Reviewer’s report

Title: Estimating the BMI-Mortality Relationship: A New Approach

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Reviewer: Ralf Bender

Reviewer’s report:

The nonlinear association between BMI and mortality is investigated by using the MFP procedure applied to data of the National Health Interview Survey. On one hand, the paper is in general well written and applied probably one of the best approaches to study nonlinear associations. However, on the other hand, the main aim of the paper remains unclear. In the present form the article represents a mixture of a methodological paper and an epidemiological paper describing and discussing epidemiological results. The paper has to be revised to get a clear methodological focus. The epidemiological results should be removed and can be submitted elsewhere.

Major Compulsory Revisions

(1) The title of the paper is misleading. The authors applied the usual MFP procedure which is not a new approach. Thus, the title has to be changed.

(2) Page 5, line 11: "The purpose of this study is to estimate the relationship between adult mortality and obesity using ...". If it is really the main aim of the paper to estimate a relationship the paper is better placed elsewhere. However, in the Abstract it is stated that "This study tests a flexible modeling approach ..." which means that the paper also has a methodological focus. The latter has to be strengthened and the main methodological aim (e.g. the comparison of the MFP procedure with common regression approaches using categorized variables) should be described consistently in the Abstract and the Background.

(3) Following comment (2) the main results are not given by the estimated regression curves or the estimated nadirs. The main results are the disadvantages (bias, power, etc.) of regression approaches using categorized variables compared to the MFP procedure. The paper (Abstract, Results, Discussion) has to be revised accordingly.

(4) Page 8, lines 8-10: Which graphical checks were used?

(5) Reasons should be presented for the chosen approach to adjust for selection bias. Sensitivity analyses should be performed to show the robustness of this approach.

(6) The complete case approach was applied to deal with missing data, which is prone to bias. The application of this approach may be adequate in a methodological paper with the main goal to compare several approaches in the
case of complete data. However, the limitation that the estimates may be biased due to missing data should be mentioned.

(7) Only 3 explanatory variables were considered: BMI, age, and smoking. Again, this may be adequate in a methodological paper with the main goal to compare several approaches in the case of only 3 important covariables. However, the limitation that the estimates may be biased due to ignorance of further covariates (e.g., physical activity) data should be mentioned.

(8) Only point estimates for the nadirs of the BMI-mortality curves are presented. The findings should be complemented by confidence intervals (see Durazo-Arvizu, R.A., McGee, D.L., Li, Z. & Cooper, R. (1997): Establishing the nadir of the body mass index-mortality relationship. J. Am. Stat. Assoc. 92, 1312-1319). A quite interesting point is to investigate the differences between the considered regression approaches regarding point and interval estimates of the nadirs.

(9) The Discussion section starts with the description of the epidemiological findings regarding the BMI-mortality relationship and includes a lengthy discussion of the own findings compared to that of other epidemiological studies. Most of this discussion should be removed and the Discussion section should concentrate on methodological issues.

(10) The paragraph on limitations contains only the model choice (logistic vs. Cox model) and the performed pooling of data. The existing further limitations (missing data, possible confounding) should be added.

Minor Essential Revisions

(1) In the Background of the Abstract it is stated that "This study tests a flexible modeling approach … to examine the relationship between mortality and obesity measured as BMI>30." However, the main approach is given by the MFP procedure in which BMI is used as continuous variable. Thus, not the relationship between mortality and obesity measured as BMI>30 is investigated but the relationship between mortality and BMI as continuous variable is investigated and compared to a common regression approach using BMI as categorized variable. Thus, the statement has to be changed.

(2) Page 11, line 1: "Figure 5" should be "Figure 4".

(3) The labeling of Table 2 is incomplete; probably, the numbers in brackets represent SEs; this should be stated clearly.

(4) The title of Table 2 is hard to read. Please move the formulas into a footnote for Table 2.

(5) Please use different line types in Figure 3 for smokers and nonsmokers.

Discretionary Revisions
Sensitivity analyses were performed by using 3-year mortality as outcome. The following sensitivity analyses would improve the paper (in addition to the sensitivity analyses concerning the authors' approach to adjust for selection bias, see above):

- Regression analyses without extreme BMI values
- Exclusion of persons that died early

If the authors consider to write an additional paper presenting the epidemiological results for another journal the following papers may be interesting:


Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.