Reviewer's report

Title: Weight change during chemotherapy is a poor prognostic in early stage breast cancer

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Reviewer: Patricia Thompson

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Review of manuscript "Weight change during chemotherapy is a poor prognostic in early stage breast cancer" offered by Thivat et al.

The objective of the study was to assess the effect of weight change defined as > 5% variation among 132 women treated with anthracycline-based chemotherapy for stage I-III breast cancer between 1976 and 1989 and followed for ~ 20 years. The authors report women who experience > 5% variation (gain or loss) in their weight with treatment have a near doubling of risk for recurrence and mortality.

The manuscript is generally well written with minor need for English editing. The study replicates findings from other studies showing that BMI at baseline is associated with later stage of diagnosis and is thus associated with higher risk of recur and mortality. This aspect of the study does not add appreciably to the existing literature except to extend the observations to a population with a lower mean BMI than the U.S. counterparts.

The rationale for combining women who gained weight (15%) with those who lost weight (17%) as a weight changing group (32%) is not provided nor is a mechanism for how weight change regardless of direction would influence outcomes. This should be addressed.

The description of the present status of the cohort of patients is confusing and suggests that the majority, if not all of the women, who did not experience a recurrence (breast cancer event) are dead from other causes and were therefore censored in the data. In contrast, they appear to be contributing as a large group to deaths in the cohort. It leads one to wonder what role age plays in the relationship between BMI and poor outcomes in this study as older women have higher BMIs. Age nor menopausal status are included in the multivariate model. There is a need to better describe the population and to consider other factors in the multivariate model of known significance for recurrence and survival (i.e., age, smoking status, menopausal status).

In general, the relevance of the manuscript is unclear given the combining of weight loss with weight gain during chemotherapy. This seems somewhat counterintuitive given the mechanisms proposed for effects of weight gain on poor outcomes and lack of discussion of effects of weight loss. The question asked in this study is not supported by an underlying unifying hypothesis about weight change. If there is one, it should be provided. In general, the sample size
is too small to conduct a well powered study of the independent effect of weight gain, weight loss or weight stability on breast cancer recurrence and overall survival. Limitations of the study should be noted.

It is further difficult to reconcile the relevance of the study in light of the observation that treatment with tamoxifen is effective independent of BMI status at diagnosis and that in more recent studies there is less support for adverse effects of BMI on outcomes with change in treatment practices. There is little generalizability of these findings to the current breast cancer patient population, thus the contribution of the study is very modest. The author’s should speak to these results in light of change in practice.

**Level of interest:** An article of limited interest

**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'