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

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

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

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

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
RE: Manuscript Number ONG-20-2143

Excess Maternal Deaths Associated with COVID-19 in Mexico

Dear Dr. Farber:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors are interested in potentially publishing your revised manuscript in a timely manner. In order to have this considered quickly, we need to have your revision documents submitted to us as soon as you are able. I am tentatively setting your due date to August 13, 2020, but please let me know if you need additional time.

The standard revision letter text follows.

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).

REVIEWER COMMENTS:

Reviewer #1: This is an interesting research letter based on Mexican Ministry of Health data. Issues to be resolved include:

1. Please add a brief description of your statistical method (Farrington surveillance algorithms based on Poisson generalized linear models with overdispersion) so the average reader will understand how you determined the number of excess maternal deaths.

2. You state that, before COVID, the MMR in Mexico was on track to be 29.5 in 2020, which (according to the Table) would be the lowest MMR in the last 10 years. Please add a sentence supporting this prediction (what aspect of maternal health or health care indicated that the MMR would be that low?).

3. A previous publication on this topic by the senior author [M Farber: Int J Gynaecology & Obstetrics, 150 (20: 266-7)] reported that as of May 17 there were 308 cases of COVID-19 in pregnant women in Mexico, of whom 7 died, indicating a case fatality rate of 2.3%. Is the current data consistent with this rate? Please update your case fatality rate, which would further confirm that the excess mortality your report is due to COVID-19.

4. In the Figure: please provide some dates or at least a week count under the bars to the reader doesn’t have to struggle to figure out which week is which. Also, please clarify what you mean by "Phase 3 of the COVID pandemic" in Mexico; in the US, "Phase 3" corresponds to a specific strategy to relax COVID-19 restrictions and reopen the economy.

Reviewer #2: The authors present a Research Letter describing maternal mortality in Mexico from 2011 through current to show the increase in mortality, and specifically from respiratory causes since COVID-19 was introduced. The data are striking.

I have several questions for the authors, as well as one larger recommendation.

1. why start in 2011 specifically? was this the year this data began to be published, or was there another reason? or was it just arbitrary

2. the maternal mortality seems to have been dropping steadily from 2011 to 2019. do the authors have a hypothesis why
that was happening? was there anything else that happened in 2020, covid-related or otherwise, that could have slowed down or reversed this trend?

3. in the Figure it appears that the actual deaths in the first 3 months of 2020 were well below the "predicted" number of deaths. the authors should comment if that is related to better health than expected, or an overestimation of predicted deaths. this would color the interpretation of the excess deaths seen in the latter half of the figure.

for the larger recommendation:
-i understand the desire to get this out quickly as a Research Letter, but i think this would be better as a full Original Research Manuscript. you would have more opportunity to describe the methods and do a deeper dive into the Results. I suspect there is a lot more analyses that can be done. if i am wrong and this is all there is, ignore this comment

Reviewer #3: The authors have submitted a timely RL on the impact of COVID-19 in the global maternal community. We are told by news outlets that it is mostly the old, infirm, ill patients at risk, but what of pregnant women in low- and middle-income countries?

Intro
1 - Provocative content. 15 million is a staggering number. The authors make a strong case for the importance of this work.

Methods
2 - Pre-existing, open-sourced reports (line 60) are utilized, and presumably accurate for this type of data capture.

3 - This reviewer is not familiar with the (line 66) Farrington surveillance algorithm, or overdispersion, but this will be appropriately explored by the stat review. I do not think the authors need to elaborate in this tightly written section.

Results
4 - Fig 1 is very powerful and well-done

5 - Table 1 would look better if there was a way to better present the 'Excess maternal deaths' data - having 6 columns with only dash marks is not very effective use of space. The authors could probably delete this whole part of the Table as Fig 1 visually presents this anyway

6 - It would be helpful to include a bit more data in the text of this section (27.8% is vastly higher than any previous year; MMR higher than its been since 2012, etc).

