Reviewer's report

Title: Leptin and smoking cessation: secondary analyses of a randomized controlled trial assessing physical activity as an aid for smoking cessation

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Reviewer: Marietta Stadler

Reviewer's report:

In the article entitled “Leptin and smoking cessation: secondary analyses of a randomized controlled trial assessing physical activity as an aid for smoking cessation” by Gonseth S. et al. the authors describe the changes in fasting serum leptin levels in a subgroup analysis of participants in a smoking cessation intervention programme. The intervention compared the group receiving moderate-intensity physical activity intervention with a control group. Both groups of participants who successfully stopped smoking gained approximately 3kg of body weight, but the increase in leptin levels adjusted to body fat increased significantly more in the non-intervention group. The authors conclude that the dynamic of leptin level changes in chronic smokers is different in those who are physically more active.

The research question is well defined, the methods are appropriate and the authors are open about the fact that this is a subgroup secondary analysis within their RCT for physical activity intervention in smoking cessation.

The data are reported clearly, the article is well written although I would suggest a few modifications to the way they are presented.

The data are interesting and worth reporting.

Strength of this article is the large number of participants and the complex lifestyle intervention, because smoking cessation studies usually come along with large drop-out rates due to the addictiveness of smoking.

A major limitation is that there is no information on insulin sensitivity and secretion which is known to change after smoking cessation and to be influenced by physical activity. Leptin levels also change with changes in insulin sensitivity—this makes the interpretations of the changes in plasma leptin levels difficult. The authors tried to overcome this issue by adding complex statistical models, but these do not help with the clarity and readability.

Major revisions

- there are no data on insulin sensitivity and insulin secretion. It seems difficult to discuss the change in leptin levels outside the context of insulin sensitivity, particularly because physical activity as well as smoking cessation impact on insulin sensitivity and secretion (Eliasson B et al Eur J Clin Invest 1997; Stadler M. et al. Eur J Endocrinol. 2014). The effects of smoking cessation on insulin
sensitivity and secretion need to be addressed in the discussion.

- Have the authors measured fasting insulin levels? If so, I would suggest calculating a fasting measurement of insulin sensitivity (e.g. HOMA-IR, QUICKI) and report these data.

- The lack of insulin sensitivity and secretion data needs to be mentioned in the limitations section.

- I would suggest simplification of the statistical methods and to clearly present what has been measured without trying to “inflate” the data by applying complex piecewise polynomial longitudinal models:

  Fasting leptin was measured at 4 time-points, there are no dynamic measurements (e.g. oral glucose tolerance test, post-meal leptin…), it was one adipokine. It would be sufficient to present clearly present the results of the measurements as 4 time points with mean and standard deviation to start with. Please put in the models and the Figures 1-2 as supplemental material rather than in the main manuscript body.

- please describe why the number of participants differs from the main publication (271 vs 481). Please describe how you dealt with missing data

Minor revision

- Table 2: the percentage body fat seems low, are you actually reporting the change percentage body weight?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

no competing interests to report