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

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RE: Manuscript Number ONG-21-115

Disease Severity and Perinatal Outcomes of Pregnant Patients with Coronavirus Disease 2019 (COVID-19): A Multistate Cohort

Dear Dr. Metz:

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 Feb 15, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

The purpose of this manuscript is to "To describe coronavirus disease 2019 (COVID-19) severity in pregnant patients and evaluate the association between disease severity and perinatal outcomes." This was an observational cohort study.

1. The authors that one of the limitations of this analysis was that "not all sites were performing universal screening." In the Materials and Method section, could the authors discuss what approach to screening was performed at the various sites? Did some sites do just symptom based screening? universal screening throughout the study? Was the protocol different for inpatient and outpatient screening?

2. The authors note "Of those with a venous thromboembolism, five received anticoagulation prior to the event, all in the severe/critical group." Were the individuals who developed a VTE while on anticoagulation on prophylactic or therapeutic doses? What anticoagulant was used in these individuals? The authors note that "Further study is needed to determine the need for anticoagulation in the setting of less severe COVID-19 illness during pregnancy as there was an isolated venous thromboembolic event in the mild/moderate group." Could the authors expand their discussion of anticoagulation? Since 63% of the patients in the severe/critical group who developed VTE were on anticoagulation, what regimen would they suggest in these patients to lower the risk? Would they suggest anticoagulation in the mild/moderate group until further data is available? If yes, prophylactic or therapeutic doses?

3. The authors note " Two other maternal deaths occurred during the study time period and were not related to infection; both had severe COVID-19 before dying of other causes." What were the other causes in these two patients?

4. The authors note "the increased risk of preterm birth was driven by indicated, rather than spontaneous..." What were the indications for induction or cesarean section? Primarily related to COVID-19?

5. "We found that 12% of pregnant patients had severe or critical COVID-19." Should this be 12% of COVID-19 infected pregnant patients?

6. In Figure 1, under the critical category would the authors consider adding the 'n' for each category; ie. respiratory failure n= , septic shock n= , multiple organ dysfunction or failure n= , and death due to COVID 19 n= .

7. In the Supplemental Appendix. In the title: could the authors add "clinical presentation for Coronavirus Disease 2019 (COVID-19)? Under the criteria for mild, "including included". Please remove included?
Reviewer #2:

Lines 59-60, 196-197 and Table 2: While it is true that the numbers and proportions were higher, the stats test used evaluated a trend, not a pair-wise comparison. Need to clarify that difference for the reader, or supply results of specific pair-wise stats test.

lines 199-201: Same issue with difference between overall trend and specific comorbidity rates in one group vs another.

Table 1: The Critical and Severe groups each had N < 100, so the corresponding %s should be rounded to nearest integer %, not cited to 0.1% precision.

Table 2: Many of the row entries had low counts and therefore many of the NS trends have low power to discern a difference. (eg., chronic CVD or renal disease). Need to enumerate the number with missing data for BMI (see lines 227-230). Also, were the missing data evenly distributed among the groups by disease severity? If not, or if a significant proportion were missing, need to justify use of imputation. (Could be in on-line material).

Table 3 and lines 203-204: Again, need to distinguish numerical differences from specific stats difference, which was not done in Table 3.

lines 208-209: Those events were rare and there would be low stats power to discern a difference based on these data. Also, in Table 4, the counts of adverse outcomes are too few to allow for precise estimate of aRRs. That is, likely the model is over fitted.

lines 241-246: These events were rare and there is low stats power to discern a trend from these data.

Reviewer #3:

The authors present an observational cohort study of pregnant women diagnosed with COVID-19 disease over a 5 month period of in mid-2020 comparing perinatal outcomes based on severity of disease.

Results

1. Of the 33 sites involved in the study, what proportion were doing universal screening at hospital admission versus symptomatic screening (since rates of COVID-19 positive vary by sampling technique)?
2. What proportion of positive COVID-19 individuals were detected in an outpatient versus inpatient setting?
3. The authors may consider presenting the rates of some of the outcomes (such as ICU admission or maternal death) as the number per 1000 cases. This will allow comparisons to other trials in the medical literature.
4. Table 2 - Since a BMI of 40 kg/m2 or greater in non-pregnant individuals is associated with a greater risk of severe morbidity or mortality with COVID-19 disease, does the author's data allow presentation of the proportion of women with a BMI greater or equal to 40 kg/m2?
5. Line 231 - The authors may consider stating the overall rate of preterm delivery of less than 37 weeks of gestation [16.7% (204/1219)] since this allows context to other studies (such as reference number 5).
6. Line 244 - The authors may consider some brief statement why they report an Apgar of 3 or less at 5 minutes. For example that this may be an indicator of encephalopathy or neonatal mortality.

