Author's response to reviews

Title: Longitudinal change in energy expenditure and effects on energy requirements of the elderly

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Author's response to reviews: see over
We have read the comments regarding the manuscript we submitted entitled "Longitudinal change in energy expenditure and effects on energy requirements of the elderly" (MS: 2055368752914241). They were quite helpful. Below you will find all of the comments from Reviewers 1 and 2. We have tried to address all of these comments in our manuscript and we feel these significant changes have greatly improved the manuscript. We have also responded to all of those comments and our response should show up in **bold** along with the place in the manuscript (in red font) where you can find those changes.

**Reviewer's report**

**Reviewer 1**

- Major Compulsory Revisions
  1. NONE.

- Minor Essential Revisions
  1. Abstract: Conclusions: … AEE decrease in men …
      **Thank you for pointing this out. We have corrected the grammar (please see line 20 on page 3).**

  2. Results: Resting Metabolic Rate (RMR): last sentence: … AEE was calculated as (?) …
      **Thank you for pointing this out. We have corrected the grammar (please see line 17 on page 9).**

  3. Discussion: first paragraph: … assessing energy requirements take a cross sectional approach …
      **Thank you for pointing this out. We have fixed this mistake (please see line 2 on page 14).**

  4. Discussion: second paragraph: delete “but there”.
      **Thank you for pointing this out. We have deleted this mistake.**

  5. Discussion: second paragraph: deleted “3” in word contributed.
      **Thank you for pointing this out. We have deleted this mistake.**

  6. Discussion: last sentence second paragraph: change wording of “This 3.0% CV a 4.2% CV to the change score,” …
      **Thank you for pointing this out. We have changed this sentence to make it clearer (please see line 6 on page 14).**

- Discretionary Revisions
  1. The term sex was used in the early sections of the Methods, then gender was used late in the Data Analysis section, as well as the Results section. I am
unclear as to why the change. Sex is the appropriate term here. Thank you for pointing this out. We have removed ‘gender’ from the manuscript and only use the term ‘sex.’

Reviewer's report
Reviewer 2:

Overall comments
This manuscript presents longitudinal energy expenditure measurements in adults in their 8th and 9th decades of life and compares these to energy expenditure derived measurements using the DRI equations. Overall, the authors should be commended on their research; however this reviewer has several issues. Firstly the authors should be consistent with their use of “1st & 2nd study” vs. “substudy” 1 & 2. This reviewer found this to be distracting. While the data were collected as sub-analyses of a larger study, the authors should present the two time-points as baseline and follow-up. Since they are not presenting any data from the main study, they don’t have to refer to their study as the substudy.

We want to thank the reviewer for this comment and suggestion. We agree that this will probably make it much clearer. We have changed this to baseline and follow-up throughout the manuscript.

Secondly, the authors have framed their study as important for understanding energy requirements later in life, in order to prevent excess weight gain/obesity. However, they have not framed the scope of this problem adequately. What is the current obesity prevalence amongst this demographic? What is the public implication/impact of this study? Furthermore, they did not address the issue of diet; there is some consensuses that as energy requirements decrease with aging, dietary intake decreases concomitantly. The authors should address this. Finally the background is missing many references; this should be addressed prior to publication.

Thank you for your comments. We have added some information to the background regarding obesity prevalence in the elderly as well as the significance of knowing energy requirements. Please see lines 4-13 on page 4.

We have also added additional, relevant references to this section of the paper.

Major Compulsory revisions
Specific comments
Abstract
1) Page 3, Line 3: remove from sentence “or not”
Thank you for pointing this out. We have removed this.

Background
2) Page 4, Line 1-3: References are missing
We have added a reference for this (line 4 on page 4).

3) Page 4, Line 7: ref for WHO equations
We have added a reference for this (line 17 on page 4).

4) Page 4, Line 8: ref for DLW
We have added a reference for this (line 18 on page 4).

5) Page 4, line 11: remove parenthesis around TEE
Thank you for pointing this out. This has been fixed (please see line 21 on page 4).

6) Page 5, Line 1: refs for equations
We have added references for this (line 12 on page 5).

7) Page 5, Line 8: Refs for Health ABC
This has been added (line 19 on page 5).

8) Page 5, line 14: remove “or not”
Thank you for pointing this out. We have removed this.

Methods
9) Page 6, line 6: define EE
Thank you for pointing this out. This has been added (please see line 16 on page 6).

10) Page 6, line 10: change use of sub-study as it indicates that there was a further sub-study within the current study.
This has been changed here and throughout the paper.

11) Page 6, line 13: complete “failure of isotope” to do what?
We have added examples of what this means. Please see lines 23 on page 6 and line 1 on page 7).

