Referee report for "Hypothesis tests for multiple responses regression: effect of probiotics on addition and binge eating disorder"

Overview

The manuscript focuses on the estimation and testing of parameters in a regression model with multivariate responses of different types. Specifically, the authors propose to use Wald tests on parameters from a *multivariate covariance generalized linear model* (McGLM). There are extensive simulation studies and example applications, and an analysis of the motivating dataset. Ultimately, however, the article's methodological contribution is limited in scope, and its practical content is mostly covered in the authors' past work. I discuss these issues further below.

Main points

1. McGLMs and the asymptotic normality of $\hat{\theta}$ were established in Bonat and Jørgensen (2016). Wald testing for estimators which are asymptotically normal is taught in introductory statistics courses. Thus, I do not believe Wald tests for McGLMs constitute a substantial methodological contribution.

2. The majority of the article's statistical content is either reviewing Bonat and Jørgensen (2016) (e.g., portions of Section 3.1 are taken *verbatim* from Section 3 of Bonat and Jørgensen (2016)) or straightforward example applications of the Wald test. It would be more appropriate if the article were framed more as a tutorial for McGLMs and hypothesis testing, though a substantial tutorial on McGLMs was recently published in the Journal of Statistical Software (Bonat, 2018).

3. As an article focused on the data analysis, I simply do not find the motivating problem compelling or substantial enough to warrant publication in Statistics in Medicine. This is my opinion, of course, but if the data analysis were to be the primary focus, much more would be needed in terms of diagnostics and discussion of the scientific implications of the results. For example, what is revealed by this analysis that would not have been revealed if another method were used?

References

Bonat, W. H. (2018). Multiple response variables regression models in r: The mcglm package. *Journal of Statistical Software*, 84:1–30.

Bonat, W. H. and Jørgensen, B. (2016). Multivariate covariance generalized linear models. *Journal of the Royal Statistical Society: Series C (Applied Statistics)*, 65(5):649–675.