

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)*

**The corresponding author has opted to make this information publicly available.*

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obgyn@greenjournal.org.

Date: Oct 22, 2021
To: "David Chelmow" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-1918

RE: Manuscript Number ONG-21-1918

Executive Summary of the Uterine Cancer Evidence Review Conference

Dear Dr. Chelmow:

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 Nov 12, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is an executive summary of the uterine cancer evidence review conference, on similar lines to the summary published after the early onset breast cancer evidence review conference (2020). The stated goal was educational materials on prevention and early detection of endometrial cancer for clinicians. This is a summary of the relevant literature, with no new meta analyses, and reads like a book chapter. The evidence used is well presented in appropriate spots. As a reader, however, the structure is confusing at times. For example Lynch syndrome may be something a clinician would like guidance with but requires 235-244, then 305 to 312, then 486 to 496 lines to get an overview. While this fits within risk factors, screening, etc. it is not helpful for a reader hoping to meet the goal of education. Screening and early detection is also falsely separated (as no pre invasive form amenable to screening is presented, rather options for detection then discussed in early detection). Combining these in one subgroup may make more sense. Having things chopped up means the reader does not easily identify all the relevant material at one time. Finally the effect of health disparities and the potential evidence that would guide improvements is separated off into another (future?) publication. Having more clear guidance about steps to take both for individual patients and as public health initiatives would be helpful here as well as in a more extensive review elsewhere.

Reviewer #2: This is an executive summary report by a panel of experts drawn from two national societies (SASGOG & SGO) sponsored by the CDC & ACOG on best evidence for the prevention and diagnosis of uterine cancer.

Overall, well researched report and well presented. Authors did well in drawing best available evidence and presenting them as such; however, this reviewer would have expected more active synthesis of guidelines and provision of clear actionable steps that practicing OBGYNs can enact. Some of the cited ACOG, SGO, NCCN guidelines are unclear, conflicting or incomplete; clarity on these will make this summary clear added value rather than restating society guidelines.

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EDITOR COMMENTS:

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- A. OPT-IN: Yes, please publish my point-by-point response letter.
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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).
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4. Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

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 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.

6. 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).

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7. 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.

8. 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.

9. 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.

10. 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.

11. 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.

12. Please review examples of our current reference style at <http://ong.editorialmanager.com> (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). 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 reference list.

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.

13. 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 Nov 12, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Jason Wright, MD
Editor-in-Chief, Elect

2020 IMPACT FACTOR: 7.661

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

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November 8, 2021

Jason Wright, MD
Editor-in-Chief, Elect
Obstetrics & Gynecology

[REDACTED]

Dear Dr. Wright,

Thank you so much for the thoughtful reviewer comments and the opportunity to submit a revised manuscript, which we have done. Below, please find a point-by-point response to the reviewer and editor comments. We have pasted the reviewer comments in black and our responses in red. Changes to the manuscript have been made with the MS Word track changes feature. Where appropriate, the response indicates the line number of the corresponding revisions as viewed in the document with the tracked changes visible. Regarding Editor Comment #1, we OPT-IN: Yes, please publish my point-by-point response letter. In addition to the responses below, Table 1, originally redacted to ensure blinding has been inserted and associated notes regarding blinding have been removed.

REVIEWER COMMENTS:

Reviewer #1: This is an executive summary of the uterine cancer evidence review conference, on similar lines to the summary published after the early onset breast cancer evidence review conference (2020). The stated goal was educational materials on prevention and early detection of endometrial cancer for clinicians.

As stated in the abstract, the goal of the panel was to “review relevant literature, best practices, and existing practice guidelines as a first step toward developing evidence-based educational materials for women’s health care clinicians about uterine cancer.” The goal of this paper is to summarize the relevant literature and existing recommendations to guide clinicians in the prevention, early diagnosis, and special considerations of uterine cancer and to note substantive knowledge gaps to provide guidance for future research. This paper is intended to be the evidence summary (condensed, with the complete evidence summary of each research question detailed in the appendices). While we think it will be educational, particularly for people who prefer text to online educational material, it is presented in a form appropriate for an evidence summary. To make this clearer, we have modified the abstract (line 68) and introduction (lines 84-85) to explicitly state that the purpose of the paper is to provide an evidence summary.

This is a summary of the relevant literature, with no new meta analyses, and reads like a book chapter. The evidence used is well presented in appropriate spots.

We worked hard to make the executive summary readable despite the large body of evidence covered, and will interpret “reads like a textbook chapter” as our having succeeded.

As a reader, however, the structure is confusing at times. For example Lynch syndrome may be something a clinician would like guidance with but requires 235-244, then 305 to 312, then 486 to 496 lines to get an overview. While this fits within risk factors, screening, etc. it is not helpful for a reader hoping to meet the goal of education.

As noted above, the reviewer has misconstrued the purpose of the paper. A person wanting comprehensive information on Lynch syndrome should look to many of the other available resources, which are noted in the references and appendices. As standard for evidence summaries, we have organized the content by research question, and we think it will be useful for readers who are looking for information in this format.

