Author's response to reviews

Title: Prenatal Micronutrient Supplementation and Postpartum Depressive Symptoms in a Pregnancy Cohort

Authors:

Brenda MY Leung (bleun@ucalgary.ca)
Bonnie J Kaplan (kaplan@ucalgary.ca)
Catherine J Field (catherine.field@ualberta.ca)
Suzanne Tough (suzanne.tough@albertahealthservices.ca)
Misha Eliasziw (Misha.Eliasziw@tufts.edu)
Mariel F Gomez (fajergom@ualberta.ca)
Linda J McCargar (linda.mccargar@afhe.ualberta.ca)
Lisa Gagnon (lisa.gagnon@albertahealthservices.ca)

Version: 3 Date: 11 September 2012

Author's response to reviews: see over
We thank both reviewers for their time and meticulous effort to help us improve this manuscript. We have addressed every one of their comments below, and again we have shaded the changes in the text.

Authors’ response to Reviewer #1

INTRODUCTION
Discretionary Revision
1. Last 2 sentences of first paragraph: Consider rewording to something like “PPD poses sig ph issue because of its impact on not only the lives of women themselves, but also on their children’s growth (3) and cognitive and social-behavioural development (4). If revised, consider removing words “health and development” from sentence above.

RESPONSE: Thank you for the suggestion to make the sentence more succinct; we have revised it as suggested.

DISCUSSION
Minor Compulsory Revision
Page 15, last paragraph.
2. Given that data on maternal diet was collected, consider examining the relations between overall maternal diet quality, prenatal micronutrient supplementation, and postpartum depression (and adjust for overall diet quality if significant relations exist). It seems possible that maternal diet quality (as an indicator for better health and health/dietary behaviors) might confound the relations between prenatal MN supplementation and postpartum depression. If not re-analyzed, consider addressing in discussion.

RESPONSE: We regret it was not clearer that the data on maternal dietary intake is not available for analysis at this time, so we simply cannot examine those relationships yet. We will certainly do so at some future date. However, given that nutrient intake from supplements surpasses the amounts from diet alone, confounding in this case should not be an issue. We have taken the reviewer’s suggestion and discussed this in the revised manuscript. In the discussion on page 16 we say, “A third limitation was that dietary (food) intake was not included in the analysis.” And on page 17 “the high supplement intake may mitigate dietary intake in this case, and would not be likely to change our findings.” However this does not negate a contribution from macronutrient intake. We have added this potential effect that differences in macronutrient intake might have on our findings in the discussion (page 17): “There is also a potential effect on our findings of differences in macronutrient intake.”

Major Compulsory Revisions
3. Authors state in their response that prenatal nutrition status (weight, iron/anemia status) was not available for the analysis, consider discussing this as limitation (e.g. the inability to test if the effect of prenatal MN supplementation on postpartum depression varied by prenatal nutritional status)

RESPONSE: Thank you -- we have added this as a limitation in the discussion, at the bottom of page 17 “In addition, as data on prenatal nutrition status was not available, we were unable to test whether the effect of prenatal micronutrient supplementation on postpartum depression varied by prenatal nutritional status. For future research, we would like to assess whether specific nutrients interact to impact postpartum depression, and also whether prenatal nutritional status modified the association of supplementation and postpartum depression.”

4. Page 17, 1st paragraph – consider revising to something like…..Implication for future research include examining objective measures of pre and postnatal micronutrient status to: 1) test relations between pre/postnatal blood nutrient levels (or changes in pre-postnatal blood levels) and postpartum depression, 2) moderating effect of prenatal blood nutrient levels on the
relations between prenatal MN supplementation and postpartum depression, and 3) interactions amongst nutrients and their effects on postpartum depression.

**RESPONSE:** Thank you for the suggestion; the text is now revised as per reviewer’s suggestion (bottom of page 18): Implications for future research include examining objective measures of pre- and postnatal micronutrient status for: 1) relations between pre/postnatal blood nutrient levels (or changes in pre/postnatal blood levels) and postpartum depression, 2) moderating effect of prenatal blood nutrient levels on the relations between prenatal micronutrient supplementation and postpartum depression, and 3) interactions amongst nutrients and their effects on postpartum depression.

5. CONCLUSION (on page 17) and ABSTRACT Major Compulsory Revisions. Given the limitations of the current study, consider limiting conclusions to considerations for future research rather than clinical practice.

