Author’s response to reviews

Title: A methodology review on the incremental prognostic value of computed tomography biomarkers in addition to Framingham Risk Score in predicting cardiovascular disease: the use of association, discrimination and reclassification

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Author’s response to reviews:

Dear Editor,

We are delighted to hear the positive news from both the reviewers and editors of BMC Cardiovascular Disorders.

Having looked at the comments, we have undergone the following revisions according to each comment specifically. Please see below:

Technical Comments:

1. Please rename 'Introduction' to 'Background' (line 130, page 7)
   Reply: changed as suggested

2. Please provide Conclusion section after Discussion section.
Reviewer reports:

Nina Paynter (Reviewer 1): The authors have performed an interesting analysis of reports comparing prediction when adding calcium measures to Framingham Risk models.

Comments

1) One important factor in addition to the variables included in the Framingham model is whether the model coefficients were re-estimated in the new population or the published coefficients or point based model was used. This could have a large impact on the baseline AUC and would be worth adding to the paper.

Reply: Agree. This specific point raised has been added to the paragraph that described limitation in the discussion section (please see line 387-390, page 18).

2) Another important question is the outcomes used in the paper. There has been much discussion of CHD vs CVD and which models can be applied to what. This would also be worth noting.

Reply: Agree. This specific point has been added to the paragraph that described limitation in the discussion section (please see line 390-392, page 18-19).

3) I am not sure why the authors reference the cancer literature on publication bias. This may play into a larger issue where it might be helpful for the authors to separate conclusion about the predictive value of calcium and conclusions about how prediction results should be reported in the literature. This could be helped by separating the key points and the findings.

Reply: Agree. All references to publication bias in cancer risk prediction confuse matters and have been removed accordingly, including:
In the “Background” section (“In a different setting, the cancer risk prediction literature is known for its publication bias”) (line 140, page 7)

In the “Discussion” section (“This adds to the known issues on publication bias and methodology in the cancer risk prediction literature) (line 344, page 16)

Lizhang Chen (Reviewer 2): This is an interesting study. Model construction are so many, but the application of model are few. The evaluation of methodology is necessary.

I have one question. Please add the quality of included studies.

Reply: Agree. The following changes have been made accordingly:

- A critical appraisal section has been added in method (line 204-207, page 10)

- Bias assessment using the Quality in Prognosis Studies Tool has been added in the results section (line 239-246, page 12).

- Figure 2 has been added as a schematic representation of the bias assessment

- Due to the addition of a new figure, the previous figure 2 is now figure 3 (line 292, page 14); figure legends have been added and changed accordingly (page 40)

I hope the above changes made according to the comments would satisfy both the reviewers and editors. Please do not hesitate to contact me for anything else we can address.
Best regards,

Chun Lap Pang

On behalf of all the authors.