Reviewer’s report

Title: Septin 9 methylated DNA is a sensitive and specific blood test for colorectal cancer

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Reviewer: Andreas Leodolter

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Warren et al. present their data concerning Septin 9 methylated DNA for detecting CRC. They have developed a promising optimised test protocol with a much higher accuracy than described before.

How much more effort are the changes in the test protocol. Can you give an example in costs and time consuming?

The control group contains patients with polyps; these are definitely no valid controls and have to be excluded.

The calculation of accuracy in the last part of the result section is misleading and somehow incorrect. It has to be clearly stated, at least in the discussion, that the adenoma detection rate is poor, and therefore this is not a promising screening marker. Detection rate was 12%, much less than with other screening methods i.e. FIT. The specificity of 3% in the screening population is not a marker for good performance of the test; it only reflects the very poor sensitivity.

The authors stated that half of the patients with pos. Sept9 testing had polyps, the PPV therefore is about only 50%, a value that has to be critically discussed.

There is no evidence at all that a test which only detects CRC and more or less no adenoma is of any value for reducing CRC mortality, therefore the authors have to be more careful in their discussion about the value of this test.

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