OBSTETRICS & GYNECOLOGY

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

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

Personal or nonessential information may be redacted at the editor's discretion.

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

Date: Aug 05, 2019
To: "Mark A. Turrentine" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1199

RE: Manuscript Number ONG-19-1199

Cost Effectiveness of Latest Recommendations for Group B Streptococcus Screening in the United States

Dear Dr. Turrentine:

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 Aug 26, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a decision analysis model to compare the outcome of GBS early onset disease (EOD) in a hypothetical cohort of births after 35 weeks EGA utilizing either the 2010 CDC GBS guidelines or the recently published protocol screening at 36w0d to 37w6d and re-screening 5 weeks later as needed. The primary outcome was cost-effectiveness based on quality-adjusted life years (QALYs) gained. The newer protocol resulted in a 6.2% increase in QALYs gained, 11.6% fewer neonatal deaths, and a 9.6% reduction in total societal health care expenditures. The new approach was cost-effective with a ratio of $43,205 per neonatal QALY gained. The authors conclude that the new strategy is more cost-effective than past strategies. Ways in which this manuscript could be improved include:

Lines 108-109: Was 100% culture sensitivity chosen to simplify the calculations? Is there utility in calculating based on real life sensitivities? Does it make a difference in the cost-effectiveness gained? I think a more in depth discuss is needed here.

Lines 208-209: Although this is very likely given the data you present, and knowing this was a well-thought out strategy, can you state this as fact? I wonder if softer language here is more appropriate.

Lines 216-218: Are you stating this based on a literature search or that this algorithm was just published. I would clarify.

Lines 230-233: Is there a way to calculate the "cost" of the 1 in a million maternal mortality rate?

Lines 250-253: Type "suggests." Was this model used to formulate the new guidelines? Any insight into how this protocol was decided on.

Reviewer #2: The is a cost effective analysis comparing two GBS screening strategies (2010 vs. 2019 recommendations) to no screening from the perspective of infant-related morbidity and mortality and health care system and societal costs.

- This is a relevant topic given the recent change in guidelines. The methods and assumptions are concise and clearly explained. The study's limitations are well outlined. Tables are clean and useful for understanding the study

- Given the current standard would be use of screening strategy (rather than no screening), did the authors consider comparing the 2019 GBS screening strategy to the 2010 GBS screening strategy as the reference group? While there is precedent in many prior studies to study a single screening strategy to no screening, this aforementioned approach may be

a more accurate reflection of the clinical question

- The authors perform one way sensitivity with tornado diagrams for variability in estimates for probability as well as costs; can the authors also perform two way sensitivity analysis (i.e., Monte Carlo simulation)

- Line 148-149: I believe the authors are referring to case-fatality rate of 0.016 for term neonatal GBS cases with long-term sequelae attributable to GBS infection. Please clarify. The way the sentence reads in context of the prior and following sentence, it can be misleading that this is a measure of quality of life score

- Line 101-105: Would include more detail related to the literature review; including search terms and who determined the USPTF level of evidence categorization

Reviewer #3: Thank you for the opportunity to review and aid in improvement of your manuscript.

The topic is very appropriate for the green journal audience.

The abstract is succinct but may need some clarification on the strategies for GBS screening that are to be examined. (Beautifully described in the methods section but not so clear in the abstract.).

Introduction reads very well and is clear, concise, and relevant.

Description of methodology may benefit from additional information. As it is stated in your limitations, the primary validity of a cost effectiveness model depends on data used to build the model. It would help me as a reader to understand a few more if the assumptions used, such as rate of deliveries over the 35-42 week time frame, where those data were from, rates of penicillin allergy (some rates of allergy were delineated in "Table One"), rates of clindamycin or erythromycin resistance. Please forgive the reviewer if this was detailed but I did not find it readily in the paper or tables.

