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: Mar 12, 2021
To: "Rebecca Feldman Hamm" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-350

RE: Manuscript Number ONG-21-350

Racially inequitable definitions of anemia perpetuate disparities in maternal outcomes: time to change

Dear Dr. Hamm:

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 as a Research Letter.

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 Apr 02, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Thank you for the opportunity to review your work. I appreciated very much this work as a clinician and educator.

1. Lines 215-226: Very helpful to help reader understand where this work falls into what's already been published. Truly hidden in plain sight.
2. Lines 243-247. Very helpful to see that your work made a difference in your own institution. Instead of waiting for ACOG to change guidelines—act local, think global! This maybe beyond scope here, but when reading this I was wondering if authors would want to comment more generally what researchers like you need to be thinking about to make a difference in dismantling current structures. You were clearly successful, but there is so much more work to do.
3. Lines 58-59. When reading this in the intro before I got to the discussion part, I was wondering how IOM arrived at those cut off levels. Now of course it seems obvious that AA women are more anemic due to higher disease/iron def burden, but how was this not even considered at the time? What lead IOM to frame it this way? Was a precedent or some other clinical consideration they had in mind? Were they considering hemoglobinopathies for example as potential confounders (I am just guessing here)? Given that complications increase with HB <11 (ref 7-8), was this because this data became avail after the guidelines, and this is something that was not updated? Or is the problem here that curves were developed outside of pregnancy? Please add IOM document as a reference here.
4. Lines 71-74. Given that this dataset came from another study as secondary analysis, please quote original study and briefly explain what it did. Helps to eval for shortfalls of retrospective data analysis
5. Line 79. Is it possible to compare demographics of excluded women to those who were included?
6. Lines 98-105. How were secondary outcomes chosen? Were they associated with complications of anemia in pregnancy?
7. Power calculation.
a. Given that you used a dataset from another study which makes this a post-hoc analysis by default, then it needs to be in results/discussion section and acknowledged as such. By definition this would not be a priori, but rather a posthoc sample size calculation. It is still of interest but needs to be clear to the reader.
b. I was not able to follow how you came up with 35% vs. 45% rate of anemia (line 111) and 5% vs. 10% transfusion rate (line 112). It seems ok but to avoid confusion it would help to quite sources of such estimate in this sentence.
8. Study was single site, but N was large and 80% of women identified as Black.
9. Study conclusions supported by data.
10. I was also thinking about how race and anemia played out outside of US. Are other countries following guidelines similar to ACOG? I found a few references below—any of those relevant?

Jans SM, Daemers DO, de Vos R, Lagro-Jansen AL. Are pregnant women of non-Northern European descent more anaemic

than women of Northern European descent? A study into the prevalence of anaemia in pregnant women in Amsterdam. Midwifery. 2009 Dec;25(6):766-73. doi: 10.1016/j.midw.2008.02.001. Epub 2008 Apr 18. PMID: 18395309.

Elion-Gerritzen WE, Giordano PC, Haak HL. De standaard 'Anemie in de eerstelijns verloskundige praktijk' van de Koninklijke Nederlandse Organisatie van Verloskundigen (KNOV): risico voor het niet onderkennen van ijzergebrek en hemoglobinopathie [The 'Anemia in the midwife practice' standard issued by the Royal Dutch Organisation of Midwives: a risk of not recognizing iron deficiency and hemoglobinopathy]. Ned Tijdschr Geneeskd. 2002 Mar 9;146(10):457-9. Dutch. PMID: 11913108.

Tran K, McCormack S. Screening and Treatment of Obstetric Anemia: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines. Canadian Agency for Drugs and Technologies in Health, Ottawa (ON); 2019.

Reviewer #2:

The authors have undertaken an analysis of the association between Black race, anemia and maternal morbidity associated with transfusions via a single-institution, prospective cohort study that consisted of a majority of women who identify as Black. They specifically sought to assess the ways in which defining anemia differently for Black and non-Black women may contribute to racial inequity in transfusion-related maternal morbidity. As many specialties reconsider the use of race-based diagnostics, labs, and predictive models, this is an important question to consider.

Overall Comments:
- Though I understand and frankly agree with the authors' enthusiasm for altering race-based definitions such as this one, I recommend the authors undertake a careful reading for editorializing in areas of the manuscript in which speculative comments, or statements that are logical extensions of (but not directly support by) the data are generally best avoided.
- Since no difference in transfusion was demonstrated in the Hgb 10.2-11.0 stratum (untreated Black women compared to ostensibly treated non-Black women), the repeated statements in the paper that treating and correcting anemia in this group will "significantly decrease [disparities in] maternal morbidity" are unsupported by these data. This may be due to sample size given the lower transfusion rates (2-3%) in this stratum, or due to bias in offering transfusions, but in any case, no disparity in maternal morbidity as defined by transfusion is found. This is a logical extension of the findings, but not demonstrated by the analysis.
- I would encourage the authors to consider using the STROBE guidelines for reporting observational studies in any revision and to include the checklist for STROBE guidelines with resubmissions. (https://www.equator-network.org/reporting-guidelines/strobe/)

Specific comments:
1) Title & Précis: The phrase "time to change" makes this reviewer feel like what follows will be a call to action or commentary piece. There is excellent data in this analysis/manuscript, and I would encourage the authors to choose a descriptive, declarative title that highlights their findings and/or objective. The same comments apply to the précis.