12) Page 6, line 18 & 19: fix inconsistencies “second” EE study and “substudy”
This has been fixed and we have removed “substudy” from the paper.

13) Page 7, line 9: which cohorts?
We should have used the wording “study” rather than “cohort” since we are referring to the full study sample – not just the subjects that completed the EE portion of the study.
This is now changed. Please see line 16 on page 7.

14) Page 8, line 15: calculated “using” IC
Thank you for pointing this out. We have changed this (please see line 4 on page 9).

15) Page 9, line 9: Body mass, composition and medical history, socio-demographic?
We apologize, but we are not sure what the reviewer is requesting here. This page and line number is describing the calibration of the DXA scanner.

16) Page 9, line 20: remove “to use”
Thank you for pointing this out. This has been removed.

Data Analysis
17) Page 10, line 7: not clear if this was performed for baseline or follow-up data
Thank you for pointing this out. We have clarified this (please see line 18 on page 10).

18) Page 10, line 8: inconsistent use of sex & gender.
Thank you for pointing this out. We have removed gender and only use the term sex through the paper.

19) Page 10, line 8: not clear if gender were used in the analysis, and if so should be an anova
We compared baseline values between men and women. For example, height in 2006 was compared between men and women (see table 1 for a visual aid for what we did here) and the t-test was the most appropriate statistical test to use.

20) Page 10, line 8: fix substudy
This has been changed.

21) Page 10, line 6-12: it’s not clear if the data were evaluated for confounders and then the data adjusted for in the analysis, for e.g. both BMI and health status effects AEE, certain medications change RMR etc
We did not adjust the data for confounders in the analysis. This was purposely not done by design. This is a unique subject population in that most of the individuals at this stage in their life are not ‘healthy’ as would be the case in a younger (20-40 y/o) population (please see page 11, lines 9-15 of the results section for a brief list of some of the diseases these individuals had). We also have a relatively small sample size that prevents inclusion of multiple covariates. In large epidemiological studies where there are hundreds or thousands of subjects, it is more common to see data adjusted for potential covariates. However, in this study, beginning to adjust for covariates can be a problem due to the small sample size and the fact that most of the subjects are not completely healthy. With a relatively small sample size plus the presence of multiple (and unique) morbidities, there becomes a problem: do we adjust for each disease or do we combine several diseases into one category (i.e. CVD, cancer, osteoporosis = disease). In the former, we do not have the replicates to run that analysis, in the latter, what would be the standard for combining some variables while excluding others? These are the issues that we saw with respect to including covariates into the analysis and we concluded that the most appropriate technique was to display the data as it is, but to also run the most logical confounders as separate variables (i.e. sex, BMI, lean body mass). However, we did add a multiple linear regression analysis (see next comment) to look at the best predictors of TEE. We have also included a brief description of this as a limitation to the study (please see page 19, lines 8-12).

22) Page 10, line 10: This reviewer suggests the authors re-analyse their data using a multiple linear regression analysis.
Thank you for the suggestion of doing multiple linear regression. We did not think this fit with the primary or first purpose of the study. However, we did think that including multiple linear regression analysis to examine the best predictors of TEE was a great idea and fit in nicely with the 3rd purpose of the study. Therefore, we have included this analysis. Please see page 13, lines 3-21 and page 18, lines 15-18.

Results
23) The authors should present the anthropometric/body composition changes in the results section
This information is in paragraph 2 of the results section. While we did not show the actual data values for anthropometrics and body composition, we refer readers to Table 2 which contains all of the data from baseline and follow-up. We chose to present both baseline and follow-up data rather than the change data to more clearly show differences between men and women as well as differences from baseline to follow-up.

24) Page 10, lines 14-18: Table 1. It is not clear why the authors chose to only present the DLW measurements from time 2?
The authors had debated including this information in Table 1. However, it was suggested by other reviewers to only include the data from 2006 in that table because we were not using the EE data from all subjects from the baseline visit. Therefore, Table 1 gives a picture of the metabolic and anthropometric variables for subjects in their 9th decade of life. Table 2 has the information from both the baseline visit and the follow-up visit. Since we did not use the baseline data from subjects who did not have follow-up TEE measurements (see explanation in next comment), we did not think it should be included in the table because we did not use it for data analysis and it is not in the manuscript.

25) Page 10, lines 18-22 Table 2. It is not clear why the authors did not include an unbalanced ANOVA to account for drop out and missing time 2 DLW measures, so that all the data could be used in the analysis.
We felt that if subjects did not have data at both visits (baseline and follow-up), we would not be as accurately studying and presenting the changes in energy requirements in late life. By including subjects that only had data at both points, we can measure within-subject changes in these important variables and give very accurate results about the within-subject changes in those variables over the 8-year period. Additionally, nearly two-thirds of the subjects from baseline did not have follow-up data, so we did not want to be reporting on the changes in energy requirements for 300 subjects if the majority of them did not have follow-up data. We felt that this was too large of a number without data at both time-points to include them in the analysis, even if statistically it is acceptable using an unbalanced ANOVA.

