Author’s response to reviews

Title: Towards Personalised Molecular Feedback for Weight Loss

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Author’s response to reviews:

Zahra Bahadoran
BMC Obesity
November 7, 2018

Subject: Submission of revised paper “Towards Personalised Molecular Feedback for Weight Loss” (OBSY-D-18-00080)

Dear Dr. Bahadoran,

Thank you for providing us with an opportunity to address the reviewers’ comments in a major revision of our manuscript. We have carefully addressed the comments and have revised the manuscript accordingly. Our responses are provided in a point-by-point manner below. Changes to the manuscript are shown using track changes.

We would like to thank you and the reviewers for helping us improve the manuscript and hope the revised version is suitable for publication. We look forward to hearing from you.
Sincerely,

Judith Klein Seetharaman

Responses to reviewer 1

The article entitled Toward Personalized Molecular Feedback for Weight Loss is quite interesting. The rational for doing the study was justified and clear. Method was also described in detail.

Response 1. Thank you for your positive response to our manuscript. However, I noticed, some aspects of methods were described in the results section, not in methods section; it is suggested to remove to methods section. For example, in page 11, 2nd paragraph, in the 1st line, the authors described how BMI was measured. It should be not in the results section. There are many other similar description of method should be in Methods section, not in results part.

Response 2. Descriptions of methods that were presented previously in the results section have been moved to the methods section and the methods section has been expanded, also see response 5.

Conclusion section should be rewritten, many sentences were repetitive what already explain in the background and methods should be excluded from the conclusion section.

Response 3. The conclusion section has been drastically shortened.

Responses to reviewer 2

Reviewer 2: I commend the authors for undertaking this study. The research is relevant and plugs a gap in the literature with regards to the measurement of metabolites in fat loss assessment. However, the write-up for this study currently requires revisions in order for it to be publishable.

Response 4. We would like to thank the reviewer for the appreciation of our study and have carried out the required revisions as per below.

Mainly, the current methods section is severely lacking and replicating the study would be difficult based on the information provided. While the authors have described the laboratory procedures with a good amount of necessary detail, description of the actual study design is not
explicitly stated. There is significant missing information with regards to how recruitment took place (where was the study advertised? Is there a potential for bias?)

Response 5. Details about the methods, recruitment and the study design have been added (line 124 page 6; line 134, page 6; line 154 page 7; line 183 page 8)

What kind of comparison was conducted, and how the survey was scored or analysed, or even linked to the metabolite data. This information needs to be explicitly stated in the methods section.

Response 6: Only those comparisons described in the results section and figures were conducted. While the survey was carried out with the participants of the study, the data from the survey was not linked to the data from the study to maintain anonymity of the participants (line 232 page 10 and line 247 page 11)

The authors used the "fatsecret" database for getting nutrient estimates from participant diets. What is the validity of the fatsecret database? Is it possible to state whether this is valid or a limitation of the study, and how this might affect or not affect the results? Is there a reason this database was picked, such as popularity, comprehensiveness or ease of use?

Response 7: A discussion of the choice of fatsecret database has been added (line 175 page 8 and line 147 page 7). Besides convenience, there are number of other reasons making the use of this database beneficial:

* FatSecret has been used in numerous large projects, such as the CORDIS European project (https://cordis.europa.eu/result/rcn/184993_en.html, http://europepmc.org/articles/PMC5789166)
* It has been used as reference comparison in https://www.ncbi.nlm.nih.gov/pubmed/28600833
* Its one of the most popularly used Apps as per https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4985610/
* Despite errors in KCal calculation, it has been estimated to be about 80 KCal/day (which is very minor as compared to the scale of the study). See Table 4 in https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4704947/ Values in the table are for three days and expressed in KJul so 1000KJul/3day-period * 0.239006 KCal/KJul =~ 80KCal/day

The authors mention controls in the abstract, specifically in the results, but the methods do not describe the type of analysis or define what constitutes a control or intervention? Was there an intervention? Was there a washout period? Was this a case-control study comparing obese with non-obese participants, or was there a meal-skip intervention?
Response 8: The intervention was indeed the meal-skipping, but the study was an observational study to see if molecular parameters correlate with weight loss. Any diet could have likely sufficed for this purpose. The goal of the study was not to compare obese with non-obese participants, but a separation of the data into BMI groups was useful to identify BMI as a source of variation and to delineate possible trends in the data that may relate to BMI. Control and diet day are explained in line 154 page 7. Description of the analysis of the study and a discussion of this comment has been added (line 183 page 8).

If it is the latter, were 3 to 24 days sufficient to assess differences (a biochemical justification)?

Response 9: This is the first study of its kind to observe if molecular parameters could be indicative of weight loss. Because we required participants to collect all of their urine samples, it was not possible to ask them to provide samples for larger number of days than they were willing to volunteer since this would have limited the number of volunteers severely. We find clear differences between diet and control days strongly supporting the value of collecting data in 24 hour intervals. The data of this study provides the basis for future longer term studies in which molecular data can be collected over the duration of an entire dieting period which typically last for several weeks. Because we found the most informative data to be evening and morning urine samples, we can ask participants to only collect those samples, which will make adherence over such long periods of time possible.

I look forward to a proper methods section for this manuscript, since the study is timely and the results could be beneficial to follow-up studies and reviews, as well as the development of fat-loss interventions that overcome current challenges.

Response 10: We would like to thank both reviewers for these excellent suggestions which have resulted in a more complete manuscript.