

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)*
- Email correspondence between the editorial office and the authors*

**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: Dec 11, 2018
To: "George R. Saade" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2031

RE: Manuscript Number ONG-18-2031

Pregnancy and the postpartum as an opportunity for health preservation and longer term disease prevention: clinical expert series

Dear Dr. Saade:

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 Jan 01, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

REVIEWER #1:

Overall:

Pregnancy can be viewed as a cardiovascular stress test as the development of certain complications has the potential to flag susceptibility to future vascular and metabolic disease. This paper reviews cardiovascular disease in women, pre-pregnancy risk factors, pregnancy and postpartum outcomes and their relationship to future cardiovascular disease (CVD), the effects of gestational weight gain and obesity, measures of CVD risk, and makes recommendations for screening and intervention. The paper is well researched, clearly written and presents multiple practical recommendations.

Abstract:

No comments.

OTHER:

Disclosures: none.

Human subjects: not applicable

Brief Summary:

For a majority of women of reproductive age, pregnancy and the postpartum period provides a new early window of opportunity to identify underlying, undiagnosed cardiovascular risks (CVRs) which increase the chances of CVD.

CVD is the leading cause of death among women in the U.S. and Canada with 88% of women over the age of 20 having at least 1 CVR. Women present with more atypical symptoms than men and are often misdiagnosed.

Preexisting vascular or metabolic dysfunction that is present before pregnancy is exacerbated by pregnancy and primes the body for later disease.

It is well established that women with adverse obstetrical outcomes (preeclampsia, gestational hypertension, gestational diabetes, IUGR or low birth weight baby) are at increased risk for CVD.

There has been a 10% increase in obesity in North America over the last 20 years. Body weight is a strong independent risk factor for CVD and death. Excess weight gain during pregnancy plays a strong role in excess weight retention/gain in the postpartum period. There is a protective effect between breastfeeding and metabolic disease.

Current CVD risk estimators are reviewed and the limitations regarding reproductive age women is discussed.

Postpartum recommendations include timing CVR screening within the first year. This also allows counseling to improve future pregnancy outcomes. The new American College of Cardiology/American Heart Association guidelines should be used for diagnosis and treatment of hypertension. Multidisciplinary postpartum screening program development is reviewed - these should include educational, nutritional and physical activity programs. As many obstetrical providers may be unaware of the link between pregnancy complications and CVR, consultation for longer term follow up should be initiated during late pregnancy or delivery through inclusion in care order sets.

References:

Extensive literature review is included.

TABLES AND FIGURES:

Seem appropriate.

REVIEWER #2:

This is a timely and important review about the link between pregnancy complications and future maternal CVD. Recognizing this link affords health care professionals the opportunity for CVD risk assessment and disease prevention. The authors list very clear recommendations that, if implemented, would have a significant beneficial effect on women's health world-wide.

Several minor points:

1. Among the pregnancy complications the authors mention at the beginning of the manuscript are "hypertensive disorders of pregnancy, gestational diabetes, preterm birth, delivery of a growth restricted baby" (lines 33-34). However, they address the latter two complications very briefly, in one sentence (lines 121-124), and again, indirectly, in another sentence (lines 256-260). I would suggest stressing the importance of recognizing the latter two complications by further expanding on them; though the reference list is quite extensive, the authors may consider adding to the reference list Kessous et al. *Am J Obstet Gynecol*, 2013, Robbins et al. *Am J Obstet Gynecol*, 2014, Anh Ngo et al, *BMC Pregnancy & Childbirth* 2015, Tanz et al. *Circulation*, 2017 (re: preterm labor), and Pariente et al. *Int J Gynaecol Obstet* 2013 (re: growth restriction).
2. Placental abruption should be added to the list of pregnancy complications linked to increased risk of CVD (Pariente et al. *Paediat Epidemiol* 2014, De Roo et al. *Eur J Epidemiol* 2016, and more).
3. Under the heading "Screening" (line 320), the last bullet is "75g oral glucose tolerance test is recommended for women with GDM be performed between 6 weeks and 6 months postpartum". The authors should add that women with impaired glucose metabolism ("pre-diabetes", IFG or IGT) should be screened annually, and those with normal GTT results should be screened every 3 years.
4. Some of the references are dated. There are many more recent studies regarding each of these topics. As an example, in their discussion of the protective effects of lactation (lines 183-198) the authors referenced four articles, all by Stube et al (2005-2015). They may want to include more recent studies, e.g. a meta-analysis by Ljun Feng et al. *J Diabetes Investig*, 2018, and Gunderson et al. *JAMA Intern Med*, 2018. Similarly the authors used the word "Recent statistics" when discussing a 2009 article (line 160), and "Recent examination" (line 378) when referencing a 2013 study. They may want to simply specify the year the article was published in the body of the manuscript.
5. The authors, who presented convincing evidence about the connection between pregnancy complications and risk of CVD, should consider changing the cautious expressions they chose with stronger statements (e.g. "Pregnancy identifies women who may be are candidates for postpartum interventions to decrease their risk for future cardiovascular disease" (lines 24-25), and, "The link between pregnancy complications and future CVD affords us with perhaps the earliest opportunity for CVD risk assessment for health preservation and disease prevention" (lines 44-46).

These issues are relatively minor, and do not subtract from the importance of this very comprehensive review.

