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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)\*

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<sup>\*</sup>The corresponding author has opted to make this information publicly available.

**Date:** Nov 07, 2019

To: "Malavika Prabhu"

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

Subject: Your Submission ONG-19-1946

RE: Manuscript Number ONG-19-1946

Universal Screening for Hepatitis B Immunity in Pregnancy

Dear Dr. Prabhu:

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 Nov 21, 2019, we will assume you wish to withdraw the manuscript from further consideration.

# **REVIEWER COMMENTS:**

Reviewer #1: Review of Manuscript ONG-19-1946 "Universal screening for Hepatitis B Immunity in Pregnancy"

Prabhu and Riley have submitted their manuscript regarding Universal Hepatitis B screening as part of a series questioning clinical practice. The manuscript is short and appears to address many of the key considerations regarding this clinical problem. The authors point out the discrepancies among various agencies in terms of recommendations at present as well as why this is an important topic for OB/GYNs. 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 - I would substitute "universal" for routine to highlight what you have pointed out.

Vignette- Did you consider having some additional sentences where you include risk factors so that the reader may think about what they are doing in clinical practice?

Current practice - The authors note the current discrepancies in testing recommendations - HbsAg +/- HbsAb based on the goal of evaluating infection and/or immunity as well as the absence of general agreement among societies and from ACOG.

Burden - Is there financial information about the costs should chronic neonatal Hepatitis B develop?

Vaccination in pregnancy - What is the usual conversion rate (you note it was comparable but do you have a point estimate) with the non-accelerate schedule? Also, how about compliance with the traditional vaccine schedule? In addition what is the reported long term immunity for those that have received the vaccine as directed? Do you have any cost data about confirming immunity?

Bottom Line - You note the perhaps extraordinary lengths that are taken in relationship to rubella - do you have any cost data for these evaluations as well?

Reviewer #2: This is a clinical practice question surrounding universal screening for hepatitis B immunity in pregnancy.

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145-149: This is an important statement within the paper. Women are often accessing care for one of the first-time during pregnancy. This is an opportunity to screen and offer vaccination.

172-175: According the CDC, the number of reported cases of rubella in the United States remains low with a median of 11 cases annually in 2005-2011. Yet we screen all pregnant women. Providing an estimate of the cost of screening for Hepatitis B could be helpful to demonstrate the impact. Given the limited amount of data surrounding a cost analysis, it would be interesting to offer a reflexive screening option (similarly to the way we often screen for thyroid disease with a TSH and reflexive FT4.

Given that a safe vaccine is available and can be offered, and there is opportunity to screen during pregnancy, this seems to be a reasonable approach.

Reviewer #3: This is questioning clinical practice manuscript that addresses our current prenatal care screening practices for hepatitis b immunity. The manuscript argues in favor of adding additional testing during pregnancy to allow for hepB vaccination during pregnancy. There are some minor to moderate weaknesses that once addressed could perhaps strengthen the manuscript.

### Moderate

- -The manuscript opens with an appropriate clinical vignette
- -Line 36-39 cites the 7th ed of the Prenatal Care Guidelines as a reference. The original recommendation is CDC, which the Prenatal Care Guidelines mention. Additionally, all pregnant women are recommended to undergo chlamydia screening, but only those considered high-risk are advised to undergo gonorrhea screening. Clinicians lump them together, most likely because the test assays are combined, but guidelines usually separate the two infections based on risk. This sentence needs editing.
- -Would suggest structuring the paragraphs differently. Lines 45-70 are confusing as screening for infection, screening for immunity, and vaccination are jumbled. This reader had to reread these paragraphs several times to determine which national organization recommended which strategy. The authors could consider a paragraph on screening for infection and another on screening for immunity and subsequent vaccination.
- -Hep B vaccination is routinely given in women living with HIV. Authors could comment on this practice.
- -Would explicitly state that Hep B transmission can occur after exposure to infected bodily fluids (eg semen, cervicovaginal secretions, saliva) and blood. This will help to clarify why travelers to countries with intermediate or high endemicity are considered high-risk (line 56). Also, it would be useful to explain why incarcerated individuals are high-risk (is this currently incarcerated or ever incarcerated)?
- -Missing a counterargument. It would be useful to understand possible reasons why universal screening for hep B immunity is not recommended. The authors did add a sentence about cost-effectiveness but nothing more.
- -Suggest detailing the "notable" racial/ethnic differences (line 78). Were they much worse?
- -The paragraph on Acute Hep B in Pregnancy" seems out of place. The manuscript is about screening for immunity, which can allow vaccination of susceptible pregnant women. It is unclear what this information adds. Also, it is confusing as it starts with acute hep b incidence data during pregnancy, but then cites the proportion of women, in general, who develop chronic hep b.
- -Does the VAERS have pregnancy specific event reports (line 121)? If not, then would edit sentence to clarify that the data represent all comers, women, etc.
- -Efficacy of hep B vaccine is mentioned on line 126. Is efficacy defined by seroconversion alone or certain titer thresholds? Have there been pK studies done in pregnancy to support efficacy?
- -It is unclear if the authors intend to highlight this as a problem or are advocating for providers to change their practice to begin screening for immunity. What should providers do? Should they write letters to an ACOG OB Committee, begin ordering it themselves, conduct more research, etc?

