that 1500-calorie frappucino isn't healthy).

4. The section on infectious diseases is really brief. While the table is helpful, at the very least HPV should be described in a lengthier manner in the text given its significance in gynecologic cancers. The authors should use this opportunity to report on the efficacy of the HPV vaccine, as well as the recent data that use of the vaccine does not negatively impact fertility or cause an increase in sexual promiscuity.

5. In the paragraph starting with line 551, the authors mention the UKCTOCS study and the potential benefits of ovarian cancer screening. There were drawbacks to screening in this population, including a number of women with benign disease who underwent surgery while trying to find patients with cancer. This should be included to give the reader a greater understanding of the potential drawbacks to this approach. Additionally, need to mention more explicitly the theoretical stage shift (i.e. diagnosis of more women in lower stages, where treatment may be more efficacious).

Minor Suggestions:

6. Line 280 - "an" should be "or"

7. Lines 532-534 - please re-write the sentence as it doesn't make sense in its current form

Reviewer #2: Thank you for the opportunity to review this invited article, "Cancer Prevention Strategies for Women." The

article is a review of the evidence and guidelines for both primary and secondary prevention strategies for several common and/or lethal cancers for women. The article is ambitious and generally overall comprehensive, but I believe that it is overly ambitious and attempts to cover too much territory. I think the review would benefit from a more limited scope (e.g. gynecologic cancers specifically, top five deadliest cancers for women, top five most common cancers, etc.).

1. INTRODUCTION: The introduction did a good job of introducing the topic and its importance. I would appreciate the authors commenting specifically on the role of the OB/GYN provider in cancer prevention, particularly for non-gynecologic cancers.

2. Line 11-12: Please add a citation for this study

3. PRIMARY PREVENTION STRATEGIES: Generally, the authors covered these very broad topics well. However, the sections seem inconsistent regarding the background and evidence. For example, many topics (e.g. coffee consumption, alcohol and arguably diet), which have less high-quality evidence for their role in cancer are discussed at much greater length than infectious agents, which have excellent evidence for their role in cancer and important prevention strategies that are very important to an OB/GYN. I think that this section would overall benefit from a clearer critique of the literature (i.e. "there are no RCTs to support the relationship between … and cancer", concern for publication bias, etc.) and more specific actual interventions or strategies (i.e. a table reviewing the doses, side effects and contraindications of NRT). In addition, a sentence or bullet point at the end of each section summarizing the proven effective preventive strategies would be helpful. Finally, one of the more common conversations around primary prevention is about salpingectomy versus tubal ligation. I think this topic would be especially beneficial to the OB/GYN audience.

4. TOBACCO: Is there any data about smoking cessation in women specifically? In pregnancy? Any specific predictors of success? Any data about the role of the PCP or gynecologist in smoking cessation?

5. OBESITY: Line 126-127: This sentence doesn't make sense here, as it begs the question about "additional strategies" without answering them in the subsequent lines. I think it needs to be moved to right before Line 132.

6. COFFEE CONSUMPTION: How do these studies define "heavy drinker"? Is this consistent across studies? Are there any RCTs about coffee? Are there any proposed mechanisms of action? Given what I suspect is a relatively weak evidence base on this topic, I recommend removing it entirely.

7. INFECTIOUS AGENTS: I would appreciate more information in this section. Table 4 is helpful, but I think the section would benefit from a more robust discussion, at least of the infections that are most relevant to OB/GYNs, perhaps HPV vaccination, hepatitis B screening and vaccination, and HIV prevention with behavior modifications and chemoprophylaxis.

8. CHEMOPROPHYLAXIS:

Aspirin: The ASPREE study just published an article in NEJM showed a causal association between aspirin and increased cancer mortality in the elderly. I recommend incorporating this. I am assuming that the studies mentioned were including average-risk patients, but it is worth specifying. Again, I recommend commenting more on the quality of the studies, and whether and how they control for confounders.

9. OCPS: The authors should include the study by Morch et al. (NEJM 2017; doi: 10.1056/NEJMoa1700732) and address the role of hormonal contraception in breast cancer.

10. Metformin: Given that one of the potential mechanisms is glycemic control, have there been any studies of insulin? Or of metformin versus insulin in cancer prevention?

11. Breast cancer: Given that the authors have already specified that the article is addressing cancer prevention strategies in low risk women, I do not think that this section needs to be included.

