Reviewer's report

Title: Comparison of Bayesian and frequentist group-sequential clinical trial designs

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Reviewer: Tu Xu

Reviewer's report:

The authors compared the GSD with Bayesian and frequentist test statistics. In general, the manuscript is well written and easy to follow. Authors' argument looks fair to me. However, I have some questions for the authors to sharing more insights.

1. In the section of Bayesian group-sequential approach, the authors mentioned that $p_1,...,p_K$ can be calculated based on the joint distribution in Equation (1). Equation (1) describes the variance-covariance structure of observed outcomes at interim analysis. As the decision criteria depends on the prior information as well in the Bayesian setting, it is clear to me how the variance-covariance structure can be easily specified.

2. As mentioned by the authors, GSD is one type of adaptive design. Beyond the typical GSD, there is also other types of adaptive design, such as sample size re-estimation approach. Specifically, for sample size re-estimation, in order to avoid the type I error inflation, the CHW method was commonly used. With the Bayesian test statistic, is there a similar approach to handle the sample size re-estimation with type I error controlled?

3. The authors did a fair comparison between the Bayesian method and frequentist approaches with GSD. Especially, their equivalence is shown when the non-informative prior is utilized, which sounds reasonable to me. However, my question would be on the use of informative prior, which is often considered as an advantage of Bayesian method. However, my concern is that with informative prior, the outcome of early interim analyses may be driven by the prior information and thus may not be interpretable? I ask the authors to provide share more thoughts on the selection of prior distribution. Also I hope to learn about authors' opinion on using Bayesian hierarchical model for the GSD.

4. The discussion in the manuscript focuses on the single endpoint scenario. In late phase confirmatory clinical trials, it is common that type I error control on multiple endpoints (i.e. FWER) is required. For Bayesian approach, I think different prior distributions applied for multiple endpoints could further complicate the control of type I error. I suggest authors to at least include additional discussion on scenarios with multiple endpoints.

Corrections:

1. Page 14, line 8, "that" should be "than".
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Unable to assess

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