# Minor

- -authors wrote "as well as" instead of "and" numerous times
- -a word is missing on line 58 between "joint...with"
- -a citation is missing on line 152 about CDC and one of its public health priorities.

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- -should be more inclusive of the different types of clinicians. There are many advanced practice providers (eg midwives) and family medicine physicians who provide prenatal care.
- -the last sentence (line 181-182) is a bit melodramatic. Would tone it down.

### **EDITOR COMMENTS:**

### 1. Dr. Prabhu,

Thank you for submitting this piece on Questioning Clinical Practice. After discussing the work at our Editorial Conference Call, the article would require a major restructuring to get it in the format for this series. However, you are advocating a unique aspect that appears to not have been brought up previously. Would you be willing to consider revising the manuscript and re-submitting as a Current Commentary to the journal? You would need to take into account the reviewers suggested edits. I also have a few things to recommend:

- a) The article would benefit from some re-focusing on a few sections, particularly the Current Practice and Bottom Line sections. These sections could be shortened. Reviewer number 3 has some helpful suggestions in regards to this.
- b) The issue of the cost-effectiveness of this practice should be expanded upon. Even describing the lack off.
- c) The current ACOG guidance (Viral Hepatitis in Pregnancy, Practice Bulletin No. 86) states the following: "In general, prevaccination testing is not recommended. It may be cost-effective to screen for the antibody to HBV in women who belong to groups with a high risk of infection in order to avoid vaccinating adults who have had or currently have hepatitis B infection. In most other low-risk groups, antibody screening before vaccination probably is not indicated." So with that in mind, could one argue to just "offer vaccination" and not screen for immunity to Hepatitis B?
- 2. 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.
- 3. 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.

- 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.
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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).
- 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: Current Commentary articles, 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.
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- 10. 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.

- 12. 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 14 days from the date of this letter. If we have not heard from you by Nov 21, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Mark A. Turrentine, MD Consultant Editor

2018 IMPACT FACTOR: 4.965

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

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November 27, 2019

Mark Turrentine, MD Consultant Editor

Re: Manuscript ONG-19-1946

Dear Dr. Turrentine.

Thank you so much for the opportunity to revise our manuscript. We appreciate your and the reviewers' helpful comments to enhance the message of our manuscript. We have made a number of revisions to the manuscript and have changed the format to meet the criteria for the Current Commentary. We have focused several sections, and recommend universal screening and immunization if borne out by cost effectiveness studies.

We note the responses to each comment below in bold. We have also reviewed the Instructions for Authors guide, and believe we have complied with the stated requirements.

Sincerely,

Malavika Prabhu, MD Laura E. Riley, MD

RE: Manuscript Number ONG-19-1946

Universal Screening for Hepatitis B Immunity in Pregnancy

Dear Dr. Prabhu:

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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.

We have updated the title to include the call to action message.

Précis - I would substitute "universal" for routine to highlight what you have pointed out. This change has been made.

Vignette- Did you consider having some additional sentences where you include risk factors so that the reader may think about what they are doing in clinical practice?

