Reviewer’s report

Title: Does Risk for Ovarian Malignancy Algorithm excel human epididymis protein 4 and CA125 in predicting epithelial ovarian cancer: a meta-analysis

Version: 2 Date: 15 May 2012

Reviewer: Mariska M. G. Leeflang

Reviewer’s report:

This report has indeed improved and especially the explanation of which studies were used for which analyses, is clearer. However, the paper remains difficult to read and to understand. Some of my suggestions have been followed-up, some have been replied to, but did not lead to changes in the text.

Major compulsory reviewsions

1. About the test comparisons: the authors state that they included "studies that investigated both serum HE4 and CA125 [...] or calculated the ROMA". Could they explain here why they only include these studies (it is now explained in the Discussion section)? And that studies only assessing one of these tests were not eligible? I think a more explicit statement about that only 'comparative' studies were included, would have resolved the confusion I had when I previously reviewed this manuscript.

2. I am a bit worried about the univariate analyses for sensitivity and specificity. I suspect they mean that they just pooled sensitivity separately and specificity separately. But then you lose the fact that every study 'delivers' a sensitivity and a specificity. I would therefore still prefer the bivariate or HSROC method, even if no threshold effect is shown. In that situation, especially the bivariate model may be very suitable.

3. Another issue that has not yet been resolved, is the interpretation of the results. I assume that an AUC of around .90 is very good and looking at the ROC curves, these curves come close to the upper left corner, but what is the clinical meaning of this? If I am a clinician, should I now turn to the ROMA-algorithm, or is HE4 / CA125 sufficient? And if the authors don't want to make any recommendation regarding that, can they perhaps explain what the consequences would be if I would use one or the other (how many patients would I miss, how many false positives)?

4. Also about the interpretation, my point remains about interpreting the accuracy estimates when such a variety of cut-offs have been used. The estimates for ROMA, for example, to which cut-off values refer these? Can I use this estimate if I use ROMA at a cut-off of 7%, 12% or 25%?

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

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I declare that I have no competing interests