Author’s response to reviews

Title: Different levels of associations between medical co-morbidities and preterm birth outcomes among racial/ethnic women enrolled in Medicaid 2014-2015: Retrospective Analysis

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COVER LETTER WITH A POINT-BY-POINT RESPONSE TO THE COMMENTS

1. Email and Editor's comments

Dear Dr. Lee,

Your manuscript "Different levels of associations between medical co-morbidities and preterm birth outcomes among racial/ethnic women enrolled in Medicaid 2014-2015: Retrospective Analysis" (PRCH-D-19-01447R1) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Pregnancy and Childbirth.

Their reports, together with any other comments, are below. Please also take a moment to check our website at https://www.editorialmanager.com/prch/ for any additional comments that were saved as attachments. Please note that as BMC Pregnancy and Childbirth has a policy of open peer review, you will be able to see the names of the reviewers.

If you are able to fully address these points, we would encourage you to submit a revised manuscript to BMC Pregnancy and Childbirth.

Once you have made the necessary corrections, please submit online at:

https://www.editorialmanager.com/prch/

Please include a cover letter with a point-by-point response to the comments, describing any additional experiments that were carried out and including a detailed rebuttal of any criticisms or
requested revisions that you disagreed with. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

Please also ensure that your revised manuscript conforms to the journal style, which can be found at the Submission Guidelines on the journal homepage. A decision will be made once we have received your revised manuscript, which we expect by 13 Dec 2019.

Please note that you will not be able to add, remove, or change the order of authors once the editor has accepted your manuscript for publication. Any proposed changes to the authorship must be requested during peer-review, and adhere to our criteria for authorship as outlined in BioMed Central's policies. To request a change in authorship, please download the 'Request for change in authorship form' which can be found here - http://www.biomedcentral.com/about/editorialpolicies#authorship. Please note that incomplete forms will be rejected. Your request will be taken into consideration by the editor, and you will be advised whether any changes will be permitted. Please be aware that we may investigate, or ask your institute to investigate, any unauthorized attempts to change authorship or discrepancies in authorship between the submitted and revised versions of your manuscript.

I look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Ashraf Nabhan, M.D.

2. REVIEWER 1 - P Dwarkanath, Ph.D

Title: Different levels of associations between medical co-morbidities and preterm birth outcomes among racial/ethnic women enrolled in Medicaid 2014-2015: Retrospective Analysis

The study has examined the different levels of association between preterm birth outcome and major medical co-morbidities among various racial/ethnic women enrolled in Medicaid. The authors have shown that the preterm birth rate was observed to be high in black women even after controlled for age, prenatal visit counts, and medical comorbidities.

General comments:

This manuscript is more of a descriptive analysis, only referring to the incidence of preterm births on adjusting to co-morbidities and other parameters during pregnancy. There is still a lacuna on various other determinants of preterm births which is not captured or mentioned.

We updated the followings based on the feedback:
Page 4, Line 14-20: “The associations of medical co-morbidities and preterm births varied across racial and ethnic groups enrolled in Medicaid. This report calls for future research on racial/ethnic disparity in preterm birth to apply more integrative and qualitative approaches to ultimately understand the disparity from a contextual perspective, especially for vulnerable pregnant women like Medicaid enrollees.”

Page 6, Line 5-6: Added “overall health, lifestyle” into the following sentence. “Medicaid beneficiaries share common characteristics, such as lower income and health literacy, among other risk factors, which in turn impact their overall health, lifestyle, and access to and utilization of prenatal health services and birth outcomes.”

Page 11, Line 18-24: “While a higher preterm birth rate in black women is a well-known finding, this study showed that racial/ethnic disparity in preterm birth persists among women enrolled in Medicaid, who are expected to share some of the common characteristics: significant financial hardship, less likely to be married, and more medical co-morbidities.”

Major comments:

The objective of the study was to examine the association of preterm births. However, there is a lot of discussion on the 0-12 weeks postnatally. What is the premise of this discussion? This information can be misleading.

The postnatal analysis part was taken out of this manuscript for future publication/analysis.

The authors mention that "The current study found that drug dependence was associated with a higher preterm birth rate in black women whereas diabetes was associated with a higher preterm birth rate in Hispanic women". There is no genetic morphology assessment or any other supporting details to confirm that racial component is predominant determinant of preterm birth.

We revised our discussion section such as the followings:

Page 4, Line 8-10: "In Hispanic women, diabetes (OR=1.44, 95% CI [1.27, 1.64]) and hypertension (OR=1.98, 95% CI [1.74, 2.26]) were associated with higher odds of preterm birth."

Page 12 Line 12 - Page 13 Line 5: "The study finding demands a better understanding of the underlying influences of various medical conditions and its associated social factors to different groups of women. Until now, it is still unclear how race and ethnicity play their role as a predominant determinant of preterm birth. Birth outcomes are different among Hispanic women with different length of immigration years. Risk behaviors like drug dependence and chronic medical conditions such as diabetes and hypertension often coincide with other medical and socioeconomic vulnerabilities and cultural contexts."
Contextual factors, such as distressed neighborhood, thought to explain up to two-thirds of racial disparity in the preterm birth rate among black and white women. In future research, different profiles of pregnant women can be introduced beyond self-reported racial/ethnic classification that may account for these contextual factors."

We also added the following in the introduction section.

- Page 5, Line 14-16: Race and ethnicity are also associated with preterm birth; Black women have higher rates of preterm birth than other racial groups.

- Page 5, Line 18-24: As race/ethnicity is interwoven with multiple social, economic, and cultural issues, however, the precise cause of this disparity is not clearly known. Social determinants of health, such as maternal educational level, family income, housing situation, partner support as well as community factors can also play an important role in accounting for these disparities in preterm birth outcomes.

Minor comments:

Types of preterm births not defined. By definition, preterm is &lt;37 weeks of gestation, as well as early preterm which are at 28 weeks with complications and difficulty in survival.

We have added the followings:

- Page 3, Line 10-15: Preterm birth, defined by delivery before 37 completed weeks of gestation, was the primary dependent variable. All single, liveborn births were dichotomously categorized as either preterm or full-term birth using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes.

- Page 3 Line 23 - Page 4 line 1: A significantly higher preterm birth rate was found in black women after controlled for medical co-morbidities, age, prenatal visit count, and high-risk pregnancy.

- Page 7, Line 7-10: In this study, preterm birth included all delivery before 37 completed weeks of gestation, including extremely preterm birth, delivery prior to 28 weeks of pregnancy.

- The list of ICD9 codes for preterm birth diagnosis is listed in the Appendix A as the following:

  - 644.20 Early onset of delivery, unspecified as to episode of care or not applicable
  - 644.21 Early onset of delivery, delivered, with or without mention of antepartum condition
  - 765.10-765.19 Disorders relating to other preterm infants
There is a mention of number of prenatal visits and its association with preterm births. But the authors have not defined the clinical examination during the prenatal visits. This is an important as the clinical intervention can help in improving the birth outcomes particularly the preterm birth.

- Page 8, Line 2-6: In this study, we focused on the mother’s access and utilization of prenatal care services rather than the actual clinical examination or intervention delivered during the prenatal visit. The ICD-9 codes for prenatal visits for normal and high-risk pregnancy are listed in Appendix B.

- In future study, it would be to meaningful to examine which prenatal intervention actually would help to reduce preterm birth events.

Explain: 'A multi-state study found that merely increasing obstetric providers was not associated with increased utilization of office-based prenatal care by black Medicaid enrolled pregnant women'. So, number of prenatal visits and obstetrics providers may not add significance to the association of preterm births.

The number of prenatal visits is associated with healthier birth outcomes, but the multi-state study found that an increased in obstetrics providers did not achieve adequate prenatal care visits.

We added the followings:

- Page 5, Line 8-13: The timing of initiation and frequency of prenatal care, often measured by the Kotelchuck or Kessner Index, were found to be significantly associated with preterm birth outcomes. Adequate prenatal care can assess a woman’s health and support for recommended care, while reducing risky behaviors.

- Page 13, Line 6-10: The study also showed adequate prenatal care visits were strongly associated with preterm birth outcomes in all racial/ethnic groups. There have been diverse approaches to support pregnant women in accessing early and adequate prenatal care and reduce preterm birth outcomes.

Page 16, lines 18-20. Funding sentence is incomplete.

- Page 16, Line 5-13: updated the funding section to “DentaQuest Partnership for Oral health Advancement purchased the access to the dataset. Mr. Ilya Okunev, Dr. Eric Tranby, and Dr. Sean Boynes are employed by DentaQuest Partnership for Oral Health Advancement. Dr. Hyewon Lee was an Academy Health Delivery System Science Fellow during the research study was conducted, and received her fellowship stipend from her host site, DentaQuest Partnership for Oral health Advancement. There is no other funding availability in completing this study.”
Mention the n's for table 1 and not only percentages. For Figure 1 & 2, mention the legends on Y-axis

- Updated Table 1 with the sample number
- Updated Figure 1 and Figure 2 with Y axis
- Deleted post natal analysis from Figure 2

3. REVIEWER 2: Guillaume Ducarme, MD, MSc, PhD

The authors reported a retrospective analysis of data from the Medicaid core dataset from January 1, 2014, and 18 September 30, 2015, including 457,200 pregnant women. They have examined the different levels of association between preterm birth and major medical co-morbidities that were shown to be associated with preterm birth (smoking, drug dependence, alcohol dependence, diabetes, and hypertension) among various racial/ethnic women enrolled in Medicaid.

