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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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Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-22-61

Neighborhood characteristics and racial/ethnic disparities in SARS-CoV-2 seropositivity in pregnancy

Dear Dr. Burris:

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).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

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 25, 2022, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

The authors present a cohort study evaluating the association between SARS CoV-2 seropositivity and neighborhood characteristics. They conclude that deprivation mediated 10% of the increase in seropositivity among non-hispanic blacks versus whites and crowding mediated Hispanic versus white seropositivity. The study is well-written, interesting and brings to light neighborhood factors that contribute to the spread of SARS-CoV 2 virus. The ability of the authors to obtain covid serology data for over 8,000 participants is impressive.

Methods:
Line 111- was this part of a larger protocol to test all pregnant inpatients for SARS CoV-2 antibodies?

With this large amount of data on COVID serology did the authors collect pregnancy outcome data?

Was maternal serum stored from April 2020-December to 2020? Was data collected prospectively?

Results:
The supplemental figure with outlining the cohort should be included in the main study.

Table 2- the first column should be clarified.

Table 3 may be cut down

Reviewer #2:

Line 176: Does the mediation analysis also take into consideration socioeconomic status that also impact neighborhood characteristics?

Line 111: What proportion of patients who present for parturition have syphilis screening lab drawn on admission? I know the following statements say that 97% of the labs obtained were obtained on admission but was this 97% of all the
patients or 97% of the labs obtained?

Line 196: This statement about the novelty is a bit misleading. There is another study that evaluated impact on neighborhood factors on COVID-19 infection in pregnancy (Emeruwa UN, Ona S, Shaman JL, Turitz A, Wright JD, et al. Associations Between Built Environment, Neighborhood Socioeconomic Status, and SARS-CoV-2 Infection Among Pregnant Women in New York City. JAMA. 2020)

Overall I think this a good paper and well done study adds to already existing literature about impact of socioeconomic status on COVID 19 diagnosis and outcomes in pregnancy. It is hard to tease out impact of neighborhood characteristics from impact of socioeconomic status which influences neighborhood characteristics. Regardless, the use of census data for analysis is quite neat.

Reviewer #3: This is a well-designed retrospective cohort study aimed to quantify how neighborhood characteristics contribute to racial/ethnic disparities in SARS-CoV-2 seropositivity in pregnancy. The authors used multivariable mixed effects logistic regression models and causal mediation analyses to investigate these aims. As expected, they found racial/ethnic disparities in SARS-CoV-2 seropositivity rates. Regarding neighborhood factors, they found that deprivation and crowding were associated with seropositivity, while segregation was not. Mediation analyses showed that crowding may explain 6.7% of the Hispanic-White disparity and that deprivation may explain 10.2% of the Black-White disparity. See below for some specific questions and suggestions.

Detailed Comments

General
-Can you consistently define and use racial/ethnic categories? You at times alternate between non-Hispanic Black and Black (i.e. line 181 says non-Hispanic Black and non-Hispanic White and line 183 says Black-White disparities). I think it would be clearer if you defined non-Hispanic Black as "Black" and non-Hispanic White as "White" at the start and then used those terms throughout.

Abstract
-Can you define the abbreviations used within your abstract?

Intro
-Can you explicitly state your hypotheses?

Methods
-How did you decide to use this measure of community-level deprivation? There seem to be others (i.e. the CDC's Social Vulnerability Index, the Area Deprivation Index (ADI) from the University of Wisconsin) that have more supporting literature.

-Did you consider dividing the neighborhood indicators into deciles or quartiles and modeling the most deprived compared to the least deprived? This has been done in other studies using on neighborhood indices (i.e. Dasgupta S, Bowen VB, Leidner A, Fletcher K, Musial T, Rose C, et al. Association between social vulnerability and a county’s risk for becoming a COVID-19 hotspot—United States, June 1-July 25, 2020. Morbidity and Mortality Weekly Report. 2020;69(42):1535.) and seems to allow for a more intuitive interpretation (as compared to your approach of calculating aORs of seropositivity per standard deviation increment increase).

