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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*
- Email correspondence between the editorial office and the authors*

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

Date: Oct 05, 2018
To: "Abriana Tasillo" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1700

RE: Manuscript Number ONG-18-1700

Title Short-term impact and long-term cost-effectiveness of universal HCV hepatitis C testing in prenatal care

Dear Dr. Tasillo:

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 Oct 26, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The purpose of the manuscript is to understand the cost effectiveness of introducing universal Hep C screening during the prenatal period through a simulation model. General comments about the draft:

The introduction needs some additional information. The trends for Hep C infection, the current impact of it and why should we be focusing on it now at the same level as we focused on HIV. I did not see that. The prevalence as given does not show me necessarily the need for this as an important or pressing issue. There are some issues with some of the language that is used, that assumes the audience is knowledgeable about the topic area. For example, the reference to "interferon era" should be explained as it might not be readily apparent to a reader who may come from non-clinical/research background. Same goes for the interferon-free direct acting antiviral treatment. What makes this unique and why should I care?

I am having a hard time understanding the purpose and need for the study based on the literature review that is provided. Some additional information pertaining to history, changes in the current environment are needed to build the case for this paper.

Reviewer #2:

Abstract:

1. Line 84 This line is confusing. I would suggest leaving out implications. It is redundant.

Introductions:

2. Line 106-111 This is a good description of the problem. For cost effectiveness and evidence based testing I would suggest further discussion of all prenatal lab panels that are recommended. Many do not stand up to the scrutiny provided in this study and would engage the general obstetrician in practice that has to decide every day which panels or tests to order.

3. Further description of effective treatment is key to reconsideration of recommendations since this was the historic reason for not testing.

4. Expand on treatment and cost of hep C to give the reader an understanding of where the rest of the article goes with linkage analysis to treatment. The model looking at this sets the framework for longitudinal effectiveness.

Methods:

5. Line 155 Why were terminations excluded? I would compare to most practices performing family planning and testing for HIV. In the age of PREP and PEP this is now a focus in the family planning community based upon regional and individual risks.

6. Line 156 Explain the assumptions in more detail related to fertility rates through 49 and miscarriage rates. What were the rates and how did they modify and change in the model over time?

7. Line 160-162 Explain why there was no analysis of the maternal infant pair? This is very important and would go a long way in making the argument for routine screening and cost effectiveness. Although the treatment and outcomes for the infant are different than HIV vertical transmission, the concept of maternal infant linkage is important to bring up.

8. Line 186-187 Why was the assumption of 100% access to treatment made?. Is there data on barriers to treatment in the public health literature and could this be incorporated into the modeling? Since many of the reasons for current Hep c infection are related to possible injection drug abuse, and this is a significant barrier to treatment I am not sure this is an accurate assumption. Millman, Alexander J. et al. "Barriers to Treatment Access for Chronic Hepatitis C Virus Infection: A Case Series." Topics in Antiviral Medicine 25.3 (2017): 110-113. Print.

9. Line 195-196 Is there a reference for 50% reduction in cost for patients treated and in SVR along with 96% reduction in the hep c attributable mortality? Is this from references 22, 23 in the beginning of this paragraph?

Model data:

10. This was a good description of the detailed assumptions and comparisons of routine vs. universal screening.

11. Line 245 Explain what is meant by 3% discounting on cost and life expectancy.

12. Line 250. Explain the choice of willingness to pay ICER at 100,000. This is a key to the conclusions and needs to be supported from a public health perspective.

13. Line 254 Sensitivity analysis is an important part of this study to effect public health policy and future recommendations.

14. Lines 283-284 Given the assumptions of 6% reduction in exposed infants can there be modeling based upon follow up cost, clearance and future outpatient pediatric visits? This would make the conclusions more robust for short term effectiveness.

15. Line 285 Cost outcomes are difficult to understand. Is the small difference the cost of actually testing? Difference $123

Results:

16. Table 1 stands by itself. It answers many of the questions in the narrative about modeling with supported references. I would recommend making reference to this table in the methods section earlier so the reader can follow the study design. The only discrepancy I see is in line 157 it implies modeling through age 49. The table uses 15-44.

17. Line 294. How were the ranges of Hep c prevalence chosen for sensitivity analysis?

18. Figure 1 It is unclear why modeling for universal screening would be less than 99-100% identification.

Discussion:

19. Overall this was a comprehensive cost analysis using multiple real world assumptions with incremental longitudinal cost assessment along the life course. The limitations of any assumption were well described along with changing sensitivities to account for variation in the population. Limitations were acknowledged and addressed thoroughly.

Reviewer #3: Thank you for the opportunity to review this manuscript.

ABSTRACT

1. It may be helpful to reframe the first sentence in the Objective as a "To" statement. Also, "the primary objective" and "secondary objectives included" will help with readability.

