Author's response to reviews

**Title:** Insulin Resistance and its Association with the Components of Metabolic Syndrome among Obese Children and Adolescents.

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To: BMC Public Health

Title of the paper: *Insulin Resistance and its Association with the Components of Metabolic Syndrome among Obese Children and Adolescents*

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On behalf of my co-authors, please find enclosed the manuscript mentioned above, submitted for consideration to BMC Public Health. The manuscript has been carefully revised and includes changes according with the suggested recommendations emitted by the referees. All changes can be identified because they are highlighted in yellow. In the following paragraphs we provide answers – in blue – to each one of the referees’ comments.

**Reviewer: Douglas Curran-Everett**

Reviewer’s report:

Q1. P values throughout manuscript and in Tables. Three decimal places for P values greater than or equal to 0.01 are unnecessary. All P values in the Tables can be rounded to the nearest 0.01. They will be easier to read. If P < 0.01, then 0.01- can be used, or P < 0.001 can be used.

A1. Following this suggestion, we have rounded P values throughout the manuscript and in tables as follows:
   If P > 0.05, we now use “ns” (not significant).
   If P is between 0.05 - 0.015, we have rounded to 0.05.
   If P is between 0.014 - 0.001, we have rounded to 0.01.
   If P is less than 0.001, we use <0.001.
   In the tables, we have used one decimal for CI values.
Reviewer: Sophie Hawkesworth
Reviewer’s report:

Major compulsory revisions

1. The manuscript would benefit from greater clarity of the purpose of this study. It seems that the hypothesis is that IR is associated with components of the metabolic syndrome in obese children, whilst I have reservations about this design I am happy to accept the authors previous explanation. However I feel that although the aim is clearly stated in the background section it is not clearly answered in the discussion. I suggest reordering the discussion so that it begins by answering the question that the paper set out to address.

A1. Following this suggestion, we now begin the discussion by answering the question posed in the background section. In the remainder of the discussion, we take IR as the independent variable and MS as the outcome variable.

2. I also think the wording throughout the manuscript but particularly in the abstract and discussion is misleading. You have presented cross-sectional data here so you are unable to say whether IR augments the risk of developing MS as this would require prospective data. All you can say is that increasing IR was associated with an increasing number of components of the MS in this population. What you are really showing is the clustering of metabolic disturbances in obese individuals.

A2. We have re-written both the abstract and the discussion taking into account that, as the reviewer rightly points out, only associations can be drawn from a study based on cross-sectional data such as this one.

3. In line with this comment, I would be cautious in the discussion of using the word ‘explain’ when talking about an association that you have reported. Rather than stating that ‘IR can explain the alterations in lipid profile etc’ I suggest rewording to ‘IR is associated with…’ as these have quite different meanings.

A3. When speaking about the association between IR and MS components in the discussion, we have followed the reviewer’s suggestion and avoided the term “explain”.

4. Figure 1 seems to be unnecessary in this manuscript. As I understand your study aims, you are primarily interested in the effect of IR (explanatory variable) on the odds of having the metabolic syndrome (outcome variable) and this analysis had been presented in Table 4. In contrast Figure 1 is presenting the effect of having components of the metabolic syndrome on the level of IR, which is the reverse association.

A4. We agree with the argument of the referee in the sense that figure 1 is showing reverse association; we have now deleted this figure.
Minor essential revisions

1. Please be consistent with the use of either boys and girls or men and women throughout the manuscript. For example on page 8 you use both terms and this is confusing for the reader.

A1. Throughout the manuscript we have now consistently used “boys and girls”.

2. Please state in the methods the statistical tests you have used to investigate the differences in metabolic variables between boys and girls.

A2. The methods section now states the statistical tests we used to investigate the difference in metabolic variables between boys and girls (Student’s t test and $X^2$). We have also stated this at the bottom of the corresponding tables.

3. In the discussion on page 11 you state that ‘The increase in BP in this population’. What is this an increase in relation to? Do you mean raised BP in individuals with IR compared to no IR? If so this isn’t shown in the data. Please clarify.

A3. In order to clarify this point, we now re-written the discussion about blood pressure according to the data shown in the new table 3. We note that an association exist between IR and OR of presenting high blood pressure; this association is, however, not statistically significant.

4. Again on page 11 there is mention of ‘the lower prevalence of MS reported in this study’. Lower in relation to what? Please clarify.

A4. In order to clarify this point we have deleted the word “lower” and stated the real prevalence (20%). This figure can now be compared with figures from other studies – mentioned in the same paragraph – that used other criteria to define MS.

5. On page 12 you state that the prevalence of ‘metabolically healthy but obese individuals’ is 9.7% in adults and go on to state that this population does not have a family history of T2DM. Which population do you mean here? Are you talking about a particular study? I think the word population is confusing here and I am not sure I understand the point you are making. Please clarify.

A5. Apologies for the lack of clarity. We were referring to another study (44). In order to eliminate the confusion, we have deleted the phrase “this population” and stated that those without a family history of T2DM were the fraction of metabolically healthy but obese adults in the study cited.

6. Thank you for discussing briefly the limitations of cross-sectional studies. Are there any other limitations of your particular study that could be raised here?

A6. We have pointed at another limitation: the fact of not having included an evaluation of adolescents’ pubertal stage.

7. In the conclusions and abstract you state that as IR increased so did BP but this is not shown in your data in Table 3.
A7. The reviewer is right. As pointed out in answer 3, we have now highlighted the association between IR and BP within the manuscript and the abstract.

8. In the conclusions you also state that HOMA values under 3.4 were associated with a decreased risk of also having MS. I would argue that the data in table 4 actually show that HOMA values above 3.4 are associated with an increased risk of having MS compared to the lowest percentile of HOMA values, which is subtly different from how you have worded it.

A8. We thank the reviewer for this thoughtful observation. We have now modified our second conclusion and stated that the values above 3.4 are associated with an increased risk of having MS compared to the lowest percentile of HOMA values.

9. In the abstract you state that ‘among those who presented disorders an increase in IR augmented…’ However, your analysis presumably includes all individuals not just those with metabolic disorders defined by the various cut-offs?

A9. Yes, our analysis included all individuals. We have corrected this in the manuscript.

10. In the abstract you state that as IR increased HDL levels decreased but in Table 3 there was very little association between these two variables and if anything HDL increased as IR increased.

A10. Thank you for this observation. We have removed this statement from the abstract. Table 3 now shows OR values instead of values of MS components.