We did consider this, however chose to leave it vague, as the ultimate argument is for universal screening for hepatitis B immunity, regardless of risk factors.

Current practice - The authors note the current discrepancies in testing recommendations - HbsAg +/- HbsAb based on the goal of evaluating infection and/or immunity as well as the absence of general agreement among societies and from ACOG.

Burden - Is there financial information about the costs should chronic neonatal Hepatitis B develop? We were unable to identify any well documented source in the literature regarding the costs of chronic neonatal hepatitis B.

Vaccination in pregnancy - What is the usual conversion rate (you note it was comparable but do you have a point estimate) with the non-accelerate schedule? Also, how about compliance with the traditional vaccine schedule? In addition what is the reported long term immunity for those that have received the vaccine as directed? Do you have any cost data about confirming immunity?

Thank you for these questions. The usual conversion rate with the non-accelerated schedule is greater than 90%, both outside and in pregnancy. This is the rate reported by the CDC.

Vaccination compliance is highly dependent on populations offered vaccination. As adult populations screened for and offered vaccination for hepatitis B are often high risk, based on current recommendations, and may have challenges in accessing healthcare, compliance with the traditional schedule ranges from 10-66% in two different populations. This information has been included in the manuscript, with appropriate citations.

We are unable to find data on long-term immunity based on the accelerated pregnancy schedule, as Sheffield et al have not published this data. However, in general, immunity lasts at least 3 decades. For most individuals (except healthcare workers), CDC/ACIP do not recommend confirming immunity if there is documentation of an appropriately completed vaccination schedule. Given this recommendation, we do not believe that the cost data to confirm immunity is relevant.

We have updated lines 255-259.

Bottom Line - You note the perhaps extraordinary lengths that are taken in relationship to rubella - do you have any cost data for these evaluations as well?

In a paper by Haas et al, Obstet Gynecol 2005;106: 295, the cost at the primary author's center (Naval Hospital) is \$4 per rubella IgG sent, in 2005 dollars. We do not have any more recent or comprehensive data on cost of screening and immunizing for rubella. We were also unable to access cost data at our institution (which only releases charge data). However, we believe the cost effectiveness information is more pertinent to the discussion rather than cost data alone, and were not able to find any contemporary papers evaluating this. We did not include this discussion about the possible cost effectiveness of rubella screening and immunization in our manuscript, as we did not want to detract from the main message regarding hepatitis B, and primarily wanted to compare a typical, accepted aspect of prenatal care, with the one we are suggesting.

Reviewer #2: This is a clinical practice question surrounding universal screening for hepatitis B immunity in pregnancy.

145-149: This is an important statement within the paper. Women are often accessing care for one of the first-time during pregnancy. This is an opportunity to screen and offer vaccination.

Thank you.

172-175: According the CDC, the number of reported cases of rubella in the United States remains low with a median of 11 cases annually in 2005-2011. Yet we screen all pregnant women. Providing an estimate of the cost of screening for Hepatitis B could be helpful to demonstrate the impact. Given the limited amount of data surrounding a cost analysis, it would be interesting to offer a reflexive screening option (similarly to the way we often screen for thyroid disease with a TSH and reflexive FT4.

We attempted to perform a simple cost calculation. However, we were unable to access true cost data from a reliable source. At our institution, the patient charge for a hepatitis B surface antibody test is \$143. We suspect this is equal to the cost, but have no data upon which to base a cost calculation, and our institution was not willing to release this data to us. Therefore, we felt including a cost calculation using this input would be inaccurate, overestimate the costs, and possibly introduce a data point into the literature that other researchers may use to base cost-effectiveness analyses on.

Moreover, cost effectiveness analyses are truly what are needed.

It is not apparent to us how a reflexive screening option would significantly decrease the costs of testing for hepatitis B immunity, as most pregnant women in the U.S. are hepatitis B surface antigen negative.

Given that a safe vaccine is available and can be offered, and there is opportunity to screen during pregnancy, this seems to be a reasonable approach.

Thank you.

