Reviewer's report

Title: Weight change during chemotherapy is a poor prognostic in non metastatic breast cancer

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Reviewer: Rebecca Cleveland

Reviewer's report:

This is a review of a resubmission of the manuscript “Weight change during chemotherapy is a poor prognostic in non metastatic breast cancer.” While somewhat improved, this manuscript still needs a lot of work. There are still a lot of gaps in the study design and analyses that need to addressed. Also, the language is awkward; the authors would greatly benefit from the help of a native English speaker to edit the manuscript. I suspect there is a language barrier at work here in the resubmission. It seems the authors did not adequately respond or responded incorrectly to several questions posed by the reviewers. For instance, one reviewer inquired about stratified analyses and the authors responded by stating that they included 3 covariates in the analysis. In addition, a reviewer asked the authors to stratify the population characteristics by BMI or WV and the authors’ reply was “Correction done” although it was not.

Major Compulsory Revisions
1) The authors have not made a convincing argument that it is appropriate to include weight loss and weight gain into the same category. While the associations may be similar and in the same direction, it is likely that there are different mechanisms at play and therefore may be affected by different covariates and making different contributions. In addition, I still wouldn’t call what they are measuring as “weight variation” as that implies measurement of fluctuations in weight at each cycle of chemotherapy treatment over the course of follow-up. What they are really measuring, from what I can discern, is absolute “weight change” from start of treatment until the end of follow up.

2) If there were so few patients who did not receive anthracycline treatment (5%), why not simply exclude them so that you are better able to assess the effects of weight change exclusively among those who received this type of treatment? This would seem logical as it is the basis of the authors’ hypothesis. The reason for including participants with other types of treatments needs to be addressed.

3) The authors need to include in their limitations the fact that they only have weight data at baseline and not the participants’ “normal” weight. This could be very important because women could have lost weight prior to diagnosis due to the course of the disease.

4) Table 1 would be more informative if the study population characteristics were stratified by Median Weight Variation and all variables included both numbers of
subjects and percentages.

5) Table 2:
a) What are the P-values at the top of the table?
b) It would be more useful if the table included the number of events (OS and DFS) as well as the total number at risk.
c) The numbers at risk in this table are not consistent. If all these variables were included in the same model, then the authors would be working with a reduced dataset that only included data for participants who had observations for all the variables in the model (i.e., had no missing values for any of the variables). For instance, the Ns for weight variation ($78+36=114$) should add up to the same number as the Ns for Nodal Involvement ($60+62+7+1=130$). Clearly this is not the case in the table.
d) The table needs to include a footnote that indicates that all the variables in the table were mutually adjusted for each other.

Minor Essential Revisions

6) There are several examples of failing to follow up on cited literature. For example, in the Background section, Paragraph 2, Sentence 2 they indicate that there are “notable” exceptions to the point they are trying to make but fail to expound on what those exceptions are and what reasons exist for why those results may or may not be different. Several sentences later the authors indicate that all 9 studies of weight gain and survival were conducted in overweight populations, but only cite 2 of them.

7) Statistical analyses, second paragraph: the sentence beginning “according to the number of events…” does not make sense.

8) Discussion, Paragraph 2: Did the authors carry out a statistical test to determine that 32% of the population with WV >5% was not significant? In this case I’m not sure it is appropriate to test the median WV in this case.

Discretionary Revisions

9) What was the lag time between diagnosis and the start of treatment on average?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests