Reviewer's report

Title: Pre-pregnancy body mass index and weight gain: Where is the tipping point for preterm birth?

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Reviewer: Maria Regina Torloni

Reviewer's report:

Review of Masho 2012.
The authors assessed the effect of gestational weight gain on the odds ratio (OR) of preterm birth (PTB) in women with different pre-pregnancy BMI categories. They used data from a large cohort of American women receiving antenatal care between 1959-1974 in 12 hospitals. Their main question is how these two factors (gestational weight gain and maternal baseline BMI) interact and influence the OR for PTB.

Their research question is valid, clear and well formulated. They performed subgroup analyses for Black and White women of various BMI categories and gestational weight gains, which is interesting and pertinent, since ethnicity plays an important role in PTB and is often neglected. Additionally, they also analyzed the effects of these variable on early PTB (<32 weeks) as well as in PTB in general (<37 weeks), which is also an important point from a clinical perspective. There are important methodological details missing (such as information on recruitment, setting, type of population and how gestational age at delivery was obtained, among others) which I trust the authors can provide. In the Results and Discussion, the authors should review some sentences on the interpretation of their findings and refrain from making so many inferences based on tendencies devoid of statistical significance, concentrating instead on their more robust findings.

My main concern with this manuscript is the fact that the authors grouped different subtypes of PTB as a single outcome. It has been recommended that the investigation of possible risk factors for PTB should distinguish between PTB with and without premature rupture of membranes and indicated PTB, since the etiology, risk factors and pathways for these various subtypes of PTB may differ considerably [Hendler et al 2005, The Preterm Prediction Study: association between maternal body mass index and spontaneous and indicated preterm birth. AJOG; Goldenberg et al 2008, Epidemiology and causes of preterm birth. Lancet; Moutquin 2003, Classification and heterogeneity of preterm birth. BJO; Savitz et al 1991, Epidemiologic characteristics of preterm delivery: etiologic heterogeneity. AJOG]. I therefore strongly recommend that the authors reanalyze their data according to subtype of PTB and resubmit this manuscript.

Abstract
MAJOR COMPULSORY REVISIONS: The 2nd and 3rd sentences of Results should be corrected to reflect significant difference in the ORs identified in this study (see comments on Results and Discussion below).

The 1st sentence of Conclusion is incorrect, based on the findings reported in the tables (see comments on Results and Discussion below). The second sentence should be removed since it is not supported by the findings of this study which was not designed to answer this specific research question (i.e., the adequacy of IOM 2009 gestational weight gain recommendations).

Introduction
The authors present well the importance of the topic as well as current controversies and knowledge gaps in the area. The research question is well stated and clear.

MINOR ESSENTIAL REVISION: Some important references on the topic of maternal prepregnancy BMI and/or gestational weight gain versus PTB are missing and should be added. This studies should also be mentioned in Discussion and their findings compared with the main outcomes of the present study:


• The association between prepregnancy maternal body mass index and preterm delivery. Zhong Y, Cahill AG, Macones GA, Zhu F, Odibo AO. Am J Perinatol. 2010 Apr;27(4):293-8

• Pre-pregnancy body mass index and weight gain during pregnancy in relation to preterm delivery subtypes. Rudra CB, Frederick IO, Williams MA. Acta Obstet Gynecol Scand. 2008;87(5):510-7

Methods
MINOR ESSENTIAL REVISIONS: 2nd paragraph, selection criteria for inclusion in analyses: the authors state they analyzed 52,574 pregnancies after excluding multiple births and fetal anomalies. How many, from the original cohort that enrolled women in their 1st antenatal care visit, were excluded due to miscarriage (< 20 weeks) and to fetal demise? How many were excluded from this original cohort due to missing information on essential variables, such as gestational age at delivery or maternal prepregnancy BMI or gestational weight gain? I suggest creating a flow chart to depict the representativeness of the included cases in relation to the original cohort.

- 3rd paragraph, Socio economic index: define how this was calculated (or
provide a brief explanation as a footnote to Table 1). (MINOR ESSENTIAL
REVISION)

MAJOR COMPULSORY REVISIONS: 4th paragraph, Gestational age (GA) at
delivery, the main outcome variable: This needs to be describe in much greater
details. Include information on the following:

- What specific subtypes of PTB included in this cohort? This information is
  critical. How many were Spontaneous PTB with intact membranes? How many
  were PTB after preterm rupture of membranes who went into labor
  spontaneously before 37 weeks? How many were induced PTB due to rupture of
  membranes or other indications such as Preeclampsia or diabetes or other
  maternal or fetal complications? How many were elective cesarean section PTB
due to medical indications? This should be clearly stated and women with
  induced PTB should be analyzed separately from those with spontaneous PTB.

- How was gestational age at delivery ascertained in this cohort: by menstrual
dates or by obstetric ultrasound? If it was the latter, at what gestational age was
  it performed? Or was gestational age assessed by physical examination of the
  neonate (Capurro)? In cases of discrepancy between these parameters, which
  one was used to determine gestational age at delivery? This information is
  crucial for the validity of the study.

MINOR ESSENTIAL REVISIONS: 4th paragraph: Add reference to BMI
categories used (WHO).

- 4th paragraph, Gestational Weight Gain:
  - use Kg instead of pounds.
  - take into account GA at delivery
  - instead of using fixed, predetermined GWG categories (e.g. 5 lbs or 10 lbs) I
    suggest that you use quintiles of your own population.

Results

MAJOR COMPULSORY REVISIONS: Incorporate in manuscript the complete
details of how the sample was drawn and describe the population from which it
was drawn. If data are missing or the sampling plan was not followed, explain
why and list all differences between data that were present in the
sample and data that were missing or excluded.