Discussion
-In line 212, you describe deprivation's contribution to the Black-White disparity as 11.6% overall and 14.6% in the sensitivity analysis in [Blinded] county. I am confused about where these numbers are coming from, as they are different from the numbers presented in your Results section and in Figure 1 (which indicate that deprivation contributes 10.2% overall and 13.8% in the sensitivity analysis).

- I was initially surprised to see the low aORs (<2) for the neighborhood factors, and that neighborhood factors accounted for a relatively small percentage of disparities in mediation analyses. The authors comment (lines 210-214) that these results are similar in magnitude to a preterm birth study, but can you comment on what else may account for disparities? This seems to be an important future direction for research in this area.

Tables
-Table 2: Please provide the range for the ICE scores in the footnote for context and interpretation of your results.
STATISTICAL EDITOR COMMENTS:

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

Table 2: The aORs for deprivation and for crowding, although statistically significant, were weak associations.

Table 3: Comparing the aORs for M1 vs M2, M3 and M4 for each of the models based on the racial/ethnic groups cited, it appears that(1) there is no statistical advantage by the addition of each of the neighborhood factors to the M1 model and (2) the M2, M3 and M4 model aORs within each racial/ethnic group are NS different from one another. That is, the largest difference (and significant) appears to be from M0 to M1, that is, by adjusting for factors age, BMI, insurance status and limited English proficiency. These observations are limited to the comparison of Hispanic-White and Black-White. For the Asian/other-White disparity, there are two issues: (1) Table 1 shows that the Other/multiple/Unknown category is a substantial (~ 40%) of the aggregated Asian/Other cohort, and (2) their numbers are relatively small (especially the counts for seropositive, n = 28 total). Thus was there sufficient stats power to generalize the NS aORs for all comparisons in that racial/ethnic group?

Fig 2a: In Fig 2a, most areas have no indication of seropositivity rates. How many neighborhood units were there and how many seropositives (out of 562) were in each of the neighborhood units? Did that in turn, limit statistic power to make inferences re: multiple factors potentially influencing seropositivity rates? Compared to Figs 2b, 2c and 2d, the seropositivity areas represent a small portion of the neighborhood areas. Suggest that it would be more easily interpreted by the reader if only the neighborhood areas highlighted in Fig 2a were highlighted in Figures 2b, 2c and 2d. All four maps could then be cropped to show only the neighborhoods tested in this study.

Supp! Fig 1: Need to compare the 699 with missing sero(+) data vs the analyzed cohort to assure the reader that missing data occurred at random, rather than a selective process that could have statistically biased the results.

EDITOR COMMENTS:

1. Please explain why consent was not (or could not) be obtained and rationale for IRB waiver of consent in greater detail in the Methods section.

2. Edit the last line of abstract to be more specific to study findings.

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

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

4. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:
   * Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors).
   * Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
   * Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
   * Name the IRB or Ethics Committee institution in the Methods section (if applicable).
   * Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

5. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you upload your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your co-authors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript’s title page.

6. 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 (e.g., 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.

6. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Methods section of the body text, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

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

* All financial support of the study must be acknowledged.
* 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.
* All and/or any 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).
* *If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: “Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL].”*

9. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

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

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

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

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

13. ACOG avoids using "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.

14. 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.

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").

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

16. 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 references you are citing are still current and available. Check the Clinical Guidance page at https://www.acog.org/clinical (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn’t listed as “Withdrawn,” it’s still a current document.

If the reference you are citing has been updated and 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.

17. Figures: Note that the manuscript cites Figures 1-3. Please update.

Figure 1: This file may be resubmitted as-is.

Figure 2: Is this figure original to the manuscript? Does any mapping program need to be credited?

18. Each supplemental file in your manuscript should be named an "Appendix," numbered, and ordered in the way they are first cited in the text. Do not order and number supplemental tables, figures, and text separately. References cited in appendixes should be added to a separate References list in the appendixes file.

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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.

If you choose open access, you will receive an Open Access Publication Charge letter from the Journal’s Publisher, Wolters Kluwer, and instructions on how to submit any open access charges. The email will be from publicationservices@copyright.com with the subject line, "Please Submit Your Open Access Article Publication Charge(s)." Please complete payment of the Open Access charges within 48 hours of receipt.