2) Abstract:
- Line 24: The authors state in the body of the manuscript that this is secondary analysis of a prospective cohort study. Please clarify in the abstract
- Line 31: Since the non-treatment of Black women for antepartum Hb 10.2-11.0 was protocol driven by the authors' institution (per the methods), it may be worth stating at the end of the sentence on Line 31 that ends "…and were not treated per institutional protocol."
- Line 32: The phrase "as a result" seems to suggest that the only reason for Black women with lower hemoglobin level antepartum to be more likely than non-Black women to present for delivery with a hemoglobin <11 is the non-treatment of their anemia. While this is likely a large contributor to this finding, unless the authors have evidence that non-Black women with Hb 10.2-11.0 were treated and adhered to their treatment, this is an association rather than causation. I would recommend leaving out the leading phrase "As a result" and simply state the result of Black women being more likely to present for delivery with anemia.
- Lines 41-42: The authors demonstrate that Black women with Hgb between 10.2-11.0 who would not have been offered iron supplementation per protocol are nearly twice as likely to present to labor and delivery with a hemoglobin <11; however, there is no difference in transfusion rate between Black and non-Black individuals in this stratum, suggesting that the increased anemia is not associated with increased maternal transfusion morbidity, at least in this cohort.
- Lines 42-43: Would consider eliminating the last sentence of the conclusion from the abstract

3) Introduction
- Lines 48-49: This short paragraph could benefit from a brief statement of the extant data connecting the successful treatment of antepartum anemia to reduced maternal and neonatal morbidity. Though the association of anemia at the time of delivery with morbidity is well-documented, and the link between appropriate antepartum treatment and decreased

morbidity is intuitive, it would be worth bolstering that intuition with available data.
- I would recommend referencing the 2019 article by Smith et al (PMID 31764734) in the first paragraph to improve the comparability of data on anemia in pregnancy to a US population.

4) Objective
- Appropriately stated and clear

5) Methods
- The authors state that this a secondary analysis of a prospective cohort study, suggesting that the original study was not aimed to study the objective under consideration in this analysis. Therefore, some details of the primary study would help the reader understand the scope and quality of the data upon which this study is based. The original study is not cited, and basic information such as a brief summary of inclusion/exclusion criteria and original objective of the primary study should be included in 1-2 sentences here. Without this information, it is not possible to determine the quality of data capture for the cohort.
- Including the details of the original study would also help to clarify the overall inclusion/exclusion criteria for this study. For instance, was the original cohort restricted to women who delivered at the University of Pennsylvania? Or is this a restriction of the secondary analysis?

6) Results and Tables
- Throughout: I would recommend using the language of "associated with" for this observational study. E.g. "In adjusted models, an antepartum hemoglobin nadir between 10.2 and 11.0 among Black women was associated with a 65% increase in the odds of presenting to labor and delivery with a hemoglobin <11"

- Lines 166-169/Table 2:
  - In addition to the overall transfusion rate in each stratum (as is currently provided in Table 2), is it possible to also provide transfusion rate by categories of hgb at admission to labor and delivery (hgb >11 or <11)?
  - Was the OR for transfusion for all individuals with hemoglobin <11 an adjusted or unadjusted analysis? If adjusted, which variables were included?
  - Perhaps the transfusion data might be better presented as a separate table to help the reader process the stratified and non-stratified transfusion analysis. The authors have done a good job of not comparing results from one stratum to another which is often a pitfall of stratified analyses. However, by presenting an un-stratified analysis in the same paragraph as the stratified results, it becomes a little muddied, especially without a table giving the n, outcome incidence, etc for the unstratified analysis.
  - A table structured to show differences by race would be particularly helpful when the authors construct arguments about anemia treatment and decreased maternal morbidity
  - Please note that it is important to describe in the methods that, in addition to the stratified analysis by antepartum hgb nadir, a non-stratified analysis of transfusion outcomes was performed and why (to preserve sample size, I presume).

- Lines 175-184/Table 3:
    - The p value for gestational age in weeks appears to round up to 0.05, and in conjunction with the fact that the difference is clinically insignificant, this is not a finding I would highlight in the results.
    - Why is an adjusted odds ratio given for preterm birth but not birthweight since both were significantly different in the mild anemia stratum?
    - If an adjusted logistic regression is performed for birthweight, I would ask the authors to consider including gestational age as a covariate, as I suspect the increased incidence of PTB in this group may skew the data toward lower birthweights.

4) Discussion
- Lines 187-194. I would recommend restructuring this paragraph such that the results associated with the primary objective are re-stated first. I would move the non-stratified transfusion analysis result to a second paragraph (see below, Line 194).
- Line 188-191. I would recommend stating this a bit differently; as it is currently written, it appears to attribute all findings to the supplementation protocol.
- Line 194 - While the authors have demonstrated that hemoglobin<11 for the entire cohort is associated with increased odds of transfusion, this was not demonstrated in the stratum of Black women with antepartum hemoglobin 10.2-11.0. I would recommend that the authors take a paragraph to fully flesh out the discrepancy (sample-size based, I presume) in these stratified and non-stratified results and carefully describe the relationships between the two.
- Lines 204-213 - I would ask the authors to reconsider this paragraph; spending a substantial argument and real-estate on an unadjusted difference in birthweights which may be driven by increased preterm birth in the group of Black women with antepartum hemoglobin 10.2-11.0 feels a bit out of place. If the authors wish to pursue this line of hypothesis generating from their secondary outcomes, I would even more strongly encourage them to perform and adjusted logistic analysis of the birthweight data which includes gestational age as a covariate. In addition, I would recommend that paragraphs based on the secondary analyses and outcomes are written from a standpoint of hypothesis generation; "these data suggest" or "raise the possibility of "
- Consider including in the limitations that the lower transfusion rate among the individuals in mildly anemic stratum limits the authors' ability to directly connect increased rates of hgb <11 among the Black women in this group to an increased risk of transfusion among the Black women in this group.

- Overall: There is a fundamental difficulty with the authors switching between statements that there is no difference in transfusion rates and stating that treating anemia will decrease disparities in maternal morbidity. I grasp the points they are trying to make, but some very careful delineation of the results and more clarity in the writing of the discussion will help even the casual reader to draw the connections more easily and clearly.