12. SECONDARY PREVENTION STRATEGIES: The introduction to this section does a nice job of explaining why the authors chose which cancers on which to focus. Given that there are multiple medical specialty societies issuing screening guidelines, I am curious how the authors chose to highlight the guidelines of the American Cancer Society, which is an advocacy organization. It might be worth considering including any recommendations from ACOG as well. I would make sure that throughout this section, mortality is clarified as being cancer-related versus all-cause. In addition, the authors should include evidence of all-cause mortality benefit in cancer screening, if any. Finally, the authors mention repeatedly the value of informed shared decision-making. I think that this is worth further discussion in the introduction to the section. Is there evidence for this? Are there recommendations for how to approach this? Are there general resources of decision-aids to assist providers?

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17. Ovarian cancer: I would move paragraph 2 to the end of the section. I found Line 557-560 unclear—what is meant by removing "prevalent cases"?

Reviewer #3: MANUSCRIPT NUMBER: 18-1662

TITLE: Cancer Prevention - Expert Series

Overall: This is an invited expert series on cancer prevention. Overall the manuscript is well written. There are some sections that could be more concise, more focused on women, and provide a little more guidance to practicing physicians. There are a lot of tables and perhaps there is a way to shorten them or combine them. In some places the tables repeat what is stated in the text.

Overall organization and structure: the overall organization is good with primary to secondary prevention strategies, and also from most common to less common cancers.

1. The title is fine

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Tobacco Use section:

3. Lines 47-55 - this seems like a lot of extra information, and the study specifically focused on men. This section would convey more information to readers if the last sentence (lines 54-55) were a topic section of a paragraph that clearly and concisely addresses evidence-based strategies to reduce tobacco use.

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5. Lines 123-127: This section would be stronger if it were at the end of the subsections on diet, physical activity and diet (@Lines 178).

6. Overall the obesity section would be strengthened if there were some concise and clear recommended therapies that physicians could provide to their patients. Perhaps a table/box might be helpful.

7. Lines 155-157 - the second section of this sentence should be the topic sentence because this is the most important statement for this section in a paper about cancer prevention.

8. The chemoprophylaxis section is very informative but a brief introductory statement that is is chemoprophylaxis for cancer in women would help prepare readers for the details provided in this section.

9. Table 1: Is there a way to make this into one single table with columns for cases, percentage, for incidence and mortality

	Incidence		Mortality	
Cancer site	Cases	Percentage	Cases	Percentage

10. The relative risk tables are informative but too long. Maybe choose to use only those activities that are associated with a certain minimal risk like 1.2 or 2.0? Or is there a way to list by activity in rows and cancer RR in the columns? There are just a lot of numbers to wade through here.

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12. Table 4 is also excellent and informative

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EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
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2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Your submission is missing a title page. Please review the Instructions for Authors for the required and optional elements of the title page.

3. Each author on this manuscript must submit a completed copy of our revised author agreement form (updated in the January 2018 issue). Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

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the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
* Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The author agreement form is available online at http://edmgr.ovid.com/ong/accounts/agreementform.pdf. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. Tables, figures, and supplemental digital content should be original. The use of borrowed material (eg, lengthy direct quotations, tables, figures, or videos) is discouraged, but should it be considered essential, written permission of the copyright holder must be obtained. Permission is also required for material that has been adapted or modified from another source. Both print and electronic (online) rights must be obtained from the holder of the copyright (often the publisher, not the author), and credit to the original source must be included in your manuscript. Many publishers now have online systems for submitting permissions request; please consult the publisher directly for more information. In addition, you must list any material included in your submission that is not original or that you are not able to transfer copyright for in the space provided under I.B on the first page of the author agreement form.

5. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Clinical Expert Series articles should not exceed 25 typed, double-spaced pages (6,250 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

7. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).

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

9. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

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

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Clinical Expert Series, 300 words. Please provide a word count.

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

12. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

14. The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, 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. 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 a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at http://www.acog.org/Resources-And-Publications.

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

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

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 Oct 26, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

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View Letter

REVIEWER COMMENTS:

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Major Suggestions:

1. The authors briefly mention in the section on smoking cessation that behavioral therapy is effective, but only elaborate on the pharmacologic treatments. Would include a sentence or two on the most effective behavioral approaches.

Thank you for the suggestion. We have discussed behavioral approaches in more detail.

2. Are there any data that quantitate the effects of bariatric surgery on cancer risk reduction? If so, would include those.

There are no high-quality studies that quantitate the effects of bariatric surgery on cancer risk reduction.