INTRODUCTION

2. While the author's succinct, short sentences are appreciated, some revision to smooth transitions between statements may improve flow. For example, "While HCV vertical transmission occurs in 6-15% of births to women with infection, infants are more like than adults to resolve the infection."

3. Further detail as to why DAA changes the calculus re: HCV screening in pregnancy would be helpful. I.e. whether treatment is safe in pregnancy for both mother and fetus, treatment during lactation, efficacy of treatment, access to treatment during pregnancy, etc. Universal screening is still theoretically problematic (though one could still argue it may change labor management) if access to treatment is limited for newer treatment modalities. While this is mentioned in the Methods as representative of current practice, the statement as it currently stands in the Introduction makes it seem that DAA is currently used for treatment during pregnancy.

METHODS

4. I am curious as to why new drug use was limited to 25 years. Certainly in may parts of the country with a high incidence of opioid use/addiction, new users do not fit into the demographic patterns seen earlier in the epidemic.

RESULTS

5. The multiple headings/sub-headings with only a few lines under each are distracting. It might be more helpful to remove these.

DISCUSSION

6. The limitation discussed above (potential decreased ability to fulfill WHO's criteria for a good screening test due to lack of access to treatment during pregnancy/lactation) should be mentioned in the discussion section to frame the issue of new trials of DAA in pregnancy and how this manuscript fills the gap in not only the SMFM/ACOG recommendations but also this aspect of an ideal screening test.

7. Given the similarities to HIV as the authors themselves alluded to in the intro, it may be helpful to discuss some of the other driving forces behind universal screening of HIV in pregnancy (i.e traditional risk factors are not 100% predictive and as the opioid epidemic is now impacting more women/older people/people of higher SES, traditional superficial risk-factor based methods in the office will be less sufficient). Furthermore and very importantly, universal screening decreases stigma and exceptionalism.

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: The estimates are mostly listed with a single value, rather than as a range or probability distribution within some bounds. Understanding how the population ages were distributed to emulate the US population, why were many of the other parameters (eg, probabilities, sensitivities or specificities etc) assumed as constant values? If they were actually within ranges, then should cite and justify the distributions etc used. Should include somewhere in model parameters the cost of therapy.

2. Table 2: Should use a consistent degree of precision for reporting results. If % infections were cited to nearest integer %, then how were life expectancies reported to nearest .01 years.

3. A flow diagram of the various branch points in the decision tree would be helpful. Could have simplified version in main text and more detailed version on-line.

EDITORIAL OFFICE COMMENTS:

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

2. Based on the forms that have been submitted, Dr. Liisa Randall has not met the criteria for authorship. On the third page of the form, under the section labeled "Authorship," items #2-4, in addition to either 1a or 1b, MUST be checked off in order to qualify for authorship. Dr. Randall should be moved to the acknowledgments, or they could resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded

with the revision in Editorial Manager.

3. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

4. 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 appendixes).

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

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

6. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. Provide a short title of no more than 45 characters (40 characters for case reports), 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, written in the present tense and stating 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. 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. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

13. The Journals' Production Editor had the following to say about the figures in your manuscript:

"Figure 1: Author needs to submit figure as a high-res (at least 300 DPI) image file (JPEG, EPS, TIFF). Suggest they submit using color bars.
Figure 2: Author needs to submit figure as a high-res (at least 300 DPI) image file (JPEG, EPS, TIFF)"

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

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.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

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If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Oct 26, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

In response to the EU General Data Protection Regulation (GDPR), you have the right to request that your personal information be removed from the database. If you would like your personal information to be removed from the database, please contact the publication office.

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



Dear *Obstetrics & Gynecology* Editorial Team,

Thank you for the opportunity to revise and resubmit our manuscript (ONG-18-1700) entitled "Short-term impact and long-term cost-effectiveness of universal hepatitis C testing in prenatal care." We are appreciative of the reviewers' time and their insightful comments. We have rewritten the introduction to include more context about hepatitis C treatment, added additional references, clarified cost-effectiveness procedures such as discounting, and added sensitivity analyses to address reviewers' questions about treatment access and costs of infant testing. Overall, we believe our response to these comments has strengthened our paper and increased clarity.

Below is a point-by-point response to each of the reviewers' comments. Each comment remains in original plain text, while our response is in italics and, where appropriate, revised manuscript text is bolded and referenced by page and line numbers. Also included with this revision are high-resolution (300 dpi) TIFF image files, and schematic diagrams of our model design. We feel that these revisions have improved our paper and made it more relevant to the *Obstetrics & Gynecology* audience.