Discussion
7 - The authors might speculate on why maternal mortality rates from COVID-19 in Mexico is 'In contrast with...economically advanced countries'. The only mention is line 103 general statement about 'Renewed focus on improving healthcare systems'. Do they need ventilators shipped to them? What are the impediments to saving these lives? The MMR had been trending downwards over the past decade - so something was improving before the pandemic.

Reviewer #4: Excellent, concise report.

1) I found the intro off point in that there are many and more likely ways to become infected with the virus than through interaction with the healthcare team;

2) It seems like causes of death other than COVID were static. This is surprising give that in my experience the extra time it takes to mobilize for emergencies such as hemorrhage in patients with COVID infection is not trivial and increases the risk for the patient. Please comment.

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

Table 1: Should include CIs for the annual maternal mortality ratios. It appears that the MMR significantly decreased during 2011-2019, and was consistently higher during 2011-2014 than since. So using all years since 2011 would have
elevated the baseline levels. In other words, the baseline was not constant over time. It is not clear from Methods whether this was addressed.

Fig: At least in my version, the dotted line representing the 95% centile is not very clear. Should use a bolder font or brighter color to show the reader the demarcation line.

EDITOR'S COMMENTS:

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

Numbers below refer to line numbers.

49. For final version, please submit updated number and date.

49. I’m not clear what the sentence starting with “as part of routine…” has to do with the paper. You are not reporting on transmission of the virus in the paper.

61-65. This is similar (but not identical) to your aim statement just above starting on line 54, Given the limitations of the research letter format, can you condense these 2 aim statements into one (I’d leave it in the introduction)? You don’t mention methods for your aim 2.

It seems that this second aim is simply a reporting of what is already in the Mexican government reports and does not need to be an “aim”.

73. number OF excess deaths.....

79. Is this 49 excess compared to year to date or overall for 2020?

81. Please give the week of the 28th week.(Example: June x-y, 2020)

In the results, please present the data to mirror the order of your aim statement. This might be Start with line 100 and moving it from the discussion to the results section.

Also please note concerns by the statistical editor regarding the falling rate of MMR that preceded 2020.

Table: We don’t uses tables formatted with 2 parts like this. Given that so much of the second half of the table is blank, is there a way to provide this data in the text or online supplemental digital content?

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.

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.
Jesus Lumbreras-Marquez and Fernando Vazquez-Alaniz will need to complete our electronic Copyright Transfer Agreement, which was sent to them by email through Editorial Manager.

3. Please change the “Year” heading in the table to a subhead. Our copy editor will format the second part of the table so that “Excess maternal deaths...” and "Week" are subheads.

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: Research Letters articles should not exceed 2.5 pages (600 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. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

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 submission, 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. Figure 1: Please upload as a figure file on Editorial Manager.

13. 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.

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

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

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.
August 13, 2020

Dear Editors of Obstetrics & Gynecology,

All of our changes in the revised manuscript are described below by page number and written in blue font.