3. Would include as a general statement in the section on coffee - though it seems obvious - that consumption of high calorie, sugar-loaded coffee drinks may mitigate any beneficial effects (i.e. that 1500-calorie frappucino isn't healthy).

At the suggestion of another reviewer, the section of coffee has been removed.

4. The section on infectious diseases is really brief. While the table is helpful, at the very least HPV should be described in a lengthier manner in the text given its significance in gynecologic cancers. The authors should use this opportunity to report on the efficacy of the HPV vaccine, as well as the recent data that use of the vaccine does not negatively impact fertility or cause an increase in sexual promiscuity.

Thank you for the suggestion. This section has been expanded.

5. In the paragraph starting with line 551, the authors mention the UKCTOCS study and the potential benefits of ovarian cancer screening. There were drawbacks to screening in this population, including a number of women with benign disease who underwent surgery while trying to find patients with cancer. This should be included to give the reader a greater understanding of the potential drawbacks to this approach. Additionally, need to mention more explicitly the theoretical stage shift (i.e. diagnosis of more women in lower stages, where treatment may be more efficacious).

Thank you for the suggestion. Information regarding false-positive surgeries and stage shifting have been added to this paragraph.

Minor Suggestions:

6. Line 280 - "an" should be "or"

Change has been made

7. Lines 532-534 - please re-write the sentence as it doesn't make sense in its current form

Sentence has been re-written

Reviewer #2: Thank you for the opportunity to review this invited article, "Cancer Prevention Strategies for Women." The article is a review of the evidence and guidelines for both primary and secondary prevention strategies for several common and/or lethal cancers for women. The article is ambitious and generally overall comprehensive, but I believe that it is overly ambitious and attempts to cover too much territory. I think the review would benefit from a more limited scope (e.g. gynecologic cancers specifically, top five deadliest cancers for women, top five most common cancers, etc.).

Thank you for the suggestion. We agree that cancer prevention strategies for women is a large topic. We chose to organize the review by the most important cancer risk factors, in order to address prevention strategies that pertain to these risk factors.

1. INTRODUCTION: The introduction did a good job of introducing the topic and its importance. I would appreciate the authors commenting specifically on the role of the OB/GYN provider in cancer prevention, particularly for non-gynecologic cancers.

Thank you for the suggestion. We have included language on the role of the OB/GYN provider in cancer prevention.

2. Line 11-12: Please add a citation for this study

The citation has been added.

3. PRIMARY PREVENTION STRATEGIES: Generally, the authors covered these very broad topics well. However, the sections seem inconsistent regarding the background and evidence. For example, many topics (e.g. coffee consumption, alcohol and arguably diet), which have less high-quality evidence for their role in cancer are discussed at much greater length than infectious agents, which have excellent evidence for their role in cancer and important prevention strategies that are very important to an OB/GYN. I think that this section would overall benefit from a clearer critique of the literature (i.e. "there are no RCTs to support the relationship between … and cancer", concern for publication bias, etc.) and more specific actual interventions or strategies (i.e. a table reviewing the doses, side effects and contraindications of NRT). In addition, a sentence or bullet point at the end of each section summarizing the proven effective preventive strategies would be helpful. Finally, one of the more common conversations around primary prevention is about salpingectomy versus tubal ligation. I think this topic would be especially beneficial to the OB/GYN audience.

Thank you for the suggestion. Many of the sections have been streamlined.

4. TOBACCO: Is there any data about smoking cessation in women specifically? In pregnancy? Any specific predictors of success? Any data about the role of the PCP or gynecologist in smoking cessation?

There is not much data about smoking cessation in women specifically, other than in pregnancy. We have added information about smoking cessation in pregnant women and the role of clinicians in smoking cessation.

5. OBESITY: Line 126-127: This sentence doesn't make sense here, as it begs the question about "additional strategies" without answering them in the subsequent lines. I think it needs to be moved to right before Line 132.

Thank you for the suggestion. The change has been made.

6. COFFEE CONSUMPTION: How do these studies define "heavy drinker"? Is this consistent across studies?

Are there any RCTs about coffee? Are there any proposed mechanisms of action? Given what I suspect is a relatively weak evidence base on this topic, I recommend removing it entirely.

Thank you for the suggestion. This section has been removed.

7. INFECTIOUS AGENTS: I would appreciate more information in this section. Table 4 is helpful, but I think the section would benefit from a more robust discussion, at least of the infections that are most relevant to OB/GYNs, perhaps HPV vaccination, hepatitis B screening and vaccination, and HIV prevention with behavior modifications and chemoprophylaxis.

