Reviewer's report

Title: Extreme Verification Bias in Paired Continuous Tests Can Cause Researchers to Choose the Wrong Screening Modality

Version: 2 Date: 25 November 2008

Reviewer: Jørgen Hilden

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Bias in trials comparing paired continuous tests can cause researchers to choose the wrong screening modality

- a revised version of Extreme verification bias in paired continuous tests can cause researchers to choose the wrong screening modality, July 2008 by Glueck et al.

There is little to criticize. The revised version is equally clear and more carefully phrased in the details.

Suggestions (discretionary suggestions for revision)

S1) If the text is going to have second round of polishing, the author may consider the following points. The new Fig. 1 is good, except that the reader cannot see where the false positives come from.

S2) 'Model …' section, paragraph 'During the…': the 'never' in the final line ought to be replaced with 'never during the available follow-up period'.

S3) 'Study design,' 3rd paragraph: The reader should be notified at the beginning of the paragraph that Fig. 1 is being explained – rather than at the end.

S4) In Tables 1 & 2 it may be very helpful to add a sentence like this to the heading: 'The signs and symptoms column is left empty in those cases where the observed disease status does not depend on the development of signs or symptoms.'

S5) The last paragraph of the Discussion jumps to the meta-question why this type of research is worth while. It deserves its own heading. Could it have it?

S6) I now realize that there is one obvious ramification that hasn't been looked at: When a patient is recalled for further testing, the investigator (who runs the potentially biased study) knows which criterion triggered the referral (essentially, which line in Tables 1 & 2 was triggered); (s)he will/may therefore also know what the patient's 'observed' diseased status would have been if only test 1 or only test 2 had been "at trial" (unpaired trials). To the extent that there is severe bias in the paired trial, my intuition tells me that there would typically also be
discrepancies between the paired and the two unpaired ROC comparisons, whereas, if the three ROCs tell essentially the same story, then a distorted conclusion is unlikely. This, of course, calls for an examination of the corners of the authors’ parameter space to see if there are any snags.

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**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests /J.Hilden