**REVIEWER COMMENTS:**

**Reviewer #1:**

<table>
<thead>
<tr>
<th>This is an interesting research letter based on Mexican Ministry of Health data. Issues to be resolved include:</th>
<th>Thank you. Now we present data up to the 32nd week of 2020.</th>
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<tr>
<td>1. Please add a brief description of your statistical method (Farrington surveillance algorithms based on Poisson generalized linear models with overdispersion) so the average reader will understand how you determined the number of excess maternal deaths.</td>
<td>Thank you for mentioning this point. We have added a brief description of our statistical method. Page 3, lines 15-16.</td>
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<td>2. You state that, before COVID, the MMR in Mexico was on track to be 29.5 in 2020, which (according to the Table) would be the lowest MMR in the last 10 years. Please add a sentence supporting this prediction (what aspect of maternal health or health care indicated that the MMR would be that low?).</td>
<td>We hypothesize that health policies implemented by the Mexican government in the last decade contributed to the significant reduction in maternal mortality in the country. Yet, the health care system has faced an unprecedented situation with the COVID-19 pandemic which hindered the positive trend observed in recent years. Due to the word count limit for research letters (600 words), we could not add a comprehensive statement regarding this subject. We plan to perform a comprehensive assessment of maternal mortality in Mexico in 2021 to describe the previous trend and to determine the impact of COVID-19 on maternal mortality in this setting.</td>
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<td>3. A previous publication on this topic by the senior author [M Farber: Int J Gynaecology &amp; Obstetrics, 150 (20: 266-7)] reported that as of May 17 there were 308 cases of COVID 19 in pregnant women in Mexico, of whom 7 died, indicating a case fatality rate of 2.3 %. Is the current data consistent with this rate?</td>
<td>The case fatality rate was retrieved from a different source where the COVID-19 test results of pregnant and nonpregnant patients are reported. According to this site (<a href="https://datos.gob.mx/busca/dataset/informacion-referente-a-casos-covid-19-en-mexico">https://datos.gob.mx/busca/dataset/informacion-referente-a-casos-covid-19-en-mexico</a>), as of 8.11.2020, the case fatality among pregnant patients was 2.64% (106/4,022). Which is consistent with our previous publication.</td>
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</table>
Please update your case fatality rate, which would further confirm that the excess mortality your report is due to COVID 19.

The maternal mortality information presented in the current submission was obtained from an epidemiological system designed to monitor maternal mortality in Mexico: [https://www.gob.mx/salud/documentos/informes-semanales-para-la-vigilancia-epidemiologica-de-muertes-maternas-2020](https://www.gob.mx/salud/documentos/informes-semanales-para-la-vigilancia-epidemiologica-de-muertes-maternas-2020)

4. In the Figure: please provide some dates or at least a week count under the bars to the reader doesn’t have to struggle to figure out which week is which. Also, please clarify what you mean by "Phase 3 of the COVID pandemic" in Mexico ; in the US, "Phase 3" corresponds to a specific strategy to relax COVID 19 restrictions and reopen the economy.

We have added the week # to the “X” axis in the Figure. Moreover, we have added the description for Phase 3 in Mexico to the Figure legend.

**Reviewer #2:**

The authors present a Research Letter describing maternal mortality in Mexico from 2011 through current to show the increase in mortality, and specifically from respiratory causes since COVID-19 was introduced. The data are striking.

Thank you, as mentioned above, now we include the data up to the 32nd week of 2020.

I have several questions for the authors, as well as one larger recommendation.

1. why start in 2011 specifically? was this the year this data began to be published, or was there another reason? or was it just arbitrary

As mentioned above, we hypothesize that health policies implemented by the Mexican government in the last decade contributed to the significant reduction in maternal mortality in the country. Yet, the health care system has faced an unprecedented situation with the COVID-19 pandemic which hindered the positive trend observed in recent years.

2. the maternal mortality seems to have been dropping steadily from 2011 to 2019. do the authors have a hypothesis why that was happening? was there anything else that happened in 2020, covid-related or otherwise, that could have slowed down or reversed this trend?
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<td>We agree, we have added this information to the Results section. (Page 4, line 12).</td>
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Discussion

7 - The authors might speculate on why maternal mortality rates from COVID-19 in Mexico is 'In contrast with...economically advanced countries'. The only mention is line 103 general statement about 'Renewed focus on improving healthcare systems'. Do they need ventilators shipped to them? What are the impediments to saving these lives? The MMR had been trending downwards over the past decade - so something was improving before the pandemic.

Thank you for this constructive comment, we agree with the reviewer, there was a favorable trend regarding maternal mortality in recent years. Unfortunately, the information about the causes of this high maternal mortality rate due to COVID-19 is scarce. Based on previous publications from the 2009 pandemic (Reference #5) where a similar situation was observed; seems like the answer to this question is quite complex and could be related to several issues including health literacy, medical education, social determinants of health, health care system infrastructure, etc.