They concluded that "The higher preterm birth rate in black women remained after controlled for age, prenatal visit counts, and medical comorbidities associated with an elevated risk of preterm birth. The associations of medical co-morbidities and preterm births varied across racial and ethnic groups".

This retrospective study is very interesting, well-written and includes a large sample of pregnant women enrolled in Medicaid in USA. A high rate of preterm birth and hypertension was observed in this cohort.

No information was noted concerning important variable about the subject: spontaneous or induced preterm birth, late-preterm or early-term birth, mode of delivery.

- Page 3, Line 10-15: Preterm birth, defined by delivery before 37 completed weeks of gestation, was the primary dependent variable. All single, liveborn births were dichotomously categorized as either preterm or full-term birth using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes.

- Page 7, Line 7-10: In this study, preterm birth included all delivery before 37 completed weeks of gestation, including extremely preterm birth, delivery prior to 28 weeks of pregnancy.

- Page 7, Line 1-3: specifies Stillbirths, multiple gestations, and low birth weight without gestation week information were excluded from the analysis.

- The list of ICD9 codes for preterm birth diagnosis is listed in the Appendix A as the following:
644.20 Early onset of delivery, unspecified as to episode of care or not applicable
644.21 Early onset of delivery, delivered, with or without mention of antepartum condition
765.10-765.19 Disorders relating to other preterm infants
765.20-765.28 Weeks of gestation (born prior to 37 week of gestation)

Appendix B has a list of ICD-9 codes that were included for full-term delivery, and the studied included both normal (vaginal) and cesarean delivery as long as it is a full term, single, hospital-based, liveborn delivery.

The authors should modulate the conclusions and clearly note that results were observed in a very biased population (pregnant women enrolled in Medicaid in USA) and no other conclusion should be done regarding association of race/ethnic, maternal co-morbidities and preterm birth.

We have updated our discussion section as the followings:

Page 12 Line 12 - Page 13 Line 5: The study finding demands a better understanding of the underlying influences of various medical conditions and its associated social factors to different groups of women. Until now, it is still unclear how race and ethnicity play their role as a predominant determinant of preterm birth. Birth outcomes are different among Hispanic women with different length of immigration years. Risk behaviors like drug dependence and chronic medical conditions such as diabetes and hypertension often coincide with other medical and socioeconomic vulnerabilities and cultural contexts. Contextual factors, such as distressed neighborhood, thought to explain up to two-thirds of racial disparity in the preterm birth rate among black and white women. In future research, different profiles of pregnant women can be introduced beyond self-reported racial/ethnic classification that may account for these contextual factors.

Page 14: Added as noted below in the section of discussion

Line 1-4: While the vast number of subjects increases the power of the study, we may not be able to generalize the study outcome to other states or non-Medicaid populations as the dataset is not a nationally representative sample.

Line 9-11: However, future research should include ways to categorize pregnant women enrolled in Medicaid, considering risky behaviors, daily lifestyle, and social support elements.

Page 14, Line 13-22: updated the section of conclusion

The associations of medical co-morbidities and preterm births varied across racial and ethnic groups enrolled in Medicaid. This report calls for future research on
racial/ethnic disparity in preterm birth to apply more integrative and qualitative approaches to ultimately understand the disparity from a contextual perspective. This comprehensive understanding will help identify prenatal care strategies and policies to reduce preterm birth outcomes among various profiles of pregnant women, especially the ones from vulnerable backgrounds, such as Medicaid enrollees.

Minor comments:

References in the text should be noted as the journal recommendations to authors.

- Reference style has been updated with the Vancouver style.

CI95% should be added in the abstract.

- Page 4, Line 4-8: Drug dependence was associated with higher odds of preterm birth in black (OR = 2.56, 95% CI [1.92-3.41]) and white women (OR = 2.12, 95% CI [1.91-2.34]), when controlled for age, other medical co-morbidities, prenatal visit counts, and high-risk pregnancy.

- Page 10, Line 15-17: In Hispanic women, diabetes (OR=1.44, 95% CI [1.27, 1.64]) and hypertension (OR=1.98, 95% CI [1.74, 2.26]) were associated with higher odds of preterm birth (Table 2).

The authors should explain the delay between Medicaid data set (2014-2015) and the submission of the manuscript.

- We have obtained access to the date in late 2017, performed the analysis in 2018. We have submitted our manuscript in Feb 2019. After seven months of review process, the manuscript was transferred to BMC Childbirth and Pregnancy in the fall of 2019.

- It is not unusual to see a few years of delay in data availability. The recent Center for Medicaid and Medicare Services’ Transformed Medicaid Statistical Information System Medicaid Analytic eXtract (MAX) is also available for data from 1999 to 2015.

Table 1: the sample size of each box should be added

- Updated with sample size

Table 2: I do not understand the line concerning the age?!!?

- Updated from 1-1 to 1.00 – 1.00e