- Specifically, the authors should provide clear information on the 12 included
  hospitals: geographic location, N of deliveries per year, level of complexity. What
  was the process used for their selection? Cluster randomization? Convenience
  sample? What were the selection criteria? Judging by the characteristics of the
  participants (Table 1), these hospitals are not representative of the whole
  spectrum of American pregnant women. This should be stated as one of the
  limitations of the study in Discussion, regarding generalizability of the findings,
even within the context of the United States population.

MINOR ESSENTIAL REVISION: On the 5th paragraph of Methods, hypertensive
disorders are apparently all grouped together. However on Table 1, the authors report the prevalence of Hypertension (presumably chronic) and Preeclampsia separately. The diagnostic criteria for these conditions should be described in Methods. And since the study spanned a period of 15 years, describe differences in these criteria over time.

Table 1.

MINOR ESSENTIAL REVISIONS: The total N of participants in the 4 BMI categories adds up to only 48,077 women. Therefore 4,497 women are missing, since in Methods the author state that they analyzed 52,574 pregnancies, after excluding multiple pregnancies and those with fetal anomalies. Explain this discrepancy.

-Title of columns: place BMI cut-offs for each of the 4 categories, under the name (e.g.: Underweight: BMI < 18.5).

-Besides the %, provide the specific Numbers for all variables presented in this table. And also add information about how many were missing for each variable presented.

-Parity: present this information as a categorical variable instead of a continuous variable: N and % of Nulliparous and of Multiparous women in the cohort.

-N of prenatal visits should be adjusted according to GA at delivery; for example, a woman who delivered before 32 wks would obviously have a lower N of visits than a woman who delivered at 40 wks and this does not imply that the former had an inadequate N of prenatal care visits.

-The overall prevalence of PE in this cohort is very high: 18.1% ! This reinforces the importance of presenting the diagnostic criteria for this condition in Methods and also the type of hospital setting (2ary? 3ary?). Could this be explained by some specific characteristic of this cohort, such as high prevalence of nulliparas (data not presented in current Results)? Or the high prevalence of Black women (47.1%) This needs to explored a bit in Discussion.

-The overall prevalence of previous PTB is very high in this cohort: 23.3% ! This indicates that this cohort is not representative of the general obstetric population and probably has a large number of high-risk women. This should be clarified, explaining the characteristics of the hospitals included in this study.

Table 2.

MINOR ESSENTIAL REVISIONS: Provide what was the reference category for maternal age and for parity.

-Provide pregnancy weight gain in Kg instead of lbs.

MAJOR COMPULSORY REVISIONS: The statement in text of Results (p 9) stating that being obese is protective against PTB is incorrect: the unadjusted OR presented in Table 2 is not significant (0.91, 95% CI 0.82 -1.02).

-The statement in text of Results stating that being obese increases the risk of early PTB (p 10 ) is incorrect: the unadjusted OR presented in Table 2 is not significant (1.03, 95%CI 0.86 -1.23).
Figures 1 and 2. Interesting and well done!

MINOR ESSENTIAL REVISIONS: I presume these ORs are unadjusted? This should be stated in the title of the figures.

-And add the 95% CI for all the ORs in the footnote table, instead of the p values. Alternatively, eliminate this footnote table and present the complete data for this in Tables 3 and 4, as additional data, grouping the Black and White women into a single group.

-Change weight gains to Kg.

Table 3.

MAJOR COMPULSORY REVISIONS: I suggest that the authors include another group for this table (as well as table 4) presenting the same data including both groups of women (Black and White together, which corresponds to the data summarized in their Figures 1 and 2, mentioned above). That way, the reader can clearly see how the OR for PTB is affected by the interaction between pre-pregnancy BMI and gestational weight gain.

-Statements referring to this table in the text (p 9-10) are incorrect and should be rephrased according to statistical significance of the ORs. For example:

-Among underweight White women, the OR for PTB was significantly higher than normal weight White women in the first three gestational weight gain categories, but was similar in the highest (30+ lbs) category (OR 1.19, 95%CI 0.79-1.79).

-In Black underweight women, the ORs for PTB was significantly higher than in normal weight Black women in the first two categories of gestational weight gain, but did not differ significantly in the last two categories (20-29 and 30+ lbs).

-Similar incorrect statements are made regarding overweight and obese categories in both races.

Table 4.

MINOR ESSENTIAL REVISION: The text referring to this table (bottom of p 10) mentions table 3 and does not specify it refers to “early PTB”. This needs to be corrected. Similarly, the paragraph on p 11 should mention “early PTB”.

MAJOR COMPULSORY REVISION: Once more, authors should limit themselves to pointing out statistically significant differences and not tendencies.

Discussion

MINOR ESSENTIAL REVISION: In addition to comparing their results with the additional references mentioned in Introduction, there are several additional studies that should be mentioned here. For example, differences in the ORs for PTB of White and Black women of different BMI should be compared to previous studies which also addressed this question. I recommend that the authors read these references:

- Ethnic disparity in spontaneous preterm birth and maternal pre-pregnancy body


MAJOR COMPULSORY REVISIONS: The 1st statement is incorrect. Based on Table 2, women with pre-pregnancy overweight do not have a higher risk for PTB, but in fact they have a significantly lower OR for these outcomes, when compared to normal weight women. And the ORs of obese women for PTB are similar to normal weight women.

- The 1st statement in the 2nd paragraph is incorrect. The data presented by the authors on Tables 1, 3 and 4 do not support their statement. Based on their Tables, this study showed that, compared to normal weight women, obese White and Black women have a significantly higher OR for early PTB if they gain at least 30 lbs during pregnancy.

- As stated by the authors, combining spontaneous and induced PTB is a weak point of their study, which in my opinion is critical. Therefore, they should reanalyze their data accordingly and rewrite their Discussion based on these findings.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.