Reviewer #3:

This is a secondary analysis of a prospective cohort study of women with antepartum Hg <11 g/dL who delivered over a one year period at a single institution. Women were stratified by race and Hg severity to determine if race-based anemia definitions influenced outcome. The authors found a similar transfusion rate among Black and non-Black women who presented with a Hg <11 and found that all women with a Hg <11 at delivery were at higher risk for transfusion than their non-anemic counterparts. This leads the authors to conclude that using a singular, non-race based anemia threshold for iron supplementation may decrease transfusion risk in Black women.

While I certainly applaud the authors for their work and wholeheartedly agree that we must work towards reducing racially-based biologic explanations to justify maternal disparities, I do have some concerns about the approach and conclusion of this manuscript. First and foremost, as the authors point out, their conclusions are largely based on an assumption that the clinicians treating women in this cohort strictly adhere to race-based definitions of anemia when deciding to recommend additional iron supplementation to patients. In my own practice and experience, there is a large amount of variation in what threshold and risk factors clinicians use to make this decision. Additionally, there is significant variation in prenatal vitamin iron content and adherence that further muddies these distinctions. Secondly, the authors are the authors really contending that anemia should be defined differently or rather that similar treatment thresholds should be applied regardless of race. The definition of anemia is, as described in the ACOG bulletin, determined by H/H less than the 5th percentile for a "healthy reference population". From my brief reading of the literature, it does appear that there may indeed be ancestral (~racial) differences in anemia prevalence because of variation in carrier status for hemoglobinopathies such as alpha thal and sickle trait. In that case, it is harder to argue that it is not appropriate from a general perspective to have different reference standards for anemia in Black and non-Black women. Therefore, the manuscript should make a consistent and clear distinction between recommending a change in the definition of anemia vs. recommending a homogenous treatment threshold that is likely to benefit all women. While this is clear in some areas of the manuscript, I see some confounding of the issue as well.

Title: I am not sure that "inequitable" is accurate here. Are the definitions really "unfair". I don't think that is necessarily true based on the reasoning above. Perhaps something more like racially-based.
Abstract: I don't think line 27 is accurate based on what was said in the limitations. This was presumed, but not confirmed. This needs to clear.
Intro: Overall, this is a comprehensive into. For the statements in line 61-65, is there any data to support that clinicians are utilizing these standards to differentially treat patients? This is important because there are other social determinant and co-variates that may confound treatment efficacy, compliance, etc.
Methods: Did the institution have a treatment algorithm for anemia that utilized racial definitions? Or where did the institutional "recommendation" referenced here originate from? How do the authors know that individual clinicians were not recommending iron even for women with Hg 10.2-11? In the limitations, anemia treatment sounds much more like an assumed approach rather than any sort of promoted or proscribed algorithm, but perhaps I am not understanding this correctly.
Results: Did the authors further stratify increasing Hg concentrations to see if there was any clearly optimal threshold? While I realize 11 was used because of the anemia definition, I am curious if there is an optimal goal that was inferred or suggested by the data.
Discussion:
- In line 204, are the authors suggesting that iron supplementation for mild anemia improves fetal growth and/or increases birth weight? Is there data to support his inference? It seems like there is a significant number of potential cofounders here.
- Do the authors have any data, even a survey, to give some idea of treatment approach for anemia? In other words, is there any support differential treatment by race?
- Again, the final paragraph should emphasize the treatment threshold rather than redefining anemia overall.
Table 3: Why are GA at delivery and birthweight not adjusted in the table since these are both significant in univariate analysis?

STATISTICS EDITOR COMMENTS:

Lines 107-113: There are actually two primary hypotheses being tested, so the alpha should be adjusted to .025, not .05, which will lower the power, but it would remain > 80%. Also, how were the rates of 10% difference in rates of Hb < 11 g/dL or of 5% difference in rates of transfusion chosen? Were those thresholds meant to be the minimum clinically important differences? Also, since this was a secondary analysis of a prospective cohort study (lines 71-72), the counts and proportion of Black vs non-Black patients was known. Therefore, those numbers should have been used to assess power, which yields different results than those cited. For example, there were 1080 Black and 1369-1080, or 289 non-Black participants, so the required difference in Hb < 11 g/dL (35% non-Black vs 45% Black) yields power = 0.87 for alpha = .05 and power = .80 for alpha = .025. For the transfusion rates of 10% vs 5%, the power corresponding to alpha = .05 is .79 (, while the power corresponding to alpha = .025 is only 0.69. In other words, the study was actually underpowered to evaluate the stated difference in transfusion rates.

lines 154-157: The adjusted odds was 1.65, but that means that the odds were 65% higher, not that those women were "65% more likely to present ...". That is, odds is not the same as risk or as rate.

Table 2: The counts for transfusion, for the antepartum Hb 10.2-11.0 groups, were low, and in fact too few to allow for multivariable adjustment with 3 variables. That is, the model is likely over fitted. The primary outcome was framed in terms of the entire cohort, while this Table shows the breakdown by strata of antepartum Hb. These subsets are not the primary outcome, nor were they the basis for the sample size/power calculation. These are all secondary outcomes, the primary outcome difference in rates of andtpartum Hb < 11.0 were 580/1080 (53%) vs 106/289 (36%). Since that is how the question was framed, that is how is should be cited as the primary outcome. The subsets are secondary outcomes. Similarly, for the rates of transfusion etc.

EDITOR COMMENTS:

Thank you very much for submitting this important work to Obstetrics and Gynecology. The editors share the same concerns as the reviewers in that the manuscript makes many inferences beyond what can be stated with the available data. The primary research question is valuable, but the results seem to get lost in some of the editorial comments that are unrelated to the research. We hope that you will consider refocusing specifically on the research question, results of the analysis, and interpretation of the results in the format of a research letter. If you elect to submit a revision, please see the author instructions for specifications of the Research Letter format and format the revision appropriately. When the editors discussed this manuscript on our conference call, we felt that the science could be succinctly presented in this format.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my point-by-point response letter.
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2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

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

3. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

4. All submissions that are considered for potential publication are run through CrossCheck for originality.

Please disclose any virtual, oral, or in-person presentations.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions and the gynecology data definitions at https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

7. 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.