**RESPONSE:** Both the abstract and the text have been revised according to the reviewer’s suggestion.

---

**Authors’ response to Reviewer #2**

Major compulsory revisions

6. The authors do not seem to realize that their description of the supplement exposure is not clear. Presumably some women were recruited during T1 and others T2 and yet others T3 (their criteria was before 28 weeks which is within t3).

**RESPONSE:** The reviewer is correct that we were unaware of the confusion, so we appreciate the opportunity to clarify, both here and in the text. As now more clearly indicated in the Methods section on page 6, women had to be \(<\ 27\) weeks gestation, to be invited into the study. This means that women could enter the study anywhere in the first (T1) or second (T2) trimester. Clinically, the second trimester ends at about 26.5 weeks; hence, we used the \(<\ 27\) weeks gestation cutoff. Our definition of trimester is consistent with every definition we have found, ranging from obstetrical texts to various government sources, so we think the confusion lies in the wording. To clarify again: women were not invited into the study if they reported being 28 weeks gestation, which the reviewer correctly points out would be within the conventional definition of T3. No women entered the study or began providing data in trimester 3. We have clarified this in the revised manuscript with the following text (page 6): “Women must be in the first (T1) or second (T2) trimester to be in this study; we did not include any woman who was 28 weeks or beyond.”

7. We don’t know what that distribution is, but we do know that the authors limited the analysis to those who had 2 EPDS values. So presumably there are 2 or 3 supplement intake measures to be combined. This should be stated.

**RESPONSE:** The reviewer is correct, that for every woman there were either 2 or 3 supplement intake measures combined. A statement about precisely how this was done is on page 8, “To obtain an average intake of each nutrient in the supplements, reported intake was averaged over the number of times data were collected. For example, if information on vitamin D supplement intake was collected at each trimester (i.e., three times), then the total amount consumed was divided by three; if information was collected at only two times, then the total was divided by two.” We have
now clarified this by adding the following (page 8): “Supplement data was collected a minimum of two times, and maximum of three times during pregnancy.”

8. The authors allude (for the first time) in the discussion section that frequency data were available but this is not described or stated in the methods section.

**RESPONSE:** In the methods section we have stated (page 8) “At each visit during pregnancy and postpartum, women were asked to describe in detail the quantity (i.e., frequency of intake and dosage) and type (e.g. prenatal multivitamins) of NHP consumed.” Now we have added in the methods section how frequency and dose were calculated (see response for next question). The number of participants per trimester varies because some people may have missed one or two visits. We had SIQ data on (n=136) 1st trimester; (n=575) 2nd trimester; (n=516) 3rd trimester. Now we have added the following (page 12): “SIQ data was available for n=136 in the first trimester, n=575 in the second trimester and n=516 in the third trimester.”

9. Presumably the authors have an intake (e.g., in mg/d based on a formulation) from some point in a trimester and some frequency such as “every day” or 3-4 times per week (the authors should provide the response categories as the reader should not have to go to the questionnaire to find this out) and then the intake was multiplied and summed across all products to project an estimate of intake per day per trimester and then given information for another trimester (or 2) these intakes similarly calculated (?) were combined as a simple average of 2 or 3 values (or not, because it could be that only 1 value was available from week 12 for example was used for one woman’s exposure during her entire pregnancy in an analysis in which another woman provided information at 3 time points in pregnancy).

**RESPONSE:** We have added the following text (page 8): “At each visit during pregnancy and postpartum, women were asked to describe in detail the quantity (i.e., frequency of intake and dosage) and type (e.g., prenatal multivitamins) of NHP consumed, using open-ended questions. To determine dose, women were asked “how much do you take?” and for frequency, women were asked “how often do you take it?” Typical responses were daily or times per week (e.g., 5 x/week). There was no menu of responses from which to choose. For example, if a woman said she consumed 700 mg/week of a nutrient, it was calculated as 100mg/day for that specific trimester. The daily value was calculated for the specific trimester, and only for that trimester, and not extrapolated for the entire pregnancy.”

