Author’s response to reviews

Title: Patient recruitment strategies for adaptive enrichment designs with time-to-event endpoints

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Author's response to reviews:

[1] Response to the comments by Reviewer 1

1. Comment: Using figures is a good way to present the results. But the authors should consider adding more legend and footnotes to each figure. For example, on Figure 4, there are three colors and different shapes (circles, squares, triangles and stars), and also looks like a combination of points, lines and boxes(?). Without more legend and notes, currently the figures are very hard to interpret.

Response: We have added more information to each figure in the form of legends and footnotes in the revised manuscript.

2. Comment: A follow up question on the previous comment 5: page 9, line 27-29 summarizes the minimum number of patients for non-enriched design. However, Figure 4 only shows the results for adaptive enrichment design with different recruitment strategies. Then why was there a conclusion about minimum number of patients in non-enriched design without any simulation results shown?

Response: We have deleted the sentence in the Results section, lines 8 to 10, page 10, of the revised manuscript with changes highlighted.
3. Comment: Page 10, line 30, what is "scenario 6"?

Response: We have corrected “scenario 6” to “scenario 5” in the Results section, line 12, page 11, of the revised manuscript with changes highlighted.

[2] Response to the comments by Reviewer 2

1. Comment: The authors have addressed in the revised manuscript most of the concerns and suggestions indicated in the original review, but the central one persists: if adaptive enrichment designs are already implemented in practice without halting recruitment (to wait for enough data to be available for the enrichment decision), what is the practical issue the paper is trying to address? Perhaps the goal is just exploring the impact of halting vs. not-halting recruitment in an adaptive enrichment design, but that's more of academic interest than of practical impact.

Response: Based on your comment, we have deleted the expression “proposed recruitment methods” throughout the revised manuscript because this expression will be inappropriate if adaptive enrichment designs are already implemented in practice with continued recruitment. Instead, we now express this as “continued recruitment method” or “alternative (recruitment) method” throughout the revised manuscript (e.g., in the Methods section, lines 26 to 33, page 6, of the revised manuscript with changes highlighted). Hence, we have modified the goal of this study in the Background section, lines 8 to 9, page 4, of the revised manuscript with changes highlighted.

[3] Other revisions:

We have re-edited the manuscript using an English proofreading service again; these have been corrected throughout the revised manuscript.