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. 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 limit for Original Research articles is 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. ACOG is moving toward discontinuing the use of "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

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. 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.

15. Please review examples of our current reference style at http://ong.editorialmanager.com (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, 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 at the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top).

16. 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.

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

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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. Do not omit your responses to the Editorial Office or Editors' comments.

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 Apr 02, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Torri D. Metz, MD

Associate Editor, Obstetrics

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

March 18, 2021

Rebecca F. Hamm, MD MSCE
Pennsylvania Hospital
800 Spruce Street, 2 Pine East
Philadelphia, PA 19107

Dear *Obstetrics & Gynecology* Editors:

The following reviews were noted for our manuscript entitled: "The negative impact of a race-based definition of antepartum anemia". We have addressed the reviewers' comments and revised the manuscript accordingly. We are grateful for the comments which have made the paper stronger and have reformatted the paper into a Research Letter. Line numbers refer to the clean version of our manuscript. We believe that this research is of significant interest to your readership. Thank you for your consideration of our work.

Reviewer #1 Comment #1:

A. Thank you for the opportunity to review your work. I appreciated very much this work as a clinician and educator. Lines 215-226: Very helpful to help reader understand where this work falls into what's already been published. Truly hidden in plain sight.
Lines 243-247. Very helpful to see that your work made a difference in your own institution. Instead of waiting for ACOG to change guidelines—act local, think global! This maybe beyond scope here, but when reading this I was wondering if authors would want to comment more generally what researchers like you need to be thinking about to make a difference in dismantling current structures. You were clearly successful, but there is so much more work to do.
B. Thank you for these thoughtful comments. Unfortunately, given the constraints of the Research Letter format, we were unable to address this addition to the text.
C. No changes were made.
D. NA

Reviewer #1 Comment #2:

A. Lines 58-59. When reading this in the intro before I got to the discussion part, I was wondering how IOM arrived at those cut off levels. Now of course it seems obvious that AA women are more anemic due to higher disease/iron def burden, but how was this not even considered at the time? What lead IOM to frame it this way? Was a precedent or some other clinical consideration they had in mind? Were they considering hemoglobinopathies for example as potential confounders (I am just guessing here)? Given that complications increase with HB <11 (ref 7-8), was this because this data became avail after the guidelines, and this is something that was not updated? Or is the problem here that curves were developed outside of pregnancy? Please add IOM document as a reference here.
B. Thank you for these comments. The IOM guidelines utilize standardized curves to define anemia. The reference for the IOM guidelines has been added.
C. See Reference 2.
D. Institute of Medicine (US). Iron deficiency anemia: recommended guidelines for the prevention, detection, and management among U.S. children and women of childbearing age. Washington, DC: National Academy Press;1993. (Level III)

Reviewer #1 Comment #3:

A. Lines 71-74. Given that this dataset came from another study as secondary analysis, please quote original study and briefly explain what it did. Helps to eval for shortfalls of retrospective data analysis

B. Thank you for this comment. We have now briefly reviewed the context of the parent study in the Methods. This data is yet unpublished.

C. Lines 30-32.

D. "We performed a post-hoc secondary analysis of a prospective cohort study that evaluated trends in intravenous iron utilization among women with an antepartum Hb<11g/dL and without hemoglobinopathy delivering at the Hospital of the University of Pennsylvania from 2018-2019."

Reviewer #1 Comment #4:

A. Line 79. Is it possible to compare demographics of excluded women to those who were included?

B. Thank you for this question. While we are unable to include this information in the manuscript to the space constraints of the Research Letter, the demographics of women excluded given they did not have a recorded self-identified race did not differ from the included cohort in any significant ways.

C. No changes have been made.

D. NA

Reviewer #1 Comment #5:

A. Lines 98-105. How were secondary outcomes chosen? Were they associated with complications of anemia in pregnancy?

B. Thank you for these questions. We did select these outcomes as known complications of anemia. However, they have been removed from the manuscript given the space constraints of the Research Letter format.

C. Secondary outcomes removed.

D. Changes made throughout.

Reviewer #1 Comment #6:

A. Power calculation. Given that you used a dataset from another study which makes this a post-hoc analysis by default, then it needs to be in results/discussion section and acknowledged as such. By definition this would not be a priori, but rather a posthoc sample size calculation. It is still of interest but needs to be clear to the reader. I was not able to follow how you came up with 35% vs. 45% rate of anemia (line 111) and 5% vs. 10% transfusion rate (line 112). It seems ok but to avoid confusion it would help to quite sources of such estimate in this sentence.

B. Thank you for these comments. The post-hoc nature of the analysis has been clarified in the methods. Due to the space limitations of the Research Letter, the post hoc power analysis has been removed.

C. Lines 30-32.

D. "We performed a post-hoc secondary analysis of a prospective cohort study that evaluated trends in intravenous iron utilization among women with an antepartum Hb<11g/dL and without hemoglobinopathy delivering at the Hospital of the University of Pennsylvania from 2018-2019."

Reviewer #1 Comment #7:

A. Study was single site, but N was large and 80% of women identified as Black. Study conclusions supported by data. I was also thinking about how race and anemia played out outside of US. Are other countries following guidelines similar to ACOG? I found a few references below—any of those relevant?

Jans SM, Daemers DO, de Vos R, Lagro-Jansen AL. Are pregnant women of non-Northern European descent more anaemic than women of Northern European descent? A study into the prevalence of anaemia in pregnant women in Amsterdam. Midwifery. 2009 Dec;25(6):766-73. doi: 10.1016/j.midw.2008.02.001. Epub 2008 Apr 18. PMID: 18395309.

