Reviewer’s report

Title Evaluating screening approaches for hepatocellular carcinoma in a cohort of HCV related cirrhosis patients from the Veteran's Affairs Health Care System

Version: 0 Date: 30 Aug 2017

Reviewer: Massimiliano Orso

Reviewer's report:
This paper is aimed to evaluate two biomarker screening approaches, a six-month risk prediction model and a parametric empirical Bayes (PEB) algorithm, in terms of their ability to improve the likelihood of early detection of hepatocellular carcinoma (HCC) compared to current alpha-fetoprotein (AFP) alone when applied prospectively in a future study.

The paper is well planned and written; I have just some comments to do.

Major comments:
- The cohort of patients was randomly split into the training and validation cohorts. I wonder if this is a robust approach. Should be a cross-validation approach a better option in this case?
- Why only the training cohort was restricted to only those with AFP < 400 ng/ml?

Minor comments:
- page 2, line 30: delete the word "trial";
- page 2, lines 37-38: "...that is widely used in screening...": Could you provide a reference for this statement or some examples of Countries in the world using AFP for HCC screening?
  Bruix and Sherman (AASLD PRACTICE GUIDELINE Management of Hepatocellular Carcinoma: An Update) do not recommend the measurement of AFP or other serum biomarkers alone or in combination with USG for surveillance.
- page 9, line 5-6: change "cummulative" with "cumulative".
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

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

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?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:
Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal