RE: Manuscript Number ONG-20-2825

Prematurity rates during the coronavirus pandemic lockdown

Dear Dr. Rolnik:

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 Nov 20, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The authors report the prematurity rates in Melbourne, comparing timeframes prior to and during the pandemic of COVID-19.

1. Lines 33; 70+: Although I respect the limited word count for this research letter, but stating that "the lockdown...has been one of the strictest in the world" could be more specific about what made this so rigid.
2. Line 50: You state the total number of liveborns since January, 2018 but not the total number of preterm births overall. I would think either include that or remove this sentence.
3. Given that the seasons in Melbourne are the reverse to those of north America (perhaps affecting indoor transmission rates), when was the largest number of affected cases during this timeframe?
4. Line 71: what is the context of the "second coronavirus wave" in Melbourne? Again, some description of this would help the context for this report. This is again referenced on line 85+ with the "milder lockdown" reference.

Reviewer #2:

The authors present data from Melbourne to estimate the impact of covid-19 quarantine/. lockdown on prematurity rates. I have several questions/comments for the authors

1. since this journal is US-based, the title should clarify that this is from an Australian population.
2. it would be important to demonstrate to the reader that delivery-location patterns didn't change due to the lockdowns, which could significantly impact the results. I, like most readers of this journal I assume, am unaware how many hospitals are in the Melbourne region, and how patients choose which ones to deliver at. In New York, for example, there are many hospitals and patients basically get to choose themselves as there isn't a single hospital for any population. as such, when the lockdowns started, patients started moving around to leave New York City, or to deliver closer to where they live, etc. As such, if I took a sample of a certain hospital, or group of hospitals, I find find differences in outcomes after the lockdown that were solely due to higher risk patients going elsewhere, for example. if this is not at all similar in Melbourne, the authors should state that specifically, or present some data to demonstrate it didn't happen.
3. the methods or introduction should be more detailed on exactly what lockdown measures were instituted and when.
4. twins should just be excluded. it does not make sense to present data with twins and then do a sub analysis to control for them.
5. similarly, I would think the denominator should be live born neonates without anomalies.
Reviewer #3:

Table 1: Since CIs are included with the OR and mean differences, the column of p-values is redundant. Should round BW differences to at most, 0.1 g, not cite to 0.01 g precision. There is a typo in the footnote "2m584 in the first epoch".

General: Should acknowledge in limitations section of Discussion that the women in the two epochs were not matched and may have differed in demographic and clinical factors, so the differences cited may not be completely attributable to the different time epochs. Also, the control group is one year prior, so there is no comparison of multiple prior years to exclude a longer trend in PTB frequency that could be independent of Covid in 2020.

Fig 1: The difference in months of PTB rate after June 2020 appears to be significant only due to the rate in Sept 2020; that month appears to be the only outlier. Also, from Table 1, the total number of PTB < 28 wks from June-Sept 2020 is only 9. The conclusion that the subset of PTB < 28 wks represents a significant trend seems equally likely due to stochastic variation. Again, there is no information re: risk factors for PTB in any of the months shown. A similar time series monthly display of all PTB from Jan 2018 would be more informative, as well as based on a larger sample of PTB.

STATISTICS EDITOR COMMENTS:

Fig 1 seems a stretch. The differences are statistically significant, but based on mostly small counts or percentages. Might be useful for a future meta-analysis.

EDITOR COMMENTS:

Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision of this Research Letter, it will be especially important to address the comment made by the statistical editor re: Figure 1 and the concern that the findings may just result from random variation in a single month.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   A. OPT-IN: Yes, please publish my point-by-point response letter.
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2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA. Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), observational studies using ICD-10 data (ie, RECORD), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic
accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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 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.

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).

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.

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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 Nov 20, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
Torri Metz, MD
Associate Editor, Obstetrics

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

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Melbourne, 31 October 2020

Professor Nancy C. Chescheir, Editor-in-Chief
c/o Obstetrics & Gynecology
409 12th Street, SW, Washington, DC 20024-2188

RE: Manuscript Number ONG-20-2825
Dear Prof Chescheir,

We would like to thank the Editor and the Reviewers for taking the time to read and provide helpful feedback on our manuscript *Prematurity rates during the coronavirus pandemic lockdown*. We have made changes accordingly and hope that it is acceptable for publication Research Letter in *Obstetrics & Gynecology*.

Please find below an itemized response to the reviewer’s comments.
Thank you for considering our submission for publication.

Yours sincerely,

Daniel L. Rolnik
REVIEWER COMMENTS:

Reviewer #1: The authors report the prematurity rates in Melbourne, comparing timeframes prior to and during the pandemic of COVID-19.

1. Lines 33; 70+: Although I respect the limited word count for this research letter, but stating that "the lockdown...has been one of the strictest in the world" could be more specific about what made this so rigid.
   **Answer:** We have now added to the Discussion “Between July 8 and September 28, one could only leave the house if they were an “essential” worker, seeking healthcare, exercising or shopping for necessities. Gatherings between more than 2 people were prohibited. A daily curfew was introduced from 8 P.M. and mask wearing became mandatory.”

2. Line 50: You state the total number of liveborns since January, 2018 but not the total number of preterm births overall. I would think either include that or remove this sentence.
   **Answer:** Thank you. We believe that for the time-series analysis, the overall number of preterm births is of little value. The figures are given for the three-month periods comparisons in Table 1. We have removed the total number of live births from January 2018 as suggested.

3. Given that the seasons in Melbourne are the reverse to those of north America (perhaps affecting indoor transmission rates), when was the largest number of affected cases during this timeframe?
   **Answer:** The peak number of daily cases in Melbourne occurred in the first week of August, with 650-750 new cases per day (please see figure below). Given the strict lockdown measures with most people staying at home and with heavy fines applied to infringements, however, it is difficult to draw conclusions about the possible association with the season. No adjustments were made.

4. Line 71: what is the context of the “second coronavirus wave” in Melbourne? Again, some description of this would help the context for this report. This is again referenced on line 85+ with the “milder lockdown” reference.
   **Answer:** Due to the word limit, we did not explain in details the incidence rates. The second wave started in July and was worse than the first, as demonstrated in the figure above. We have changed “during the second wave” to “from July” (Line 46 of the manuscript).
The authors present data from Melbourne to estimate the impact of covid-19 quarantine/lockdown on prematurity rates. I have several questions/comments for the authors.

1. since this journal is US-based, the title should clarify that this is from an Australian population.
   Answer: Thank you kindly for taking the time to review our manuscript and for your insightful comments. We have modified the title as suggested.

2. it would be important to demonstrate to the reader that delivery-location patterns didn't change due to the lockdowns, which could significantly impact the results. I, like most readers of this journal I assume, am unaware how many hospitals are in the Melbourne region, and how patients choose which ones to deliver at. In New York, for example, there are many hospitals and patients basically get to choose themselves as there isn't a single hospital for any population. as such, when the lockdowns started, patients started moving around to leave New York City, or to deliver closer to where they live, etc. as such, if I took a sample of a certain hospital, or group of hospitals, I find find differences in outcomes after the lockdown that were solely due to higher risk patients going elsewhere, for example. if this is not at all similar in Melbourne, the authors should state that specifically, or present some data to demonstrate it didn't happen.
   Answer: Thank you. Due to word count constraints, we did not provide many details about the setting. Our three maternity hospitals serve a large population in metropolitan Melbourne and the State of Victoria, with about 10,000 deliveries a year. Patients are allocated to public hospitals according to area of residence, and as such very few would change maternity during antenatal care (unless they move to a different area). Additionally, our tertiary hospital is one of only three in Melbourne, and the other two are relatively distant. We could not include a baseline characteristics Table, but the demographic and baseline characteristics of the women who delivered during lockdown are very similar to those of women who delivered before lockdown. We modified slightly the results to reflect this: “There were no differences in demographic or baseline characteristics (age, weight, height, region of birth, smoking, marital status and parity).” (Line 31 of the manuscript).

3. the methods or introduction should be more detailed on exactly what lockdown measures were instituted and when.
   Answer: See our response on referee 1; point 1.