10. This algorithm needs to be described in detail. I use the word "project" because a woman may have provided an estimate for the 2nd trimester at week 15 and another at week 23 (start and end of T2) and one has an estimate which is projected forward (as a planned behavior) and the other has an estimate which recalls presumably their actual behavior. We do not have information on the week of gestation for enrolment in the study or the weeks’ gestation that correspond to the t1, t2 or t3 questionnaire administration. Did the authors query back from t3 for information at t2 or t1? The authors should state yes or no on this point. In sum, the authors need to state the algorithm used, the degree of completeness of the information with respect to trimesters, and the timing at which the information per trimester was collected.

**RESPONSE:** All of the information on supplement use was collected with the 24h recall and reflected use at the time of the interview. The answer to the question posed by the reviewer is NO, the authors did not ‘query back from t3 for information at t2 or t1.’ We have added to the text (page 6): “Windows for data collection were defined *a priori* as week 10 ±2 for first trimester, week 18 ±
2 for second trimester, and week 32 ± 2 for third trimester. Every attempt was made to meet these specific timepoints as closely as possible (see Figure 1).” At the visit we asked about the use of supplements and the frequency at which the women took them to generate an average for that trimester. The mean nutrient intake from supplements, standard deviation and range are in Table 2. If a woman missed her trimester visit, then this was treated as missing data and no estimation was made. We agree with the reviewer that there was some degree of projection as the women were not asked at the end of each trimester for the entire trimester. We have added this limitation in the discussion (page 17): “Thus, there was some degree of projection as the women were asked for information for the entire trimester at the trimester midpoint and not the end, making this a limitation to our estimates.”

11. On a similar vein, Table 2 does not inform us of the distribution of the calculated exposure. The mean intake (95% CI) in the table provides an estimate of the CI around the mean rather than telling us about the distribution of the exposure across women. This was made clear to me when looking at the values for selenium intake and the tight bounds around the mean and then looking at the results in table 3 which suggest an effect per 10 mg/d which would suggest that the authors are estimating effects beyond the range of observed exposures as shown in Table 2! This brings up a related point in that the distributions for some intakes (from supplements) are not likely to be normal but are treated as such in the paper as we find reported mean intakes in Table 2. This may be true for nutrients found in multivitamin/mineral (MVM) which perhaps all women take (?) with varying frequency, but not so for selenium and omega-3 FA which are not (?) provided in some prenatal or other MVM and for which some (?) woman will have 0 intakes, and other may have higher intakes as they may be taking specialty products (?). The authors should provide the mean and SD for the distribution of intakes and I think the range as well. If the distribution is not normal, provide appropriate alternate characteristics to describe the distribution and state how this was handled during analysis.

RESPONSE: The reviewer raises an important point. We have revised Table 2: for each nutrient, we now provide the mean and SD, and the range for intake, which will assist the reader in identifying the variation in the intakes and the supplement intakes that are not normally distributed. We have added also to the text (page12): “In fact, the upper ranges for intake were higher in almost all nutrients (except for folic acid) in women with EPDS <10 than women with EDPS ≥10.” The statistical model we used was logistic regression which does not rely on the predictors being normally distributed. We have added this information to the description of the statistics (page 10) and acknowledged that the supplement intake for many of the nutrients is not normally distributed (page 12).

12. The authors now recognize that multicollinearity may have been a problem, but a few more sentences are really needed as it relates to broader issues common to these types of analyses. The intakes of nutrients from supplements are highly correlated because a woman takes a supplement with a given formulation, and in fact for most nutrients there is a standard formulation across brands, and this is true across MVM, those for women and in fact prenatal formulations. For these nutrients, variance is driven by frequency differences across women (and we have no information to see what true differences are – see point above). For other nutrients there are perhaps differences depending on the type chosen. And for others (such as selenium and omega) are likely to vary the most because they are not found in many MVM but found in some products which leads to projected differences across subjects. Thus, there may be reduced
inter-subject variance in nutrient intakes for many nutrients and an inability to find differences in models (the multicollinearity) and findings for selenium may be more related to the fact that you had the ability to see (between subject variance) but which is based on behavioral choices which are endogenous to your model (determined by social factors).