Discussion

7. Lines 298 to 311 - Some additional limitations that should be discussed:
   a) Is there a risk of sampling bias? This study notes a rate of maternal ICU admission of 48.4/1000 cases and a risk of maternal death of 3/1000 cases. For a comparison, references 5 and 6 report a rate of maternal ICU admission of 14.6/1000 and 10.5/1000 cases or a rate of maternal death of 1.9/1000 and 1.5/1000 cases, respectively. Is the current study potentially overestimating these outcomes? Please comment.
   b) One suspects that the treatment modalities utilized in severe or critical COVID-19 infections were not standardized between the various institutions. Thus outcomes may have been affected by hospital or institutional treatment practices.
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   A. OPT-IN: Yes, please publish my point-by-point response letter.
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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. 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.

5. 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.

6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

   * All financial support of the study must be acknowledged.
   * 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).

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

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

8. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

9. 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.

10. 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").

11. 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.

12. 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.

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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).

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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 Feb 15, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
John O. Schorge, MD
Associate Editor, Gynecology

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

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REVIEWER COMMENTS:

Reviewer #1:

The purpose of this manuscript is to "To describe coronavirus disease 2019 (COVID-19) severity in pregnant patients and evaluate the association between disease severity and perinatal outcomes." This was an observational cohort study.

1. The authors that one of the limitations of this analysis was that "not all sites were performing universal screening." In the Materials and Method section, could the authors discuss what approach to screening was performed at the various sites? Did some sites do just symptom based screening? universal screening throughout the study? Was the protocol different for inpatient and outpatient screening?

Response: Thank you for requesting clarification. The study protocol detailed the research questions, study population and the data that were abstracted. The data abstraction was the same regardless of the setting in which the test was obtained, and patients were followed through 6 weeks postpartum. The SARS-CoV-2 testing employed at each site was dictated by the site’s clinical protocols. We have clarified in the Methods section that some centers were screening all patients admitted to L&D during this time period.

See Methods, p. 7: “Both symptomatic patients and asymptomatic patients were included. During the study time period, some of the centers performed SARS-CoV-2 testing for all patients admitted for delivery regardless of symptoms or known exposures.”

This is also addressed in the results on p.10 as follows:

“Of those who were asymptomatic with a positive SARS-CoV-2 test, 97% were tested in the context of universal screening at the time of delivery admission.”

2. The authors note "Of those with a venous thromboembolism, five received
anticoagulation prior to the event, all in the severe/critical group.” Were the individuals who developed a VTE while on anticoagulation on prophylactic or therapeutic doses? What anticoagulant was used in these individuals? The authors note that “Further study is needed to determine the need for anticoagulation in the setting of less severe COVID-19 illness during pregnancy as there was an isolated venous thromboembolic event in the mild/moderate group.” Could the authors expand their discussion of anticoagulation? Since 63% of the patients in the severe/critical group who developed VTE were on anticoagulation, what regimen would they suggest in these patients to lower the risk? Would they suggest anticoagulation in the mild/moderate group until further data is available? If yes, prophylactic or therapeutic doses?

Response: We appreciate that this is a very important question for clinical practice, and have expanded the discussion on p. 14 related to VTE events. All of the patients who were receiving anticoagulation prior to the VTE event were receiving prophylactic doses, which was clarified in the manuscript.

“We observed a 6% VTE rate in the critical/severe group. NIH treatment guidelines recommend prophylactic anticoagulation in pregnant hospitalized patients with COVID-19. Nonetheless, our data are consistent with those in non-pregnant patients in that critically ill patients with COVID-19 have a high rate of VTE even when receiving prophylactic anticoagulation. Ongoing randomized controlled trials are evaluating if therapeutic anticoagulation reduces risk of VTE when compared with prophylactic anticoagulation. Further study is also needed to determine the need for anticoagulation in the setting of less severe COVID-19 illness during pregnancy as there was an isolated venous thromboembolic event in the mild/moderate group (1 in 499).”

3. The authors note “Two other maternal deaths occurred during the study time period and were not related to infection; both had severe COVID-19 before dying of other causes.” What were the other causes in these two patients?