Respectfully,

Abriana Tasillo

REVIEWER COMMENTS:

Reviewer #1: The purpose of the manuscript is to understand the cost effectiveness of introducing universal Hep C screening during the prenatal period through a simulation model. General comments about the draft:

The introduction needs some additional information. The trends for Hep C infection, the current impact of it and why should we be focusing on it now at the same level as we focused on HIV. I did not see that. The prevalence as given does not show me necessarily the need for this as an important or pressing issue. There are some issues with some of the language that is used, that assumes the audience is knowledgeable about the topic area. For example, the reference to "interferon era" should be explained as it might not be readily apparent to a reader who may come from non-clinical/research background. Same goes for the interferon-free direct acting antiviral treatment. What makes this unique and why should I care?

I am having a hard time understanding the purpose and need for the study based on the literature review that is provided. Some additional information pertaining to history, changes in the current environment are needed to build the case for this paper.

We have rewritten the introduction in order to provide more context. We have also included a reference to a paper recently published in Clinical Infectious Diseases entitled "Universal Screening of Pregnant Women for Hepatitis C: The Time Is Now."

Page 4-5, Lines 99-115

"Hepatitis C virus (HCV) is a virulent, chronic, blood-borne infection which causes progressive liver damage and death.(1) Until recently, the only treatments available for HCV had serious side effects, were contraindicated for many, and cured fewer than 60% of those treated.(2) In 2013, the first direct-acting antiviral (DAA) treatment for HCV was approved. Today, DAAs can cure 95-99% of disease regardless of subtype.(3) However, as treatments improve, HCV incidence is rising among individuals under the age of 30 due to the opioid epidemic.(4, 5)

In reproductive age women, HCV prevalence doubled between 2006 and 2014, but many cases remain unidentified and untreated.(1, 6) For HIV, a reasonable analogy for HCV, guidance began with targeted risk-factor testing, as is currently recommended for HCV. Providers did not adequately identify stigmatized HIV risk behaviors, and targeted testing missed too many cases of HIV. A large proportion of pregnant women with an identified risk factor are not tested for HCV.(7) Eventually, guidance expanded to universal one-time HIV testing, which is both effective and cost-effective.(8, 9) Universal HCV testing in adults is also likely cost-effective.(10, 11)

Prenatal care may provide an ideal venue to diagnose HCV in reproductive age women.(12) Low absolute prevalence, lack of available treatment during pregnancy, and the extremely high cost of HCV treatment raise questions of overall impact and resource allocation. A study conducted before the approval of DAAs found that testing in pregnancy was not likely cost-effective,(13) but with an effective HCV cure, these findings are due for reconsideration."

Reviewer #2:

Abstract:

1. Line 84 This line is confusing. I would suggest leaving out implications. It is redundant.
The word "implications" has been deleted.
Page 3, Line 78
"To estimate the clinical impact and cost-effectiveness of universal prenatal hepatitis C screening."
Introductions:

2. Line 106-111 This is a good description of the problem. For cost effectiveness and evidence based testing I would suggest further discussion of all prenatal lab panels that are recommended. Many do not stand up to the scrutiny provided in this study and would engage the general obstetrician in practice that has to decide every day which panels or tests to order.
We have added additional information on prenatal testing in the methods section, which places the ICER willingness-to-pay threshold into context.
Page 9-10, Lines 250-256
"We interpret ICERs assuming a willingness to pay (WTP) threshold of $100,000 per QALY gained. There is no universal WTP threshold, and so we chose $100,000 per QALY to maintain consistency with other analyses and recommendations.(36) For context in benchmarking of cost-effectiveness ratios, comparison to other accepted interventions may be useful. Screening for gestational diabetes, for example, is associated with an ICER of approximately $20,000 per QALY, screening for postpartum depression was found to have an ICER of approximately $14,000 per QALY and fetal echocardiography to detect congenital heart disease was found to have an ICER of $113,000 per QALY.(37, 38)"

3. Further description of effective treatment is key to reconsideration of recommendations since this was the historic reason for not testing.

We substantially edited the entire introduction (please see reviewer #1 comment #1 above) and it now includes discussion of new HCV treatments.
Page 4, Lines 100-102
Until recently, the only treatments available for HCV had serious side effects, were contraindicated for many, and cured fewer than 60% of those treated.(2) In 2013, the first direct-acting antiviral (DAA) treatment for HCV was approved. Today, DAAs can cure 95-99% of disease regardless of subtype.

4. Expand on treatment and cost of hep C to give the reader an understanding of where the rest of the article goes with linkage analysis to treatment. The model looking at this sets the framework for longitudinal effectiveness.
Please see above.

Methods:

5. Line 155 Why were terminations excluded? I would compare to most practices performing family planning and testing for HIV. In the age of PREP and PEP this is now a focus in the family planning community based upon regional and individual risks.

