Reviewer's report

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

Version: 2 Date: 17 August 2012

Reviewer: Laura Caulfield

Reviewer's report:

Major compulsory revisions

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). 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. 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. 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). 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.

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 omeg-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.

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). 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? Can you say it is selenium and not the decision to buy a product?

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.

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.

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.

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

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?

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 there 3, 2, or 1 measure used?

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).

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

Minor essential revisions

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.
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).

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.

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.

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?

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.

Bottom of page 13, change levels to concentrations

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