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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 as a Microsoft Word document. 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 25, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
February 22, 2022

RE: Manuscript Number ONG-22-61

Dear Dr. Carter:

Thank you for the opportunity to revise our manuscript, “Neighborhood characteristics and ethnic disparities in SARS-CoV-2 seropositivity in pregnancy” to be considered for publication in Obstetrics & Gynecology. We removed “racial/ethnic” in the title to conform to the desired avoidance of “/” and to remain within character count. If allowed, I'd love to leave in “racial/ethnic” in the title but will defer to you.

Below is a point-by-point response. We look forward to hearing from you.

Sincerely,

Heather H. Burris, MD, MPH

Reviewer 1:

Point 1: “Was this part of a larger protocol to test all pregnant inpatients for SARS CoV-2 antibodies?”
Response: This study did not involve clinical testing of patients but instead was research surveillance of the prevalence of seropositivity. The scavenged serum samples were prospectively collected before they would have otherwise been discarded.

Change to manuscript: none
Lines: N/A

Point 2: “With this large amount of data on COVID serology did the authors collect pregnancy outcome data?”
Response: We did collect some pregnancy outcome data (birthweight, gestational age) through electronic query. The relationship of COVID serology with specific pregnancy outcomes is a separate study question. We do not know when all patients became positive, making it difficult to determine the relationship of virus exposure, immune response and specific pregnancy outcomes. In addition, if we analyzed seropositivity with pregnancy outcomes, seropositivity would be the exposure instead of the outcome and would require additional adjusted analyses that would detract from the focus of the manuscript.
Change to manuscript: none
Lines: N/A

Point 3: “Was maternal serum stored from April 2020-December to 2020? Was data collected prospectively?”
Response: Samples were collected as available when they were otherwise scheduled for discard by hospital laboratories. They were analyzed in batches at the convenience of the research laboratory. Clinical and demographic data were retrospectively collected on an ongoing basis.
Change to manuscript: none
Lines: N/A

Point 4: “The supplemental figure with outlining the cohort should be included in the main study.”
Response: We moved supplemental figure 1 to the main document.
Change to manuscript: Figures renumbered.
Lines: N/A

Point 5: “Table 2- the first column should be clarified.”
Response: First column renamed.
Change to manuscript: Column now states “at the census tract level”
Page/line numbers: Table 2 first column.

Point 6: “Table 3 may be cut down”
Response: We have removed the list of individual covariates included and put into the footnote. We defer to the reviewer and editor as to which version is preferred.
Change to manuscript: Simplified the description of M1 in Table 3 to “individual covariates”
Lines: Table 3 M1 and footnote
Reviewer 2:

**Point 7:** “Line 176: Does the mediation analysis also take into consideration socioeconomic status that also impact neighborhood characteristics?”

**Response:** Thank you for noticing that we had not clarified that the mediation model adjusted for covariates. The mediation analysis adjusted for insurance status and limited English proficiency (the two socioeconomic variables available). Other variables in the model included age and body mass index. These are the same variables in the models from Table 3.

**Change to manuscript:** Methods: “Mediation models included adjustment for individual-level age, body mass index, insurance status, and limited English proficiency.” And Results: “Mediation analyses, adjusted for individual-level age, body mass index, insurance status, and limited English proficiency…”

**Lines:** 246

**Point 8:** “Line 111: What proportion of patients who present for parturition have syphilis screening lab drawn on admission? I know the following statements say that 97% of the labs obtained were obtained on admission but was this 97% of all the patients or 97% of the labs obtained?”

**Response:** By policy, both birth hospitals universally obtain serum for syphilis screening on admission for parturition. Residual serum is prioritized for clinical use. This study scavenged serum that was scheduled for discard; missing serum had been used for clinical purposes and was not available for scavenge. During the study, 6,095/6,556 pregnant patients had serum available for antibody testing (93%)(Figure 1). A new Supplemental Table 1 comparing those with and without testing is now included.; 3% had the screening lab sent at a prior visit close enough to parturition to not have it repeated (e.g. evaluated for labor but sent home).

