Reviewer’s report

Title: Assessing the effect of a partly unobserved, exogenous, binary time-dependent covariate on survival probabilities using generalised pseudo-values

Version: 0 Date: 05 May 2017

Reviewer: Per Kragh Andersen

Reviewer’s report:

The authors propose a novel approach for comparing survival curves when an exogeneous time-dependent covariate is operating.

The motivating example comes from pediatric oncology where the exogenous covariate is 'donor availability'.

I have some problems with the properties of the quantity defined in equation (5) in the paper. The suggested pseudo-value for subject i is based on observed survival for all (n_i) patients (with or without a transplant) who are alive at the observed time, w_i of transplant for that patient. This pseudo-value seems to be used only for patient i, i.e. 'a single, special patient', and yet reference is made to 'general properties of pseudo-values' that rely on an i.i.d. assumption. I am not convinced that the property of the resulting pseudo-value for patient i can be derived without further arguments.

Some further comments:

The crucial word 'exogeneous' correctly appears in the title of the paper. It should also be emphasized in the abstract.

p.6: please elaborate a bit on the 'clear and unambiguous interpretation' of a cumulative hazard ratio. To me, the interpretation is not quite clear.

p.7: do you need the hazard \( \lambda_{01} \) of V? It must be a strange non-integrable function on the interval from 0 to t-search. Perhaps you only need the density?

p.8: Shouldn't X(u) (and X(t)) in the exogeneity property by \{X(s),s<=u}\)?

p.10 (top): where has pseudo-values been used for estimating a cumulative hazard?


Equation (8) seems to require density estimation. How is that done in general?
A general comment: Perhaps the problem studied could be tackled using methods from 'causal inference' (e.g., Daniel et al., Stat. in Med., 2013) though donor availability is not a confounder?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
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I am able to assess the statistics

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