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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)*

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.

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

Date: Nov 20, 2019

To: "sammy saab"

From: "The Green Journal" em@greenjournal.org

Subject: Your Submission ONG-19-2004

RE: Manuscript Number ONG-19-2004

The Need for Hepatitis C Screening in Pregnant Women

Dear Dr. saab:

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 14 days from the date of this letter. If we have not heard from you by Dec 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The commentary is very well written and timely. The data that is presented is clear. The authors base their opinion on factually data and thus their argument is strong.

The manuscript may be even more powerful if the authors more directly addressed why ACOG's current risk based screening is not felt to be adequate. The data is in the body of the paper, but perhaps a reference back to ACOG risk based screening may make the argument even more robust

There are few areas where the sentence structure could be enhanced.

Line 44 and 45 Due to the changing epidemiology of HCV infection from the baby boomer generation to 45 younger non-Hispanic white adults aged 20-39 years, this sentence seems out of context and perhaps may be deleted to allow the next sentence to be clear.

Line 62 please add the word "and" before the word their "current screening paradigm and treatment options for pregnant women their infant"

There is always a cost to adding additional screenings. The authors should comment on the cost of the test to the US population. This may then lead to a brief discussion on cost savings by early treatment of HCV thus mitigating the need for transplant and chronic care.

Reviewer #2: Hepatitis C is of potentially serious consequence to mother and developing fetus and has been a topic of discussion for awhile. In 2017 this topic was reviewed in another journal Hepatitis C in pregnancy: screening, treatment, and management. Am J Obstet Gynecol 2017 11;217(5):B2-B12 (ISSN: 1097-6868)

Hughes BL, et al. This article covers the basic topic as in this other article, but updates other organization's positions, adds in an article about current screening of drug users (not necessarily pregnant), and reviews what is being done in a current phase I study of medication use in pregnancy. The article proposes that risk based screening is not necessarily the best way to identify all (almost all) HSV individuals who are pregnant. The changing face of HSV discussion quotes rates from 1999-2015, as with other epidemics, data lags behind the actual clinical scenarios we see, but does seem to represent the current available documents. The thesis of the commentary states that universal screening can be beneficial, and recommends this based, in part on the fact that pregnancy might be the 'only' point of contact to the medical system. It

seems to me that that shouldn't mean that the best way to handle this is through better screening, but more universal health care, contraception access, and care and testing but this is beyond the scope of the article. The authors propose a registry to track those infected, but there is no data given for how this registry would function, or whether this strategy would work for this condition. Women with risk factors or infection for HCV would likely have the same risk factors for other STIs, and wouldn't screening and tracking in conjunction with other STIs be useful as well, which is not proposed in this article.

Reviewer #3: Review of Manuscript ONG-19-2004 "The Need for Hepatitis C Screening in Pregnant Women"

Saab and colleagues have submitted their manuscript regarding Hepatitis C screening as a clinical commentary. Although not a review metrics, the authors left an "x" on the title page for the word count, figure and tables. Did you consider at least a comment on current strategies in Hepatitis B screening? I have the following questions and comments.

Title - Consider making the title more provocative or as a call to action as written it is bland and I think it detracts from an otherwise cogent argument for universal screening.

Précis - None provided

Introduction - The authors appropriately note the current discrepancies in testing recommendations, be it universal or risk factor based among various professional societies.

Changing Face... - Line 95 - "...study..." not "...studied...".

Hepatitis C Screening - Do you have any information about the costs and/or potential cost effectiveness if this testing?

HCV Transmission... - No comments

Antiviral therapy... - How many and what type of trials are needed?

Conclusion - Reasonable summary of issues at hand.

Figure - Acceptable

EDITOR COMMENTS

Line 33: We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting.

For instance, Current Commentary features require an abstract and Line 79: WOCA is not an acceptable abbreviation.

In the introduction, can you tell how many (%) of adults typically spontaneously clear the infection vs who many remain as chronic carriers? Also, isn't one of the current impetuses for screening because there are now treatments for HCV available? (one of the requirements for a good screening test is that there needs to be something one does w/ the information obtained).

Line 47: please spell out CDC on first use

Line 73: Is heroin as the first IV opioid used relavant?