This section has been expanded as suggested by the reviewer.

8. CHEMOPROPHYLAXIS:

Aspirin: The ASPREE study just published an article in NEJM showed a causal association between aspirin and increased cancer mortality in the elderly. I recommend incorporating this. I am assuming that the studies mentioned were including average-risk patients, but it is worth specifying. Again, I recommend commenting more on the quality of the studies, and whether and how they control for confounders.

Thank you for the suggestion. A discussion of the ASPREE trial has been added.

9. OCPS: The authors should include the study by Morch et al. (NEJM 2017; doi: 10.1056/NEJMoa1700732) and address the role of hormonal contraception in breast cancer.

Thank you for the suggestion. This study has been included.

10. Metformin: Given that one of the potential mechanisms is glycemic control, have there been any studies of insulin? Or of metformin versus insulin in cancer prevention?

There have not been any studies of metformin versus insulin in cancer prevention.

11. Breast cancer: Given that the authors have already specified that the article is addressing cancer prevention strategies in low risk women, I do not think that this section needs to be included.

Thank you for the suggestion. This section has been removed.

12. SECONDARY PREVENTION STRATEGIES: The introduction to this section does a nice job of explaining why the authors chose which cancers on which to focus. Given that there are multiple medical specialty societies issuing screening guidelines, I am curious how the authors chose to highlight the guidelines of the American Cancer Society, which is an advocacy organization. It might be worth considering including any recommendations from ACOG as well. I would make sure that throughout this section, mortality is clarified as being cancer-related versus all-cause. In addition, the authors should include evidence of all-cause mortality benefit in cancer screening, if any. Finally, the authors mention repeatedly the value of informed shared decision-making. I think that this is worth further discussion in the introduction to the section. Is there evidence for this? Are there recommendations for how to approach this? Are there general resources of decision-aids to assist providers?

Thank you for your comments. In this section we presented guidelines from several national organizations such as the USPSTF and NCCN, and have especially made sure to include relevant ACOG recommendations. We have included information regarding shared decision-making.

13. Breast cancer: Much controversy and lack of clarity exists around the frequency of breast cancer

screening. While this is referred to in Table 6, I think it warrants a more thorough discussion here.

We acknowledge in the paper that there is controversy regarding breast cancer screening recommendations ("Differing opinions regarding the appropriate balance of benefits vs. consequences has led to non-uniform screening recommendations across the major guideline groups regarding age at initiation, frequency, age to stop screening, and use of screening modalities other than mammography for women at average risk for developing breast cancer."). With the intentions of brevity, we have chosen to highlight ACOG's Practice Bulletin on this topic.

14. Cervical cancer: This section should be updated with the USPSTF's final statement and ACOG's subsequent statement regarding cytology versus HPV.

This section already references the USPSTF final statement (Curry et al, JAMA 2018) and ACOG's subsequent statement.

15. Lung cancer: Line 519-520: Are there any recommendations for providers who do not have access to high-volume, high-quality lung cancer treatment centers?

This is an excellent question. Providers who do not have access to high-volume, high-quality lung cancer treatment centers should not perform screening for lung cancer because the risks of cancer screening may be substantially higher and therefore not be outweighed by the benefits of screening. This information has been added to the paper.

16. Endometrial cancer: Please describe the evidence more thoroughly for why screening is not recommended (i.e. most endometrial cancers present at early stages and screening has not been shown to improve outcomes, etc.).

Thank you for the suggestion. This has been added.

17. Ovarian cancer: I would move paragraph 2 to the end of the section. I found Line 557-560 unclear—what is meant by removing "prevalent cases"?

Thank you for the suggestion. Paragraph 2 has been moved to the end of the section. Line 557-560 has been edited to be clearer. Excluding prevalent cases means excluding pre-existing cases of ovarian cancer, in order to look specifically at the detection of incident cases.

Reviewer #3: MANUSCRIPT NUMBER: 18-1662

TITLE: Cancer Prevention - Expert Series

Overall: This is an invited expert series on cancer prevention. Overall the manuscript is well written. There are some sections that could be more concise, more focused on women, and provide a little more guidance to practicing physicians. There are a lot of tables and perhaps there is a way to shorten them or combine them. In some places the tables repeat what is stated in the text.

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Thank you for the suggestion. We have streamlined this paragraph and better addressed evidence-based strategies to reduce tobacco use.

4. Lines 70-86: This whole paragraph seems disingenuous. There seem to be current clear data that e-cigarettes are harmful especially to young people. To this reviewer that seems like the most important thing to deter anyone from using e-cigarettes - even to quit tobacco use.