We modeled pregnancies that progressed past the first trimester, which would exclude the more than 90% of induced abortions that are performed during this time (Jatlaoui, 2017). To our knowledge, there are no available data to inform an estimate of linkage to HCV care following an induced abortion. However, if linkage to care and subsequent treatment management were equivalent to those seen in women who remained pregnant, the cost-effectiveness conclusions would not change. We agree that induced abortion is an opportunity to engage women in HCV care.

6. Line 156 Explain the assumptions in more detail related to fertility rates through 49 and miscarriage rates. What were the rates and how did they modify and change in the model over time?

We inserted the following sentence
Page 6, Lines 148-149
"Our fertility data came from the U.S. Vital Statistics 2017 preliminary report on births."

and included a link to the citation: **Hamilton BE, Martin JA, Oseterman MJK, Driscoll AK, Rossen LM. Births: Provisional Data for 2016: National Center for Health Statistics; June 2017.**

We also added more detail to the model data section, and recorded the rates in Table 1.
Page 8, Lines 207-213
"Because a substantial proportion of pregnancies prove unviable during the first trimester and spontaneously terminate prior to initiation of routine prenatal care, we modeled only pregnancies that passed beyond the first trimester. We constructed our pregnancy rates by working backwards from the number of live births and adjusting for multiple births and miscarriage and stillbirth rates after the first trimester.(16, 25) The final fertility estimates were highest for women ages 30-34 (approximately 104 pregnancies per 1,000 women) and lowest for women ages 45-49 (approximately 0.9 pregnancies per 1,000 women)."

7. Line 160-162 Explain why there was no analysis of the maternal infant pair? This is very important and would go a long way in making the argument for routine screening and cost effectiveness. Although the treatment and outcomes for the infant are different than HIV vertical transmission, the concept of maternal infant linkage is important to bring up.

To be clear, this analysis does focus on maternal infant pairs. We report the proportion of infants exposed to HCV in utero and at risk for infection, as well as the proportion of those with in utero HCV exposure who are identified as such secondary to HCV identification in the mother. We do not include infant outcomes in the cost-effectiveness estimates, which are calculated based on the health and cost outcomes of the women being screened. Pediatric HCV infection is clinically distinct from adult infection, and much of the data needed to model pediatric HCV infection are not available in the literature. DAAs were only recently approved in children, with the first DAA approved for children 12-17 years old in 2017. No DAAs are FDA-

approved yet in children under age 12. Consequently, there are no data to inform linkage of infants or children to DAA treatment.
In this analysis, therefore, we focused on outcomes for pregnant women and made infant outcomes a secondary objective. We note that routine testing among pregnant women is cost-effective, even when we do not consider benefits to infants. Were we to include infant benefits, routine testing among pregnant women would likely remain cost-effective.
To clarify these points, we added to the methods section.
Page 6, Lines 151-157
"We tracked the number of infants born to women with HCV infection and calculated the proportion of those exposed infants in whom maternal HCV infection was identified such that the infant could be appropriately screened. Because infant and childhood HCV infection are clinically distinct entities from adult infection, and because there are no data to inform linkage rates in the future when infants born with infection become eligible for HCV treatment, we did not simulate the lifetime of HCV-infected infants, nor did we include infant outcomes in calculations of ICERs. We did, however, conduct sensitivity analyses on the cost of testing among infants born to mothers identified with HCV infection while pregnant."
To explore the effects of subsequent infant testing on the cost burden, we added the cost of an antibody test to each infant identified as exposed to infection. Even adding this additional cost without considering additional health benefits due to early detection of vertical transmission, the intervention remained cost-effective. The ICER associated with prenatal HCV screening remained $41,000 per QALY. We added the following to the text, and included results in the table of sensitivity analyses.
Page 12, Lines 320-322
"When we added the additional cost of antibody testing for infants identified as being exposed to HCV to the ICER calculation, the ICER rose slightly (from $41,275 to $41,317) but remained $41,000 per QALY when rounded to the nearest thousand"
8. Line 186-187 Why was the assumption of 100% access to treatment made?. Is there data on barriers to treatment in the public health literature and could this be incorporated into the modeling? Since many of the reasons for current Hep c infection are related to possible injection drug abuse, and this is a significant barrier to treatment I am not sure this is an accurate assumption. Millman, Alexander J. et al. "Barriers to Treatment Access for Chronic Hepatitis C Virus Infection: A Case Series." Topics in Antiviral Medicine 25.3 (2017): 110-113. Print.

