Reviewer’s report

Title: Prospective association between ultra-processed food consumption and incident depressive symptoms in the French NutriNet-Santé cohort

Version: 0 Date: 20 Oct 2018

Reviewer: Kaijun Niu

Reviewer's report:

The authors reported a positive association between the proportion of UPF (%UPF) in diet and incident depressive symptoms. The conclusion was drawn from a large prospective cohort. Although the paper concerns an interesting topic, I have some concerns:

1. It is unclear why so many subjects did not complete 2 CES-D questionnaire assessments (N=84,094). If possible, could the authors make some comparison of baseline characteristics between the excluded and included populations? Could the authors report how many subjects among them have completed the first assessment, then compare these participants with those who had at least 2 assessments? Perhaps subjects that completed the first but not the second assessment is more likely to have depressive symptoms. The authors should also describe this study limitation in the Discussion/limitation section.

2. The survey included volunteers who might be more interested in health issues and all questionnaires and diet records were web-based self-administered, which may be associated with selection bias.

3. Table 1 (baseline characteristics) revealed that CES-D scale is strongly associated with the quartiles of ultra-processed food consumption. Therefore, baseline CES-D scale should be adjusted in the final model.

4. In introduction, the reasons why did the author study the association between UPF and depressive symptoms is not enough. What is the study basis of the hypothesis?

5. The authors should provide detailed inclusion and exclusion criteria. For example, whether baseline chronic diseases, such as hypertension, diabetes, CVD and cancer were excluded or not, which may affect the incident depressive symptoms.

6. page 10 and 11, lines 237-243: "The first model (main model) was adjusted for age, sex, marital status, educational level, occupational categories, monthly household income per
consumption unit, residential area, energy intake without alcohol, number of 24h records and inclusion month, smoking status, alcohol consumption, physical activity and BMI (continuous variable). Three additional models were created to also account for a) PCA-extracted dietary patterns, or b) nutrient intakes, namely carbohydrates, lipids and salt intakes or c) for health events occurring during follow-up (cancer, type 2 diabetes and cardiovascular diseases).” Is baseline health status adjusted?

7. Over a mean follow-up of 5.4 years, are there any lifestyle changes (including dietary, smoking, drinking, etc) among participants during follow-up?

8. The prevalence of depressive symptoms is higher in males than in females. In the present study, is there a difference between males and females?

9. Page 7, line 150-151: "validated against blood and urinary biomarkers [24]" It seems that only urinary biomarkers were mentioned in reference 24. Please clarify.

10. Page 11, lines 242 and 243: "c) for health events occurring during follow-up (cancer, type 2 diabetes and cardiovascular diseases)."; Table 1: "b Incident cases of cancer, Type 2 diabetes, and cardiovascular diseases". The incidence rate (34.6~44.0%) of chronic diseases is fairly high in this study. Please explain in detail.

11. Table 3 - Can the authors present the age, sex and BMI-adjusted model before the multivariate model?

12. Page 15, line 344-345: "more 370 scientific papers than" a typo, should be "more than 370 scientific papers"

13. A statistic test of the model's significance is also useful for demonstration. The authors need to assess the proportional hazards assumption, and report the result in the "Statistical Analysis" section.

14. Please provide more detail on what cardiovascular diseases was included. Information on hypertension and hyperlipidemia would add much value to the paper.

15. No interactions with chronic diseases and BMI were observed?
16. Because dementia is frequently associated with symptoms of depression, and the quality of the questionnaire was also affected by dementia, please consider excluding subjects with dementia in the final model.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Not applicable

**Are the conclusions drawn adequately supported by the data shown?**
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No

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