Screening and early detection is also falsely separated (as no pre invasive form amenable to screening is presented, rather options for detection then discussed in early detection). Combining these in one subgroup may make more sense. Having things chopped up means the reader does not easily identify all the relevant material at one time.

We inadvertently wrote “early detection” when we meant “early diagnosis.” This has been replaced in the text in the four instances where it was used (lines 61, 69, 437, and 697). “Screening” and “early diagnosis” have distinct definitions, were searched as separate research questions, and, following the usual format of an evidence summary, are presented separately.

Finally the effect of health disparities and the potential evidence that would guide improvements is separated off into another (future?) publication. Having more clear guidance about steps to take both for individual patients and as public health initiatives would be helpful here as well as in a more extensive review elsewhere.

The topic of health disparities is covered in the companion paper that is also being revised and will hopefully be published in the same issue.

Reviewer #2: This is an executive summary report by a panel of experts drawn from two national societies (SASGOG & SGO) sponsored by the CDC & ACOG on best evidence for the prevention and diagnosis of uterine cancer.

Overall, well researched report and well presented. Authors did well in drawing best available evidence and presenting them as such;

Thank you

however, this reviewer would have expected more active synthesis of guidelines and provision of clear actionable steps that practicing OBGYNs can enact. Some of the cited ACOG, SGO, NCCN guidelines are unclear, conflicting or incomplete; clarity on these will make this summary clear added value rather than restating society guidelines.

The panel was charged with reviewing the high-quality evidence and guidelines. Synthesizing, particularly making recommendations between competing guidelines, was beyond the scope of the panel’s charge. While guidelines were at times summarized in the interest of keeping the paper to a manageable length, they are presented in increased detail where relevant in the appendices.

Specific suggestions for consideration;

1. Lines 125-133; a brief textual description of these molecular subtypes will be useful here.

This information (now lines 185–193) is presented in Table 2 and is more concise in this format than it would be in text. We are grateful that we have not been asked to shorten the manuscript, and do not think we should include duplicate information in text and table.

2. Line 150; "in Western countries" seem a Cold War anachronistic term. Does that exclude Eastern Europe including unified Germany?

The citation is US SEER data. The text in question (now line 211) has been changed to “In the United States . . .”

3. Lines 148-275; it would seem appropriate to discuss the physiologic basis of each of these associations/risk factors where known. It's helpful to declare when unknown as in tubal ligation.

This section (now lines 210-340) includes several dozen different risk factors. The physiologic basis for many is speculative. This would add significant length and include information that was beyond the scope of the evidence review.

4. Lines 436-447; how does the use of HRT impact evaluation of endometrial stripe >4mm in postmenopausal women with or without bleeding episodes?

Our search did not find any studies about this.

5. Line 446; "we found no guidelines regarding evaluation of.." should that be "treatment" since the question really is whether to remove asymptomatic polyps or not.

The text was changed to “evaluation or treatment” (line 517).

6. Lines 514-21; So what is this panel's recommendation? It doesn't seem clear that women with confirmed diagnosis of EC should be operated on by trained oncologists in high volume centers? Perhaps an itemized summary of key recommendations will be useful

The panel's charge was to summarize existing recommendations, not to make new ones, so we want to be careful here. As ACOG makes the only statement about this, we changed “ACOG states. . .” to “ACOG recommends . . .” to better convey that it is a recommendation (line 588).

7. Lines 522-32; When EIN is diagnosed by the primary OBGYN, what is the recommendation for next steps in evaluation- give the quoted risks of concurrent EC? Hysteroscopy & D&C? What is the role of MR imaging in the initial evaluation of EC and EIN?

We did not find any recommendations regarding the role of imaging in EIN or hysteroscopy and D&C prior to hysterectomy and have added a sentence to this effect (lines 603–604). The role of imaging in the initial evaluation of endometrial cancer is covered in Appendix 6.

8. Lines 576-579; what is the role MR imaging in treatment surveillance?

None of the recommendations include imaging as part of surveillance. We have added a sentence stating this (lines 654-655).

9. Lines 601-625; one area of gathering investigation is early detection of EC using molecular tests on vaginal fluids obtained with self-administered tampons ie, non-invasive diagnostic tests.

“Development of noninvasive diagnostic tests for endometrial cancer” added to the list of research gaps and opportunities (line 707).

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- * Name the IRB or Ethics Committee institution in the Methods section (if applicable).
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All applicable information is included in the title page, which has been incorporated into the main manuscript file.

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The manuscript uses the standard reVITALize definitions.

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- * 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).
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The abstract accurately reflects the body of the paper.

8. 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;!!JqxBPMk!y-hlEPVDL1dS1pEXyg-jpkq9A7YxOKv-8YGd_MZMHj6QlrSjP5_dwGcR35ySMzgT6TA\\$](https://urldefense.com/v3/http://edmgr.ovid.com/ong/accounts/abbreviations.pdf;!!JqxBPMk!y-hlEPVDL1dS1pEXyg-jpkq9A7YxOKv-8YGd_MZMHj6QlrSjP5_dwGcR35ySMzgT6TA$). 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.

Standard abbreviations and acronyms are used and introduced appropriately.

9. 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.

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10. 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.

The term "provider" has been replaced throughout the manuscript.

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