**Change to manuscript:** “93% had available samples for analysis of which 97% were collected during the labor and delivery admission, with 3% of those collected within the month prior”

**Lines:** 172-3

**Point 9:** “Line 196: This statement about the novelty is a bit misleading. There is another study that evaluated impact on neighborhood factors on COVID-19 infection in pregnancy (Emeruwa UN, Ona S, Shaman JL, Turitz A, Wright JD, et al. Associations Between Built Environment, Neighborhood Socioeconomic Status, and SARS-CoV-2 Infection Among Pregnant Women in New York City. JAMA. 2020 )”

**Response:** Thank you for pointing this research letter out to us.

**Change to the manuscript:** “Additionally a study of 434 patients admitted for labor and delivery at a New York City hospital with universal PCR testing from the first month of the COVID-19 pandemic (March 22 through April 21, 2020) demonstrated that lower neighborhood socioeconomic status and more household crowding were associated with COVID-19 infection. Our study differs from these prior reports in that it interrogated seroprevalence which captures information about past infections in patients who may not test positive using a PCR at the time of admission for parturition. Furthermore, we examined the extent to which neighborhood factors might explain racial and ethnic disparities in seropositivity.”

**Lines:** 280-7

Reviewer 3:
Point 10: “Can you consistently define and use racial/ethnic categories? You at times alternate between non-Hispanic Black and Black (i.e. line 181 says non-Hispanic Black and non-Hispanic White and line 183 says Black-White disparities). I think it would be clearer if you defined non-Hispanic Black as "Black" and non-Hispanic White as "White" at the start and then used those terms throughout.

Response: Change made

Change to manuscript: “For brevity, we refer to non-Hispanic Black, non-Hispanic White, and non-Hispanic Asian patients as Black, White, and Asian, respectively.” (and deleted non-Hispanic thereafter).

Lines: 142-4

Point 11: “Can you define the abbreviations used within your abstract?”

Response: Change made

Change to Manuscript: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus that causes Coronavirus Disease-19 (COVID-19); United States; Immunoglobulin G (IgG) and Immunoglobulin M (IgM); (adjusted odds ratio (aOR)

Lines: 59,60,62,63,64,75

Point 12: “Can you explicitly state your hypotheses?

Response: Hypotheses added

Change to the manuscript: “Our hypotheses were that in the pre-vaccination era, neighborhood characteristics would be associated with the odds of seropositivity and might partially explain racial and ethnic disparities in seropositivity. Specifically,”

Lines:120-3

Point 13: “How did you decide to use this measure of community-level deprivation? There seem to be others (i.e. the CDC's Social Vulnerability Index, the Area Deprivation Index (ADI) from the University of Wisconsin) that have more supporting literature.”

Response: The index we used specifically is for census tracts whereas the ADI is for block groups. We chose census tracts so as to use ICE (a correlate of segregation) which is less stable at smaller units. Additionally, the ADI has a coefficient for crowding which we chose to analyze separately as we hypothesized it would be associated specifically with viral transmission. The CDC SVI includes a measure of minority status which we wanted to analyze separately using ICE. We added it to the discussion.

Change to the manuscript: “There are other measures of neighborhood deprivation in the literature. We chose to use a specific material community deprivation index because it did not have an indicator for the proportion of “minority” residents like the Centers for Disease Control and Prevention Social Vulnerability Index does or an indicator for “crowding” which is included in the Area Deprivation Index. We wanted to assess segregation and crowding separately. Nonetheless, findings might vary with the choice of neighborhood deprivation index.”

Lines: 340-6

Point 14: “Did you consider dividing the neighborhood indicators into deciles or quartiles and modeling the most deprived compared to the least deprived? This has been done in other studies using on neighborhood indices (i.e. Dasgupta S, Bowen VB, Leidner A, Fletcher K, Musial T,
Rose C, et al. Association between social vulnerability and a county's risk for becoming a COVID-19 hotspot—United States, June 1-July 25, 2020. Morbidity and Mortality Weekly Report. 2020;69(42):1535.) and seems to allow for a more intuitive interpretation (as compared to your approach of calculating aORs of seropositivity per standard deviation increment increase).

