Author's response to reviews

Title: Effects of Lifestyle Modification on Metabolic Syndrome: A Meta-analysis

Authors:

Kazue Yamaoka (kazue@med.teikyo-u.ac.jp)
Toshiro Tango (tango@medstat.jp)

Version: 2 Date: 16 July 2012

Author's response to reviews: see over
RE: Effects of Lifestyle Modification on Metabolic Syndrome: A Meta-analysis

Dear Editors:

We would like to express our deep appreciation for the valuable comments made by reviewers. Based on these recommendations, we have revised the manuscript and attached our responses to the reviewers’ comments.

The attached paper has been carefully reviewed by an experienced medical editor whose first language is English and who specializes in the editing of papers written by physicians and scientists whose native language is not English.

We are submitting two versions of this paper, both of which are the same except in presentation. The first is a clean copy with no strike-out marks. Red font reflects areas where changes were made. The second version shows the changes and additions in red font and the deletions in blue using the strike-out feature. The reason that we are sending two versions is that the paper was somewhat heavily edited and it would be difficult to get the meaning and flow of information because of the interruptions. Perhaps you will want to supply the reviewer with both copies.

We hope that this revised paper is satisfactory and that our responses are clearly presented so that our revised manuscript will be accepted for publication in *BMC Medicine*. If you require further revisions that would make this paper acceptable, we would be glad to make them. We certainly have appreciated your very careful review and would be more than happy to follow any further suggestions.

Thank you again for considering our manuscript. We look forward to hearing from you.

Sincerely yours,

Kazue Yamaoka
For Dr. M. Hassan Murad’s Comments:

Thank you very much for your valuable comments concerning our manuscript. We found these most helpful and have revised the manuscript accordingly. Based on the recommendations, we excluded the sensitivity analyses using simulated data and reanalyzed in order to make it simple and represent the core result more clearly. In this process, we excluded one study. In the clear version of the manuscript, red font reflects areas where changes were made. We hope that the corrections are satisfactory. Responses to specific comments are as follows.

MAJOR COMPULSORY REVISIONS

1. **Authors did not report the risk of bias in individual studies (methodological quality) or describe the quality of the evidence (strength of inference). This is a mandatory procedure that is always needed to interpret this body of evidence.**

   We evaluated RCT studies, including a variety of different interventions and participants. Therefore, we descriptively report study quality and risk of bias from the viewpoint of study design, response rate, type of data, and outcome measures. As suggested, we have certainly revised the method section and result section by adding these issues.
   Method section → P7L2-4
   Result section “Type of intervention and risk of bias” → P10 last lines
   Discussion section → P12L

2. **Authors report following the PRISMA statement but they clearly did not do that (no quality assessment, no measure of consistency (i.e., I², only p value is reported), and importantly, no description of search strategy.**

   Thank you for your critical comment on the explanation of “PRISMA” contents. We added the explanations to make it clear. Furthermore, we added the search strategy as an appendix table.
3. The review is clearly affected by publication bias (by definition, restricting the review to English language). Funnel plot assessment is absolutely useless here (small number of studies with high heterogeneity).

Thank you for your important comment. For this point, we added the description about the bias in the discussion section.

4. In two areas (abstract and results section), author state that Lifestyle Modification reduced HDL (the correct inference is it increased HDL)

We appreciate your reminding us about the HDL. Since we agree with your valuable comments about the RR, quality of study, and statistical method, we reanalyzed data as mentioned in the above. In the new results, HDL did show a similar positive effect, but it was not significant. Accordingly, we rewrote the explanation.

Abstract→P4L1

5. Pooling risk difference is flawed in this situation (associated with significant heterogeneity due to baseline risk heterogeneity) and is rarely done. The appropriate measure for the effect size in this analysis should be a relative association measure (RR or OR).

The authors agree that the RD is not an appropriate measure for the effect size and that RR is a better measure. In order to avoid confusion, we used RR as a primary effect size and excluded RD results. We hope that the corrections are satisfactory.

Abstract methods section→P2L1
   Results section →P2L1-3

Methods section →P6L6-9
Result RR section → P10

6. Sensitivity analysis for several correlation coefficients is needed.
Thank you for your critical comment on the sensitivity analysis. We added the sensitivity analyses for r=0.3 and r=0.7. The results were similar and the effect of variability of the correlation coefficients was not so large. We added the explanation for this in the legend of Table 2 and the results and discussion sections.

