

Peer Review File

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Reviewer Comments

Reviewer A

Comment 1: This manuscript describes a use case of using the IPDmada tool to perform an individual patient data meta-analysis of diagnostic test accuracy (DTA). The already published tool IPDmada is a UI-based R Shiny application that reduces the barrier for users without a strong statistical background to analyze data in DTA study.

Requested Revisions:

- It is unclear to what extent this article contributes an original novelty/ new insight, that was not already described in the cited article <https://doi.org/10.1002/jrsm.1444> of the IPDmada tool. Please clarify how this work extends the previous publication.

Reply 1: This manuscript was submitted to a Special session in JLPM: Statistics Corner, which aims to introduce statistical methods and provide tutorial of statistical tools to JLPM audiences. The current manuscript did not extend the IPDmada in its methodology or implementation, however, we explained how to use this tool (which is originally not designed for primary studies) to perform statistical analyses in primary DTA studies.

Comment 2: Since the focus of the manuscript is on the exemplary analysis of a concrete data set and the manuscript and the tool are aimed at statistically inexperienced users, an interpretation of the visualizations and a more detailed explanation of the statistical methods/the particular question that can be answered by using the software would be very helpful. An additional idea could be to describe how the thresholds influence the results and compare the different threshold options.

Reply 2: Thanks for the suggestion. We have added some interpretation of the visualizations, the following changes are made to the manuscript:

“The first option is useful when different thresholds are used in different centers, e.g. index test is from different manufacturers and the recommended thresholds are different; the second option is often desired when we need to determine an optimal threshold; the third option allows the users to tune the threshold for sensitivity analysis and data visualization purposes, to have a better understand how sensitivity and specificity will change when the threshold changes.”

“This ridgeline plot shows the distribution of index test in diseased group (Present) and non-diseased group (Absent), and smaller overlap between the two groups indicates better discrimination power of the index test.”

“ROC curve shows the relation between true positive rate/sensitivity (y-axis) and false positive rate/1-specificity (x-axis) at all possible threshold values.”

“Investigating the distributions of covariates can help to identify differences in patient characteristics in diseased and non-diseased groups, which may influence the true test performance. If substantial differences are observed, we can consider using covariate

adjusted ROC curve for further analysis.”

Comment 3: - The import of comma-separated values (.CSV file) into Excel is trivial. Please consider shortening the Data preparation section.

Reply 3: Thanks for the suggestion. Since after uploading data, most of analyses will be done by IPDmada automatically, the only work needs to be done manually by users is importing CSV file into Excel and adjusting the variable names. Thus importing CSV file is an essential step in this process, and the authors also received feedback from users that most errors happened in this step. For these reasons, we prefer to keep the detailed description.

Comment 4: - Please rewrite the section Data preparation to make clear that three columns are required and have to be named “Study”, “test.results”, and “disease”.

Reply 4: Thanks for the suggestion. We have rewritten the Data preparation section to emphasize that the three columns are required and have to be named “Study”, “test.results”, and “disease”: “To facilitate the analyses provided in IPDmada, three columns are required and have to be named “Study”, “test.results”, and “disease”, and the variable names are case sensitive (e.g. Study must has a capital S).”

Comment 5: Conclusion:

Unfortunately, the content of this manuscript in the current version is very close to the earlier publication of the application and offers little added value. All IPDmada visualizations are already explained in the previous publication. Thus, the content can only be considered as a software accompanying vignette but not a stand-alone publication.

Reply 5: As we explained in the reply to the first comment, this manuscript was submitted to a Special session in JLPM: Statistics Corner, which aims to introduce statistical methods and provide tutorial of statistical tools to JLPM audiences. We agree with the reviewer, the manuscript did not provided primary results, and the data analysis was only illustration purposes thus not contributing original content. We will discuss with the Editor about the suitable label.

Reviewer B

Comment 1: Although presented as an "Original Article", the manuscript is in practice only a brief manual on the usage of the Shiny web application IPDmada, which was already described in the published journal article available at this link: <https://onlinelibrary.wiley.com/doi/epdf/10.1002/jrsm.1444>

The paper does not present any particular inaccuracy, but it lacks the originality in content that an original article should have. Indeed, it's main contribution is the discussion on data preparation details for app usage, which I believe should be better published on the app itself, which it is currently lacking any documentation on usage,

and not in an "Original Article". Indeed, if the goal of the app is to provide a easier experience to practitioners, the app itself should also be self-explanatory and contain detailed information on how to use it. Further, the analysis of the data does not concern novel data and it is only performed as a pretest. Indeed at lines 88-91 the authors claim "Please note that, all the analyses presented in this report are only for illustration purposes, and sometimes variables are analyzed as a hypothetical example without practical meaning, thus no clinical conclusions should be drawn from these results.". Thus, the article carries no original content in its data analysis part.

Reply 1: This manuscript was submitted to a Special session in JLPM: Statistics Corner, which aims to introduce statistical methods and provide tutorial of statistical tools to JLPM audiences. We agree with the reviewer, the manuscript did not provided primary results, and the data analysis was only illustration purposes thus not contributing original content. We will discuss with the Editor about the suitable label.