OBSTETRICS & GYNECOLOGY

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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.*

Personal or nonessential information may be redacted at the editor's discretion.

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

Date: Aug 07, 2019
To: "Joshua A. Copel" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1231

RE: Manuscript Number ONG-19-1231

Gottesfeld Hohler Memorial Foundation Risk Assessment for Early-Onset Preeclampsia in the United States Think Tank Summary

Dear Dr. Copel:

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 Aug 28, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Great presentation on potential benefits and risks of implementation of risk stratification with use of aspirin prophylactically to prevent preeclampsia with delivery before 32 weeks!

Specific issues:

1- Precis: Line 64: please include the year!

2- Abstract: Line 73: "We reviewed" was that a systematic search or not and what was the timeline?

3- Introduction:
a. Line 154: "severe preeclampsia" or "preeclampsia with severe features"?
b. Line 170: "screen positive rate of 11%"; it might be interesting to add information about the percentage of patients who were missed by the model and how much overall rate of preeclampsia in this cohort. Was the overall rate 5% as cited in the literature or not? What is the C-statistic of that model?
c. It would be great to have an outline of the aims and approach for this article included at the end of the Introduction!

4- Prevention, Current research in the US sections, research gaps

5- Conclusions:
a. Line 382: "severe preeclampsia" or "preeclampsia with severe features"
b. Line 387: "sonologists"

6- Tables:
a. Table 3: do we have a nomogram for this model?

Reviewer #2: General:
This is a consensus article via a working group of experts reviewing the current literature and guidelines on risk assessment for early onset preeclampsia in the United States.

Specific:
Well written, concise and easy to read.

No specific changes.

Reviewer #3: This manuscript by Copel et al. is the summary of an expert committee convened to assess the optimal risk assessment strategy and associated interventions to reduce the impact of early-onset preeclampsia. This summary clearly documents the important issues involved, and the panel of convened experts is impressive.
Specific criticisms are listed below:

1. Your assertion that the rate of preeclampsia is rising "more rapidly" than diabetes or obesity (lines 96, 379) seems unsupported. The references cited detected small increases and suggest demographic changes in pregnancy and/or changes in diagnostic criteria may explain all or most of this increase. I cannot argue with stating that the incidence is rising, but comparing this to other morbidities and stating it is rising faster seems to be overreaching.

2. The manuscript compares several approaches for identifying a population at "high-risk" of preeclampsia. Option 1 is ACOG, option 2 is USPSTF, and option 3 is the Fetal Medicine Foundation and associated NICE guidelines. The Committee neglects to provide its opinion on these approaches, and makes no recommendations regarding current screening for preeclampsia (other than to say you should use one of these schemes). What was your expert opinion on these guidelines and how should the clinician proceed?

3. The research gaps section appropriately documents many clinical questions concerning preeclampsia that need to be answered. I would hope that a body as august as this the one would make more specific research recommendations. If the Committee was going to propose a study design what would it look like? Your recommendations may help clarify for funding agencies how to approach this important issue.

4. Concerns regarding patient compliance with aspirin treatment are described. Do you recommend serologic assays to assess compliance?

In conclusion, the Foundation's working committee did a good job outlining the relevant issues in identifying parturients at risk for preeclampsia and the best prophylaxis strategies. I hope the final manuscript will be more explicit in documenting the committee's specific opinions regarding screening approaches, aspirin dosing, and future research.

EDITORIAL OFFICE COMMENTS:

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

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

4. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

5. 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).

6.
Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

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.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Executive Summaries, Consensus Statements, and Guidelines, 250 words. Please provide a word count.

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. 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%").

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. 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 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 (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 (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

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Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at

http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Aug 28, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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

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Dear Editors

We are grateful for the opportunity to revise our manuscript. Specific responses are in red below, and the manuscript is submitted with “Track Changes” used for any revisions.

