

Reviewer's report

Title: A randomized, controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial)

Version: 2 Date: 30 Dec 2016

Reviewer: Eiko Fried

Reviewer's report:

I thank the authors for addressing my comments. Regarding best practices in correcting for multiple testing, we have to agree to disagree, and I leave the final decision to the Editor. I have taken the time to talk about this (anonymously) with multiple colleagues one more time, and posted this question on 2 statistics mailing lists. The large majority of answers was consistent with my position, which I will clarify one last time.

If you want to find out whether eating any of 50 different types of M&Ms (in 50 colors) impact on your dependent variable (e.g. antidepressant efficacy), and you write a study protocol, a study protocol should include the sentence: "To avoid finding false positives, we will correct for multiple testing". Forgetting to put this into the study protocol does not mean the study should not correct for multiple testing, the same way forgetting to put using non-parametric tests into a study protocol in case of non-parametric data does not mean you should not use non-parametric tests with non-parametric data.

If the study protocol, however, lists "We expect that for the light green and dark blue M&M, the dependent variable will be higher" — in other words, if the study protocol lists very specific hypotheses between specific variables and the outcome, *including* a specific direction (higher vs lower) — which also means statistical tests have to be one-tailed tests, not two-tailed significance tests — the argument can be made that multiple correction is not necessary.

But after re-reading the authors' study protocol a second time, I can find many pre-registered tests and outcomes (which is great), but not specific pre-registered hypotheses and directions. This is a crucial difference, and means that consistent with the literature, the authors have to balance type-I and type-II errors, because they are genuinely interested in describing what the data tell them. In this case, the authors chose to use a Frequentist framework with a p-value $\leq 5\%$ as evidence for the H1, and this framework demands attention to inflated error rates through multiple testing.

But, as I said above, I leave the decision about this to the Editor. I am very worried about promoting depression treatments for which there is little to no evidence — the field of depression treatment research would likely be in a much better state had we been more open and honest about efficacy — and I hope the authors understand my attention to multiple testing from this perspective. I think they have written a great paper, but my work in depression trials has made me wary of overinterpreting results that lead to great economic loss and add substantial burden to patients.

Are the methods appropriate and well described?

If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?

If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?

If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?

If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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