Response to 'Can collider bias fully explain the obesity paradox?'

Matthew Sperrin*¹, Jane Candlish¹², Ellena Badrick¹, Andrew Renehan³, Iain Buchan¹

¹ Division of Informatics, Imaging and Data Science, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre
² School of Health Related Research, University of Sheffield, UK
³ Division of Cancer, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre

Correspondence to: Dr Matthew Sperrin, Health eResearch Centre, Farr Institute, University of Manchester, Manchester M13 9PL, United Kingdom. Tel: +44 (0)161 306 7629, E-mail: matthew.sperrin@manchester.ac.uk

Conflicts of Interest and Source of Funding

This work was supported by the University of Manchester's Health eResearch Centre (HeRC) funded by the Medical Research Council Grant MR/K006665/1.

Conflicts of interest: None declared.

Editor’s Note: A related Commentary appears on p. XXX.
To the Editor:

We thank Viallon and Dufournet for their letter\(^1\), and agree with the concerns raised regarding our paper\(^2\). As the letter points out, the effect we calculated was not equal to \(\Delta_{CE}\), because it is *not* true that \(Y^a \perp A|M, U\). Thus, the bias in estimating \(\Delta_{CE}\) may be much larger than we stated. Fortuitously, this has given rise to an interesting discussion about the various causal effects that can be calculated in this framework.

In fact, the effect we have calculated can be shown to be the controlled direct effect, conditioned on the level of \(M\), \(\Delta_{CDE|M=1}\); we give a proof in the eAppendix, http://links.lww.com/EDE/B217. This is similar to the controlled direct effect derived by Viallon and Dufournet (the red line in their Figure 2), the difference being that we condition on those patients who had diabetes (and intervene to ‘maintain’ their diabetes).

We agree with Viallon and Dufournet that controlled direct effects are more likely to be the effects of interest in discussions around the obesity paradox; this has been noted by others as well\(^3\). In this setting, the effect of collider stratification is to induce a (or strengthen an existing\(^4\)) relationship between \(U\) and \(A\), and hence induce (or strengthen) confounding.

Viallon and Dufournet have also shown how the extent of the bias between controlled direct effects and observed associations can become larger than in the scenarios we considered, when interactions are present.

To conclude, we feel our results remain useful as an illustration of the extent of bias in using an observed association to estimate the controlled direct effect, \(\Delta_{CDE|M=1}\), under the scenarios we considered. Collider bias is one possible explanation for the obesity paradox, among many. It seems most likely to us that a combination of these explanations act together, possibly in synergy, to generate an observed obesity paradox.
References:

1. Viallon V, Dufournet M. Re. Collider bias is only a partial explanation for the obesity paradox. *Epidemiology* 2017;28:xxx.