Elion-Gerritzen WE, Giordano PC, Haak HL. De standaard 'Anemie in de eerstelijns verloskundige praktijk' van de Koninklijke Nederlandse Organisatie van Verloskundigen (KNOV): risico voor het niet onderkennen van ijzergebrek en hemoglobinopathie [The 'Anemia in the midwife practice' standard issued by the Royal Dutch Organisation of Midwives: a risk of not recognizing iron deficiency and hemoglobinopathy]. Ned Tijdschr Geneeskd. 2002 Mar 9;146(10):457-9. Dutch. PMID: 11913108.

Tran K, McCormack S. Screening and Treatment of Obstetric Anemia: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines. Canadian Agency for Drugs and Technologies in Health, Ottawa (ON); 2019.

B. Thank you so much for this thoughtful question. We are unaware of any race-based anemia in pregnancy guidelines outside of the US.

C. No changes were made.

D. NA

Reviewer #2 Comment #1:

A. The authors have undertaken an analysis of the association between Black race, anemia and maternal morbidity associated with transfusions via a single-institution, prospective cohort study that consisted of a majority of women who identify as Black. They specifically sought to assess the ways in which defining anemia differently for Black and non-Black women may contribute to racial inequity in transfusion-related maternal morbidity. As many specialties reconsider the use of race-based diagnostics, labs, and predictive models, this is an important question to consider. Since no difference in transfusion was demonstrated in the Hgb 10.2-11.0 stratum (untreated Black women compared to ostensibly treated non-Black women), the repeated statements in the paper that treating and correcting anemia in this group will "significantly decrease [disparities in] maternal morbidity" are unsupported by these data. This may be due to sample size given the lower transfusion rates (2-3%) in this stratum, or due to bias in offering transfusions, but in any case, no disparity in maternal morbidity as defined by transfusion is found. This is a logical extension of the findings, but not demonstrated by the analysis. Though I understand and frankly agree with the authors' enthusiasm for altering race-based definitions such as this one, I recommend the authors undertake a careful reading for editorializing in areas of the manuscript in which speculative comments, or statements that are logical extensions of (but not directly support by) the data are generally best avoided.

B. Thank you for this comment. We have removed speculative comments and statements regarding unfounded extensions from the data.

C. Changes made throughout.
D. Changes made throughout.

Reviewer #2 Comment #2:

A. I would encourage the authors to consider using the STROBE guidelines for reporting observational studies in any revision and to include the checklist for STROBE guidelines with resubmissions. (https://www.equator-network.org/reporting-guidelines/strobe/)
B. Thank you for this comment. STROBE reporting guidelines were used to guide this resubmission.
C. No changes were made to the document.
D. NA

Reviewer #2 Comment #3:

A. Title & Précis: The phrase "time to change" makes this reviewer feel like what follows will be a call to action or commentary piece. There is excellent data in this analysis/manuscript, and I would encourage the authors to choose a descriptive, declarative title that highlights their findings and/or objective. The same comments apply to the précis.
B. Thank you for this comment. We agree, and have changed the title in response to this comment. The precis has been removed given the Research Letter resubmission format.
C. Line 1.
D. “The negative impact of a race-based definition of antepartum anemia”

Reviewer #2 Comment #4:

A. Abstract:
- Line 24: The authors state in the body of the manuscript that this is secondary analysis of a prospective cohort study. Please clarify in the abstract
- Line 31: Since the non-treatment of Black women for antepartum Hb 10.2-11.0 was protocol driven by the authors' institution (per the methods), it may be worth stating at the end of the sentence on Line 31 that ends "…and were not treated per institutional protocol."
- Line 32: The phrase "as a result" seems to suggest that the only reason for Black women with lower hemoglobin level antepartum to be more likely than non-Black women to present for delivery with a hemoglobin <11 is the non-treatment of their anemia. While this is likely a large contributor to this finding, unless the authors have evidence that non-Black women with Hb 10.2-11.0 were treated and adhered to their treatment, this is an association rather than causation. I would recommend leaving out the leading phrase "As a result" and simply state the result of Black women being more likely to present for delivery with anemia.
- Lines 41-42: The authors demonstrate that Black women with Hgb between 10.2-11.0 who would not have been offered iron supplementation per protocol are nearly twice as likely to present to labor and delivery with a hemoglobin <11; however, there is no difference in transfusion rate between Black and non-Black individuals in this stratum, suggesting that the increased anemia is not associated with increased maternal transfusion morbidity, at least in this cohort.
- Lines 42-43: Would consider eliminating the last sentence of the conclusion from the abstract
B. Thank you for these comments. The abstract has been removed given the Research Letter resubmission format.
C. Abstract has been removed.
D. NA

Reviewer #2 Comment #5:

A. Introduction

- Lines 48-49: This short paragraph could benefit from a brief statement of the extant data connecting the successful treatment of antepartum anemia to reduced maternal and neonatal morbidity. Though the association of anemia at the time of delivery with morbidity is well-documented, and the link between appropriate antepartum treatment and decreased morbidity is intuitive, it would be worth bolstering that intuition with available data. I would recommend referencing the 2019 article by Smith et al (PMID 31764734) in the first paragraph to improve the comparability of data on anemia in pregnancy to a US population.

B. Thank you for these comments. Due to the word constraints of the Research Letter format, we were unable to keep the first paragraph in the resubmitted version.

C. The first paragraph has been removed.

D. NA

Reviewer #2 Comment #5:

A. Objective

- Appropriately stated and clear

Methods

- The authors state that this a secondary analysis of a prospective cohort study, suggesting that the original study was not aimed to study the objective under consideration in this analysis. Therefore, some details of the primary study would help the reader understand the scope and quality of the data upon which this study is based. The original study is not cited, and basic information such as a brief summary of inclusion/exclusion criteria and original objective of the primary study should be included in 1-2 sentences here. Without this information, it is not possible to determine the quality of data capture for the cohort.
- Including the details of the original study would also help to clarify the overall inclusion/exclusion criteria for this study. For instance, was the original cohort restricted to women who delivered at the University of Pennsylvania? Or is this a restriction of the secondary analysis?