**RESPONSE:** We agree with the reviewer’s assessment that a number of nutrients (e.g. B vitamins) are highly correlated; as shown in Table 2, a majority of women are above the RDA for several nutrients, and thus we conclude that women have adequate intake of those nutrients. Our focus then is on nutrients that have received little attention or research that may still influence depression. In our sample, about 99% of women took some form of supplement, using over 400 brands; thus we also conclude there is variability for intake of some nutrients impacting depression (see response to next question). We did not go into details on the characteristics about supplement intake (frequency, dose, above/below RDA, etc) as another paper on this topic is currently under review for publication. In the current manuscript we focused on the specific topic of supplement intake in relation to postpartum mood. We have also added to the text (page 16): “Multicollinearity is a common problem in nutrition studies, particularly those that examine the intake of nutrients from supplements as supplements include multiple nutrients and many are in similar amounts and combinations due the nutrient recommendations by health agencies.” We hope the various changes to both this and the other questions that are related are sufficient, and appreciate the reviewer emphasizing these important points.

13. My question to the authors is whether there is another nutrient which is found in products and has enough variance in the right part of the distribution (I get what you say about omega-3) for which you did not find an effect?

**RESPONSE:** Another nutrient that may be comparable is magnesium (i.e., mean intake and range). As shown in table 2, and shown below,

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>EPDS&lt;10 (n=416)</th>
<th>EPDS≥10 (n=59)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>67 (65)</td>
<td>59 (39)</td>
<td>0.19</td>
</tr>
<tr>
<td>Range</td>
<td>0 – 1025</td>
<td>0 – 208</td>
<td></td>
</tr>
<tr>
<td>Below RDA (n (%))</td>
<td>415 (87.5)</td>
<td>59 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Above RDA (n (%))</td>
<td>1 (100.0)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Selenium (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>25 (17)</td>
<td>19 (13)</td>
<td>0.0015</td>
</tr>
<tr>
<td>Range</td>
<td>0 – 125</td>
<td>0 – 45</td>
<td></td>
</tr>
<tr>
<td>Below RDA (n (%))</td>
<td>401 (87.2)</td>
<td>59 (12.8)</td>
<td></td>
</tr>
<tr>
<td>Above RDA (n (%))</td>
<td>15 (100.0)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

However, magnesium was not statistically significant as a predictor of PPD when used in the initial model that incorporated all the nutrients. This is indicated in the text.
14. Can you say it is selenium and not the decision to buy a product?  
**RESPONSE:** As reviewed in the discussion (page 14 – 16), there is a strong literature on selenium in terms of its neuroprotective properties, and other studies have shown its association with depressive symptoms. We do not know why people may have chosen “special supplements” that contained more selenium or more omega-3s. Thus we cannot comment on whether the behaviour of seeking these types of supplements is more or less of a contributing factor to the significant finding for selenium.

15. The authors state as a limitation the lack of data on biochemical indicators but that does not really respond to the point made by the reviewer that anemia is not adjusted for in the analysis and that this is a well established determinant of depression including postpartum depression.  
**RESPONSE:** We have added this detail to the Discussion (page 17): “We did not have lab values at present to assess anemia in our sample. Although anemia is known to be a risk factor for depression, we also know that women are routinely supplemented with iron when anemia is diagnosed during pregnancy. In this study, for women below RDA, 82.9% scored <10 EPDS, 17.1% scored ≥10 EPDS; for women above RDA, 88.5% <10 EPDS, and 11.5% were ≥10. p = 0.84 (see Table 2), indicating that there was no difference of scoring ≥10 EPDS between being above or below the RDA for iron. While we recognize this is not the ideal measure for iron associated form of anemia, it served as a proxy for iron status.”

16. The authors seem now to back away from the selenium finding to say that nutrients still matter for preventing depression. I suppose this is in response to thinking about the fact that they can't really evaluate the separate effects of intake of nutrients when they are delivered in a combined MVM supplement. But this is not made clear and it makes the paper look flip-floppy. I would suggest editing to clarify these points.  
**RESPONSE:** We have revised the abstract and conclusion to specify that our results focus on supplementary selenium intake, as multiple factors, including selenium, are associated with the risk of postpartum depression.

