Reviewer’s report

Title: Effect of folate intake on health outcomes in pregnancy: a systematic review and meta-analysis on birth weight, placental weight and length of gestation

Version: 2 Date: 8 May 2012

Reviewer: Radek Bukowski

Reviewer’s report:

Dear Editor,

This manuscript is a systematic review and meta-analysis of the randomized controlled trials of the effect of folate intake on birth weight, placental weight and duration of pregnancy. Such synthesis of the literature is important because of the clinical and research significance of the role of folate in pregnancy outcome. The manuscript is well written and methodologically is appropriate. The authors may consider these suggestions to clarify its findings.

Major comments

1. The outcomes of pregnancy in this study birth weight and placental weight and duration of pregnancy are important because they function as proxies for perinatal mortality and morbidity. However, the extremes of birth weight, small for gestational age birth weight and duration of pregnancy preterm birth are predominantly associated with mortality and morbidity. The studies included in this meta-analysis evaluated approximately 700 birth weights and 400 durations of pregnancy, which would correspond to about 70 small for gestational age birth weights and 40 preterm births in both interventional groups together. Thus this study is underpowered to make inferences about those most important outcomes.

2. It appears that all the studies included in the meta-analysis were evaluating post-conceptional supplementation and intake of folate. It would be important to emphasize that the findings do not allow inferences about pre-conceptional supplementation or intake which differ substantially from intake and supplementation during pregnancy.

3. Related to previous point is importance to clarify not only the average duration of intervention (Table 1), but also in what gestational age interval was it implemented.

4. Similarly, authors could comment on the effect in the dosage of folate supplementation in the interventions. Both differences in gestational age, duration and dosage of intervention could explain the observed heterogeneity of intervention effect and perhaps shed light on the underlying mechanisms.

5. The readership would benefit from expansion of limitation section on the aspect of the findings that significant association was observed among birth
weights outcomes with larger number of data points while non-significant
associations were observed with less numerous outcomes. Could those
differences be ascribed to differnces in subject numbers and variance?

6. To facilitate the interpretation of the findings it would be helpful to develop the
argument and evidence supporting the assumption that the relationship between
intake and outcomes follows natural logarithm function.

7. The authors noted a substantial risk of bias but should expend discussion of
arguments for and against its effect on the study findings.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

Declaration of competing interests:

'I declare that I have no competing interests'