B. Thank you for these questions. We have expanded upon the description of the parent cohort study in the methods, as well as the description of the inclusion and exclusion criteria. The original cohort was only women who delivered at the University of Pennsylvania. The only change from the original cohort was that we excluded those without a recorded self-identified race for this secondary analysis.

C. Lines 30-33.

D. “We performed a post-hoc secondary analysis of a prospective cohort study that evaluated trends in intravenous iron utilization among women with an antepartum Hb<11g/dL and without hemoglobinopathy delivering at the Hospital of the University of Pennsylvania from 2018-2019. Those without recorded self-identified race were excluded from this secondary analysis.”

Reviewer #2 Comment #6:

A. Results and Tables

- Throughout: I would recommend using the language of "associated with" for this observational study. E.g. "In adjusted models, an antepartum hemoglobin nadir between 10.2 and 11.0 among Black women was associated with a 65% increase in the odds of presenting to labor and delivery with a hemoglobin <11"

B. Thank you for this comment. We have edited our language to refer to associations within our results.
C. Lines 50-55.
D. “For our first primary outcome, among women with an antepartum Hb=10.2-11g/dL, Black race was associated with 65% increased odds of presenting for delivery with Hb<11.0g/dL compared to non-Black women, even when controlling for confounders (aOR=1.65 95%CI[1.10-2.47]; Table 2). When evaluating the same outcome among women with antepartum Hb<10.2g/dL, Black race was associated with increased odds of presenting for delivery with Hb<11.0g/dL in only unadjusted models.”

Reviewer #2 Comment #7:

A**.** - Lines 166-169/Table 2:

- In addition to the overall transfusion rate in each stratum (as is currently provided in Table 2), is it possible to also provide transfusion rate by categories of hgb at admission to labor and delivery (hgb >11 or <11)?
- Was the OR for transfusion for all individuals with hemoglobin <11 an adjusted or unadjusted analysis? If adjusted, which variables were included?
- Perhaps the transfusion data might be better presented as a separate table to help the reader process the stratified and non-stratified transfusion analysis. The authors have done a good job of not comparing results from one stratum to another which is often a pitfall of stratified analyses. However, by presenting an un-stratified analysis in the same paragraph as the stratified results, it becomes a little muddied, especially without a table giving the n, outcome incidence, etc for the unstratified analysis.
- A table structured to show differences by race would be particularly helpful when the authors construct arguments about anemia treatment and decreased maternal morbidity
- Please note that it is important to describe in the methods that, in addition to the stratified analysis by antepartum hgb nadir, a non-stratified analysis of transfusion outcomes was performed and why (to preserve sample size, I presume).

B. Thank you for these thoughtful comments related to our analysis surrounding transfusion rates by admission for delivery hemoglobin. This entire analysis has been significantly truncated due to the size limitations of the Research Letter. We did add a sentence to the methods stating the plan to perform this analysis.
C. Lines 41-42.
D. “Transfusion rate was also compared for the entire cohort by Hb at admission for delivery (<11g/d; ≥11g/dL).”

Reviewer #2 Comment #8:

A. - Lines 175-184/Table 3:

- The p value for gestational age in weeks appears to round up to 0.05, and in conjunction with the fact that the difference is clinically insignificant, this is not a finding I would highlight in the results.
- Why is an adjusted odds ratio given for preterm birth but not birthweight since both were significantly different in the mild anemia stratum?
- If an adjusted logistic regression is performed for birthweight, I would ask the authors to consider including gestational age as a covariate, as I suspect the increased incidence of PTB in this group may skew the data toward lower birthweights.

B. Thank you for these thoughtful comments related to our analysis surrounding neonatal outcomes. This entire analysis has been removed from our manuscript due to the word limitations of the Research Letter format.
C. The analysis has been removed.
D. NA

Reviewer #2 Comment #9:

A. Discussion
- Lines 187-194. I would recommend restructuring this paragraph such that the results associated with the primary objective are re-stated first. I would move the non-stratified transfusion analysis result to a second paragraph (see below, Line 194).
- Line 188-191. I would recommend stating this a bit differently; as it is currently written, it appears to attribute all findings to the supplementation protocol.
B. Thank you for this comment. We have restructured our discussion.
C. Lines 61-65.
D. “Recently, the negative impact of race as an adjustment within algorithms and guidelines has come to light [3-5]. Our data demonstrate that, with race-based definitions of anemia, Black women with antepartum Hb=10.2-11g/dL are at increased odds of arriving for delivery <11g/dL when compared to non-Black women despite the same antepartum Hb. Hb<11g/dL at delivery is a significant risk factor for transfusion.”

Reviewer #2 Comment #10:

A. - Line 194 - While the authors have demonstrated that hemoglobin<11 for the entire cohort is associated with increased odds of transfusion, this was not demonstrated in the stratum of Black women with antepartum hemoglobin 10.2-11.0. I would recommend that the authors take a paragraph to fully flesh out the discrepancy (sample-size based, I presume) in these stratified and non-stratified results and carefully describe the relationships between the two.
B. Thank you for this comment. We have addressed this in the discussion.
C. Lines 64-67.
D. “Hb<11g/dL at delivery is a significant risk factor for transfusion. While we did not see a significant racial disparity in transfusion in this cohort, we were likely underpowered for this outcome given a low rate of transfusion when antepartum Hb=10.2-11g/dL.”