17. The results as presented suggest that prenatal selenium intake affects the likelihood of pp depression symptoms independent of pregnancy depression symptoms! Why would that be? What was the effect of selenium on the outcome prior to putting the pregnancy depression variables in the model? Was prenatal depression associated with selenium intake? How does that association affect your interpretation? These considerations should be added to results and the discussion.  
**RESPONSE:** Given the need to focus on a single topic for the manuscript, some details were left out (e.g. details about the social support questions, which we now have added in response to the reviewer’s request). Thus, the analyses presented in the paper focused on those that were statistically significant (e.g. in building the most parsimonious model). Not presented were regressions for prenatal depression and the key nutrients found to be significantly associated with postpartum depression. The results (not shown) were that supplementary selenium was not a predictor of prenatal depression at second or third trimesters (information added to the Results section, bottom of page 11). This may be due to the fact that women who scored >10 on the EPDS prenatally are not the same as the women who scored >10 postnatally. We have not explored the possible reasons behind this difference. In the final model, we adjusted for perinatal depression, and...
selenium was still statistically significant, which adds credence to our conclusion. Given the multitude of underlying factors in pregnancy, this may be a topic worthy of investigation for another paper, but may be beyond the scope of this current article to cover. As with other research, we are providing one small piece of the puzzle in an effort to understand the overall association between nutrients and postpartum depression.

18. Page 10, I do feel strongly that the sentence on power analysis should be part of the methods section.

**RESPONSE:** As requested by the reviewer, the statement on power analysis has been moved to the Methods section, under the EPDS description, page 9.

19. I also don’t understand the power calculation as I would think that some distinction would need to be made about the prevalence of the exposure (supplement consumption above/below the RDA). Also this does not appear to be the way the data were analyzed, and the authors suggest that power may have prevented their ability to find an effect for omega-3 FA, so more text is needed. In addition, there may not be sufficient between subject variance in take for some nutrients to find effects. If these matters are addressed they would make for a stronger paper.

**RESPONSE:** The power was calculated to determine the minimum number required to adequately detect the outcome of depression in the sample. We are unclear as to the reviewer’s comment about “supplement consumption above/below RDA” and whether the reviewer is asking for power to be calculated for each nutrient? Furthermore, the reference to omega-3 was talking about the proportion taking omega-3 compared to the proportion who took selenium. However, we did talk about the lack of variance for some nutrients: as stated on page 16, “the effect of multicollinearity as a number of variables were closely correlated (e.g. various B vitamins with each other, and with vitamin C and E).” We have now added the following: “Multicollinearity is a common problem in nutrition studies, particularly those that examine the intake of nutrients from supplements as supplements include multiple nutrients and many are in similar amounts and combinations due the nutrient recommendations by health agencies.”

20. Not much information is provided about what kind/type/level of social support is characterized in this variable. For example, does professional intervention count? Medication? Or are we looking at having family and friends to do housework share in child care? This relates to the literature on which we should compare findings?

**RESPONSE:** As social support was a covariate, we had not provided details on the specific questions used. In response to the reviewer’s question, we have now added the following text in the Methods section, page 6: “Perceived social support was measured with questions from the National Population Health Survey (NPHS) – Social Support section (Statistics Canada, 1994/95 & 1996/97 cycles) [31] with response options modified for the APrON study. The NPHS-Social Support section is comprised of four statements about having “someone to confide in”, “someone one can count on in a crisis”, “someone one can count on for advice”, and “someone who makes one feel loved and cared for”, with Yes/No response options. Guided by expert advice from team members, the APrON study kept the wording of the statements, but modified the response options to five possible answers: none of the time, a little of the time, about half of the time, most of the time, all of the time. Each response option was then assigned a numerical value, “none of the time” was assigned a value of 0 and ranged up to a value of 4 for “all of the time”. By summing the scores of each statement, an overall score of 16 indicated the highest
possible level of perceived social support, while an overall score of 0 was the lowest possible level of perceived social support.”

21. Page 16, the authors cite the use of multiple measures over time to record intake but we don’t have that information to be able to recognize that as a strength. For how many women are their 3, 2, or 1 measure used?

**RESPONSE:** We have added, under Methods section, page 8, the following text: “Supplement data was collected a minimum of two times, and maximum of three times during pregnancy.” And on page 12 we added: “SIQ data was available for n=136 in the first trimester, n=575 in the second trimester and n=516 in the third trimester.”

22. Page 16, bottom of para 2, how can the authors draw conclusions that the biological and social risk factors are not mutually exclusive? Where is the evidence for that? I believe that the factors in the model represent mutually exclusive (independent) effects but rather the authors are saying that factors influencing the likelihood of pp depression are not exclusively biological or social (although we can’t know that from this analysis when the two other factors besides selenium in the model are the outcome at an earlier period, and potentially treatment during perinatal period (the social support variable which we need to know more about what it is and what it is not).