We assumed that 92% of patients prescribed DAAs would initiate therapy based on real-world cohort data (Younossi, 2015). In order to explore the effect that restricted access to treatment would have, we conducted two sensitivity analyses. In the first, we reduced the percentage of patients initiating care to 64.5%, based on a 35.5% absolute denial found in one study (Gowda, 2017). In this case, the ICER associated with universal prenatal HCV testing rose from $41,000 per QALY to $49,000 per QALY. In the second, we restricted treatment to only those patients who were not currently injecting drugs. In this case, the ICER associated dropped to $34,000. In both cases, the health benefit of prenatal screening (as measured in additional life expectancy) decreased from the base case. These findings were added to the sensitivity analysis table as well as the main results section.
Page 12, Lines 314-318
"If current PWID were not eligible for treatment, universal prenatal HCV screening was cost-effective with an ICER of $34,000 per QALY. If treatment was denied to 35.5% of the linked population, as was found in a recent study, the ICER was $49,000 per QALY. Both of these restricted treatment scenarios resulted in reduced life expectancies compared with the base case, with a population-level average decrease of 0.004 and 0.009 life years for PWID restriction and overall limitation, respectively."

9. Line 195-196 Is there a reference for 50% reduction in cost for patients treated and in SVR along with 96% reduction in the hep c attributable mortality? Is this from references 22, 23 in the beginning of this paragraph?

We updated this paragraph to include the appropriate citations. The 96% reduction in HCV mortality comes from van der Meer, et al as published in JAMA in 2012.
The 50% reduction in HCV-related costs comes from expert opinion and is a parameter we give special attention to during sensitivity analysis. Even assuming no cost reduction in HCV prior to cirrhosis, universal prenatal HCV screening is still cost-effective.

Model data:

11. Line 245 Explain what is meant by 3% discounting on cost and life expectancy.
We have added the following, and included references two papers discussing the reasons and strategies for discounting over time: Severens, 2004 and Attema, 2018.
Page 9, Lines 242-245
Costs and quality-adjusted life expectancy were discounted at a rate of 3% per annum in accordance with best practices defined by the second panel on cost-effectiveness. Discounting is a standard procedure in economic evaluations research that accounts for the theoretical and observed reality that future costs and benefits are less acute and therefore valued less relative to costs in the present.

12. Line 250. Explain the choice of willingness to pay ICER at 100,000. This is a key to the conclusions and needs to be supported from a public health perspective.
We added more context around the willingness-to-pay threshold; please see reviewer #2, comment #2 response above.

14. Lines 283-284 Given the assumptions of 6% reduction in exposed infants can there be modeling based upon follow up cost, clearance and future outpatient pediatric visits? This would make the conclusions more robust for short term effectiveness.
Please see our discussion of infant outcomes above and the modifications we made to address this concern (reviewer #2, comment #7).

15. Line 285 Cost outcomes are difficult to understand. Is the small difference the cost of actually testing? Difference $123
We have added the following information to increase clarity:
Page 11, Lines 291-297
"These cost differences of $123 (undiscounted) and $78 (discounted) represent the total net increase in lifetime healthcare costs per patient. These numbers include the cost of universal HCV prenatal testing, treatment and any other medical care received over the lifetime, and the future cost savings of averted liver failure and further cirrhosis. The small incremental cost difference reflects that fact that for a small portion of the total population – those with HCV infection – the cost of screening and HCV treatment is high, whereas for the large majority who are not HCV-infected, the cost is only the cost of HCV testing. When these two populations are averaged, the resulting incremental cost for the entire population is expectedly small."

Results:

16. Table 1 stands by itself. It answers many of the questions in the narrative about modeling

with supported references. I would recommend making reference to this table in the methods section earlier so the reader can follow the study design. The only discrepancy I see is in line 157 it implies modeling through age 49. The table uses 15-44.
The initial cohort is age 15-44, but future pregnancy is possible at a much lower rate until age 49. Please see our response to reviewer #2, comment #6 for more information on pregnancy rates. We added the following line to direct readers to Table 1 earlier in the manuscript.
Page 5, Lines 129-130
"Important input parameters are discussed below as well as recorded in Table 1."

17. Line 294. How were the ranges of Hep c prevalence chosen for sensitivity analysis?
For HCV prevalence, we conducted a threshold analysis to determine the prevalence below which universal prenatal HCV screening would no longer be a cost-effective intervention. This analysis took us well below the range of estimates for HCV available in the literature. We added the following to the methods section.
Page 10, Lines 262-263
"We performed a threshold analysis on HCV prevalence to determine the lowest prevalence below which routine testing is not likely to be cost-effective."

18. Figure 1 It is unclear why modeling for universal screening would be less than 99-100% identification.
Universal screening is likely to identify nearly 100% of initial infections, but we do not model perfect screening throughout the lifetime, as that is not a realistic assumption. Even a recommendation for universal prenatal HCV screening will be unable to identify every infection, because some infections occur after the start of the simulation, either through reinfection after cure, or through first-time infection due to risk behaviors.

ABSTRACT

1. It may be helpful to reframe the first sentence in the Objective as a "To" statement. Also, "the primary objective" and "secondary objectives included" will help with readability.