Reviewer #2 Comment #10:

A. - Lines 204-213 - I would ask the authors to reconsider this paragraph; spending a substantial argument and real-estate on an unadjusted difference in birthweights which may be driven by increased preterm birth in the group of Black women with antepartum hemoglobin 10.2-11.0 feels a bit out of place. If the authors wish to pursue this line of hypothesis generating from their secondary outcomes, I would even more strongly encourage them to perform and adjusted logistic analysis of the birthweight data which includes gestational age as a covariate. In addition, I would recommend that paragraphs based on the secondary analyses and outcomes are written from a standpoint of hypothesis generation; "these data suggest" or "raise the possibility of "
B. Thank you for these thoughtful comments related to our analysis surrounding neonatal outcomes. This entire analysis and associated discussion has been removed from our manuscript due to the word limitations of the Research Letter format.
C. The analysis has been removed.
D. NA

Reviewer #2 Comment #11:

A. - Consider including in the limitations that the lower transfusion rate among the individuals in mildly anemic stratum limits the authors' ability to directly connect increased rates of hgb <11 among the Black women in this group to an increased risk of transfusion among the Black women in this group.

B. Thank you for this comment. This limitation has been added.

C. Line 65-67.

D. “While we did not see a significant racial disparity in transfusion in this cohort, we were likely underpowered for this outcome given a low rate of transfusion when antepartum Hb=10.2-11g/dL.”

Reviewer #2 Comment #12:

A. Overall: There is a fundamental difficulty with the authors switching between statements that there is no difference in transfusion rates and stating that treating anemia will decrease disparities in maternal morbidity. I grasp the points they are trying to make, but some very careful delineation of the results and more clarity in the writing of the discussion will help even the casual reader to draw the connections more easily and clearly.

B. Thank you for this comment. We have removed all references to the conclusion that treating anemia will decrease disparities in maternal morbidity based on our study.

C. Changes made throughout.

D. Changes made throughout.

Reviewer #3 Comment #1:

A. This is a secondary analysis of a prospective cohort study of women with antepartum Hg <11 g/dL who delivered over a one year period at a single institution. Women were stratified by race and Hg severity to determine if race-based anemia definitions influenced outcome. The authors found a similar transfusion rate among Black and non-Black women who presented with a Hg <11 and found that all women with a Hg <11 at delivery were at higher risk for transfusion than their non-anemic counterparts. This leads the authors to conclude that using a singular, non-race based anemia threshold for iron supplementation may decrease transfusion risk in Black women. While I certainly applaud the authors for their work and wholeheartedly agree that we must work towards reducing racially-based biologic explanations to justify maternal disparities, I do have some concerns about the approach and conclusion of this manuscript. First and foremost, as the authors point out, their conclusions are largely based on an assumption that the clinicians treating women in this cohort strictly adhere to race-based definitions of anemia when deciding to recommend additional iron supplementation to patients. In my own practice and experience, there is a large amount of variation in what threshold and risk factors clinicians use to make this decision. Additionally, there is significant variation in prenatal vitamin iron content and adherence that further muddies these distinctions.

B. Thank you for these comments. We agree that a limitation of this study is that we did not measure compliance with iron supplementation, stated in the limitations. However, at our institution, we did have a clearly written protocol for the management of antepartum anemia that differed by race, that was well-known and advertised, as well as published on our institutional guideline site. This guideline was created and approved by a multidisciplinary hospital committee in order to keep with the recommendations as outlined in the ACOG practice bulletin.

C. Lines 36-38; 67-68.

D. “During the study period, our institution’s algorithm for defining and treating antepartum anemia differed by race, consistent with ACOG (6).”; “Additionally, compliance with the institutional antepartum anemia guideline or with iron supplementation was not directly measured.”

Reviewer #3 Comment #2:

A. Secondly, the authors are the authors really contending that anemia should be defined differently or rather that similar treatment thresholds should be applied regardless of race. The definition of anemia is, as described in the ACOG bulletin, determined by H/H less than the 5th percentile for a "healthy reference population". From my brief reading of the literature, it does appear that there may indeed be ancestral (~racial) differences in anemia prevalence because of variation in carrier status for hemoglobinopathies such as alpha thal and sickle trait. In that case, it is harder to argue that it is not appropriate from a general perspective to have different reference standards for anemia in Black and non-Black women. Therefore, the manuscript should make a consistent and clear distinction between recommending a change in the definition of anemia vs. recommending a homogenous treatment threshold that is likely to benefit all women. While this is clear in some areas of the manuscript, I see some confounding of the issue as well.

B. Thank you for these comments. We are arguing that both the definition of anemia should be the same regardless of race, and that treatment thresholds should be the same for all women. While we agree with the reviewer that Black women are more likely to have lower hemoglobin levels, we respectively argue that this does not mean anemia should be defined any differently in the Black population. It just means more Black women are anemic (whether from underlying genetic issues or not).

C. No changes have been made.

D. NA

Reviewer #3 Comment #3:

A. Title: I am not sure that "inequitable" is accurate here. Are the definitions really "unfair". I don't think that is necessarily true based on the reasoning above. Perhaps something more like racially-based.

B. Thank you for this comment. We have changed the title in response.

C. Line 1.

D. “The negative impact of a race-based definition of antepartum anemia”

Reviewer #3 Comment #4:

A. Abstract: I don't think line 27 is accurate based on what was said in the limitations. This was presumed, but not confirmed. This needs to clear.

B. Thank you for these comments. The abstract has been removed given the Research Letter resubmission format.

C. Abstract has been removed.

D. NA

Reviewer #3 Comment #5:

A. Intro: Overall, this is a comprehensive into. For the statements in line 61-65, is there any data to support that clinicians are utilizing these standards to differentially treat patients? This is important because there are other social determinant and co-variates that may confound treatment efficacy, compliance, etc.