Could the authors please further describe the value in using GBS Early onset disease and it's treatment as the reference group for comparison? If screening is already accepted and demonstrated as superior then why not compare the standard screening to screen and re-screen method and emphasize the value of infants saved at post dates where screening tools are weakest? Or propose a better window for screening during weeks of gestation ?

Results are well described and succinct. It may strengthen this section to include or to mention if you've included the stated risk of anaphylaxis/ treatment in the treatment arm? Healthcare cost savings are mentioned, but it would also be interesting to know cost comparison with screen and re-screen strategies.

Conclusion paragraphs are well thought out and nicely organized. Like 250, last paragraph may contain a type- "our study suggest" rather than suggests.

Thank you for the opportunity to review your manuscript.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 49-50: Minor point, but since the difference was 4/34, I would suggest rounding to nearest integer %, rather than 0.1%, in deference to the precision allowed by the data.

Tables 1 and 2: The probabilities, costs and their ranges are given with references. What distributions within the ranges were assumed?

I think that the appendices 1 and 2 are important and should be in the main text, if they were being considered as supplemental material.

The incremental cost effectiveness ratios, as shown in Appendix 1 and 2 are actually very narrow but they represent one way sensitivities. If one were to simulate 10,000 repetitions using all the values in the ranges cited, were there any scenarios where the $100,000 per QALY threshold was crossed?

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.

- Seems reasonable to mention that these are the new vs old GBS screening guidelines and to give the dates of publication.

- This is a very precise number of women to be included and as such, I'd like some more clarity about who you excluded. For instance, please state that # excluded are based on population frequency of these events, not actual data about # of women with GBS bacteruria? Could you state that it is women with GBS bacteriuria and prior infant loss. For the livebirths < 35 weeks it makes sense to say "births from 23 to 34" but after that it should be "women with GBS bacteriuria....

- total health care expenditures related to GBS?

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

- was it starting at this range or during this range of weeks of gestation?

- what about the women from 36 0/7 to 37 weeks 6 days who have not yet been screened? Since the screening range is 36 0/7-37 6/7 some women won't get screening done til 36 6/7.

- were they compared to each other and then also to the reference group of no screening or preventive therapy? Lines 87-88 state that you you compared the 2 screening strategies but here on 99 you state you compared to no screening/treatment. Please clarify.

- how long did you assume it took to get GBS results? Not sure what "no delay" means.

- 2019 recommendations? To avoid confusion, instead of "current" please give the year.

- and how many retested?

- therapeutic or prophylactic?

- what do you mean by sentence starting on line 228? Presumably most fetuses exposed to intrapartum antibiotics won't develop a disease so how would exposure to the antibiotics PRECEDE a role in pathogenesis? Also, unclear what you mean by 'preceded a role" to begin with.

- Again, please use the year rather than say "new" or "current" just to avoid ambiguity.

2. It is important in the abstract and paper to be clear that your results reflect estimates of outcomes and costs, not actual costs. As an example, your precis currently reads "New recommendations for Group B Streptococcus screening in the United States result in fewer cases of neonatal death and less societal health care expenditures" and should be edited to read something like "New recommendations for Group B Streptococcus screening in the United States are estimated to result in fewer cases.....". Please edit your paper to reflect this type of wording throughout.

3. 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.

4. 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.

5. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works.

- Lines 106-126: A large portion of the methods is section is very similar to another paper published by the authors. Please try to add more variance.

6. 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.

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

8. 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).

9. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

10. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Current Commentary articles, 250 words. Please provide a word count.

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. 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.

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.

17. Figure 1 may be resubmitted as-is.

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.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

19. If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and
* A point-by-point response to each of the received comments in this letter.