The objective statement was changed to increase readability and now reads as follows:
Page 3, Lines 78-81
"To estimate the clinical impact and cost-effectiveness of universal prenatal hepatitis C screening. Primary objective was to establish whether universal prenatal hepatitis C screening was cost-effective. Secondary objectives were to calculate life expectancy, quality of life and healthcare costs associated with universal prenatal hepatitis C screening and linkage to treatment."

INTRODUCTION

3. Further detail as to why DAA changes the calculus re: HCV screening in pregnancy would be helpful. I.e. whether treatment is safe in pregnancy for both mother and fetus, treatment during lactation, efficacy of treatment, access to treatment during pregnancy, etc. Universal screening is still theoretically problematic (though one could still argue it may change labor management) if access to treatment is limited for newer treatment modalities. While this is mentioned in the

Methods as representative of current practice, the statement as it currently stands in the Introduction makes it seem that DAA is currently used for treatment during pregnancy.
We made substantial revisions to the introduction to address this and other concerns. Please see above, reviewer #1, comment #1.

METHODS

4. I am curious as to why new drug use was limited to 25 years. Certainly in may parts of the country with a high incidence of opioid use/addiction, new users do not fit into the demographic patterns seen earlier in the epidemic.
To clarify, we modeled initiation to injection drug use up until the age of 25, such that the prevalence of injection drug use among those aged 26 matched that of national data, but we allowed for prevalent injection and non-injection drug use throughout the lifespan. While this is a simplification of substance use behavior, we feel it is a reasonable simulation for the purpose of modeling HCV reinfection after cure among drug users. We also conducted sensitivity analyses on the prevalence of drug use, which did not change our cost-effectiveness conclusions. We adapted the limitations section in order to acknowledge this.
Page 13, Lines 356-360
"A second limitation concerns HCV transmission and drug use. We used available data to model periods of drug use, but with limited data and changes in opioid use in the U.S., this is imperfect. While we included infection and re-infection for those with injection drug use behaviors, we did not consider that community-level treatment may decrease transmission rates. If so, then we likely underestimated positive effects."

RESULTS

5. The multiple headings/sub-headings with only a few lines under each are distracting. It might be more helpful to remove these.
We removed the subheadings from the main section of the results, but kept them to demarcate separate sensitivity analyses.

DISCUSSION

6. The limitation discussed above (potential decreased ability to fulfill WHO's criteria for a good screening test due to lack of access to treatment during pregnancy/lactation) should be mentioned in the discussion section to frame the issue of new trials of DAA in pregnancy and how this manuscript fills the gap in not only the SMFM/ACOG recommendations but also this aspect of an ideal screening test.
The reality that it is not possible to treat pregnant women for HCV is sometimes discussed as a reason to not offer routine testing in prenatal care. This analysis demonstrates, however, that HCV testing in the venue where a woman is present (prenatal care) improves clinical outcomes and is cost-effective, even when the treatment comes later, after delivery and a period of recovery or breast-feeding. Not all medical services that are delivered in the prenatal care venue need to provide explicit prenatal benefits. Prenatal care is one component of a larger healthcare delivery system and can play a role in HCV diagnosis, even if it is not possible to treat women during the relatively short period of their lives when they are pregnant or nursing. We added the following to the discussion

Page 13, Lines 341-344

"Although one WHO criteria for ideal screening tests is the availability of treatment, we have shown a benefit even with delayed treatment. Furthermore, our analysis demonstrated that universal hepatitis C testing followed by DAA treatment during pregnancy could improve cure rates from 60% to 67%, at an ICER of $19,000 per QALY gained."

7. Given the similarities to HIV as the authors themselves alluded to in the intro, it may be helpful to discuss some of the other driving forces behind universal screening of HIV in pregnancy (i.e traditional risk factors are not 100% predictive and as the opioid epidemic is now impacting more women/older people/people of higher SES, traditional superficial risk-factor based methods in the office will be less sufficient). Furthermore and very importantly, universal screening decreases stigma and exceptionalism.

We have made the parallels between HIV stronger in the introduction. Please see reviewer #1, comment #1 above. We added the following to the discussion to address the important point of decreasing exceptionalism.

Page 14, Lines 380-382

"We have an opportunity to identify and treat HCV infection in women of reproductive age, to circumvent difficulties of risk-based testing and to reduce stigma of HCV testing in general."

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: The estimates are mostly listed with a single value, rather than as a range or probability distribution within some bounds. Understanding how the population ages were distributed to emulate the US population, why were many of the other parameters (eg, probabilities, sensitivities or specificities etc) assumed as constant values? If they were actually within ranges, then should cite and justify the distributions etc used. Should include somewhere in model parameters the cost of therapy.

The cost of therapy has been included in Table 1. Sensitivity analysis ranges were included for relevant parameters, and citations were updated.

