Reviewer's report

Title: Effectiveness of a low-fructose and/or low-sucrose diet in decreasing insulin resistance. DISFRUTE STUDY: study protocol for a randomized controlled trial

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Reviewer: Gareth Wallis

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The article describes the protocol for a field-based assessment of the effects of reducing fructose intakes in overweight and obese participants on insulin resistance as assessed by HOMA2-IR.

The Background summarizes the efficacy of reducing fructose intakes on various body metabolic health outcomes, and thus studies of effectiveness in the real-world are warranted. In the Background, references are made to 'Excessive', 'large' and/or 'moderate' amounts of mono/disaccharide ingestion and their health effects - its would be helpful to clarify quantitatively what amounts these qualitative descriptors refer to.

The Methods largely describe the protocol to be followed, some further clarification /justification is sought in the following areas:

a) What formula is used to estimate dietary energy requirements and why was an energy-reduced diet prescribed? Presumably, the intervention is therefore also an energy-reduced diet, so how is it possible to conclude on independent effects of low fructose? What reductions in fructose are expected based on habitual consumption patterns in this population?

b) The dietary prescription for the control group needs clarification - e.g., in the Discussion it is stated that both groups will be advised to reduce added sugar consumption - thus the control group is also making dietary changes - this should be justified (is this 'usual care' for example).
c) Statistical analysis clarity is sought. For example, sample size calculations are based on the primary outcome, which is discussed, but are the authors then suggesting a mean difference of 4 kg between interventions? If so, further justification is needed as to why the authors feel this is acceptable to translate to a different primary outcome. As well, the overall statistical analysis plan requires a more detailed description, such as issues around performing multiple t-tests, how the regression analysis will help with confounding, what about the influence of baseline IR on outcomes, plus a consideration of how to control for potential systematic effects of dividing the intervention on the basis of eastern vs. western health centers?

At the end of the Abstract and in the Discussion, it is suggested that this is a tool for preventing type 2 DM. Without follow up of cases of type 2 DM this is not possible to conclude, so perhaps it is more about risk factor management. If this is about tool development, it has to be acknowledged that this is quite an intensively supported intervention, so the take up in clinical practice might require a modification to reduce the burden on resources. The Discussion should also acknowledge that a difference in weight loss is expected, so isolating the intervention effects to reduced fructose should be taken with caution, and probably all conclusions related to a diet that is low in fructose and leads to weight loss.

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