Reviewer’s report

Title: A general approach to risk modeling using partial surrogate markers with application to perioperative acute kidney injury

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Reviewer: Jason Oke

Reviewer's report:

The authors do not seem to have access to the true outcome (T) but only another surrogate marker (eGFR90). I think that paper which aims to resolve methods for dealing with partial surrogates should start with an example in which the true outcome is known. Another problem here is eGFR90 itself. It is not clear from the manuscript how GFR has been estimated. They seem to be skirting around the issue of GFR being estimated at all. eGFR90 (and once or twice just eGFR) is used in the text many times but in the list of abbreviations it is written as just GFR?, there is no mention of estimated GFR. The problem with this is, is that GFR is often estimated using serum creatinine which is the partial surrogate in the example. Even if GFR is not estimated but measured using something like inulin clearance then I am still not sure that this is as good as a clinical diagnosis of AKI Finally, the suggested change of 20 is not standard as far as I am aware and probably too stringent given the reference change value of eGFR using the MDRD equation is 15%. Sensitivity analyses would be required to assess the importance of setting change at this level.

The simulation method as per the introduction difficult to follow. The analysis was also incomplete. I want to know when using this approach might go wrong (fitting a two-mixtures when there are three) and I would want to know about coverage and bias. This is what I would expect in a methods paper. I am also surprised to see that there are no tables showing detailed results of the simulations. In addition, it would be nice to have as an appendix, the code used to do the simulations as this is often much easier to follow than text

Finally, the title of the paper suggest that this will be a methods paper but the abstract reads as if the paper is setting out to apply this method to a particular clinical setting (AKI). I wonder whether this has been submitted previously to a clinical journal? I would suggest that if this were to be accepted then this abstract should be amended.

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