Response: This is indeed another approach that may be more intuitive. However, our primary goal wasn’t to quantify the exact increase in odds at a certain level but to determine the extent to which neighborhood factors might explain disparities. Leaving the exposures as continuous variables preserves the power necessary for the mediation analyses. The presented adjusted effect sizes are per 1SD unit change in the variable. But we have now added an interpretation of what the increased odds of seropositivity would be comparing the midpoint of the highest vs. lowest quartile of exposure. For example, when we use this unit of comparison (2.3 SD units in a normal distribution), the corresponding odds ratio is 1.40, corresponding to 40% higher odds of seropositivity among individuals from the highest quartile compared to the lowest quartile of deprivation.

Change to the manuscript: “These effect estimates correspond to 40% and 38% increased odds of seropositivity for individuals residing in the midpoint of the highest quartile compared to the midpoint of the lowest quartile (2.3 standard deviation units apart) of deprivation and crowding respectively.”

Lines: 228-231

Point 15: “I was initially surprised to see the low aORs (<2) for the neighborhood factors, and that neighborhood factors accounted for a relatively small percentage of disparities in mediation analyses. The authors comment (lines 210-214) that these results are similar in magnitude to a preterm birth study, but can you comment on what else may account for disparities? This seems to be an important future direction for research in this area.”

Response: This may be because of our approach pointed out in the prior comment #14. This is per 1 SD increment increase. Additionally, often individual factors will explain more of the variance as we can see the attenuation in adjusted models in Table 2. We have added speculation regarding other factors that could explain the disparities.

Change to the manuscript: “Nonetheless, it is clear that unmeasured factors are explaining the disparity in seropositivity that persisted after adjusting for individual and neighborhood factors with adjusted odds ratios of seropositivity among Hispanic and Black patients compared to White exceeding three. Additional work to determine the extent to which occupational, transportation, or other socioenvironmental factors explain persistent disparities in seropositivity, and many other health outcomes, is warranted.

Lines: 293-8

Point 16: “Table 2: Please provide the range for the ICE scores in the footnote for context and interpretation of your results.”

Response: Change made

Change to the manuscript: “range -1 to 1 with”

Lines: Footnote of Table 2

Statistical Editor Comments
**Point 17:** “Table 2: The aORs for deprivation and for crowding, although statistically significant, were weak associations.”  
**Response:** We were not surprised that these were relatively weak associations; this is often the case with environmental studies when we use continuous exposures with a 1 SD unit increment as the exposure. Additionally, individual variables often explain more of the variance. We chose to leave the exposures as continuous because our main area of interest was in the mediation analysis which is more powerful with continuous exposures. Nonetheless, we now acknowledge the weakening of associations in the Discussion. Please also see response to **Point 14 above.**  
**Change to the manuscript:** “While the effect estimates in models of associations of deprivation and crowding with seropositivity were substantially weakened by the addition of individual covariates, they remained significant.”  
**Lines:** 299-301

**Point 18:** “Table 3: Comparing the aORs for M1 vs M2, M3 and M4 for each of the models based on the racial/ethnic groups cited, it appears that(1) there is no statistical advantage by the addition of each of the neighborhood factors to the M1 model and (2) the M2, M3 and M4 model aORs within each racial/ethnic group are NS different from one another. That is, the largest difference (and significant) appears to be from M0 to M1, that is, by adjusting for factors age, BMI, insurance status and limited English proficiency. These observations are limited to the comparison of Hispanic-White and Black-White. For the Asian/other-White disparity, there are two issues: (1) Table 1 shows that the Other/multiple/Unknown category is a substantial (~40%) of the aggregated Asian/Other cohort, and (2) their numbers are relatively small (especially the counts for seropositive, n = 28 total). Thus was there sufficient stats power to generalize the NS aORs for all comparisons in that racial/ethnic group?  
**Response:** The purpose of showing the models in Table 3 was to show a more interpretable “old school” mediation analysis. For example, we can see minor attenuation of effect estimates between M1 and Ms 2, 3, 4 if there is potential mediation. However, this cannot test whether there is statistical mediation. We show it for interpretability. We were not trying to generate the “best model” for prediction. We have added a line to explain this goal in the results.  
For the Asian/other/multiple, we were underpowered as we can observe with the wide confidence intervals. A limitation is now added.  
**Changes to the manuscript:** “In models with race or ethnicity as the independent (predictor) variable and seropositivity as the dependent (outcome), adding individual age, body mass index, insurance status and limited English proficiency substantially attenuated Hispanic-white and Black-white disparities (Table 3). The addition of neighborhood factors appeared to subtly attenuate disparities. Formal mediation analyses”  
**Lines:** 242-7

