Author’s response to reviews

Title: When to keep it simple – adaptive designs are not always useful

Authors:

James Wason (james.wason@mrc-bsu.cam.ac.uk)

Peter Brocklehurst (P.Brocklehurst@bham.ac.uk)

Christina Yap (C.Yap@bham.ac.uk)

Version: 1 Date: 08 Apr 2019

Author’s response to reviews:

We thank the editorial board member for reviewing our paper and providing useful suggestions that have helped improve it. Our specific response to each comments is below:

1.) "I believe that the paper would be improved if additional “real life” examples were included."

Agreed, we have now added several other trials that provide useful additional illustration to our points.

2.) "Some additional simulations that provide comparisons under a range of scenarios expected to cover REALISTIC situations would also be helpful to readers. The simulations would ideally be modeled after some real trials that the authors had encountered and should demonstrate advantages and disadvantages in a range of situations expected to be favorable or unfavorable to use of adaptive designs. Performance should be assessed not only in terms of expected total sample size but also in terms of BOTH proportion and absolute number of patients who end up on the inferior arm of the trial."

We have added a simulation based on the TAILoR trial, which is a MAMS study where information on the delay and planned recruitment rate is given. We have conducted simulations exploring the effect of delay on the expected sample size and the proportion of patients who are allocated to a truly effective arm. We noted the comment about ‘absolute and relative number given the inferior arm’ but believe that all the required information on these is given by the two new plots. We are happy to add more if requested.
3.) "The submission might emphasize more the logistical issues of delay in obtaining endpoint and unreliability of endpoint."

This is a good point, and we have expanded the logistical section to address this.