Author's response to reviews

Title: Lifestyle precision medicine: the next generation in type 2 diabetes prevention?

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REVIEWER 2

Reviewer 2, comment 1: The authors have done an excellent job in addressing my concerns in this revised paper. I have only one small suggestion. In Table 1 it would be helpful to mention that issues related to regression to the mean are overcome in RCT study designs where the difference in change from baseline in intervention and control conditions is considered.

Response to R2.1:

The Reviewer refers to the section of Table 1 shown below. We agree that when RCTs are used to assess the effect of an intervention, the comparison with a control condition helps remove the influence of non-intervention factors. When interventions are assessed in the absence of a control condition, the observed effect may be over- or under-estimated if there are background (non-intervention) factors that influence the outcome. The latter reflects the impact of confounding.

Regression to the mean does not usually cause an intervention’s effects to be under- or over-estimated (it simply results in greater error and thus reduced statistical power). We agree with the reviewer that in principle, one could use data collected in the control arm to reduce the impact of regression to the mean in analyses designed to detect responders and non-responders to a given intervention. However, studies in the published literature on responders and non-responders have not to our knowledge adopted such an approach (usually subgrouping is done only in the intervention arm).
Whilst conditioning treatment-response values, and identifying responders and non-responders, to an intervention on the response data obtained in the control arm of an RCT is worthy of greater discussion, we feel that this would go beyond the scope of the current paper, given that this is not common practice. We have added to the text in Table 1 (page 13) to briefly address this point as below (please also see revised document and tracked changes).

"This problem could in principle be overcome in an RCT by conditioning treatment response on response to the control intervention, although this is not conventionally done in studies of responders and non-responders, which generally focus only on intervention groups."