

Consistency, conditional exchangeability and positivity in hypothetical weight change interventions

We would like to thank MacDonald and Frenoy[1] for their commentary on our study[2] and for giving us the opportunity to broaden the discussion.

We agree with them that our interventions are not well-defined, and had made this clear in our paper[2]. Their comment expands on the impact that this has on the identification assumptions. Below, we explain the steps we took to attenuate these well-known problems[3].

Consistency: This assumption implies that any treatment-variation is irrelevant or that there are no multiple treatment versions[4]. In other words, individuals considered as being on the same arm should actually undergo the same intervention. This is indeed a problem in our paper, which we highlighted in the Discussion[2]: “Different methods of modifying bodyweight may have different effects on CVD risk”. Thus, the potential outcomes of individuals who experienced a given weight change regime may not be the same as their observed outcomes. We tried to partially tackle this problem by restricting the analyses to healthy individuals, thus minimising the chance of weight change due to illness. With respect to achieving weight change by smoking cessation or uptake, we believe that any indirect effect would have a limited impact because our findings were robust to restrictions involving only people who remained non-smokers during the first year.

Conditional exchangeability: Apart from the problem of unmeasured confounding which is inevitable to some degree in observational studies, MacDonald and Frenoy[1] mentioned that confounding factors for physical activity and diet are not the same. We had pointed this out in our paper “Ill-defined interventions also affect our ability to define and address confounding too”. However, we tried to minimize this problem by restricting the interventions to healthy individuals. We did not extend the inferences to non-healthy individuals, as it is very likely that the effect of this type of interventions would differ by baseline health status.

Positivity: The interpretation of the positivity assumption is that there must be a non-zero probability of having treated and untreated individuals across all strata defined by the confounders. We stratified the population according to baseline BMI and performed three separate emulated trials. In this way, we attempted to address the problem mentioned by Hernán and Taubman[3] that people with high BMI may have different distributions of (some) confounders compared to people with low BMI (which could potentially affect the positivity assumption). In practice, we didn’t face this problem as, within each emulated trial, inverse probability weight estimates were not large (near-positivity violations would have resulted in inflated weights).

In conclusion, by adopting a target trial emulation approach, stratified by baseline BMI, we utilised a robust study design, albeit considering hypothetical weight change interventions which cannot be seen as “actionable” real-world interventions. We believe that our study addresses some of the knowledge gaps in this area and provides some evidence on what might work in healthy individuals. However, as we mentioned in our paper[2], future research in the field should focus on well-defined interventions for which more detailed data than ours would be needed.

References

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