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

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Aug 26, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

August 20, 2019

Editor

Obstetrics & Gynecology

RE: Manuscript ID ONG-19-1199

Dear Editor,

We wish to thank the Editor and Reviewers for their comments. We also want to thank you for the opportunity to do the revisions. The suggestions were fantastic, and the manuscript is stronger from them. We will address each comment individually. We have attached a manuscript version with the Track Changes as well as a "clean version" with the Track Changes accepted for ease of readability. The line numbers refer to the revised Track Changes version. Each author has approved the final form of the revision, and the agreement form signed by each author and submitted with the initial version remains valid. Regarding the inquiry of transparency around peer-review, yes, please publish our point-by-point response letter (OPT-IN). This letter serves as confirmation we have read the Instructions for Authors for this article type (i.e. Original Research). Finally, we have followed in the document the CHEERS guideline for economic evaluations of health interventions.

Best regards,

Mark Turrentine, MD

REVIEWER COMMENTS:

Reviewer #1:

This is a decision analysis model to compare the outcome of GBS early onset disease (EOD) in a hypothetical cohort of births after 35 weeks EGA utilizing either the 2010 CDC GBS guidelines or the recently published protocol screening at 36w0d to 37w6d and re-screening 5 weeks later as needed. The primary outcome was cost-effectiveness based on quality-adjusted life years (QALYs) gained. The newer protocol resulted in a 6.2% increase in QALYs gained, 11.6% fewer neonatal deaths, and a 9.6% reduction in total societal health care expenditures. The new approach was cost-effective with a ratio of $43,205 per neonatal QALY gained. The authors conclude that the new strategy is more cost-effective than past strategies. Ways in which this manuscript could be improved include:

Lines 108-109: Was 100% culture sensitivity chosen to simplify the calculations? Is there utility in calculating based on real life sensitivities? Does it make a difference in the cost-effectiveness gained? I think a more in depth discuss is needed here.

Yes, for simplifying calculations it was assumed the antenatal GBS culture had 100% sensitivity for detecting GBS colonization. We have clarified in the Methods section the assumptions for simplifying calculations that were made, lines 115 to 119. While we think this assumption would

not impact the cost-effectiveness gained, we have added to the Discussion (lines 266 to 274) this as a potential limitation of our analysis and why we think this will not substantially affect the cost effectiveness analysis.

Lines 208-209: Although this is very likely given the data you present, and knowing this was a well-thought out strategy, can you state this as fact? I wonder if softer language here is more appropriate.

We appreciate the Reviewer's interpretation that our analysis may support our statement. However, we do agree this is a decision analysis and not an actual prospective trial looking at these outcomes. We have "softened" the sentence on line 227.

Lines 216-218: Are you stating this based on a literature search or that this algorithm was just published. I would clarify.

This was based on the ACOG algorithm just published. We have modified the sentence (lines 235 to 237) to reflect this for clarification.

Lines 230-233: Is there a way to calculate the "cost" of the 1 in a million maternal mortality rate?

The costs of maternal mortality were incorporated into the analysis (as stated on lines 176 to 178, and Table 2). However, for clarification for readers we added lines 255 to 256.

Lines 250-253: Type "suggests." Was this model used to formulate the new guidelines? Any insight into how this protocol was decided on.

Thank you, we have corrected this typographical error. This model was not utilized to formulate the current ACOG guideline on GBS screening. However, from the explanation in that document on why the culture interval was changed is what inspired this cost-effectiveness analysis. This background was summarized in the Introduction. We have modified lines 80 to 81 to clarify this better.

Reviewer #2:

The is a cost effective analysis comparing two GBS screening strategies (2010 vs. 2019 recommendations) to no screening from the perspective of infant-related morbidity and mortality and health care system and societal costs.

- This is a relevant topic given the recent change in guidelines. The methods and assumptions are concise and clearly explained. The study's limitations are well outlined. Tables are clean and useful for understanding the study

- Given the current standard would be use of screening strategy (rather than no screening), did the authors consider comparing the 2019 GBS screening strategy to the 2010 GBS screening strategy as the reference group? While there is precedent in many prior studies to study a single screening strategy to no screening, this aforementioned approach may be a more accurate reflection of the clinical question

The Reviewer is correct that the current precedent is to use as a "base rate" in cost-effectiveness analysis a "no prevention" comparison. We are slightly confused by the Reviewer's suggestion since 2019 versus 2010 GBS screening strategies were compared directly to each other through the incremental cost-effectiveness ratio. This is described in lines 180 to 183. However, to help with the understanding of the analysis, we did add lines 205 to 209 and 216 to 218 to better drive home this point.