Response: These two other maternal deaths were due to a gunshot wound and rejection of a solid organ transplant. Given the highly identifying nature of both of these events, these details were intentionally not included in the manuscript.
4. The authors note "the increased risk of preterm birth was driven by indicated, rather than spontaneous..." What were the indications for induction or cesarean section? Primarily related to COVID-19?
Response: The proportion of preterm births that were induced or underwent cesarean with a primary indication of COVID-19 are now included. We also included the other most common indications for induction or cesarean on p. of the Results.
“COVID-19 was the primary indication for induction of labor in 3% of those induced preterm (n=67). The most common indications for induction among the preterm births were hypertensive disorders of pregnancy (33%), stillbirth (16%), and preterm premature rupture of membranes (13%). COVID-19 was the primary indication for cesarean birth in 22% of those who underwent preterm cesarean (n=106). The other common indications for cesarean among preterm births were non-reassuring fetal status (29%), hypertensive disorders of pregnancy (15%), and abnormal presentation (11%).”

5. "We found that 12% of pregnant patients had severe or critical COVID-19." Should this be 12% of COVID-19 infected pregnant patients?
Response: Yes, thank you for catching this error. We have edited the sentence in the Discussion on p. 13 to read as follows:
“We found that 12% of pregnant patients with COVID-19 had severe or critical illness.”

6. In Figure 1, under the critical category would the authors consider adding the 'n' for each category; ie. respiratory failure n= , septic shock n= , multiple organ dysfunction or failure n= , and death due to COVID 19 n= .
Response: These data are included in Table 1, in which we detail how patients were categorized into each of the NIH severity categories. It seems repetitive to add this to Figure 1, but can certainly do so if that is the editor’s preference.

7. In the Supplemental Appendix. In the title: could the authors add "clinical
presentation for Coronavirus Disease 2019 (COVID-19)? Under the criteria for mild, "including included". Please remove included?

Response: Thank you for catching this typo. It has been corrected, and the title was changed as requested as follows in the supplementary appendix:

“Supplementary Table 1. Modified National Institutes of Health (NIH) guidelines for severity of clinical presentation of coronavirus disease 2019 (COVID-19)”

Reviewer #2:

1. Lines 59-60, 196-197 and Table 2: While it is true that the numbers and proportions were higher, the stats test used evaluated a trend, not a a pair-wise comparison. Need to clarify that difference for the reader, or supply results of specific pair-wise stats test.

Response: Thank you for this point of clarification. The results reported in Lines 59-60, 196-197 were compared using a test for trend only; pairwise comparisons were not made. The methods of the abstract state that trends were examined, so no change was made to the descriptive reporting of baseline characteristics in the abstracts. The sentence in the results was changed to clarify that this was a trend across severity.

Lines 59-60: Those with more severe illness had older mean age, higher median body mass index, and pre-existing medical comorbidities.

Lines 196-197: Tests of trend were significant for differences in age, median BMI, and insurance status across disease severity (Table 2).

2. lines 199-201: Same issue with difference between overall trend and specific comorbidity rates in one group vs another.

Response: We also clarified this sentence to indicate that we are referring to a test of trend.

“Tests of trend were significant for differences in frequency of medical comorbidities including asthma or chronic obstructive pulmonary disease, chronic hypertension, pre-
pregnancy diabetes, chronic liver disease, and seizure disorder across disease severity.”

3. Table 1: The Critical and Severe groups each had N < 100, so the corresponding %s should be rounded to nearest integer %, not cited to 0.1% precision.

**Response:** All values with groups less than 100 were rounded to the nearest integer.

4. Table 2: Many of the row entries had low counts and therefore many of the NS trends have low power to discern a difference. (eg., chronic CVD or renal disease). Need to enumerate the number with missing data for BMI (see lines 227-230). Also, were the missing data evenly distributed among the groups by disease severity? If not, or if a significant proportion were missing, need to justify use of imputation. (Could be in online material).

**Response:** BMI was missing in n=159 (13%), representing 28/141 (20%) of severe/critical, 47/499 (9%) of mild/moderate, and 84/579 (15%) asymptomatic. Pre-pregnancy BMI is frequently missing in the medical record, and is an important covariate when studying COVID-19 outcomes. Rather than select any available BMI, we thought it was important to approximate pre-pregnancy BMI for all participants. We were able to calculate pre-pregnancy BMI based on BMI at the time of delivery using a generalized linear model. Imputed pre-pregnancy BMI was only used for sensitivity analyses. The proportion of patients with missing BMI was added to the Results on p. 12:

“In a sensitivity analysis in which BMI was imputed for those with missing values (n=159, 13%), the adjusted association between critical/severe and postpartum hemorrhage was no longer significant (aRR 1.68, 95% CI 1.00-2.84).”

