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)*

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Date: Dec 06, 2019
To: "Mona Prasad" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-2108

RE: Manuscript Number ONG-19-2108

Hepatitis C Virus Screening in a Cohort of Pregnant Women

Dear Dr. Prasad:

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 Dec 27, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is a case controlled study through the NICHHD Maternal-Fetal Medicine Units (MFMU) Network of 28 academic and 4 non-academic hospitals to determine the prevalence of hepatitis C infection through HCV antibody (anti-HCV) testing in an obstetric population over a 3 year period (2012- 2015). HCV RNA status was also assessed, of which those with negative RNA viral levels underwent supplemental HCV antibody testing to rule out false positive screens. Risk factors were evaluated by patient interview and chart review in the attempt to classify composite risk factors for identification of groups most likely to demonstrate anti-HCV seropositivity. The emerging arguments for and against universal screening are presented and recommendations regarding HCV screening in pregnancy are put forth.

Reviewer #2: Hepatitis C Virus Screening in a Cohort of Pregnant Women
ONG-19-21-2108
The manuscript describes an observational study with clear aims to understand the epidemiology of HCV infection in pregnancy. The study is well designed and described. The subject is of interest to general practitioners of obstetrics and newborn medicine, infectious disease experts and epidemiologists.

1. Despite the analysis of 100K+ patients, the frequency of the potential covariates are quite low, i.e. prostitution, and destabilize the reliability of the regression analysis. A larger sample size would improve the reliance on the conclusions.

2. As a corollary of above comment, the number of missing data points of number of lifetime partners might affect the reliability of > 3 lifetime partners in predicting HCV given the marginally significant values in the final adjusted models. A sensitivity analysis on lifetime partners and comment in the discussion would improve reader interpretation.

3. Line 227. What was the correlation coefficient for inclusion in a cluster set?

Reviewer #3: Our understanding of HCV, and our ability to treat it, have evolved at a rapid pace. In order to determine how best to identify carriers, to start to eradicate its spread, and to prevent progression, there is a need to identify appropriate groups to screen. In that regard this team of investigators has made a major contribution. A few points are

worth considering:

1. While it would have been impossible for the authors to know about unpublished work in progress, the CDC is proposing a change in standards for screening which will include universal screening for all pregnant women in communities with a prevalence of 0.1% or greater. While this does not distract from their findings it will make some of their discussion about screening seem a bit less germane, if the CDC recommendations appear before their manuscript is published, particularly if they don't have a chance to say how their findings fit once the new screening policy is adapted. Even some of their asides—"the seroprevalence of anti-HCV was low" (0.24%), needs to be reconsidered in light of the CDC's new practical definition of low (i.e., low enough not to screen—0.1%)

2. They offered screening to all women. Were there differences between those who accepted the offer and those that did not?

3. When they say there are risks of over screening (line 139) they give a reference but provide no discussion. They may want to expand by a sentence or two.
4. The give a few reasons why screening is not particularly useful during pregnancy (line 140) but don't acknowledge that some women are only seen for care while pregnant, and even if treatment has to be delayed, those women could at least be linked into a care system that will allow for subsequent therapy.
5. Why were multi-fetal pregnancies excluded for a serosurvey?
6. How was "substance abuse" history obtained? Were there Q by Qs so that each site used the same instrument applied the same way?
7. Did all sites test for all the STIs they list on page 11? Was HSV testing by antibody or antigen?
8. On page 12 they only explain half of the reasons for failure to participate.
9. On page 13 (line 281) they note that there were no associations with medical comorbidities. Did that include hepatitis B?
10. They note no association with known risk factors (line 290). How many patients in the cohort were on dialysis or had HIV or organ transplant? Was the lack of an association evidence of absence or absence of evidence?
11. The specificity of IVDU for HCV of 97% is remarkably high, even given the known association. How would they explain that? Similarly almost 1 in 4 women who had more than 3 lifetime sexual partners—which doesn't seem like a notably high number—had hepatitis C (line 324). Am I misunderstanding something?
12. When they are discussing geographic variability, is their data robust enough to sustain their assertions? Have they controlled for risk factors in the hospitals representing each geographic are? In other words, if one region screened a higher drug using population, it might not reflect the full geographic population; rather it might reflect the subpopulations using the particular hospitals chosen to represent those regions.

STATISTICAL EDITOR'S COMMENTS:

1. lines 79-80: Although numerically highest, this is statistically equivalent to 74/82 (known risk factors or >3 sexual partners). Also, see comments re: Table 3.

2. Fig 1: For the n = 254 (Ab (+)) vs the n = 131 cases enrolled in risk analysis, did the excluded group (n = 123, or ~ 1/2 of the original group of cases) differ in any of the characteristics cited in Table 1 in ways that could have affected the generalizability of the conclusions re: case-control analysis?