Reviewer #3: This is questioning clinical practice manuscript that addresses our current prenatal care screening practices for hepatitis b immunity. The manuscript argues in favor of adding additional testing during pregnancy to allow for hepB vaccination during pregnancy. There are some minor to moderate weaknesses that once addressed could perhaps strengthen the manuscript.

#### Moderate

- -The manuscript opens with an appropriate clinical vignette
- -Line 36-39 cites the 7th ed of the Prenatal Care Guidelines as a reference. The original recommendation is CDC, which the Prenatal Care Guidelines mention. Additionally, all pregnant women are recommended to undergo chlamydia screening, but only those considered high-risk are advised to undergo gonorrhea screening. Clinicians lump them together, most likely because the test assays are combined, but guidelines usually separate the two infections based on risk. This sentence needs editing.

Thank you for this comment. We have made this change in lines 58-59.

-Would suggest structuring the paragraphs differently. Lines 45-70 are confusing as screening for infection, screening for immunity, and vaccination are jumbled. This reader had to reread these paragraphs several times to determine which national organization recommended which strategy. The authors could consider a paragraph on screening for infection and another on screening for immunity and subsequent vaccination.

This paragraph has been revised. Lines 67-85 describe various societies' recommendations for screening for hepatitis B immunity in pregnancy. Lines 87-92 discuss the societies' recommendations on hepatitis B vaccination in pregnancy. As all societies recommend screening for hepatitis B infection, and this is concordant with ACOG recommendations, we removed discussion of screening for infection, to make these paragraphs easier to digest. Thank you for the suggestion.

-Hep B vaccination is routinely given in women living with HIV. Authors could comment on this practice. We agree that there are certain comorbidities for which Hep B vaccination is recommended – for instance, in type 2 diabetes, hepatitis B vaccination is also recommended. The purpose of our manuscript is to consider the strengths of universal screening and vaccination, not risk-based screening and vaccination.

-Would explicitly state that Hep B transmission can occur after exposure to infected bodily fluids (eg semen, cervicovaginal secretions, saliva) and blood. This will help to clarify why travelers to countries with intermediate or high endemicity are considered high-risk (line 56). Also, it would be useful to explain why incarcerated individuals are high-risk (is this currently incarcerated or ever incarcerated)?

Thank you. We have added the mechanism of transmission in lines 77-79. The ACIP does not distinguish between current or ever incarcerated women and the level of risk, thus we do not wish to make any assumptions on this point.

- -Missing a counterargument. It would be useful to understand possible reasons why universal screening for hep B immunity is not recommended. The authors did add a sentence about cost-effectiveness but nothing more. We suspect the primary counterargument would be one of cost effectiveness, as this will take into account the prevalence of hepatitis B nonimmunity, the risks of not vaccinating, averted lost QALYs for mother and neonate. Other counterarguments may include relative prioritization of public health needs and resources. Therefore, we emphasize the need for cost effectiveness analyses prior to the adoption of this approach, and do not detail other counter arguments for not pursuing screening and immunization.
- -Suggest detailing the "notable" racial/ethnic differences (line 78). Were they much worse? We have included the point estimates for the racial/ethnic differences in lines 141-142.
- -The paragraph on Acute Hep B in Pregnancy" seems out of place. The manuscript is about screening for immunity, which can allow vaccination of susceptible pregnant women. It is unclear what this information adds. Also, it is

confusing as it starts with acute hep b incidence data during pregnancy, but then cites the proportion of women, in general, who develop chronic hep b.

We agree this paragraph appears misplaced in the manuscript. We do believe that without universal screening and vaccination, there is a small risk for incident hepatitis B to occur during pregnancy, and as such, should be considered as a risk of not screening and vaccinating women. We have reorganized the manuscript to improve the flow, and this point is now discussed in lines 156-163.

-Does the VAERS have pregnancy specific event reports (line 121)? If not, then would edit sentence to clarify that the data represent all comers, women, etc.

Thank you. We clarify to note that all 110 events were in pregnant women, but none were thought to be associated with the vaccine in line 244.

-Efficacy of hep B vaccine is mentioned on line 126. Is efficacy defined by seroconversion alone or certain titer thresholds? Have there been pK studies done in pregnancy to support efficacy?