We agree with the reviewer that deterring smoking of any form should be the goal. We have added language to this paragraph to make this intent clearer.

5. Lines 123-127: This section would be stronger if it were at the end of the subsections on diet, physical activity and diet (@Lines 178).

Thank you for the suggestion. These lines have been edited and moved to a more appropriate place.

6. Overall the obesity section would be strengthened if there were some concise and clear recommended therapies that physicians could provide to their patients. Perhaps a table/box might be helpful.

This information is available in Table 3.

7. Lines 155-157 - the second section of this sentence should be the topic sentence because this is the most important statement for this section in a paper about cancer prevention.

Thank you for the suggestion, change has been made.

8. The chemoprophylaxis section is very informative but a brief introductory statement that is chemoprophylaxis for cancer in women would help prepare readers for the details provided in this section.

Thank you for the suggestion. This has been added.

9. Table 1: Is there a way to make this into one single table with columns for cases, percentage, for incidence and mortality
Incidence Mortality
Cancer site Cases Percentage Cases Percentage

Table 1 displays the estimated incidence and mortality of the leading sites of new cancer cases and deaths. There is not 100% overlap in the cancers listed under incidence and the cancers listed under mortality, so the data on incidence and mortality is best presented separately.

10. The relative risk tables are informative but too long. Maybe choose to use only those activities that are associated with a certain minimal risk like 1.2 or 2.0? Or is there a way to list by activity in rows and cancer RR in the columns? There are just a lot of numbers to wade through here.

Thank you for the suggestion. The table has been streamlined

11. Table 3 is excellent

Thank you

12. Table 4 is also excellent and informative

Thank you

13. Tables 5 and 6 may have too much detail - rather than actually publishing those tables is there a way to provide succinct paraphrasing so busy clinicians can easily pick out the salient points?

Tables 5 and 6 have been removed due to space constraints and their content has been summarized in the body of the paper.

EDITORIAL OFFICE COMMENTS:

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

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All tables are original.

5. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

Not applicable

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Clinical Expert Series articles should not exceed 25 typed, double-spaced pages (6,250 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

The revised manuscript, as well as the introduction and conclusion sections adhere to length restrictions.

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* 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).

Acknowledgments have been included.

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

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9. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

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Tables conform

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not applicable

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Daniel Mosier

From: Tergas, Ana I. [redacted]
Sent: Wednesday, January 16, 2019 4:22 PM
To: Daniel Mosier
Subject: Re: Manuscript Revisions: ONG-18-1662R1
Attachments: 18-1662R1 ms (1-16-19v2)_AT.docx

Dear Daniel,

I agree with the changes on the manuscript. I changed the corresponding author information. Please find attached an updated version of the manuscript.

Thank you

From: Daniel Mosier <dmosier@greenjournal.org>
Date: Wednesday, January 16, 2019 at 4:16 PM
To: "Tergas, Ana I." [redacted]
Subject: Manuscript Revisions: ONG-18-1662R1

Dear Dr. Tergas,

Thank you for submitting your revised manuscript. It has been reviewed by the editor. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.

If you need to make changes, please use the attached version of the manuscript. Leave the track changes on, and do not use the "Accept all Changes" function prior to re-submission.

Your prompt response would be appreciated be appreciated; please respond no later than COB on **Friday, January 18th.**

Sincerely,

-Daniel Mosier

Daniel Mosier
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Daniel Mosier

From: John Schorge
Sent: Friday, January 18, 2019 6:43 AM
To: Daniel Mosier
Subject: Re: 1/17 ECC Follow-Ups
Attachments: 18-1662R1 ms (1-15-19v1)-v2jos.docx

2204 is ready to go - no changes

1662 - i made changes ONLY to the Abstract and now this is ready to move also

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From: Daniel Mosier
Sent: Thursday, January 17, 2019 4:06:15 PM
To: John Schorge
Subject: 1/17 ECC Follow-Ups

John,

Just wanted to follow-up really quickly about the Accepts in this week's ECC, since these are both nearly ready to go to Denise and the publisher:

1. 18-1662R1: Dwight said during the call that the abstract could use some "Examples," and you agreed. Did you mean examples of the primary and secondary prevention strategies? If so, should I send an email to the authors?
2. 18-2204R1: Did you have anything to add/change with this post- ECC, or can I send this on to Denise for final approval?

Thanks,
-Dan

Daniel Mosier
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