4. twins should just be excluded. it does not make sense to present data with twins and then do a sub analysis to control for them.
   Answer: Some authors have suggested that lockdown worked almost like a natural experiment. As such, it has affected the entire population, including twins. Additionally, multiple pregnancies are at much higher risk of preterm birth, and so it is important to understand the effect of lockdown in this high-risk subgroup, and to understand how much of the effect is independent of a possible reduction in multiple pregnancies.

5. similarly, I would think the denominator should be live born neonates without anomalies.
   Answer: Thank you. We agree with the reviewer that cases of major fetal anomalies should be excluded from the neonatal outcome analysis (stillbirth, birthweight and admission to neonatal intensive care or special care units). We have simplified and modified Table 1 to represent these changes. However, we believe that cases with fetal abnormalities that did not lead to termination of pregnancy or stillbirth should be included in the denominator for prematurity rates, since prematurity is also an important determinant of survival and prognosis in such cases (excluding cases of major abnormalities would lead to similar estimates for preterm birth).

Reviewer #3:

Table 1: Since CIs are included with the OR and mean differences, the column of p-values is redundant. Should round BW differences to at most, 0.1 g, not cite to 0.01 g precision. There is a typo in the footnote “2m584 in the first epoch”.
   Answer: We have adjusted the rounding of birthweight and gestational age differences, and corrected the typo. We have removed the columns with p-values as suggested from the table.

General: Should acknowledge in limitations section of Discussion that the women in the two epochs were not matched and may have differed in demographic and clinical factors, so the differences cited may not be completely attributable to the different time epochs. Also, the control group is one year prior, so there is no comparison of multiple prior years to exclude a longer trend in PTB frequency that could be independent of Covid in 2020.
   Answer: Thank you, we have modified the discussion and it now reads: “A limitation of our study is that women and children who qualify for our cohorts do so conditional on delivery which, together with possible unmeasured confounding by differences in maternal demographics and clinical characteristics, may affect the comparability and likely explains the difference in multiple pregnancy rates between the two groups.”

The reviewer is right about the control group being only from the previous year. Including individuals from previous years, however, could also bias the estimates if significant changes on the incidence of preterm birth occurred across time. Hence why for the time trend analysis, we included monthly data since January 2018.
Fig 1: The difference in months of PTB rate after June 2020 appears to be significant only due to the rate in Sept 2020; that month appears to be the only outlier. Also, from Table 1, the total number of PTB < 28 wks from June-Sept 2020 is only 9. The conclusion that the subset of PTB < 28 wks represents a significant trend seems equally likely due to stochastic variation. Again, there is no information re: risk factors for PTB in any of the months shown. A similar time series monthly display of all PTB from Jan 2018 would be more informative, as well as based on a larger sample of PTB. 

Answer: We have now modified Figure 1 to include rates of overall preterm birth and preterm birth < 28 weeks. The rates are lower in September but also consistently low in the last three months. Extreme preterm birth is a relatively uncommon event and, unsurprisingly, the study is underpowered for rare outcomes. However, we do observe a biological gradient, with larger effect size in earlier forms of preterm birth that, although not statistically significant, may reflect a delay or a shift in distribution of gestational age at birth (as also evidenced in Table 1).

STATISTICS EDITOR COMMENTS:
Fig 1 seems a stretch. The differences are statistically significant, but based on mostly small counts or percentages. Might be useful for a future meta-analysis.

Answer: Our study was initially motivated by the previous reports and the impression that the occupancy of our neonatal intensive care unit during lockdown dramatically decreased. We agree that the numbers and rates of extreme preterm birth are too low to draw definite conclusions and that three months after start of lockdown may be too short a period to assess the trend in the second period. Nevertheless, we wanted to demonstrate the monthly rates of extreme preterm birth and how they have been consistently low in the last three months. We now also include preterm birth before 37 weeks in the graph. We would be happy to remove the figure if the reviewer believes that it would be best not to include it.

EDITOR COMMENTS:
Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision of this Research Letter, it will be especially important to address the comment made by the statistical editor re: Figure 1 and the concern that the findings may just result from random variation in a single month.

Answer: We hope that the changes made have significantly improved the quality of the letter.