Dr. Catherine Spong asked that her name be removed from the manuscript as she was invited due to her role at NICHD, but she felt that she did not wish to be an author.

We hope that the responses below and our revisions will be sufficient for acceptance of the manuscript. Given the diversity of opinions represented in our expert group, we never assumed we would reach a single consensus opinion on correct current management.

All authors have had the opportunity to review the revised manuscript and been reminded to update any disclosures. We have read the instructions for authors.

Joshua Copel

On 8/7/19, 2:02 PM, "em.ong.0.6519b1.30d8a1d0@editorialmanager.com on behalf of The Green Journal" <em.ong.0.6519b1.30d8a1d0@editorialmanager.com on behalf of em@editorialmanager.com> wrote:

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Reviewer #1: Great presentation on potential benefits and risks of implementation of risk stratification with use of aspirin prophylactically to prevent preeclampsia with delivery before 32 weeks! Thank you

Specific issues:

1- Precis: Line 64: please include the year! Done, thank you

2- Abstract: Line 73: "We reviewed" was that a systematic search or not and what was the timeline? There was no formal systematic review. Key articles were identified in a Pub Med search and supplemented by suggestions from the participants. “We reviewed” refers to our discussion process. The wording in lines 79-81 have been revised to reflect this.

3- Introduction:

a. Line 154: "severe preeclampsia" or "preeclampsia with severe features"? This has been corrected throughout.

b. Line 170: "screen positive rate of 11%"; it might be interesting to add information about the percentage of patients who were missed by the model and how much overall rate of preeclampsia in this cohort. Was the overall rate 5% as cited in the literature or not? What is the C-statistic of that model? This (ref 27) was a modeling study based on a large population of normal and preeclamptic pregnancies, so no patients were missing. The detection rates are shown in lines 181-186

c. It would be great to have an outline of the aims and approach for this article included at the end of the Introduction! We believe this is addressed in lines 117-133 of the Introduction.

4- Prevention, Current research in the US sections, research gaps

5- Conclusions:

a. Line 382: "severe preeclampsia" or "preeclampsia with severe features" See above

b. Line 387: "sonologists" I'm not sure what is intended by this comment. "Sonologists" is the term for physicians who perform sonography, and we intended to refer to physicians here rather than sonographers. Note this is now line 404 in the revised manuscript.

6- Tables:

a. Table 3: do we have a nomogram for this model? Not currently, the underlying RR information is from the Fetal Medicine Foundation, but there is no formula that we can include to weight the factors.

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2. The manuscript compares several approaches for identifying a population at "high-risk" of preeclampsia. Option 1 is ACOG, option 2 is USPSTF, and option 3 is the Fetal Medicine Foundation and associated NICE guidelines. The Committee neglects to provide its opinion on these approaches, and makes no recommendations regarding current screening for preeclampsia (other than to say you should use one of these schemes). What was your expert opinion on these guidelines and how should the clinician proceed? Given the diversity of opinions presented, a single consensus was not possible from the short time we had. The last paragraph of the conclusions represents our best consensus, that clinicians should use one of the varied options for now, pending definitive comparison between them.

3. The research gaps section appropriately documents many clinical questions concerning preeclampsia that need to be answered. I would hope that a body as august as this the one would make more specific research recommendations. If the Committee was going to propose a study design what would it look like? Your recommendations may help clarify for funding agencies how to approach this important issue. We had extensive discussions of study design, but in the interests of complying with necessary manuscript length, we did not go into the many considerations of such studies. Lines 380-383 now summarize those discussions.

4. Concerns regarding patient compliance with aspirin treatment are described. Do you recommend serologic assays to assess compliance? That was not discussed

In conclusion, the Foundation's working committee did a good job outlining the relevant issues in identifying parturients at risk for preeclampsia and the best prophylaxis strategies. I hope the final manuscript will be more explicit in documenting the committee's specific opinions regarding screening approaches, aspirin dosing, and future research.