26) Page 11, lines 18-23: What were the limits for the bland altman plots in both the men/women.
We have added the limits of agreement for each plot (please see lines 15-18 on page 12).

Discussion:
27) Page 12, line 5: ref for other study.
We have added the reference for this (line 2 on page 14).

28) Page 12, line 8, same
We have added a reference for this (line 5 on page 14).

29) Page 12, line 9-11: are these results in line with the other study? What about other studies looking at decreases from 60-70yr?
We have added information regarding TEE values reported in other studies and how those relate to our study results. One is the population of subjects greater than 90 years of age, and the other two are elderly populations that were younger than ours (ages of 55-79).
Please see page 14, lines 7-13.

30) Page 12, line 11-15: The change in FFM was only significant in the men, the women decreased FFM by 0.5 kg, and therefore we would not expect their RMR to change?
FFM did actually significantly decrease in women; however, this decrease was not great enough to lead to a significant decrease in RMR. The men showed decreases in FFM by about 2.5kg vs. 0.5kg in women. Therefore, it appears that 0.5kg is not enough to significantly decrease RMR in this population (at least we were not able to detect it in this study). We have added a sentence about this in the paper. Please see lines 17-18 on page 16.

31) It seems that if the women weren’t very active to begin with, so then their change would not be very great?
We agree with your observation that women were not as active as the men at the baseline measures. However, the calculated PAL of 1.68 for women in 1999 is greater than that of a very sedentary person (a PAL around 1.4). This indicates that it would have been plausible for women to still be able to significantly decrease their activity levels. If you look at percent change, the men decreased AEE about 20% while the women only decreased about 5%. However, we acknowledge your point as important and have included information about this in the paper. Please see page 15, lines 17-21.

32) The authors make recommendations of improving FFM using strength training; the applicability of this is questionable at best. Using NHANES data it is known a very small % of the US population does any form of PA.
We agree that this recommendation is only effective if participants actually engage in strength training. However, we did feel that it was the best recommendation to be made regarding FFM. Your point is a good one, however, and we have included this in the manuscript. Please see page 16, lines 7-11.

33) Page 13, line 24: would not use the word sarcopenia here. Also are the authors implying that it was only applicable to the men? Is it not a case of the men were more physically active than the women to start with? Please discuss.
We have removed the word sarcopenia and used muscle mass instead. We also acknowledge your point regarding men vs. women with this application. We have modified our statement to say aging adults, especially men. Yes, the men were more physically active than the women at baseline. However, we only saw decreases in FFM in men.
Therefore, we feel most comfortable making this recommendation more specified to men and do not feel as justified making this recommendation in women since their RMR and AEE levels did not decrease. Please see page 16, lines 7-11.

34) Page 14, line 5-18: the authors conclude that women behave differently to men, whereas this may just be a reflection of the small sample size and low levels of PA to start with, please discuss.
This paragraph now reflects the low sample size and variation among women in AEE and RMR data, and the lower levels of PAL to start with. Please see page 16, line 20 through page 17, line 12).

35) Page 15, lines 7-19: what were the limits of agreement for the Bland Altman plot? Discuss the variation in the measurement please. (actually lines 16-19)
We have now included the limits of agreement in the results section and on the figure (please see lines 15-18 on page 12 and Figure 3). We have also discussed these results in more detail in this part of the discussion (please see lines 12-13 on page 18).

36) Page 16, lines 1-8: it seems that the cohort that completed the study were very different to those who could not and while is stated, these discrepancies should be further discussed in the results section.
Thank you for pointing this out. It is an important point. We have expanded on this and provided some more information in the results section. However, we had to limit the expansion and amount of data from this since it is a primary focus on a different paper that is currently being written on the same subjects from the Health ABC data set. Please see page 11, lines 9-15.

Conclusion
37) Page 16, lines 10-17: this reviewer feels that the authors have over-stated their results, not providing enough evidence that lack of change in the women, was simply not as a result of their AEE levels being low to start with, compared to the men, who had higher levels of AEE at baseline. This should be addressed.
We have adjust our conclusion to reflect the lower AEE and PAL levels of women at baseline and how that could have impacted the changes (or lack thereof) in the women in this study. Please see page 19, lines 19-22.

Figures 3: please include the limits of agreement.
The limits of agreement have been added to Figure 3.