3. Table 1: Income should be cited as annual income.

4. Table 2: There are > 20 variables used as adjustors in the full model and 5 variables in the final model. Compared to the counts with the risk factors among cases and controls, the ratio of adverse counts vs variables is not favorable for most of the comparisons in the fully adjusted column and also unfavorable for the "injected any drugs", "blood transfusion", "partners with HCV" in the final adjusted model. That is, the models are likely over fitted, for all but the comparisons based on # of sexual partners comparisons or on smoking status.

5. Table 3: Should include CIs with the sens and spec estimates. There is a trade-off of sens vs spec apparent for most of these variables, with most of the AUCs being statistically indistinguishable. In fact, it appears for "known risk factors, partner with HCV, smoking or > 3 sexual partners" (AUC = 0.65 (0.60-0.69)) is statistically worse than e.g., "known risk factors or smoking" (AUC = 0.73 (0.67-0.79).

6. Appendices 4, 5: The previous comments re: Table 2 and over fitting apply to these Tables, with even fewer entries.

7. General: As just a suggestion, perhaps citing the prevalence and its CIs in terms of cases per 1000 women, rather than as 0.24% would be more useful for the reader.

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:
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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. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

4. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric 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.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 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.

7. 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).

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: Original Research articles, 300 words. Please provide a word count.

10. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

11. 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.

12. 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.

13. 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%").

14. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

15. 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.

16. 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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If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

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* 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 Dec 27, 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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Dr. Nancy C Chescheir
Editor-in-Chief
Obstetrics and Gynecology

December 23, 2019

Dear Dr. Chescheir,

I am pleased to submit the requested revisions after review of our article: **Hepatitis C Virus Screening in a Cohort of Pregnant Women** (ClinicalTrials.gov: NCT01959321).

We have followed the STROBE guidelines, as appropriate for our work, and the checklist is included in this submission.

The response to reviewers and editorial comments follow.

REVIEWER COMMENTS:

Reviewer #1:

This is a case controlled study through the NICHHD Maternal-Fetal Medicine Units (MFMU) Network of 28 academic and 4 non-academic hospitals to determine the prevalence of hepatitis C infection through HCV antibody (anti-HCV) testing in an obstetric population over a 3 year period (2012- 2015). HCV RNA status was also assessed, of which those with negative RNA viral levels underwent supplemental HCV antibody testing to rule out false positive screens. Risk factors were evaluated by patient interview and chart review in the attempt to classify composite risk factors for identification of groups most likely to demonstrate anti-HCV seropositivity. The emerging arguments for and against universal screening are presented and recommendations regarding HCV screening in pregnancy are put forth.

We appreciate Reviewer #1's evaluation of the paper.

Reviewer #2: Hepatitis C Virus Screening in a Cohort of Pregnant Women
ONG-19-21-2108
The manuscript describes an observational study with clear aims to understand the epidemiology of HCV infection in pregnancy. The study is well designed and described. The subject is of interest to general practitioners of obstetrics and newborn medicine, infectious disease experts and epidemiologists.

1. Despite the analysis of 100K+ patients, the frequency of the potential covariates are quite low, i.e. prostitution, and destabilize the reliability of the regression analysis. A larger sample size would improve the reliance on the conclusions.

Our analysis included all women that were screened for the observational study. Any covariates that appear to be low would be a description of our population. For covariates that have been mentioned to appear low (i.e. prostitution), we re-ran the model selection without the covariate and yielded the same set of significant covariates.

2. As a corollary of above comment, the number of missing data points of number of lifetime partners might affect the reliability of > 3 lifetime partners in predicting HCV given the marginally significant values in the final adjusted models. A sensitivity analysis on lifetime partners and comment in the discussion would improve reader interpretation.

Our analysis had 19 women (5%) that did not report the number of lifetime partners.
As a sensitivity analysis, we re-ran the analysis grouping lifetime partners as 1, 2-3, 4-5, 6-10, and >10 partners. This yielded similar adjusted odds ratio estimates that ranged from 5 to 6, where the reference group was 1 partner.

3. Line 227. What was the correlation coefficient for inclusion in a cluster set?

The correlation coefficient for inclusion in a cluster set was $R^2 \geq 0.70$. This information has been included in the Results section.

