Author's response to reviews

Title: A Randomized Controlled Trial to Investigate the Impact of a Low Glycemic Index (GI) Diet on Body Mass Index in Obese Adolescents

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Author's response to reviews: see over
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Dr. Wei Bao  
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Dear Dr. Wei Bao,

Ref: Manuscript number- MS:1686808131091137  
Title: A Randomized Controlled Trial to Investigate the Impact of a Low Glycemic Index (GI) Diet on Body Mass Index in Obese Adolescents

We would like to express our most sincere gratitude to you for the time and effort spent with this manuscript and the reviewers for their valuable comments. We have revised the manuscript with full consideration of your and the reviewers’ feedback. Our responses to the comments are listed below with amended parts in the revised manuscript highlighted in yellow:

Reviewer 1
Major compulsory revisions:
1. Some editing with regards to English language would be needed to improve comprehension, and I suggest the authors have someone whose first language is English proof-read their manuscript.

Response: Co-authors of this manuscript, Prof. C. Jeya K. Henry and Dr. Risa Ozaki, are the one whose first language is English. The revised manuscript has been sent to them for editing the English again.

2. Methods- Intervention, 2nd paragraph: Please provide information (earlier than this section) on how desirable weight status was defined for each subject. Later on you mention that a 20% caloric reduction was applied. However, some might argue that there are issues to consider when applying weight loss diets to children and adolescents, since that might affect their growth. In fact, a common practice for weight loss in this age group is to increase physical activity (and therefore energy expenditure) and focus on improvement of eating habits rather than caloric restriction. Can you please clarify/discuss this? Also, in the 3rd paragraph, please define low-calorific products.

Response: Most, if not all, of the study subjects had their baseline dietary caloric intake being excessive than what they needed before entering into this study. Therefore, what we suggested to them, 20% caloric restriction to their current diet, should not affect their growth. Moreover, our study subjects were all post-pubertal and weight loss diets would not have negative impact on their growth spurts. For desirable weight status, we aimed to have body weight <85th percentile of the local age- and sex-specific reference (see reference 16). For the definition of low calorific products, they are those equal to or less than 100kcal per serving, and the fat and sugar content should also be equal to or less than 5gm and 30% of the total calorie respectively. The definition had been added in the revised manuscript.
3. Methods- Interventions: The information discussed in the counseling sessions really complicated to be explained to parents and children in either 20 or 30 minutes.

Response: The counseling provided by the dietitian would not convey all information within one counseling session. Instead, in each counseling session, the dietitian applied motivational interviewing approach to encourage the participants to share any personal and environmental barriers to lifestyle change. The dietitian also assessed the participant’s feelings about the dietary advice and the progress, provided ongoing support and encouragement for the participants, re-defined goals based on participant’s feeling and progress, and affirmed participant’s efforts and achievements to enhance participant’s self-efficacy. Moreover, the study subjects were provided with telephone reinforcement (telephone calls around 10 to 15 minutes each time for a total of 5 times in 6 months) to make sure the information was conveyed to them.

4. Results: As this was an intervention promoting a low-GI diet, the results (e.g. in Table 2) should contain information on the baseline and post-test GI of the adolescents’ diets in the two groups. This is important to examine compliance levels with the study’s intervention but also to examine whether it was indeed the low-GI advice provided to the intervention group that caused the favourable changes in the intervention group. This is needed before the authors can reach the conclusion that “The results of our study provide additional evidence and important insights regarding the role of low GI diet in obesity management of our youth population”.

Response: Thank you for your suggestion to include the baseline and post-intervention GI values of the study subjects. Table 2 was revised accordingly. In addition, we also analysed the glycemic load (GL). However, we could not show a significant difference in GI and GL between the two groups from baseline to month 6. The discussion part was revised with inclusion of explanations as below:

i) It might be possible that the compliance of the study subjects randomized to low GI diets did not comply satisfactorily. From our observation, most participants in the intervention group did not include at least one low GI food per meal. Only some of them were able to replace high GI food items with low GI ones, such as white rice with brown or red rice, white bread with whole wheat bread, or classic coke with diet coke.

ii) The energy and macronutrients, including energy, carbohydrate, fat and protein were estimated by 3-day record which was considered more accurate in capturing current energy and macronutrient intakes. However, the GI and GL values from diet were estimated by a food frequency questionnaire (FFQ). The FFQ used in the present study had only been validated for quantifying common nutrient intakes but had not been validated for estimating dietary GI and GL values.

iii) Many Chinese foods did not have published GI values and were actually difficult to have GI values, such as Dim Sum. The GI values from diets of the study subjects in this present trial were estimated mainly from the GI values of international published data which might account for some bias in the accurate estimation of GI values of Chinese foods.

5. Discussion- 5th paragraph (limitations): “This may account for the insignificant differences in carbohydrate intake between the adolescents in the control and low GI group”. Although this is potentially a valid point, these questionnaires did manage to detect differences in fat, energy, protein and fibre intake, so this reviewer does not
understand why differences in carbohydrate intake might not have been detected as well. Nevertheless, and similar to my previous comment, the effect of the intervention on GI values would be more important to present here.