5. Table 3 and lines 203-204: Again, need to distinguish numerical differences from specific stats difference, which was not done in Table 3.
Response: Data presented in Table 3 are descriptive and not compared statistically. Any interpretation of these data in the results section was removed.

6. lines 208-209: Those events were rare and there would be low stats power to discern a difference based on these data. Also, in Table 4, the counts of adverse outcomes are too few to allow for precise estimate of aRRs. That is, likely the model is over fitted. 

Response: Per reviewer recommendations, reporting of adjusted relative risks was removed from Table 2 for fetal and neonatal death due to low frequency of these events. An explanation was added to the Methods section on p. 9:

“Multivariable modeling was not performed for outcomes with low frequencies including maternal death, stillbirth or neonatal death, maternal venous thromboembolism, or positive SARS-CoV-2 results for the neonate.”

7. lines 241-246: These events were rare and there is low stats power to discern a trend from these data.

Response: We agree with the reviewer and removed statistical comparisons between the groups. These data are now just presented descriptively in the Results on p. 13-14.

“The rate of positive neonatal SARS-CoV-2 tests among live births was 1.5% in the severe/critical group, 0.6% in the mild/moderate group, and 1.2% in the asymptomatic group. The percent of neonates with a 5-minute Apgar score less than or equal to 3 was 2.9% in the severe/critical, 0.2% in the mild/moderate, and 0.7% in the asymptomatic group.”

Reviewer #3:

The authors present an observational cohort study of pregnant women diagnosed with COVID-19 disease over a 5 month period of in mid-2020 comparing perinatal outcomes based on severity of disease.

Results
1. Of the 33 sites involved in the study, what proportion were doing universal screening
at hospital admission versus symptomatic screening (since rates of COVID-19 positive vary by sampling technique)?

**Response:** Please see response to reviewer #1, comment #1. We are unable to include exactly how many centers were performing universal testing as it changed over the course of the study. There were only 3 sites who never did universal testing during the study period. We added information to clarify this in the Methods, and included a result indicating that 97% of the patients who were asymptomatic were detected upon universal testing at delivery admission.

2. What proportion of positive COVID-19 individuals were detected in an outpatient versus inpatient setting?

**Response:** We added the percent of patients who had SARS-CoV-2 testing performed in the inpatient setting to the Results on p. 10:

“*The majority of positive SARS-CoV-2 tests were performed in the inpatient setting (67%).”*

3. The authors may consider presenting the rates of some of the outcomes (such as ICU admission or maternal death) as the number per 1000 cases. This will allow comparisons to other trials in the medical literature.

**Response:** The maternal death rate of 3 per 1,000, and the maternal ICU rate of 48 per 1,000 are now reported in the Discussion for context and comparison to the existing literature. This change is on p. 15 in the Discussion.

“*CDC MMWR data* demonstrate an increased risk of death from COVID-19 and ICU admission among pregnant patients compared with non-pregnant patients. Recent hospital-level administrative data also demonstrate increased risks of both of these outcomes among COVID-19 positive compared with COVID-19 negative patients. Our maternal death rate was 0.3%, or 3 per 1,000 patients with COVID-19, and ICU admission rate was 4.8%, or 48 per 1,000. Both of these rates are higher than those previously published. A small proportion of the increase may reflect transports requiring
critical care from other facilities to MFMU tertiary centers. However, transports only comprised 11% of the severe/critical study population. Therefore, the higher rates may also reflect increased ascertainment of these outcomes through manual medical record abstraction rather than relying on administrative data.”

4. Table 2 - Since a BMI of 40 kg/m2 or greater in non-pregnant individuals is associated with a greater risk of severe morbidity or mortality with COVID-19 disease, does the author’s data allow presentation of the proportion of women with a BMI greater or equal to 40 kg/m2?

Response: At the reviewer’s request, we added a category for BMI ≥ 40 kg/m² to Table 2.

5. Line 231 - The authors may consider stating the overall rate of preterm delivery of less than 37 weeks of gestation [16.7% (204/1219)] since this allows context to other studies (such as reference number 5).

Response: Thank you for this suggestion. We have added the overall rate of each of the main outcomes of interest to the Results on p.12:

“Overall, the rates for cesarean birth, postpartum hemorrhage, hypertensive disorders of pregnancy and preterm birth were 36.9%, 8.9%, 23.4% and 16.7%, respectively.”

