Author's response to reviews

Title: The impact of a cancer diagnosis on weight change: findings from prospective, population-based cohorts in the UK and the US

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Author's response to reviews: see over
Dear Dr Keku,

The impact of a cancer diagnosis on weight change: findings from prospective, population-based cohorts in the UK and the US [MS 9142471431339054]

We should like to thank you for considering this manuscript for publication in *BMC Cancer*, and for the valuable comments from the reviewers. This letter outlines the revisions we have made in response to these comments. Page numbers refer to the document with tracked changes. We hope that you find the revised manuscript suitable for publication, but would of course be happy to make further changes where required.

**Reviewer 1’s comments**

*This is an interesting study examining changes in weight in 2 large population-based cohorts of older adults of cancer survivors and cancer-free controls. This manuscript has many strengths including the use of prospective data, replication of findings in two cohorts, and examining differences by pre-diagnosis weight status. Despite the strengths of this study there are a few limitations and concerns.*

*What is missing for me is an explanation of the significance of these findings, in light of the many limitations. The meaningfulness of your main finding, that obese cancer survivors are more likely to lose weight, is difficult to interpret as the authors point out that for some this could mean greater mortality risk some and for others this could be reducing their risk. I think this manuscript would be strengthened if more focus was given to importance and usefulness of these findings.*

**Response:** We believe that our findings are important because they provide evidence for differential patterns of weight change in normal weight, overweight, and obese individuals diagnosed with cancer; which has not previously been reported. While we are unable to tell whether weight loss will increase or reduce obese cancer survivors’ risk of mortality, our results highlight important directions for future research. We have added a paragraph to our discussion making clear the importance of our findings (page 11).
Additionally, in the introduction you state that a previous study found differences between men and women. Why for this study did you control for sex and not look at sex differences?

- **Response:** We combined the data to maximise power, but we appreciate it would be useful to examine differences between men and women given previous findings, so we have added sex-stratified analyses to offer insight into sex differences in effects (page 9).

**Reviewer 2’s comments**

The paper deals with an interesting topic that so far is not extensively explored.

**Major compulsory revisions**

1. **The Authors should report on the validation of the cancer diagnosis.** From the manuscript they look as self-reported without any confirmation. Most other studies using self-reported cancer diagnosis have a subsequent validation through writing to the patients and obtaining hospital reports. Misclassification of outcome is more severe than exposure misclassification. If the outcome variable cancer is not validated the Authors should carefully consider the public interest of the analyses since there are so many cohort studies with validated cancer information.

   - **Response:** Data are not yet available validating the self-reported cancer diagnoses in either ELSA or HRS. However, several previous studies have shown high agreement between self-reported and validated cancer diagnoses, which we now cite in our manuscript (page 13).

2. **Another major issue is the use of cancer NOS.** Do the authors think that different sites and degrees of disease like metastasis is the same for all subgroups?

   - **Response:** We appreciate that there is substantial heterogeneity across the different cancers, and the relationship between weight loss and incidence/progression may vary by site. However, with relatively small numbers of diagnoses for each cancer site, we did not have power to analyse them separately and therefore followed the approach that many others have used and combined all cancers. This may not be entirely inappropriate because people who have had a cancer diagnosis – regardless of the effect on survival – tend to be interested in maximising their general health status. We have made more of this limitation of combining cancers in our discussion (page 13) and also mention the need for future research to investigate this issue in different cancers (page 11).

3. **Looking at figure 2 and 3 the impression is that there are very small, but significant differences in the obese group.** Is it reasonable to put any weight in the interpretation on such small differences partly due to a relatively large study and the use of BMI as continuous variable.

   - **Response:** We acknowledge that the differences we observed between the cancer and comparison groups are relatively small. However, we believe that having seen the same pattern
of results in two independent cohorts is suggestive of a true, robust effect. We have amended the wording of the opening paragraph of our discussion to make it clear that the effects observed were small (page 9).

**Minor revisions.**

4. Most epidemiological studies on cancer have sex-specific analyses, not only sex adjustment. A gender stratified analysis should be shown With a test for heterogeneity.

   - **Response:** As described in response to a comment by Reviewer 1, we have repeated our analyses stratifying by sex.

5. Argue more clearly why the data was not pooled.

   - **Response:** We chose not to pool data from the two cohorts because they are from different populations and use some different measures, so we were advised by our statistician that it would be of greater value to have replication in two independent samples. We now argue this in our method (page 6).

**Discretionary revisions.**

6. The BMI cutoff point for obese etc should be given.

   - **Response:** Thank you for highlighting this omission. We have added BMI cut-offs to our description of our statistical analyses (page 6).

Once again, we are grateful for your interest in the paper. We look forward to hearing your response.

Yours sincerely

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