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Dear Editor:

We read with great interest 'The Oral Health Statistics Guidelines for Reporting Observational Studies and Clinical Trials in Oral Health Research: Explanation and Elaboration'.<sup>1</sup> We are members of the United Kingdom National Institute for Health and Care Research Statistics Group, which aims to translate best methodological practice into applied research. We are therefore delighted to see collaborative efforts to improve reporting, and hope that other health areas might follow, but believe the guidelines are unclear on some important points.

Multivariable modelling is used for many different purposes throughout health research; despite both involving modeling, predicting an outcome versus understanding what causes it (and how to change it) are different tasks requiring tailored analytical approaches rather than a one-size-fits-all solution.<sup>2</sup> The artificial intelligence explosion within health requires researchers to understand this distinction because here inappropriate methodology can have huge impact.

The guidance does not encourage clarity regarding predictive vs causal aims. Specifically, items 15 (variables), 29 (multivariable modeling) and 40 (modeling) do not highlight that variable roles, variable selection and model interpretation differ between the two. Therefore, we suggest that a future revision of the guidelines should go beyond simply classifying items as predictors and response in the context of multivariable modelling.

It is well established, but not widely understood, that you cannot interpret the effects of multiple variables from the same multivariable model. This is deemed the Table 2 Fallacy, because multivariable models are often presented in Table 2 of a publication.<sup>3</sup> To understand whether one particular variable (exposure) is causing an outcome, we need to estimate the strength and direction of that specific relationship, adjusting for confounders, i.e. variables that cause both the exposure and the outcome, but should not include mediators, which sit between them on the causal pathway. This a) adjusts away some of the total causal effect of the exposure, which operates through the mediator (Figure 1) and b) introduces unpredictable

biasing effects that can even reverse the apparent direction of effect.<sup>3</sup> Therefore, if we switch focus to a different exposure variable, we will need a different analysis model, because variables that are confounders of one exposure-outcome relationship will be mediators of another.

The elaboration paper refers to the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines, which pay greater attention in this regard. Section 16a states: *Decisions about excluding or including variables should be guided by knowledge, or explicit assumptions, on causal relations. Inappropriate decisions may introduce bias, for example by including variables that are in the causal pathway between exposure and disease (unless the aim is to assess how much of the effect is carried by the intermediary variable).*<sup>4</sup> We believe that item 29 might ask whether directed acyclic graphs were used to guide model development and covariate selection<sup>5</sup> and that item 40 should be reworded to clearly discourage interpretation of multiple ‘primary factors of interest’ from the same model.

We appreciate the huge effort that went into the creation of these excellent guidelines but believe they would be further enhanced were these distinctions to be drawn.

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## References

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## Figure legend

**Figure 1:** Basic directed acyclic graph highlighting that including a mediator adjusts away some of the total causal effect of an exposure on an outcome