B. Thank you for these comments. While there is data supporting that Black women are more likely to have lower hemoglobin levels, there is no data to our knowledge that supports differential treatment by race.
C. No changes have been made.
D. NA

Reviewer #3 Comment #6:

A. Methods: Did the institution have a treatment algorithm for anemia that utilized racial definitions? Or where did the institutional "recommendation" referenced here originate from? How do the authors know that individual clinicians were not recommending iron even for women with Hg 10.2-11? In the limitations, anemia treatment sounds much more like an assumed approach rather than any sort of promoted or proscribed algorithm, but perhaps I am not understanding this correctly.
B. Thank you for these comments. We agree that a limitation of this study is that we did not measure compliance with iron supplementation, stated in the limitations. However, at our institution, we did have a clearly written protocol for the management of antepartum anemia that differed by race, that was well-known and advertised among providers, as well as published on our institutional guideline site. This guideline was created and approved by a multidisciplinary hospital committee in order to keep with the recommendations as outlined in the ACOG practice bulletin.
C. Lines 36-38; 67-68.
D. “During the study period, our institution’s algorithm for defining and treating antepartum anemia differed by race, consistent with ACOG (6).”; “Additionally, compliance with the institutional antepartum anemia guideline or with iron supplementation was not directly measured.”

Reviewer #3 Comment #7:

A. Results: Did the authors further stratify increasing Hg concentrations to see if there was any clearly optimal threshold? While I realize 11 was used because of the anemia definition, I am curious if there is an optimal goal that was inferred or suggested by the data.
B. Thank you for this comment. An optimal threshold for treatment of anemia is difficult to determine by this dataset, as the number of transfusions overall is not high enough to evaluate for a Hb cutoff predictive of transfusions. This is a goal of future work.
C. No changes have been made.
D. NA

Reviewer #3 Comment #8:

A. Discussion:
- In line 204, are the authors suggesting that iron supplementation for mild anemia improves fetal growth and/or increases birth weight? Is there data to support his inference? It seems like there is a significant number of potential cofounders here.
B. Thank you for these thoughtful comments related to our analysis surrounding neonatal outcomes. This entire analysis and associated discussion has been removed from our manuscript due to the word limitations of the Research Letter format.
C. The analysis has been removed.
D. NA

Reviewer #3 Comment #9:

A. Do the authors have any data, even a survey, to give some idea of treatment approach for a nemia? In other words, is there any support differential treatment by race?
B. Thank you for this question. Unfortunately, we do not have that data available at our institution.
C. No changes have been made.
D. NA

Reviewer #3 Comment #10:

A. Again, the final paragraph should emphasize the treatment threshold rather than redefining anemia overall.
B. Thank you for this comment. Please see Reviewer #3 Comment #2 for responses.
C. See above.
D. See above.

Reviewer #3 Comment #11:

A. Table 3: Why are GA at delivery and birthweight not adjusted in the table since these are both significant in univariate analysis?
B. Thank you for this question related to our analysis surrounding neonatal outcomes. This entire analysis and associated discussion has been removed from our manuscript due to the word limitations of the Research Letter format.
C. The analysis has been removed.
D. NA

Statistics Editor Comment #1:

A. Lines 107-113: There are actually two primary hypotheses being tested, so the alpha should be adjusted to .025, not .05, which will lower the power, but it would remain > 80%. Also, how were the rates of 10% difference in rates of Hb < 11 g/dL or of 5% difference in rates of transfusion chosen? Were those thresholds meant to be the minimum clinically important differences? Also, since this was a secondary analysis of a prospective cohort study (lines 71-72), the counts and proportion of Black vs non-Black patients was known. Therefore, those numbers should have been used to assess power, which yields different results than those cited. For example, there were 1080 Black and 1369-1080, or 289 non-Black participants, so the required difference in Hb < 11 g/dL (35% non-Black vs 45% Black) yields power = 0.87 for alpha = .05 and power = .80 for alpha = .025. For the transfusion rates of 10% vs 5%, the power corresponding to alpha = .05 is .79 (, while the power corresponding
to alpha = .025 is only 0.69. In other words, the study was actually underpowered to evaluate the stated difference in transfusion rates.
B. Thank you for these comments. The post-hoc nature of the analysis has been clarified in the methods. Due to the space limitations of the Research Letter, the post hoc power analysis has been removed.
C. Lines 30-32.
D. “We performed a post-hoc secondary analysis of a prospective cohort study that evaluated trends in intravenous iron utilization among women with an antepartum Hb<11g/dL and without hemoglobinopathy delivering at the Hospital of the University of Pennsylvania from 2018-2019.”

Statistics Editor Comment #2:

A. lines 154-157: The adjusted odds was 1.65, but that means that the odds were 65% higher, not that those women were "65% more likely to present ...". That is, odds is not the same as risk or as rate.

B. Thank you for this comment. We have adjusted the results accordingly.

C. Lines 50-55.

D. “For our first primary outcome, among women with an antepartum Hb=10.2-11g/dL, Black race was associated with 65% increased odds of presenting for delivery with Hb<11.0g/dL compared to non-Black women, even when controlling for confounders (aOR=1.65 95%CI[1.10-2.47]; Table 2). When evaluating the same outcome among women with antepartum Hb<10.2g/dL, Black race was associated with increased odds of presenting for delivery with Hb<11.0g/dL in only unadjusted models.”

Statistics Editor Comment #3:

A. Table 2: The counts for transfusion, for the antepartum Hb 10.2-11.0 groups, were low, and in fact too few to allow for multivariable adjustment with 3 variables. That is, the model is likely over fitted. The primary outcome was framed in terms of the entire cohort, while this Table shows the breakdown by strata of antepartum Hb. These subsets are not the primary outcome, nor were they the basis for the sample size/power calculation. These are all secondary outcomes, the primary outcome difference in rates of andtpartum Hb < 11.0 were 580/1080 (53%) vs 106/289 (36%). Since that is how the question was framed, that is how is should be cited as the primary outcome. The subsets are secondary outcomes. Similarly, for the rates of transfusion etc

B. Thank you for these comments. We did design our study with the plan to primarily analyze by strata. This has now been clarified in the methods.

C. Lines 39-40.

D. “Primary outcomes (1) Hb<11g/dL at admission for delivery and (2) blood transfusion were compared by race, within antepartum Hb strata.”