- The authors perform one way sensitivity with tornado diagrams for variability in estimates for probability as well as costs; can the authors also perform two way sensitivity analysis (i.e., Monte Carlo simulation)

We did not perform a two-way sensitivity analysis due to the complexity of performing this on the statistical program utilized (Excel) and that our current input data does not contain any distribution information for any predictors and parameters. In addition, the multivariate association information for us to model the correlation among different input covariates would be difficult to estimate, so it might make the result in our estimates less robust. We consulted a statistician to confirm this. We have added this as a limitation of the study in the Discussion, lines 275 to 286 and added an additional reference discussing this aspect.

- Line 148-149: I believe the authors are referring to case-fatality rate of 0.016 for term neonatal GBS cases with long-term sequelae attributable to GBS infection. Please clarify. The way the sentence reads in context of the prior and following sentence, it can be misleading that this is a measure of quality of life score

This is the proportion of term neonates with long-term sequelae as provided from the medical literature. We have clarified the beginning of this sentence, line 161.

- Line 101-105: Would include more detail related to the literature review; including search terms and who determined the USPTF level of evidence categorization

We have added lines 106 to 115 to address this suggestion.

Reviewer #3:

Thank you for the opportunity to review and aid in improvement of your manuscript.

The topic is very appropriate for the green journal audience.

The abstract is succinct but may need some clarification on the strategies for GBS screening that are to be examined. (Beautifully described in the methods section but not so clear in the abstract.).

Although we are open to suggestions, due to the 300 word limit of the Abstract, it would be difficult to expand the wording of the Methods section in the Abstract.

Introduction reads very well and is clear, concise, and relevant.

Description of methodology may benefit from additional information. As it is stated in your limitations, the primary validity of a cost effectiveness model depends on data used to build the

model. It would help me as a reader to understand a few more if the assumptions used, such as rate of deliveries over the 35-42 week time frame, where those data were from,

We have a detailed description of the source (2017 national birth data) and calculations in lines 147 to 153. We would not know how to make this clearer. This is reflected by Reviewer #2, indicating “the methods and assumptions are concise and clearly explained.” However, this may be clearer from the legend to Figure 1, and we added a reference to this figure on line 152 to help the reader.

rates of penicillin allergy (some rates of allergy were delineated in "Table One"), rates of clindamycin or erythromycin resistance. Please forgive the reviewer if this was detailed but I did not find it readily in the paper or tables.

This is explained in detail in lines 133 to 141 and Table 1. The assumptions from Table 1 explain how patients would be treated, and the literature referenced for these assumptions. Erythromycin is no longer recommended as an antibiotic prophylactic agent.

Could the authors please further describe the value in using GBS Early onset disease and it's treatment as the reference group for comparison? If screening is already accepted and demonstrated as superior then why not compare the standard screening to screen and re-screen method and emphasize the value of infants saved at post dates where screening tools are weakest? Or propose a better window for screening during weeks of gestation ?

The purpose of screening for antenatal GBS screening in the U.S. is to prevent GBS EOD. This has been recommended since 2002 by the CDC. The typical standard for cost-effectiveness analysis is to use a reference group of no treatment. The incremental cost-effectiveness ratio does compare the “new” (2019) to the “old” (2010) strategy. However, we have added lines 216 to 218 to make this point stronger. The purpose of this cost-effectiveness analysis was to compare 2019 to the 2010 strategy. While it would be an excellent analysis to calculate which gestational age is optimal to screen for antenatal GBS, this would have to be left for another manuscript.