2. Table 2: Should use a consistent degree of precision for reporting results. If % infections were cited to nearest integer %, then how were life expectancies reported to nearest .01 years.

We increased precision of our Table 2 values to report to the nearest 0.01%.

3. A flow diagram of the various branch points in the decision tree would be helpful. Could have simplified version in main text and more detailed version on-line.

We have included flow diagrams for liver fibrosis progression, pregnancy throughout the life span, and HCV cascade of care. These will be uploaded to the Editorial Manager.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental

digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.
In the interest of transparency, we elect to opt-in to publishing this letter response and subsequent email correspondence related to author queries.

2. Based on the forms that have been submitted, Dr. Liisa Randall has not met the criteria for authorship. On the third page of the form, under the section labeled "Authorship," items #2-4, in addition to either 1a or 1b, MUST be checked off in order to qualify for authorship. Dr. Randall should be moved to the acknowledgments, or they could resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.

Dr Randall meets criteria for authorship. An uploaded form will be submitted to the Editorial Manager.

3. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515<http://links.lww.com/AOG/A515>>, and the gynecology data definitions are available at http://links.lww.com/AOG/A935<http://links.lww.com/AOG/A935>>.

We changed the phrase “elective termination” to “induced abortion” in order to be more consistent with the definitions provided.
Page 6, Line 145-146
“We excluded induced abortions from consideration and assumed all pregnancies resulted in a live birth except in the case of a) maternal death or b) miscarriage.”

4. 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 appendixes).

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

Our introduction is 249 words and our discussion is 750 words. The main text of our manuscript is 4,065 words, and there are 21 pages total.

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

We shortened our title to 100 characters:
Page 1, Line 1: **"Short-term impact and long-term cost-effectiveness of universal hepatitis C testing in prenatal care"**

6. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

We added a separate acknowledgements section to include our funding information. This paper has not been presented in whole or in part at any organizational meeting.
Page 3, Lines 66-71
"This project was funded by the CDC, National Center for HIV, Viral Hepatitis, STD, and TB Prevention Epidemiologic and Economic Modeling Agreement (NEEMA, # 5U38PS00-4644) and the Center for Health Economics of Treatment Interventions for Substance Use Disorder, HCV and HIV (NIDA, #P30DA040500). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention."

7. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.
We included a short title with length 38 characters.
Page 1, Line 3: **Universal prenatal hepatitis C testing**

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, written in the present tense and stating 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."
Our précis can be found on page 3; it totals 21 words.
Lines 73-75 "Universal testing for hepatitis C in pregnancy is cost-effective and would increase average life expectancy by 1.21 years for infected women."

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.

We added a word count to our abstract (250 words).

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf<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.
We removed the abbreviation HCV from the title.

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.

We replaced the virgule symbol with the words "and" and "or" as appropriate.

12. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf<http://edmgr.ovid.com/ong/accounts/table_checklist.pdf>>.

13. The Journals' Production Editor had the following to say about the figures in your manuscript:

"Figure 1: Author needs to submit figure as a high-res (at least 300 DPI) image file (JPEG, EPS, TIFF). Suggest they submit using color bars.
Figure 2: Author needs to submit figure as a high-res (at least 300 DPI) image file (JPEG, EPS, TIFF)"

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or

Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

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.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp<http://cjs.cadmus.com/da/index.asp>) for more direction on digital art preparation.

We have created new, high-resolution TIFF files for our images. Both images are 300 dpi and we added color bars to Fig 1.

Daniel Mosier

From: Denise Shields
Sent: Friday, November 9, 2018 11:37 AM
To: Tasillo, Abriana
Cc: Daniel Mosier
Subject: RE: Manuscript Revisions: ONG-18-1700R1

Dear Dr. Tasillo,

Thank you for answering our queries. There are three flowcharts in your article that should be cited as Appendix 1, Appendix 2, and Appendix 3. Would you add these citations to your manuscript?

Regards,
Denise

Denise Shields
Senior Manuscript Editor
Obstetrics & Gynecology
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Facebook (https://www.facebook.com/greenjournal/)
Instagram (https://www.instagram.com/greenjrnl/)
LinkedIn (https://www.linkedin.com/groups/4058408)

From: Tasillo, Abriana [redacted]
Sent: Thursday, November 8, 2018 2:41 PM
To: Daniel Mosier <dmosier@greenjournal.org>
Cc: Denise Shields <DShields@greenjournal.org>
Subject: Re: Manuscript Revisions: ONG-18-1700R1

Atta hAtAttached is is a revised version of the manuscript with requested edits. I emailed Dr Vellozzi with a reminder to confirm her authorship. Please let me know if there is anything else required. Thank you.
BBB
Best,

B

1.
Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes. I agree with these changes
2.
LINE 3: Please ask the following authors to respond to the authorship confirmation email we sent. We sent an email from em@greenjournal.org. The message contains a link that needs to be clicked on. We emailed the authors below at the email addresses listed– are these the correct addresses? Claudia Vellozzi: [redacted] i sent a reminder as well.