Reviewer #3: Our understanding of HCV, and our ability to treat it, have evolved at a rapid pace. In order to determine how best to identify carriers, to start to eradicate its spread, and to prevent progression, there is a need to identify appropriate groups to screen. In that regard this team of investigators has made a major contribution. A few points are worth considering:

1. While it would have been impossible for the authors to know about unpublished work in progress, the CDC is proposing a change in standards for screening which will include universal screening for all pregnant women in communities with a prevalence of 0.1% or greater. While this does not distract from their findings it will make some of their discussion about screening seem a bit less germane, if the CDC recommendations appear before their manuscript is published, particularly if they don't have a chance to say how their findings fit once the new screening policy is adapted. Even some of their asides—"the seroprevalence of anti-HCV was low" (0.24%), needs to be reconsidered in light of the CDC's new practical definition of low (i.e., low enough not to screen—0.1%)

Reviewer #3 is correct in that the authors were not aware of this planned change in recommendation. We are aware of work of Tasillo et al., as well as Chaillon et al. that suggests that universal screening of pregnant women is a cost effective strategy based upon the assumptions they make in their models. The authors feel that the data included in this paper inform such assumptions, and that our findings could be used to reconsider the recommendation based upon contemporary and real-world findings. Interestingly, Chaillon et al. suggests that the strategy is cost effective with a prevalence rate of 0.1%, Tasillo et al.

suggests that the strategy is cost effective unless the prevalence falls below 0.16%. Our data suggests that we have identified a population appropriate to treat at 0.16%. In sum, modeled outcomes and actual data do not obviously support the proposed strategy to change recommendation for universal screening. In fact, one could argue that these three papers identify that controversy remains. We have revised the discussion to reflect this as well.

2. They offered screening to all women. Were there differences between those who accepted the offer and those that did not?
Potential participants were approached and asked for consent to be screened for the observational study. We did not collect and we do not have data on participants that did not consent to be screened.

3. When they say there are risks of over screening (line 139) they give a reference but provide no discussion. They may want to expand by a sentence or two.
Line 139 does not discuss the risks of over screening; rather it acknowledges the limitation of a risk factor based strategies for screening.

4. The give a few reasons why screening is not particularly useful during pregnancy (line 140) but don't acknowledge that some women are only seen for care while pregnant, and even if treatment has to be delayed, those women could at least be linked into a care system that will allow for subsequent therapy.
We have added the following line at line 141: Universal screening additionally has the advantage of identifying women who may not have contact with health care or health insurance were it not for their pregnancy state.

5. Why were multi-fetal pregnancies excluded for a serosurvey?
Our analysis is based on participants that were screened for the ongoing HCV observational study, the study design was not a serosurvey or true population based screening. It was unselected screening of an obstetric cohort. Screening for the HCV observational study was limited to singletons, as the primary outcome of the larger observational study is mother to child transmission (MTCT) of HCV. For clearer interpretation of the results for the primary outcome of MTCT from the observational study, singletons were only included.

6. How was "substance abuse" history obtained? Were there Q by Qs so that each site used the same instrument applied the same way?
Data on substance abuse was collected via participant interview and review of medical records. This was described in the Methods section (Lines 183-186). The protocol did not call for a screening tool to be uniformly used to elicit substance abuse history.

7. Did all sites test for all the STIs they list on page 11? Was HSV testing by antibody or antigen?
All STIs were based on a clinical diagnosis. Herpes was based on a clinical diagnosis and does not include women with serology alone without clinical symptoms.

8. On page 12 they only explain half of the reasons for failure to participate.
All reasons were listed in Figure 1. The number of participants that were ineligible for the observation study and all reasons for non-participation are now included in the text (Lines 263-266).

9. On page 13 (line 281) they note that there were no associations with medical comorbidities. Did that include hepatitis B?
Although hepatitis B was not mentioned in the text, Table 1 does show that there was no association between case-control status and hepatitis B or hepatitis D. Note that there were only 3 women with either hepatitis B or hepatitis D, and data obtained regarding Hepatitis B and Hepatitis D were obtained in combination.

10. They note no association with known risk factors (line 290). How many patients in the cohort were on dialysis or had HIV or organ transplant? Was the lack of an association evidence of absence or absence of evidence?
There were little to no enrolled participants that had these risk factors (zero women with dialysis or HIV, only 1 woman was a tissue/organ transplant recipient). The lack of an association would be based on evidence of absence based upon the number of women screened and enrolled. We deem it unlikely that, were our entire cohort of anti-HCV women enrolled, we would find evidence of these risk factors.
We can expand upon this in the text if deemed important.

11. The specificity of IVDU for HCV of 97% is remarkably high, even given the known association. How would they explain that? Similarly almost 1 in 4 women who had more than 3 lifetime sexual partners—which doesn't seem like a notably high number—had hepatitis C (line 324). Am I misunderstanding something?
A specificity of 97% for injection drug use (IVDU) means that a high percentage of non-injection drug use (non-IVDU) were negative for HCV. For lifetime sexual partners, the majority of women overall in both groups had >3 lifetime sexual partners (63%). This means that we would expect to capture a greater number of HCV cases.