“While diverse, our study population had few cases of seropositivity among Asian patients (n=13) and patients self-designated as other, multiple, or unknown race or ethnicity (n=15) which necessitated combining this group for modeling and likely resulted in lack of power to rule out disparities.”
Lines: 330-3

Point 19: “Fig 2a: In Fig 2a, most areas have no indication of seropositivity rates. How many neighborhood units were there and how many seropositives (out of 562) were in each of the neighborhood units? Did that in turn, limit statistic power to make inferences re: multiple factors potentially influencing seropositivity rates? Compared to Figs 2b, 2c and 2d, the seropositivity areas represent a small portion of the neighborhood areas. Suggest that it would be more easily interpreted by the reader if only the neighborhood areas highlighted in Fig 2a were highlighted in Figures 2b, 2c and 2d. All four maps could then be cropped to show only the neighborhoods tested in this study.

Response: You are correct. We chose only to show the seropositive rates for tracts with at least 20 humans. A table showing the n of tracts with n positive is here:

<table>
<thead>
<tr>
<th>Positive (n)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>&gt;5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tracts (n)</td>
<td>143</td>
<td>76</td>
<td>34</td>
<td>22</td>
<td>10</td>
<td>7</td>
<td>14</td>
</tr>
</tbody>
</table>

The total number of tracts analyzed (where participants lived) was 306. The total number of tracts with at least 1 positive was 163.

However, the unit of analysis in this study is the patient. We weren’t testing the spatial units themselves, but assigned each individual the value of their residential census tract. We then used a random intercept for each tract to account for shared variance for humans when they resided in the same tract.

With respect to showing the seropositive rates, we chose to limit to a minimum of 20 subjects because if a tract had 2 subjects and one was positive it would appear as 50% positivity which is not a stable estimate. We added a footnote to explain that subjects may have lived in greyed out tracts but rates are not shown because they would be too unstable and potentially identifiable. If this is too confusing, we could remove the map and defer to the editor.

Change to manuscript: “Map of seropositivity rates in census tracts with at least 20 study subjects; study subjects lived in other tracts, but rates would be too unstable and individuals too potentially identifiable to depict.”

Lines: Figure 2 legend

Point 20: “Suppl Fig 1: Need to compare the 699 with missing sero(+) data vs the analyzed cohort to assure the reader that missing data occurred at random, rather than a selective process that could have statistically biased the results.”

Response: Supplemental Table added. When generating this table we noticed that those missing seropositivity samples were more likely to have preterm birth. In retrospect, we are not surprised
given that the primary reason serum was unavailable is that it was used by the care team for “add-on” clinical tests. One might imagine that more tests would be ordered on women who were sicker. Another issue is that women transferred from another facility to a Penn hospital for delivery might not have the RPR repeated. We now note this in the results and limitations.

**Change to manuscript:**

“Comparisons of patients with and without sera available for testing are shown in Appendix Table 1”

“Comparisons of patients with and without seropositivity data showed that patients without these data were older, less likely to be obese, more likely to be privately insured, more likely to self-identify as non-Hispanic White, and more likely to have preterm birth (Appendix Table 1)”

“There were some differences between patients with and without (7%) seropositivity data which could affect generalizability of findings. Specifically, patients without available samples were more likely to be older, White, privately insured, and have preterm birth suggesting this may have been a population referred into the hospital from other hospitals where the sample had already been drawn or were so sick that add-on tests used up the sample and there was no volume left for our assay.”

Methods lines: 174-5
Results lines: 210-3
Discussion lines: 335-8

**Editor comments:**

**Point 21:** “Please explain why consent was not (or could not) be obtained and rationale for IRB waiver of consent in greater detail in the Methods section.”