Results are well described and succinct. It may strengthen this section to include or to mention if you've included the stated risk of anaphylaxis/ treatment in the treatment arm? Healthcare cost savings are mentioned, but it would also be interesting to know cost comparison with screen and re-screen strategies.

The treatment of maternal anaphylaxis and the economic value of maternal death were included in the cost analysis. This was described in lines 176 to 178. However, to make this point clearer, we did add lines 255 to 256 in the Discussion.

Conclusion paragraphs are well thought out and nicely organized. Like 250, last paragraph may contain a type- "our study suggest" rather than suggests.

Thank you, this has been corrected.

Thank you for the opportunity to review your manuscript.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 49-50: Minor point, but since the difference was 4/34, I would suggest rounding to nearest integer %, rather than 0.1%, in deference to the precision allowed by the data.

This has been changed in both the Abstract and the Results, thank you for the suggestion.

Tables 1 and 2: The probabilities, costs and their ranges are given with references. What distributions within the ranges were assumed?

Thank you for pointing this out. We have added wording to the legends of Tables 1 and 2 to clarify this.

I think that the appendices 1 and 2 are important and should be in the main text, if they were being considered as supplemental material.

Thank you for this suggestion. We were trying to stay within the word limit. However, we will add these back as a new Figure 2 and Figure 3. The figure legends have been renamed.

The incremental cost effectiveness ratios, as shown in Appendix 1 and 2 are actually very narrow but they represent one way sensitivities. If one were to simulate 10,000 repetitions using all the values in the ranges cited, were there any scenarios where the $100,000 per QALY threshold was crossed?

We did not perform a two-way sensitivity analysis due to the complexity of performing this on the statistical program utilized (Excel) and that our current input data does not contain any distribution information for any predictors and parameters. In addition, the multivariate association information for us to model the correlation among different input covariates would be difficult to estimate, so it might make the result in our estimates less robust. We consulted a statistician to confirm this. We have added this as a limitation of the study in the Discussion, lines 275 to 286 and added an additional reference discussing this aspect.

EDITOR COMMENTS:

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- Seems reasonable to mention that these are the new vs old GBS screening guidelines and to give the dates of publication.

This has been added to the Abstract as suggested and is on lines 35 to 36.

- This is a very precise number of women to be included and as such, I'd like some more clarity about who you excluded. For instance, please state that # excluded are based on population frequency of these events, not actual data about # of women with GBS bacteruria? Could you state that it is women with GBS bacteriuria and prior infant loss. For the livebirths < 35 weeks it makes sense to say "births from 23 to 34" but after that it should be "women with GBS bacteriuria....

Thank you for pointing this out. We have made this suggestion both in the Abstract (lines 41 to 43) and the Methods section (lines 148 to 150). This is only the proportion of women with a previous infant treated for GBS disease, not infant loss. The data available for that statistic (infant with GBS disease) does not split the outcomes in that fashion. Just to note, these suggestions will put the Abstract slightly over the 300 word limit (303 words).

- total health care expenditures related to GBS?

We have made this suggested change in both the Abstract (lines 52 to 53) and the Results (lines 207 to 208).

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

We have carefully reviewed the guidelines to the authors for Original Research submissions. While our Introduction is 350 words, the complex nature of describing the background for this cost-effectiveness analysis necessitated this length. In addition, while the Discussion was expanded to 900 words due to suggestions from the Reviewers. The overall total manuscript word count (approximately 4725 words) and references (46 total) is still well within the limits recommended in the Instructions to the Authors.

- was it starting at this range or during this range of weeks of gestation?

Thank you for noting this, the correction was made on line 64.

- what about the women from 36 0/7 to 37 weeks 6 days who have not yet been screened? Since the screening range is 36 0/7-37 6/7 some women won't get screening done till 36 6/7.

Any women that presented before 37 0/7 weeks in labor would receive default intrapartum antibiotic prophylaxis. We had to make the assumption that this would be similar between the two groups since calculating the number in both strategies would be difficult, and the impact would be similar. The available literature for the 2010 strategy does indicate that 95% of women present in labor with GBS screening results being known.