Reference #6 describes a comprehensive framework to improve the structural competency of health care systems. We have modified this paragraph to highlight the importance of such strategies in low- and middle-income countries (Page 5 lines 4-8).

Reviewer #4:

Excellent, concise report. Thank you.

1) I found the intro off point in that there are many and more likely ways to become infected with the Thank you for mentioning this point. We have modified the Introduction section. (Page 3, lines 2-12).
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<td>We agree with the reviewer, in previous years, postpartum hemorrhage was the leading cause of maternal mortality in Mexico. With the COVID-19 pandemic a delay in the diagnosis and management of postpartum hemorrhage, hypertensive disorders of pregnancy, and other obstetric complications was expected. Since the data from this open source is provisional, further analysis in the following months/years could help to elucidate if the pandemic impacted the management of other pregnancy complications.</td>
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**STATISTICAL EDITOR COMMENTS:**
The Statistical Editor makes the following points that need to be addressed:

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| Thank you for this valuable feedback. We have added the CIs for the MMRs.

We performed a post-hoc analysis (not shown in the research letter) that shows that starting at 2014 makes the baseline (i.e., the upper limit of the 95% prediction interval) lower so it makes results during COVID-19 even more striking. We are taking a more conservative approach by including the time period when the baseline was higher. |

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<td>Per your request, we have moved the aims sentence to the Introduction section. (Page 3, lines 6-12).</td>
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<td>It seems that this second aim is simply a reporting of what is already in the Mexican government reports and does not need to be an “aim”.</td>
<td>Thank you for mentioning this point, we have modified this sentence. (Page 3, lines 11-12).</td>
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<td>We have added “OF” to this sentence, page 4, line 1.</td>
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<td>79. Is this 49 excess compared to year to date or overall for 2020?</td>
<td>This refers to year to date (weeks 1-32 for 2020). Now we report 86 excess deaths. (Page 4, line 15).</td>
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<td>81. Please give the week of the 28th week.(Example: June x-y, 2020)</td>
<td>We have added this information to the Results section. (Page 4, line 9).</td>
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<td>In the results, please present the data to mirror the order of your aim statement. This might be Start with line 100 and moving it from the discussion to the results section.</td>
<td>Thank you, we have moved this sentence to the Results section. (Page 4, lines 6-15).</td>
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Also please note concerns by the statistical editor regarding the falling rate of MMR that preceded 2020.

| Table: We don’t uses tables formatted with 2 parts like this. Given that so much of the second half of the table is blank, is there a way to provide this data in the text or online supplemental digital content? | We have addressed this point. Please see response above. |
| Table: We don’t uses tables formatted with 2 parts like this. Given that so much of the second half of the table is blank, is there a way to provide this data in the text or online supplemental digital content? | Thank you for mentioning this important point, we have moved the second part of the Table to the Figure legend. According to the Journal guidelines, we cannot attach any online supplemental digital content. |

**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:
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| Fernando Vazquez did not receive the eCTA via email. Could you please send it again? This is the correct email address: feralaniz1@hotmail.com |
| ___________________________________________ | OPT-IN |

Fernando Vazquez did not receive the eCTA via email. Could you please send it again? This is the correct email address: feralaniz1@hotmail.com
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.

Jesus Lumbreras-Marquez and Fernando Vazquez-Alaniz will need to complete our electronic Copyright Transfer Agreement, which was sent to them by email through Editorial Manager.

3. Please change the “Year” heading in the table to a subhead. Our copy editor will format the second part of the table so that “Excess maternal deaths...” and “Week” are subheads.

We have modified the Table. Now we present the second part of the Table as text in the Figure legend.

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

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On behalf of my co-authors, I would like to thank you for the opportunity to revise our manuscript. We look forward to hearing from you.

Sincerely,

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