Method Data extraction and risk of bias in individual studies section → P6 last line
Results Difference in means for the components of MetS section → P11L7-8
Discussion section → P11L6

7. Clusters RCTs were included but there was no clear description of how the design effect was adjusted for in analysis.

There was a study (Bo, 2007) to treat family member as a cluster but the study performed individual randomization, not cluster. They stratified some groups and used a minimization method for randomization.

MINOR ESSENTIAL REVISIONS
1. Awkward writing: (for example, repeating “random effects model” 3 times in abstract). Numerous grammatical errors (for example, missing “of” in “proportions of patients”, page 6, line 7

Thank you for your appropriate suggestion for the sentence. We corrected those.

2. Authors use 3 analytical models which is confusing to readers with limited statistical background and takes away from the message of this review. They should choose one model (a priori) and provide justification of their choice (at the least, take that out of the abstract).

Thank you for your critical comment on the analytical models. The authors agree with this comment. We chose a random-effects model with DerSimonian-Laird method as the primary method considering the small sample size. We took out other results from the abstract and excluded all the result of the random-effects model with REML. We hope that the corrections are satisfactory.

Method Statistical analysis section → P7L1
3. Life style modification follows a dose related fashion so when they decided include only RCTs they could underestimated the effect size of LSM programs. This should be acknowledged in discussion.

We do not understand what you mean. It seems to us that including only RCT in meta-analysis do not always underestimate the effect size.

**Discretionary Revisions**

1. We would like to see implications for future research about LSMs in this review. For instance, evaluate LSM with and without weight loss, LSM diet vs anaerobic exercise vs aerobic exercise vs combination, etc.

Following your suggestion, we added implications in the discussion section.

Discussion Implications for practice and research section ➔ P15L1-5

**Quality of written English: Needs some language corrections before being published**

We asked a company to make language correction.
For Dr. Michel de Lorgeril’s Comments:

Thank you very much for your valuable comments concerning our manuscript. We found these most helpful and have revised the manuscript accordingly. Based on the recommendations, we excluded the sensitivity analyses using simulated data and reanalyzed in order to make it simple and represent the core result more clearly. In this process, we excluded one study. In the clear version of the manuscript, red font reflects areas where changes were made. We hope that the corrections are satisfactory. Responses to specific comments are as follows.

The big problem of this systematic review and meta-analysis is the huge heterogeneity of the included studies, which has been acknowledged by the authors. Also, data are lacking in several studies (for instance the standard deviations, SD) and the way the authors did calculate them require the expertise of a statistician. Some missing data have even been "modeled" by using a Metabolic syndrome "simulator" and once again the opinion of an expert statistician is required ...

Thank you for your critical comment on the statistical method. In the analysis we used “Metabolic syndrome simulator” to cover the missing data. The authors agree that this is confusing in some degree. We chose not to use “MetS simulator” in order to avoid complexity. Although the number of studies used for the estimation of overall estimates became less, the results were not largely different from the former analyses and the results also supported the efficacy of lifestyle modification compared to control. We removed the descriptions related to MetS simulator and it’s results throughout the method, results, and discussion sections.

Minor issues:

1) the Methods and Results sections are mixed. Most of the "results" should be inserted in the Methods.
Thank you for your comment. We moved several sentences from the results section to the methods section.

Methods Study selection section → P5L6-11
Methods Statistical Analysis section → P7L6-9

2) References do not follow the BMC "guidelines"

We corrected the references following the BMC guidelines. Thank you for reminding us about the reference.

Quality of written English: Needs some language corrections before being published

We asked a company to make language correction.
For Dr. Melania Manco’s Comments:

Thank you very much for your review of our manuscript. We found the reviewers' comments most helpful and have revised the manuscript accordingly. Based on the recommendations, we excluded the sensitivity analyses using simulated data and reanalyzed in order to make it simple and represent core result clearer. In this process, we excluded one study. In the clear version of the manuscript, red font reflects areas where changes were made. We hope that the corrections are satisfactory.