Reviewer’s report

Title: Intake of non-nutritive sweeteners is associated with an unhealthy lifestyle. A cross-sectional study in subjects with morbid obesity

Version: 0 Date: 25 Oct 2017

Reviewer: Sigrid Gibson

Reviewer's report:

Reviewer's comments on Winther et al. Intake of Non-nutritive sweeteners is associated with an unhealthy lifestyle.

Whether NNS help or hinder achievement of a healthy nutritious diet is less studied than the weight loss outcomes. Studies on morbidly obese subjects are relatively infrequent. Hence studies on these topics are needed. However, in this paper there are significant limitations in the sample size and ability to control for confounders. The results section requires more detail in order to justify the conclusions.

This is a very small cross-sectional study of morbidly obese, mainly female subjects attending a hospital clinic. Only 100 subjects were included and a potential control group (52 who did not report NNS use) appear to have been excluded. Hence the study is about the amount of NNS used within a group of morbidly-obese self-reporting NNS consumers and cannot be generalised to users of NNS in general, or all morbidly obese in general. These are all study limitations.

An FFQ was used to assess intake of NNS from beverages and table-top sweeteners, but more detail is needed on the range of possible responses (frequency and portion). (eg less than once a month, (min) to twice a day (max), how much is a portion? State reasoning for 100ml = 2NNS tablets (eg equivalent sweetening to 100ml of a regular beverage at 10% sugar)

The results and tables giving median (3.3 units) and min/max range (0 to 43 units) give too little information to understand the distribution of intakes and the clusters that drove the choice of statistical models. Please define no/low/medium/high in Figure 2.

The results need to be interpreted and discussed more fully. For example, with regard to the main finding lines 28-30 simply state "high intake of NNS was associated with diabetes, reduced physical activity, fatigue, reduced wellbeing and diarrhea". It would be meaningful to discuss and interpret the size of effect (B value) as this can't be judged easily from the tables. How much greater is the diabetes prevalence with "high" intake of NNS?

The energy and nutrient outcomes are analysed as correlations, these are weak, mostly (rho<0.2) even if the P values are significant (see below). For example a value of 0.14(energy) indicates that NNS only explains 2% of the variance in energy intake.
There may be too much reliance on the P values as an indication of significance. Given the large number of variables there is also a danger of Type 1 error; some of the significant P values may be due to chance. Was any correction made (eg Bonferroni)?

My main concern is the possibility of confounding from the positive association between NNS and diabetes, which was not adjusted for in the analysis. Could this have contributed to the fatigue, reduced activity and lower wellbeing associated with NNS? Adjusting for age, gender and BMI may not be sufficient.

Introduction

The prevalence figures for obesity are quoted from WHO but this needs to state the population it refers to (i.e. globally). Data for Norway would be a useful comparison.

Some statements are supported by selective use of references. For example Line 39 -40 states "that the effect of NNS on weight prevention and reduction is controversial and serious safety concerns have been raised", citing 5 refs. However, the largest systematic review (Rogers et al) concluded that NNS has benefits for weight loss (when replacing sugar) and regulatory authorities worldwide approve NNS as safe. The tone of the paper seems to be that concerns over safety are widespread and well-founded, and that evidence of efficacy with regard to bodyweight is equivocal. I would suggest that discussion of other references, is warranted to provide more balance. The issue of diet quality is little discussed (refs to Gibson et al. and Drewnowski & Rehm are mentioned briefly but others are not, notable the intervention trial CHOICE, which found that consumption of desserts decreased more in the group given NNS beverages. (Piernas C, Tate DF, Wang X, Popkin BM. Does diet-beverage intake affect dietary consumption patterns? Results from the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. Am J Clin Nutr. 2013;97(3):604-11).

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.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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