REVIEWER #3:

The authors of this clinical expert series submission provide an insightful and informative evidenced-base review on the relationship between pregnancy complications and the considerable increased risk for future cardiovascular health.

This topic has received a significant amount of attention during the past few years and several editorials and reviews have been published dealing with this important topic. The link between common obstetrical complications such as preeclampsia, IUGR, preterm birth, gestational diabetes future cardiovascular disease certainly affords practicing obstetricians with an opportunity to reduce the lifetime risk of these serious conditions.

The manuscript is well-written, structured, and evidence-based and contains a large number of references of recent publications. However, I was surprised to see that the authors failed to discuss the relationship between pregnancy complications and later-life cardiovascular health in women of different races, ethnicity, and socioeconomic status. Perhaps they can expand on this.

Are there any studies that have shown proven success at reducing cardiovascular risk factors in patients with increased risks identified in a previous pregnancy? If so, these need to be discussed. We need studies showing that interventions during the postpartum period bestow significant lifetime cardiovascular health.

A few minor points:

1. Should the authors refer to the postpartum period instead of the "postpartum"?
2. Should the title mention cardiovascular disease prevention?
3. The institution of the second authors is the University of South Florida, not Southern Florida. I was surprised that the author from that institution missed the typographical error.

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:

1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. 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.

3. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works. Variance is needed in the following sections:

- a. Please cite or rework lines 59-60 (for the majority...opportunity to identify).
- b. Please cite lines 248-249 (the lifetime risk...significantly younger individuals).
- c. Please cite lines 324-326 (an opportunity...body weight).
- d. Additionally, there are several places in the manuscript where large chunks of text are taken nearly verbatim from another source. While these instances are cited, it is simply too much borrowed text. Lines 155-159 (a nearly 10%...an individual risk), lines 206-216 (place significant weight...secondary prevention), lines 373-387 (next step requires...inflammatory factors).

4. 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>.

5. 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 appendices).

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

6. 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.

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. 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.

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. 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.

13. 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>.

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 Jan 01, 2019, we will assume you wish to withdraw the manuscript from further consideration.

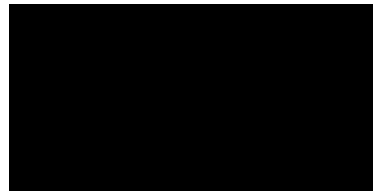
Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982

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

In compliance with data protection regulations, please contact the publication office if you would like to have your personal information removed from the database.



January 7, 2019

RE: ONG-18-2031, entitled "Pregnancy and the postpartum as an opportunity for health preservation and longer term disease prevention: clinical expert series"

Dear Editor:

Thank you for the opportunity to submit responses to reviewers of our Clinical Opinion and a revised manuscript. Please find below our point-by-point responses to the reviewer's and Editorial comments. We are also submitting a tracked-version and a clean version of the manuscript. We hope that you will find our submission complete and acceptable. On behalf of my co-authors and myself, I would like to thank you for bringing the attention to this important medical issue.

Reviewer #1: No recommendations

Reviewer #2:

1. We have added the references as suggested (new references #29-33). Line 126
2. We agree and have added "placental abruption" to the list of complications associated with future cardiovascular disease. Line 125
3. As suggested the line "Women with impaired glucose metabolism ("pre-diabetes") should be screened annually and those with a normal glucose tolerance test should be screened every three year." has been added (Line 335-337).
4. Two of the articles by Stuebe have been replaced with the recommended articles (line 194). The term "recent" has been removed and the lines edited as suggested (line 161-162 and 379).
5. As recommended, we have changed the cautious expression of recommendations to be more definitive. Line 23 and Line 48.

Reviewer #3:

1. The reviewer identifies a lack of discussion regarding women of different races, ethnicity and socioeconomic status which is true because little work has been done. We have added a line identifying this and the need for future research in these areas. Ln 155-158.
2. As recommended, where appropriate the term "postpartum" has been replaced with "postpartum period".
3. As suggested, the title has been altered to identify "cardiovascular" disease prevention.
4. The mislabelling of the University of South Florida has been corrected.

Editorial Office Comments:

1. "OPT-IN" Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. All material in the submission is original.
3. a. Lines 59-60 have been reworked: see Line 62-63
b. The reference for lines 248-249 has been added (line 253)
c. The reference for lines 324-326 has been added (line 329)
d. The parts of text identified that were nearly verbatim from another source originate from manuscripts by the authors. We have chosen to rewrite the identified sections.
-Line 155-159; see Line 158-162
-Line 206-216; see Line 210-221
-Line 373-387; see Line 376-386
4. The obstetric data definitions have been reviewed and the manuscript is in line with this document.
5. The Introduction is 167 words. The Discussion is 477 words. The entire manuscript is 25 typed, doubled-spaced pages.
6. The title has been reduced to less than 100 characters.
7. There is no acknowledgement section. No financial support for this manuscript was provided to any of the authors. The listed authors were solely responsible for the writing, reviewing and editing of this manuscript.
8. Short title: "Postpartum cardiovascular risk screening" (40 characters including spaces)
9. The abstract aligns with the recommendations in the manuscript.
10. Abstract word count: 263
11. Abbreviations and acronym rules have been adhered to.
12. The virgule symbol (/) has been removed from the manuscript where possible.

Sincerely,

George R. Saade, MD



GS/amb