- were they compared to each other and then also to the reference group of no screening or preventive therapy? Lines 87-88 state that you you compared the 2 screening strategies but here on 99 you state you compared to no screening/treatment. Please clarify.

We have rearranged a sentence (now lines 89 to 91) to clarify this point. Guidelines for cost effectiveness analysis in health and medicine recommend a reference case as a set of standard methodological practices that all cost-effectiveness analyses should follow to improve comparability. We chose as our reference case a no-treatment group (as in past cost effectiveness analysis on this topic). We then compared the incremental cost-effectiveness ratio between the two strategies (2019 versus 2010).

- how long did you assume it took to get GBS results? Not sure what "no delay" means.

We have clarified this in lines 116 to 117.

- 2019 recommendations? To avoid confusion, instead of "current" please give the year.

We have gone through the document and corrected reference to the year of screening for clarity.

- and how many retested?

The proportional increase in screening has been added to line 205.

- therapeutic or prophylactic?

Thank you for catching this. This should be prophylactic. We have corrected this on line 243.

- what do you mean by sentence starting on line 228? Presumably most fetuses exposed to intrapartum antibiotics won't develop a disease so how would exposure to the antibiotics PRECEDE a role in pathogenesis? Also, unclear what you mean by 'preceded a role" to begin with.

We have clarified this sentence and is now lines 248 to 251.

- Again, please use the year rather than say "new" or "current" just to avoid ambiguity.

We have gone through the document and clarified the year of the strategies.

2. It is important in the abstract and paper to be clear that your results reflect estimates of outcomes and costs, not actual costs. As an example, your precis currently reads "New recommendations for Group B Streptococcus screening in the United States result in fewer cases of neonatal death and less societal health care expenditures" and should be edited to read something like "New recommendations for Group B Streptococcus screening in the United States are estimated to result in fewer cases.....". Please edit your paper to reflect this type of wording throughout.

We have made this suggested edit in the Precis (lines 32 to 33) and throughout the document.

3. 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 have chosen to OPT-IN.

4. 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.

There are no changes in the author's disclosures.

5. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works.

- Lines 106-126: A large portion of the methods is section is very similar to another paper published by the authors. Please try to add more variance.

Sorry for this, it is sometimes difficult being the original author that wrote a previous publication that has a very similar topic to not overlap in phrases, particularly in the Materials and Methods. More variance has been added in lines 106 to 132.

6. 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 are compliant with the reVITALize definitions.

7. 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, tables, boxes, figure legends, and print appendixes) but exclude references.

Our total word count is 4725. While our total page number will exceed 22, this is due to the Statistical Editor's suggestion of including the supplemental material as part of the manuscript. If the page length is too long, we are willing to relabel Figure 2 and Figure 3 as a supplemental material with a hyperlink.

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines: These guidelines have been followed.

* 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).

9. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

Our Precis is compliant with this recommendation.

10. 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. The Abstract has been checked carefully and matches the body of the text.

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.

This has been done on the Title page.

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.

We are compliant with this recommendation.

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.

We did not use the virgule symbol.

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.

This does not apply to this type of article.

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.

We have added lines 210 to 212 to address this. The outcomes of the comparison are 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%").

We have standardized the presentation of the data as recommended by the Statistical Editor.

14. 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.

We have updated the checklist for our manuscript.

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.

We have done this in the checklist.

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.

Our cover letter indicates that CHEERS guidelines were followed.

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 have confirmed our Tables are compliant with the journal's checklist.

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 are citing the current version of the Committee Opinion.

17. Figure 1 may be resubmitted as-is.

Thank you. We thought this figure was pretty cool to.

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.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

19. If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following: Our cover letter is compliant with both of these points.

* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf), and

* A point-by-point response to each of the received comments in this letter.