6. Line 244 - The authors may consider some brief statement why they report an Apgar of 3 or less at 5 minutes. For example that this may be an indicator of encephalopathy or neonatal mortality.

Response: Yes, as the reviewer notes, we used a low 5-minute Apgar score as a surrogate marker for significant adverse neonatal outcomes. Apgar scores of 3 or less at 5-minutes have been associated with neonatal mortality (Cnattingius et al NEJM 2020). A brief explanation and reference was added to the Methods on p. 9:

“Among live births, additional outcomes included neonatal intermediate or intensive care
unit (NICU) admission, birthweight, 5-minute Apgar score ≤ 3 as a marker of adverse neonatal outcomes, and small-for-gestational-age birthweight less than the 10th percentile based on the Duryea et al nomogram.”

Discussion

7. Lines 298 to 311 - Some additional limitations that should be discussed:

a) Is there a risk of sampling bias? This study notes a rate of maternal ICU admission of 48.4/1000 cases and a risk of maternal death of 3/1000 cases. For a comparison, references 5 and 6 report a rate of maternal ICU admission of 14.6/1000 and 10.5/1000 cases or a rate of maternal death of 1.9/1000 and 1.5/1000 cases, respectively. Is the current study potentially overestimating these outcomes? Please comment.

Response: We anticipate that the higher rates of maternal death and ICU admission in our study are likely related to transport of critically ill patients to tertiary centers in the MFMU. We have added a paragraph to our Discussion to address this concern. Please see text in response to reviewer #3, comment # 3.

b) One suspects that the treatment modalities utilized in severe or critical COVID-19 infections were not standardized between the various institutions. Thus outcomes may have been affected by hospital or institutional treatment practices.

Response: We agree that treatments were unlikely to be standardized across sites, especially early in the pandemic when there were no data to guide therapy. We have added this as a limitation on p. 16 in the Discussion:

“Finally, treatment for COVID-19 was rapidly evolving during the study period, and the effect of current treatments on outcomes could not be evaluated.”

EDITORIAL OFFICE COMMENTS:

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

A. OPT-IN: Yes, please publish my point-by-point response letter.
B. OPT-OUT: No, please do not publish my point-by-point response letter.

**Response:** OPT-IN

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.

**Response:** Dr. Metz disclosed her conflicts. No other authors noted a conflict of interest.

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.

Response: Race and ethnicity are reported in our study. These data were abstracted from the EMR at each site based on what was self-reported by the patient when presenting for clinical care. All missing data are enumerated in the table footnotes. We have added information about the abstraction of the race-ethnicity variable to the Methods on p. 9:

“Race and ethnicity data were abstracted from the medical record, and were based on patient self-report at the time of clinical care. All patients identified as Hispanic ethnicity, regardless of race, were categorized as Hispanic. The “other race” category includes non-Hispanic Asian, Native Hawaiian or Pacific Islander, American Indian/Alaskan Native, unknown or more than one race. These categories were collapsed in order to make comparisons between groups with low frequency of patients in the other race categories.”

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

Response: Standard definitions are used throughout.

5. 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.

**Response:** The manuscript word count for the precis, abstract, text and tables is 5,488. I cannot reduce the number of authors or affiliations so this was not included, but can reduce the text further if required to meet journal page limits.

6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.
* 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).

**Response:** All requested elements are included.

7. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.
In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words. Please provide a word count.

Response: The abstract and manuscript include the same information. The abstract word count is 299.

8. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

Response: Abbreviations are not used.

9. 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.

Response: We do not use the term “and/or”. The virgule symbol is used to present data for the combination of the severe and critical groups as severe/critical, and the same for mild/moderate. We can replace the virgule symbol for these analysis groups with “or” throughout if that is preferred.

10. 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").

Response: Data are presented as relative risks. The only p values are those for test of trend which cannot be reported as an effect size. We are consistent with decimal places in our results tables.

11. 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.

Response: We have reviewed the journal’s Table Checklist. Symbols for footnotes were updated per journal specifications.

12. 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).

Response: DOI numbers were added to the referenced manuscripts per journal specifications.

13. 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.
Response: Figure 1 is now included as a separate file.

14. 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 https://wkauthorservices.editage.com/open-access/hybrid.html.

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.

Response: Given the funding source (NICHD), this article will need to be made available on PubMed Central. We do not plan to pay the additional fee to publish with open access prior to that time.