**Response:** The Institutional Review Board at the University of Pennsylvania approved this study with a waiver of consent (Protocol # 834240). Infection epidemiology data are not accurate if only reflective of a select population. Determining generalizable and population-based seroepidemiology data is crucial to inform public health policy and vaccination strategy. Therefore, to avoid selection bias, we pursued a waiver of consent for collection of discarded specimens in order to include a broad demographic population and as many participants as possible in a limited timeframe. Our request for waiver of informed consent was approved by the University of Pennsylvania IRB based on the following:

- the research involved no more than minimal risk to the subjects because it used discarded specimens and already collected data;
- the waiver would not adversely affect the rights and welfare of the subjects;
- the research could not practicably be carried out without the waiver (>9000 individuals)

**Change to the manuscript:** “The Institutional Review Board at the University of Pennsylvania approved this study with a waiver of consent because there was no more than minimal risk to participants since the protocol called for discarded samples and existing data (Protocol # 834240).”
Lines: 149-52

Point 22: “Edit the last line of abstract to be more specific to study findings.”

Response: Change made

Change to the manuscript: “Investing in structural neighborhood improvements may reduce inequities in viral transmission.”

Lines: 351-2

Point 23: “The Editors of Obstetrics & Gynecology have increased 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:”

Response: OPT-IN: Yes, please publish my point-by-point response letter.

Point 24: When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:

Response: Done

Point 25: Responsible handling of race as a variable.

Response: We attended to these details upon initial submission and have clarified in response to Reviewer 3, Point 10.

Changes in the manuscript: None

Lines: N/A.

Point 26: IRB documentation

Response: Included

Changes in the manuscript: None

Lines: N/A.

Point 27: Word count <5500 including everything but references

Response: We are below word count

Changes in the manuscript: None

Lines: N/A.

Point 28: Acknowledgements

Response: Included

Changes in the manuscript: None

Lines: N/A.
**Point 29:** Short title <=45 characters  
**Response:** Included  
**Changes in the manuscript:** None  
**Lines:** N/A.

**Point 30:** Abstract, consistency and word count <=300  
**Response:** Checked, Word count is 299  
**Changes in the manuscript:** None  
**Lines:** N/A.

**Point 31:** Standard abbreviations  
**Response:** We left the SARS-CoV-2 in precis. Please let us know if you want that spelled out.  
**Changes in the manuscript:** None  
**Lines:** N/A.

**Point 32:** No virgule symbol (/)  
**Response:** removed throughout although I’d love to re-add to title if allowed. Now only have “ethnic” or could choose “racial” but can’t fit both under character limit.  
**Changes in the manuscript:** removed throughout  
**Lines:** throughout

**Point 33:** ACOG avoids using "provider."  
**Response:** changed to “physician, nurse practitioner or other clinician, because more than just physicians care for patients in our system  
**Changes in the manuscript:** changed throughout  
**Lines:** 106, 320

**Point 34:** “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.”  

“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:** Our manuscript adheres to these recommendations.  
**Changes in the manuscript:** none  
**Lines:** N/A

**Point 35:** Footnotes changed in tables  
**Response:** Done  
**Changes in the manuscript:** *, ††§||  
**Lines:** Tables 2 and 3, appendix 2
Point 36: Reference formats  
Response: Edited  
Changes in the manuscript: Non-italicized  
Lines: References

Point 37: Figures: Note that the manuscript cites Figures 1-3. Please update.  
Response: Edited order

Point 38: “Figure 2: Is this figure original to the manuscript? Does any mapping program need to be credited?”  
Response: Now ArcMap is cited.  
Changes in the manuscript: “ArcMAP 10.8, Environmental Systems Research Institute (ESRI), Redlands, CA”  
Lines: Figure 2 legend

Point 39: Supplemental should be appendix.  
Response: Renamed  
Changes in the manuscript: Changes from supplemental to appendix  
Lines: 176, 214, 222, 241

Point 40: Open access  
Response: no thank you  
Changes in the manuscript: N/A  
Lines: N/A