Line 79: How many 1000's?

Line 91: Is this 0.7% of all pregnancies complicated by IV drug use? If not, can you provide that data?

Line 95: is there a typo? Should this be "in this study? "

EDITOR 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. 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.

Please add a citation to lines 131-134 (The treatment goal...indicative of HCV cure).

- 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 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.
- 5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.
- 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).
- 7. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.
- 8. 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 that states 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."
- 9. Please include an abstract with your revised manuscript.

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: Current Commentary articles, 250 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. 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.
- 13. Figure 1 may be resubmitted as-is.
- 14. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

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.

- 15. 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:
- ${\rm * A\ confirmation\ that\ you\ have\ read\ the\ Instructions\ for\ Authors\ (http://edmgr.ovid.com/ong/accounts/authors.pdf),} and$
 - * 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 14 days from the date of this letter. If we have not heard from you by Dec 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD Editor-in-Chief

2018 IMPACT FACTOR: 4.965

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

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

4 of 4 11/26/2019, 10:41 AM

Dear Editor,

We appreciate the opportunity to submit our revised manuscript for publication. We have addressed the editors' and reviewers' concerns and believe the manuscript is much improved.

Thank you for your time and consideration,

Sammy Saab, MD, MPH, AGAF, FAASLD, FACG

Reviewer #1:

1) The manuscript may be even more powerful if the authors more directly addressed why ACOG's current risk based screening is not felt to be adequate. The data is in the body of the paper, but perhaps a reference back to ACOG risk based screening may make the argument even more robust.

Response: Agree. We have included a discussion on the limitation to ACOG risk based screening in our manuscript on Page 4, paragraph 2 and Page 9, first sentence.

2) Line 44 and 45 Due to the changing epidemiology of HCV infection from the baby boomer generation to younger non-Hispanic white adults aged 20-39 years, this sentence seems out of context and perhaps may be deleted to allow the next sentence to be clear.

Response: We have re-written the sentence and reviewed the entire manuscript for clarity.

3) Line 62 please add the word "and" before the word their "current screening paradigm and treatment options for pregnant women their infant"

Response: We have corrected the sentence (Page 5; Paragraph 1).

4) There is always a cost to adding additional screenings. The authors should comment on the cost of the test to the US population. This may then lead to a brief discussion on cost savings by early treatment of HCV thus mitigating the need for transplant and chronic care.

Response: We have included discussion on the pharmacoeconimic benefits on screening pregnant women for HCV. We specifically highlight the results of a recent publication assessing the cost-effectiveness on Page 7, paragraph 1.

Reviewer #2:

The thesis of the commentary states that universal screening can be beneficial, and recommends this based, in part on the fact that pregnancy might be the 'only' point of contact to the medical system. It seems to me that that shouldn't mean that the best way to handle this is through better screening, but more universal health care, contraception access, and care and testing but this is beyond the scope of the article. The authors propose a registry to track those infected, but there is no data given for how this registry would function, or whether this strategy would work for this condition. Women with risk factors or infection for HCV would likely have the same risk factors for other STIs, and wouldn't screening and tracking in conjunction with other STIs be useful as well, which is not proposed in this article.

Response: We appreciate the insightful comments by Reviewer #2. We agree with the Reviewer of the importance of the above topics but they are unfortunately beyond the scope of the paper.

We have removed discussion of the Registry because of it surrounding confusion and space limitations.

We have added a comment that patients with HCV may share risk factors for other STIs, and should be screened accordingly on Page 4 paragraph 2.

Reviewer #3:

1) Although not a review metrics, the authors left an "x" on the title page for the word count, figure and tables.

Response: We have corrected the word, figure, and table counts on the Title Page.

2) Did you consider at least a comment on current strategies in Hepatitis B screening?

Response: We have included a comment on current strategies in Hepatitis B screening on page 9, paragraph 1.

3) Title - Consider making the title more provocative or as a call to action as written it is bland and I think it detracts from an otherwise cogent argument for universal screening.

Response: We appreciate the reviewer's comments and have changed the title to "A Call to Action: The Urgent Need for Hepatitis C Screening in Pregnant Women" (Page 1).

