Author’s response to reviews

Title: Molecular essence and endocrine responsiveness of estrogen receptor-negative, progesterone receptor-positive, and HER2-negative breast cancer

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Author’s response to reviews:

Dear Senior Editor,

Please reconsider our manuscript "Molecular essence and endocrine responsiveness of estrogen receptor-negative, progesterone receptor-positive, and HER2-negative breast cancer" (MS#: 1470587730167927 and BMED-D-15-00216R1) for publication in BMC Med.

Thank you very much for reviewing our previous manuscript. We would also like to thank the reviewers for their thoughtful and constructive comments. According to the editor’s suggestions and the reviewers’ concerns, we have revised our manuscript and added new information where appropriate. We are pleased to resubmit our modified manuscript to you for further consideration.

Below, we include a point by point response to the reviewers’ concerns

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1. Remaining concern from statistical advisor: The authors have stated the statistical tool used to implement the methods, but not the methods. I think they should state what method they used, they say “implemented using...”

Our response:
Yes, we have revised it. According to the previous study[1], the score methods are recommended for interval estimates of proportion and in our study the Wilson score confidence intervals were computed.

Reference:

2. Remaining concern from statistical advisor: The authors do not appear to have followed this suggestion. The reviewer offers them an elegant multivariate approach, or a simpler but still valid approach of comparing each group with all the others combined. They appear to have opted to use the simpler approach, but have not compared each group with the others combined. Instead they appear to have gone with the method the reviewer warns against, thereby introducing potential bias. I recommend they follow the approach suggested by the reviewer.

Our response:
We probably misunderstood the original comments. We thought that the former advisor suggested us to calculate the survival estimates of ER-/PgR+ vs ER+/PgR+ and ER-/PgR- vs ER+/PgR+ using the simple approach. However, according to remaining concern from statistical advisor, the advisor actually suggested us to present the results of ER+/PgR+ vs all others and ER-/PgR- vs all others (if we used the simple two 2-way comparison method). We believe that the pooled survival estimates of ER-/PgR+ vs ER+/PgR+ and ER-/PgR- vs ER+/PgR+ would be more helpful for readers. Therefore, in the revised manuscript, we employed the elegant multivariate meta-analysis (in Stata program “mvmeta”) to give pooled estimates of both ER-/PgR+ vs ER+/PgR+ and ER-/PgR- vs ER+/PgR+ simultaneously. Multivariate meta-analysis has been described previously[1, 2]. In this analysis, the method we used was restricted maximum likelihood (REML) and the variance-covariance matrix was defined as “unstructured”. The revised results were as following: the pooled HR by multivariate meta-analysis was 2.67 (95% CI 1.77-4.05) for ER-/PgR+ versus ER+/PgR+ and 3.97 (95% CI 3.38-4.66) for ER-/PgR- versus ER+/PgR+.

References:

We hope that the editors as well as reviewers can satisfy our answers.

Thank you for your consideration.

Sincerely yours,

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