Efficacy is defined in these studies by a titer threshold - >= 10 mlU/mL for the Sheffield study, >=15 mlu/mL for the Gupta study, and >= 10mlu/mL in the Grosheide study. I was unable to identify any pK studies in pregnancy. We have not added these titer thresholds to the manuscript, but would be happy to do so, if the Editors believe this will clarify our point on efficacy.

-It is unclear if the authors intend to highlight this as a problem or are advocating for providers to change their practice to begin screening for immunity. What should providers do? Should they write letters to an ACOG OB Committee, begin ordering it themselves, conduct more research, etc?

Our recommendation is for universal screening for hepatitis B immunity in pregnancy, with hepatitis B vaccination among susceptible pregnant women, if cost effectiveness analyses bear out the value of this strategy. We note this in lines 437-442. This is also included in the abstract (line 45-47).

### Minor

-authors wrote "as well as" instead of "and" numerous times

Thank you. We have made changes in places to use the conjunction and.

-a word is missing on line 58 between "joint...with"

Thank you. We have used a different conjunction.

-a citation is missing on line 152 about CDC and one of its public health priorities.

We have removed this sentence in an effort to streamline the overall manuscript.

-should be more inclusive of the different types of clinicians. There are many advanced practice providers (eg midwives) and family medicine physicians who provide prenatal care.

Thank you. We agree, this is a good point. In the final section, we refer to all individuals who provide prenatal care in lines 267 and 268.

-the last sentence (line 181-182) is a bit melodramatic. Would tone it down.

Thank you. We have edited the concluding line and paragraph.

## **EDITOR COMMENTS:**

## 1. Dr. Prabhu,

Thank you for submitting this piece on Questioning Clinical Practice. After discussing the work at our Editorial Conference Call, the article would require a major restructuring to get it in the format for this series. However, you are advocating a unique aspect that appears to not have been brought up previously. Would you be willing to consider revising the manuscript and re-submitting as a Current Commentary to the journal? You would need to take into account the reviewers suggested edits.

This manuscript has been reformatted to meet the article criteria for Current Commentary. We have restructured the manuscript headings to streamline the message, and have added an abstract. We maintained the clinical vignette in the body of the commentary, as we felt this introduced the clinical question, but are open to eliminating this if that would fit better with the typical Current Commentary format. We have also taken into account the reviewers' comments, and hope they strengthen our perspective.

I also have a few things to recommend:

a) The article would benefit from some re-focusing on a few sections, particularly the Current Practice and Bottom

Line sections. These sections could be shortened. Reviewer number 3 has some helpful suggestions in regards to this

As above, the Current Practice section has been revised, per the suggestions of Reviewer 3. The Bottom Line section has been retitled and the prior content streamlined. However, to address reviewer comments regarding costs and cost effectiveness, the length of this section remains unchanged. We would be happy to work with you to further streamline this section if desired.

- b) The issue of the cost-effectiveness of this practice should be expanded upon. Even describing the lack off. We discuss that there are no cost effectiveness studies that we identify on either screening alone or screening + vaccination in pregnancy. We have discussed further the cost effectiveness studies in high risk populations (driven by immigration) in the U.S. and European Union in this manuscript, and state that this is an area of need for further research. This is included in lines 426-432.
- c) The current ACOG guidance (Viral Hepatitis in Pregnancy, Practice Bulletin No. 86) states the following: "In general, prevaccination testing is not recommended. It may be cost-effective to screen for the antibody to HBV in women who belong to groups with a high risk of infection in order to avoid vaccinating adults who have had or currently have hepatitis B infection. In most other low-risk groups, antibody screening before vaccination probably is not indicated." So with that in mind, could one argue to just "offer vaccination" and not screen for immunity to Hepatitis B?

We believe offering vaccination alone as the primary strategy for increasing hepatitis B coverage could be effective in some populations. However, in a cohort of pregnant women, many of whom have reticence and challenges with uptake of other recommended vaccinations in pregnancy, we believe that documenting a lack of immunity will increase the chance that a patient accepts the vaccination series in pregnancy.

- 2. 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.

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3. 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.

- 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 <a href="https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize">https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize</a>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.
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Sincerely,

Mark A. Turrentine, MD Consultant Editor