**RESPONSE:** We appreciate the opportunity of revising this sentence, which gave the wrong impression. We have deleted the term “mutually exclusive” and revised the text (now on page 18) to read “biological and social risk factors are involved”.

23. Conclusions are broad to bring in intakes of multiple nutrients which is odd given the results.

**RESPONSE:** We have revised the conclusion (page 19) to read “Thus, a future research focus on dietary supplementation with special attention to the intake of selenium in the pregnant population is warranted.”

Minor essential revisions

24. In the intro, the authors use the word challenge in one way and then use challenge in another way which is not consistent with the prior sentence, depression is a challenge in a general sense but it is not an inherent part of pregnancy which is what those two sentences together seem to suggest. Rather it would seem to be an indication that psychological adaptation to pregnancy is not good (an outcome of the challenge but not the challenge itself). I would urge the authors to change the second use of challenge, and re-write that sentence.

**RESPONSE:** Thank you for pointing that out; we have deleted the first sentence and modified the second sentence to read: “Postpartum depression is a serious mental health problem”.

25. Page 6, what do the authors mean by the “first cohort”? This is repeated and it is not clear. Are their waves? Or do you mean a cohort of the first 600 women? Although a design paper is in press, key details need to be provided on the design, methods for these analyses. For example, this paper excluded women with missing data on some variables, and we need to know the methods (timing of data collection, gestation at enrollment) for those included here (as an example).

**RESPONSE:** Thank you for mentioning this confusion; the text is now revised to read: “Participants for this study are the first 600 pregnant women from the APrON study”. We have corrected the wording in other places throughout the text: in the Abstract, it now reads “Participants came from a cohort of the first 600 APrON women”; in the Results, it now reads “Of the 600 pregnant women in the study
To provide clarification on data collection, we have included a diagram of the timepoints for data collection, see Figure 1. The design paper is now accessible, and the citation has been updated in the manuscript.

26. Page 9, methods to describe an investigation of selection bias is now detailed, but what was the conclusion? I would rather have the conclusion in the methods than in the results section, but I defer to the Editor on this point.

RESPONSE: Page 9 discussed missing values and statistical methods, thus we do not understand the “selection bias” the reviewer is referring to, or what is meant by “have the conclusion in the methods than in the results section.”

27. Page 10, that first para does not fit under the sub-title. If it will remain in the results, the sub-title should be moved/retitled.

RESPONSE: If we understand correctly, the reviewer does not like the subtitle “sociodemographic variables” as the subheading for the section where we describe the sample, the comparison of the report of whether they were born in Canada, number of chronic conditions, stressful life events, and social support. We agree that it is not a perfect descriptor for that information and so we have deleted it.

28. Page 12, the authors state that they adjusted for nutrients known to be associated with depression but there are no other nutrients in the model. Perhaps they mean that they were adjusted for in that it wasn’t necessary?

RESPONSE: As stated on page 11, “The third model assessed nutrients from supplement intake (see Table 2), and the fourth model incorporated significant (and close to significant) variables from models one, two, and three”. The nutrients included in the third model were the ones listed in Table 2; given that most of the nutrient variables were not significant in the third model, we followed statistical protocol, and removed the non-significant variables the next step (model) as we were aiming for a parsimonious model for the final model. At this point, we are unsure what revision the reviewer is requesting, but perhaps the slight wording change we have made regarding Table 2 will clarify things.

29. Top of page 13, who would argue that pp depression is the result of a single cause or mitigating factor? I found this statement to be unusually strong and unnecessary. I also think that the statement that the findings support prior findings on nutritional factors to be too general/sweeping. The authors should add specificity to this comment.

RESPONSE: We had not intended to sound so broad; we thank the reviewer for drawing it to our attention, and have softened the wording on page 14 to read: “The results of this research support previous studies on the nutritional and social factors associated with depression [5,42,43] and are consistent with the finding that multiple factors are involved the development of postpartum depression.”

30. Bottom of page 13, change levels to concentrations

RESPONSE: We have revised the term as suggested (now on page 14).

31. Page 14, middle, “associated with the likelihood of depression”, “mood and mental health in pregnancy

RESPONSE: The text has been revised to read as suggested by the reviewer (now on page 15).