Author's response to reviews

Title: The Impact of Waist Circumference on Function and Physical Activity in Older Adults: Longitudinal Observational Data from the Osteoarthritis Initiative

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Author's response to reviews: see over
Dear Dr. Reyes:

I would like to thank you and the reviewers for your critical review of our manuscript titled, *The Impact of Waist Circumference on Function and Physical Activity in Older Adults: Longitudinal Observational Data from the Osteoarthritis Initiative*. We have attempted to address all the concerns and have edited the manuscript accordingly. Comments were addressed as follows:

**Reviewer #1:**
We would like to thank Dr. Stommel’s input and suggestions. The authors have addressed each point as indicated below:

**Major Compulsory Revisions:**  
(1) This paper offers some (though not surprising) evidence about the association between waist circumference (a measure of visceral adiposity) and physical functioning and quality of life. However, it does not make the case that waist circumference (WC) is a better predictor of these outcomes than the BMI. After citing one article that the BMI has poor sensitivity and specificity in identifying adiposity, the authors report a high correlation (+0.79) between the BMI and waist circumference in the data. Subsequently, the BMI is simply dropped from the analysis. This poses the question, would the BMI, separated into quartiles like the WC, have produced very similar results? Does the WC measure predict the chosen outcomes better than the BMI? Does it add anything to predictability based on the BMI? Without addressing this basic question, one does not really have any reason to use the WC instead of the BMI.

The question raised is whether WC, or WC combined with BMI, is superior to BMI in predicting distal functional outcomes. The purpose of this manuscript was not to answer that particular question. We recognize that there are a number of different anthropometric indices that can be utilized. As waist circumference often is argued to be a surrogate of visceral (central) adiposity, our intent was to see whether waist circumference predicted functional decline, and not whether it was a better predictor than BMI. Our previous work suggested that BMI in older adults suboptimally identifies adiposity. We have argued that other anthropometric measures, either in lieu of BMI or in addition to BMI should be used in older adults (Batsis et al Under Review J General Internal Med). We agree that there is some overlap and strong correlation between BMI and WC. However, by using inverse probability weighting, we were unable to account for both measures due to their collinearity.

Furthermore, stratifying BMI into quartiles (as opposed to standard BMI categories) we believe would not provide as much information. BMI categories are well established, while, to our
knowledge, there are only dichotomous cutoffs for waist circumference by sex. The quartiles of BMI were as follows in this analysis: 18.5-25;25.1-28;28.1-31.2; 31.3-48.7 which do not necessarily correspond to the standard BMI categories. This is most likely due to the fact that the cohort was skewed to having higher BMIs (since BMI is a risk factor for knee OA). Lastly, we have previously submitted a manuscript that is examining standard BMI categories with these outcomes (Under Review – Public Health Nutrition) and felt that each of these manuscripts examined different anthropometric variables providing different information in terms of associations.

We believe there are equal advantages and disadvantages in using either anthropometric variable. For example, this study shows that participants with elevated WC (that may have normal or overweight BMI) may be at increased risk for long-term impairment. The corollary can be said about BMI. Hence, the authors believe that both of these anthropometric measures can be considered to inform clinical care independently. Our intent was not to compare the predictive nature of each of these models but to determine (as others have) whether WC was independently associated. We would agree that since our results do demonstrate an impact on long-term function, that advanced modeling to ascertain which anthropometric measure is superior could be considered as a subsequent paper.

We have inserted this limitation in our discussion to address this concern and trust that this is satisfactory. The authors would be happy to consider any further alterations that are requested:

BMI fails to differentiate between central and peripheral fat stores.

These results focus solely on the impact of central adiposity on functional outcomes in older adults. We previously demonstrated in a similar population that BMI impacts quality of life and physical function [Batsis et al Under Review, Public Health Nutrition], and this current study suggests that abdominal obesity could be a separate predictor of poor functional outcomes. Future analyses could determine the impact of the combined or independent use of these metrics, in addition to evaluating the incremental predictive nature of these variables on long-term outcomes.

(2) Regarding the specific analyses chosen, it is not clear why the authors chose to divide their sample into 4 WC quartiles, rather than using the continuous WC scores as predictors; if the associations between the SF-12 and the WC scores are non-linear, this could have been explored with continuous scores as well.

We proposed using the approach of quartiles as argued by Katherine Flegal’s group at the CDC (see reference below) who argued that using cutoffs may lead to differences introduced simply because categories (like BMI) reflect different points in the distribution. These authors note (and others referenced in their manuscript) that to control for this effect, researchers not infrequently divide all variables into comparable categories of equal sizes, as we did. We felt that we were limited by study power to subcategorize into quintiles. Furthermore, representing the categories in quartiles allow one to aid in the interpretation of the data for possible clinical application.

To explore the relationship with WC as a continuous variable, we re-ran the models and presented the information within the existing tables using β-coefficients and 95% confidence
intervals and the resultant p-value in Table 3+4. As can be appreciated, since we are not dealing with a categorical variable, we felt that this was the most appropriate manner in representing the results. We have indicated in the results section some brief comments on this data.