12. When they are discussing geographic variability, is their data robust enough to sustain their assertions? Have they controlled for risk factors in the hospitals representing each geographic are? In other words, if one region screened a higher drug using population, it might not reflect the full geographic population; rather it might reflect the subpopulations using the particular hospitals chosen to represent those regions.
We emphasize that the summarization by geographic region is solely for descriptive purposes and further analysis by geographic region or hospital would deviate from our primary objectives. We agree that geographic variability may be due to particular subpopulations at our hospitals that represent these regions, although our results appear consistent with national trends. We made this more evident in the Methods section.

STATISTICAL EDITOR'S COMMENTS:

1. lines 79-80: Although numerically highest, this is statistically equivalent to 74/82 (known risk factors or >3 sexual partners). Also, see comments re: Table 3.
The risk factors noted in the abstract provided the highest sensitivity. The point was that only identifying certain risk factors resulted in very high sensitivity (91%). We agree that injection drug use, ever receiving blood transfusion, and/or >3 lifetime sexual partners provided similar results.

2. Fig 1: For the n = 254 (Ab (+)) vs the n = 131 cases enrolled in risk analysis, did the excluded group (n = 123, or ~ 1/2 of the original group of cases) differ in any of the characteristics cited in Table 1 in ways that could have affected the generalizability of the conclusions re: case-control analysis?
Characteristics cited in Table 1 were only collected on enrolled participants (i.e. post-screening at the Enrollment visit). Maternal age and insurance status were the only characteristics data collected at screening. As mentioned in the Results section (Lines 261-263), there were no differences between those enrolled and not enrolled with respect to anti-HCV level and these two characteristics.

3. Table 1: Income should be cited as annual income.
This has been updated.

4. Table 2: There are > 20 variables used as adjustors in the full model and 5 variables in the final model. Compared to the counts with the risk factors among cases and controls, the ratio of adverse counts vs variables is not favorable for most of the comparisons in the fully adjusted column and also unfavorable for the "injected any drugs", "blood transfusion", "partners with HCV" in the final adjusted model. That is, the models are likely over fitted, for all but the comparisons based on # of sexual partners comparisons or on smoking status.
Cluster analysis among all potential covariates was performed prior to model selection. This resulted in combining history of sexual abuse and self-mutilation (R^2=0.73) in our model selection. Additionally, prior to model selection, we followed a rule of thumb of 'one predictive variable can be studied for every ten events' (e.g. model selection did not include variables with less than 10 observations).

5. Table 3: Should include CIs with the sens and spec estimates. There is a trade-off of sens vs spec apparent for most of these variables, with most of the AUCs being statistically indistinguishable. In fact, it appears for "known risk factors, partner with HCV, smoking or > 3 sexual partners" (AUC = 0.65 (0.60-0.69)) is statistically worse than e.g., "known risk factors or smoking" (AUC = 0.73 (0.67-0.79).
We agree. The 95% confidence intervals for sensitivity and specificity have been included.

6. Appendices 4, 5: The previous comments re: Table 2 and over fitting apply to these Tables, with even fewer entries.
Tables in the Appendices were subgroup analyses to observe how our final model from Table 2 applies to the two different subgroups. Please see our previous comments for Comment #4.

7. General: As just a suggestion, perhaps citing the prevalence and its CIs in terms of cases per 1000 women, rather than as 0.24% would be more useful for the reader.
We agree. Prevalence and its confidence interval are now presented as 'per 1000 women'.

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.

We choose to opt in.

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.

We will address this upon resubmission.

3. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

Data for this analysis is based on an observational study.

4. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

We have completed the checklist.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize

initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric 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.

We do not believe that this is an issue in our manuscript.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 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.

Our work adheres to this limitation.

7. 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).

We believe this manuscript to be adherent to the guideline.

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

Hepatitis C Virus Screening in Pregnancy

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: Original Research articles, 300 words. Please provide a word count.

Our abstract is consistent with our paper, and the appropriate word count.

10. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

Our manuscript is not a randomized, controlled trial but we believe it complies with standard format.

11. 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.

All abbreviations and acronyms are spelled out the first time they are used in abstract and again in body of manuscript.

12. 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.

Edits have been made to remove this symbol from the text.

13. 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%").

Edits have been made to ensure our values are consistent with the specifications outlined.

14. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the

other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

We do not make such claims in this paper.

15. 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.

We believe our tables conform to the style of the journal.

16. 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.

We have reviewed this suggestion and feel the manuscript is compliant.

17. The Journal's Production Editor had the following to say about this manuscript:

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Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

We have addressed this request.

18. 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.

We would not be interested in open access.

Thank you for your consideration! We hope that this response adequately answers your questions. We would be happy to continue the discourse if any further discussion is required.

Sincerely,

Mona Prasad DO MPH
[redacted]