Response: We have deleted this statement and revised the paragraph as follows: First, we used dietary questionnaires to assess macronutrients of the study subjects before, during and after intervention. Due to the fact that self-reported dietary intake measures is a common research limitation, there has been increasing use of dietary biomarkers for research in the field of nutrition.

6. Discussion- 5th paragraph (limitations): “Third, our study captures outcome measures at 6 month which may be too short to detect any significant changes in lipid profile and glucose tolerance”. I agree with this argument, however a longer intervention might further increase attrition rates. Please discuss this.

Response: Further discussion of this point had been added in the revised manuscript.

7. Discussion- last paragraph (conclusion): Please tailor your conclusions to the methods applied. This was not only a low-GI intervention, since there were other intervention components as well (e.g. weight loss). For example, the DiOGenes study involved an ad libitum energy intake, whereas the present study was a weight loss study promoting a low-GI diet. Therefore, it might be difficult to distinguish whether the effects observed were due to the low-GI advice provided or the reduction in energy intake that was promoted (especially since no data on GI are reported). Please acknowledge this.

Response: I agree with your point and this was acknowledged in the revised manuscript.

Discretionary revisions:
1. I recommend that the authors consider also presenting intention-to-treat analyses (in addition to the per protocol analyses), to account for the high attrition rates that occurred during the study.

Response: Sorry for the confusion. The statistical analyses of the outcome variables presented in Table 4 were actually based on intention-to-treat principle. We used mixed effects model to analyse those outcome variables. This kind of model can account for intra-correlated repeated measures data and accommodate missing data caused by incomplete visits or dropout, provided the data are missing at random, and thus is particularly suitable for intention-to-treat analysis without the need of imputation for missing data. We have clarified in the revised statistical analyses part that intention-to-treat principle was adopted in analysing the outcomes.

Reviewer 2

Major compulsory revisions:
1. It will be interesting to examine which changes in dietary/nutrient components (i.e. decreased calorie intake, increased fiber intake, reduced fat intake, or increased protein, or any combinations) could explain the larger reduction in obesity indices among the low GI group.

Response: We agree that it is interesting to examine such attributable effects. We understand that a well planned factorial experimental design would allow us to estimate
the effect of each dietary/nutrient component of our low GI intervention on the obesity index outcomes. However, such design would need an accordingly larger sample size. In view of the difficulty of recruiting and following-up obese adolescents, we have not taken into consideration of estimating such attributable effects when planning our study.

2. The completion rate was higher in the low GI group (65.4%) than that in the control group (51.9%). How much does this contribute to the observed differences in obesity indices between the two groups?

Response: We have clarified in the revised statistical analyses part that intention-to-treat principle was adopted in analysing the outcomes. The observed differences in obesity indices between the two groups were therefore unlikely due to the differences in completion rates between the two groups.

3. The participants’ acceptance may be an important factor for both short-term and long-term success of any obesity intervention programs like this study, especially if calorie restriction is used. Was the information of acceptance collected in this study? If so, which diet is more acceptable by subjects, low GI or conventional diet?

Response: The acceptance rate was not collected in this study. Nonetheless, all eligible participants who agreed to enter this study, they were randomized into either low GI or conventional diet with randomization carried out using computer-generated random numbers (see Methods-second paragraph). Therefore, the acceptance rate should not be a confounding factor to the success of the intervention.

4. How many of the study participants finally met the dietary requirements of low GI diet or American Diabetes Association convention diet? It is useful to address participants’ compliance during the intervention and follow-up.

Response: We did not document the data on the compliance to the dietary requirements of low GI diet or American Diabetes Association convention diet. Nonetheless, in each counseling session, the dietitian did review the diet records and provided recommendations accordingly. We shall address this lack of documentation on compliance as one of the limitations in the revised manuscript.

5. Was statistical power estimated during study design? Is current sample size (52 per group at baseline, 27/34 at 6-month follow-up) sufficient to detect the changes/differences in cardiometabolic risk factors?

Response: As stated in the first paragraph under the session of Methods, this present manuscript was based on the interim analysis of an ongoing study started since February 2010. The planned sample size for this ongoing study was 140 subjects per study arm. The sample size calculation was based on the primary outcome, i.e. changes in body mass index at 0 and 12 months between the two groups. Based on a meta-analysis of randomized controlled trials including both adults and adolescents studies that assessed the effects of low GI diet versus high GI or other diets for change of body mass index (Thomas DE, et al. Cochrane Database Syst Rev 2007(3):CD005105, i.e. reference 36 of the manuscript), the mean (95% confidence intervals) decrease in body mass index was -1.3 kg/m² (95% CI -2.0 to -0.5, p<0.05). Using the freeware R MASS2 (accessed at http://tiger.uic.edu/~hedeker/ml.html), 140 subjects per study arm would give the study 80% power at 5% level of significance to detect a mean difference of
1.5kg/m\(^2\) in body mass index between the two groups at month 12 assuming 40% dropout rate. Therefore, the current sample size had not reached the planned sample size and it would be possible that we could detect significant differences in cardiometabolic risk factors after more subjects were recruited. The more detailed elaboration of the sample size calculation and the possible contribution due to the under-power to our insignificant results in cardiometabolic risk factors had been included in the revised manuscript.

Yours sincerely,

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