3.
LINE 4: We use up to two academic degrees per author in the byline. We used “MD, MPH” for Dr. Schillie and not “MD, MPH, MBA.” If “MBA” should be used instead of “MPH,” please edit. MD, MPH is fine, thank you.
4.
LINE 93: Please be sure this is stated in the body of your paper. Statements and data that appear in the Abstract must also appear in the body text for consistency. I changed degree of precision reported in body of manuscript to match what is in abstract
5.
LINE 124: Did you receive IRB approval or exemption? Please add text describing IRB approval to this section. If the study was found to be exempt, explain why. Not human subjects research; note added.
6.
LINE 290: I changed the “less than” symbol to “below” here, to match what is stated in the abstract. If the “less than” symbol should say “below” in the phrase, “<$100,000 per QALY” throughout, please edit. I changed < to "below" where it appeared
7.
FIGURE 1: Please cite Figure 1 within the main text of the manuscript. I cited Figure 1 in line 286.
8.
TABLES: Please shorten the titles of your tables so that they are more concise. Tables have shortened titles.

Abriana Tasillo

Research Assistant
Boston Medical Center
[redacted]

_____
From: Daniel Mosier <dmosier@greenjournal.org>
Sent: Thursday, November 8, 2018 9:29:35 AM
To: Tasillo, Abriana
Cc: Denise Shields
Subject: Manuscript Revisions: ONG-18-1700R1

Dear Dr. Tasillo,

Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:

1.
Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.
2.
LINE 3: Please ask the following authors to respond to the authorship confirmation email we sent. We sent an email from em@greenjournal.org. The message contains a link that needs to be clicked on. We emailed the authors below at the email addresses listed– are these the correct addresses? Claudia Vellozzi: [redacted]

3.
LINE 4: We use up to two academic degrees per author in the byline. We used “MD, MPH” for Dr. Schillie and not “MD, MPH, MBA.” If “MBA” should be used instead of “MPH,” please edit.
4.
LINE 93: Please be sure this is stated in the body of your paper. Statements and data that appear in the Abstract must also appear in the body text for consistency.
5.
LINE 124: Did you receive IRB approval or exemption? Please add text describing IRB approval to this section. If the study was found to be exempt, explain why.
6.
LINE 290: I changed the “less than” symbol to “below” here, to match what is stated in the abstract. If the “less than” symbol should say “below” in the phrase, “<$100,000 per QALY” throughout, please edit.
7.
FIGURE 1: Please cite Figure 1 within the main text of the manuscript.
8.
TABLES: Please shorten the titles of your tables so that they are more concise.

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on Friday, November 9th.

Sincerely,

-Daniel Mosier

Daniel Mosier

Editorial Assistant

Obstetrics & Gynecology

The American College of Obstetricians and Gynecologists

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From: Stephanie Casway
To: [redacted]
Subject: RE: O&G Figure Revision: 18-1700
Date: Friday, November 9, 2018 10:50:00 AM
Attachments: 18-1700 Legend.pdf
18-1700 Appendices 1-3.pdf

Good Morning Abriana,

Thank you so much for your review and reply. I have added an explanation of the dotted line to the legend for Figure 2 (see attached legend). I have also created Appendices 1-3 out of the 3 flowcharts (see attached). If you have any questions, concerns, or edits, just let me know.

Have a great weekend!

From: Tasillo, Abriana [redacted]
Sent: Thursday, November 8, 2018 2:47 PM
To: Stephanie Casway <SCasway@greenjournal.org>
Subject: Re: O&G Figure Revision: 18-1700

Thank you for sending these for review. They look good to me.

The solid lines are the data; the dotted line represents the $100,000 per QALY willingness-to-pay threshold.

The model diagrams should be supplemental digital content.

Please let me know if you have any other questions or require additional review.

Thank you,

Abriana

Abriana Tasillo

[redacted]

From: Stephanie Casway <SCasway@greenjournal.org>

Sent: Thursday, November 8, 2018 7:33:42 AM
To: Tasillo, Abriana
Subject: O&G Figure Revision: 18-1700

Good Morning Dr. Tasillo,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes. In addition, please see our queries below.

AQ1: What do the solid and dotted lines represent in Figure 2. We usually like to include this information in the legend or figure key.

AQ2: Two flowcharts were uploaded to Editorial Manager; however, they are not referenced in the manuscript. Would you like these to be included as figures or supplemental digital content?

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article's publication.

To avoid a delay, I would be grateful to receive a reply no later than Monday, 11/12. Thank you for your help.

Best wishes,

Stephanie Casway, MA
Production Editor

Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
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