(3) Concerning the control variables in tables 3 and 4, the authors do not make a distinction between true confounders and mediating/intervening variables: what is the meaning of “controlling for” the Charlson co-morbidity index, if several of the comorbidities in this index are themselves likely outcome of high-level adiposity? A similar point can be made about OA and hip pain in Table 3.

We controlled for the Charlson co-morbidity as we intended on looking for the independent effects of visceral adiposity on functional outcome that were not related to co-morbid conditions. Additionally, we did believe that level of co-morbidity as reflected by the Charlson score should indeed be included as we have done in our other work. Additionally, each of these co-variates that were included a priori in our analysis could potentially be a confounding variable and thus needed to account for this. Lastly, we struggled (again a priori) as to whether we should include hip pain and knee OA in the multivariable model as both may indeed be affected by visceral adiposity (knee OA more so). However, both of these variables also influence our outcomes of choice, hence we decided to keep those in the model. Lastly, co-morbidity influences disability and quality of life and a multitude of other studies include these variables in modeling.

We have inserted a statement in our discussion to this effect and trust that this is satisfactory to the reviewer. We would be happy to further clarify any statements or definitions made.

Reviewer #2:
We appreciate Dr. Vincent’s critical appraisal of the manuscript and we have attempted to address and acknowledge the comments as indicated below:

Minor essential revisions

Introduction:
1. Paragraph 3: The introduction could be strengthened with the addition of a previous review that addressed which measure of adiposity could best predict lower levels of mobility (Vincent, Vincent and Lamb. Obes Rev. 2010 Aug;11(8):568-79. Waist and BMI could predict lower mobility levels and that longitudinal data are needed to show the relationship between waist/ BMI and disability.

The authors appreciate the reviewer raising it to our attention and have inserted it in paragraph 3 as requested. We also included a statement: “Cross-sectional and longitudinal studies suggest an association of increased BMI with mobility impairments.”


We have altered the sentence to read as follows:
“Obesity is a major risk factor for increasing severity of early degenerative changes and cartilaginous lesion progression of knee OA, placing older patients at risk for worsened musculoskeletal disorders and functional decline.”

**Methods:**
This was very well written. There are only minor comments:
3. Under Study Measures: “Questionnaires ascertained…” Questionnaires collected data on….”
4. Statistical analyses; “All data is..” should be “All data are…”
The authors have made these changes.

Do you have a rationale for choosing the quartiles for the waist circumference values? If so, please cite.
Dr. Vincent raises an important point. We chose to use quartiles in line with previous methods discussed and argued for comparison of anthropometric variables as outlined by Flegal et al Am J Clin Nutr 2009. The groupings used in this study divide the cohort equally and hence allow for comparisons of equal counts. Flegal’s group argues that when observing differences of one anthropometric variable with another, differences may be introduced simply because categories reflect different points in the distributions for each variable. To control for this effect, we chose to divide all variables into comparable categories of equal size, following the model of prior research. This allows for comparisons across studies. We have referenced this article and noted this in our Statistical analysis section as well.

**Results:**
5. “Minimal clinical differences were….” Do you have a citation to reference here about what is considered the MCD?
The authors apologize for using this terminology. While the difference in age (range 67.5 to 68.7) is minimal from a clinical significance standpoint, they were indeed statistically significant across tertiles. Hence, we have changed the sentence to read as follows:
   “Statistical differences were observed in age, although….”

Second paragraph: “The unadjusted functional outcome data is..” should be “…data are..”.
This was altered.

6. Paragraph 3, line 2: SF-12 decline appear..” should be “..appears..”
We have made this change.

**Discussion:**
7. This section was straightforward, and agrees with the published literature in the area. The main conclusion may be modified, however, to include a statement that strengthening exercise and increased physical activity levels – even if weight change is not dramatic – can significantly improve joint pain and may help improve walking performance.
The authors altered the concluding sentence to read as follows:
“Clinicians should consider not only targeting this subgroup for aggressive weight management, but also encourage strengthening exercises and increased physical activity levels, both of which can improve joint pain and overall walking performance.”

**Editorial Requests:**

**Title page**

Please include a title page as page 1. The title page should provide the title of the article, list the full names, institutional addresses and email addresses for all authors, indicate the **corresponding author**.

The authors have made these corrections.

**Ethics**

As your research involves humans please include a statement of ethical approval in the **Methods section** of the manuscript, including the name of the body which gave approval, with a reference number where appropriate. Any experimental research on humans must be in compliance with the Helsinki Declaration.

This study utilized secondary (de-identified) data and hence was deemed an exempt study for the purposes of our Institutional Review Board. We have inserted the name of our IRB.

**Authors Contribution**

Please include an **Authors' Contributions** section at the end of the manuscript, before the Acknowledgement list. We suggest the following kind of format (please use initials to refer to each author's contribution).

The authors altered the contributions section to include their initials and moved the section as requested.

We hope that the Reviewers and the Editorial team are satisfied with the above clarifications and responses of the concerns brought forth. We hope that this revised manuscript merits publication in Nutrition Journal and we would welcome any further comments or criticisms that could improve the quality of this manuscript, in an effort to publish this work. Please do not hesitate to contact me at john.batsis@gmail.com should you have any questions or concerns.

Sincerely yours,

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