4) Précis - None provided

Response: This has now been provided on page 2: "Universal hepatitis C screening should be performed in all pregnant women to meet the World Health Organization (WHO) 2030 elimination goal."

5) Changing Face... - Line 95 - "...study..." not "...studied...".

Response: "Study" has been changed to "studied" (Page 6; Paragraph 1)

6) Hepatitis C Screening - Do you have any information about the costs and/or potential cost effectiveness if this testing?

Response: We have included discussion the cost-effectiveness of screening pregnant women on Page 7, paragraph 1.

7) Antiviral therapy... - How many and what type of trials are needed?

Response: We have added to underlined portion of the following sentence to "There is a need for more well-designed trials <u>either in a prospective or randomized controlled trial design</u> in a larger cohort in this patient population to assess for lower incidence of side effects or toxicities in women and their babies." (Page 8; Paragraph 2).

EDITOR COMMENTS

1) Line 33: We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting. For instance, Current Commentary features require an abstract and Line 79: WOCA is not an acceptable abbreviation.

Response: We have reviewed the manuscript in its entirety and have carefully reviewed the Journal Instructions to assure formatting is in accordance.

2) In the introduction, can you tell how many (%) of adults typically spontaneously clear the infection vs who many remain as chronic carriers? Also, isn't one of the current

impetuses for screening because there are now treatments for HCV available? (one of the requirements for a good screening test is that there needs to be something one does w/ the information obtained).

Response: We have updated the introduction with these values (Page 4; Paragraph 1 and Pages 4-5; Paragraph 2).

3) Line 47: please spell out CDC on first use

Response: CDC has been spelled out as "Centers for Disease Control and Prevention." (Page 4; Paragraph 2)

4) Line 73: Is heroin as the first IV opioid used relevant?

Response: We have deleted the statement "...with heroin often being the first opiod tried." (Page 5; Paragraph 2)

5) Line 79: How many 1000's?

Response: We have removed this statement (Page 5; Paragraph 3).

6) Line 91: Is this 0.7% of all pregnancies complicated by IV drug use? If not, can you provide that data?

Response: This has been expanded to state: "...with results showing that over (0.7% of all pregnancies a 4-year period only 123 of 16,918 pregnant women (0.7%) seen in their healthcare system had a documented HCV test in their electronic health record (EHR)." (Page 6; Paragraph 1)

7) Line 95: is there a typo? Should this be "in this study?"

Response: This has been changed. The entire manuscript has been re-reviewed for accuracy.

EDITOR 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:

OPT-IN: Yes, please publish my point-by-point response letter.

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

Response: Disclosures are correct as stated on Page 1

3. Please add a citation to lines 131-134 (The treatment goal...indicative of HCV cure).

Response: The AASLD/IDSA HCV guidelines have been added

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 has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response: We thank the editor for this reference and we have used the definitions, when applicable.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

Response: We have assured that the revised manuscript has adhered to the above length restirctions.

- 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).
- 7. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

Response: This is stated in the title page. "Pregnancy Hepatitis C Screening" (Page 1).

8. 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 that states 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."

Response: We have included this on Page 2 prior to the abstract: "Universal hepatitis C screening should be performed in all pregnant women to meet the World Health Organization (WHO) 2030 elimination goal."

9. Please include an abstract with your revised manuscript.

Response: An abstract has been included on Page 3.

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: Current Commentary articles, 250 words. Please provide a word count.

Response: An abstract has been included on Page 3. The Word count is 250 words.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.proofpoint.com/v2/url?u=http-

 $3A__edmgr.ovid.com_ong_accounts_abbreviations.pdf\&d=DwIGaQ\&c=UXmaowRpu5bLSLE\\ QRunJ2z-YIUZuUoa9Rw_x449Hd_Y\&r=UjtOPL-$

qhyQ1iEqXSI8cP3Pvs4Mk27vE_vInSzVQmfc&m=ag-

KSlxJbwUQj5gIFi7FKL31RfmaSXVyys711k-sLj4&s=9nF0gfJ5ZUvxHAslNFHQ7kf-8ZfP3lSwK00K651QzyU&e= . 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.

Response: We thank the editor for this information and have adhered to this.

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.

Response: We have removed all sections where "/" is used.