Author's response to reviews

Title: Determinants of patient recruitment in a multicenter clinical trials group: trends, seasonality and the effect of large studies

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Version: 3 Date: 8 Jun 2001

PDF covering letter
June 7, 2001

The Editor,
BioMedCentral

Re: Determinants of patient recruitment in a multicenter clinical trials group: trends, seasonality and the effect of large studies

Dear Editor:

We were pleased to see that BMC Medical Research Methodology is interested in publishing our work. We are grateful to the reviewer for the constructive comments. Some amendments have been made and we have the following replies for each comment:

Reviewer: Dr. Scott Halpern

We thank the reviewer for the kind appreciation of our work.

Major comments

1. The reason we did not provide separate analyses for the randomized and non-randomized studies is that non-randomized trials included here are still clinical trials. They are not traditional epidemiological studies. Also our aim was to investigate the overall enrollment of a multicenter clinical trialist group in all clinical trials examined together.

2. We have performed analyses involving the ratio of patients recruited over the number of active studies in each quarter as the outcome measure. While the models are qualitatively similar to those we obtain with crude quarterly recruitment, the significance of the coefficients and the model fit are not as good using the suggested metric. We suspect that the problem with the proposed metric there is a difference when a trial is in its early rapid enrollment phase or is simply still being open, but with declining enrollment. Nevertheless, as suggested, we have modified the alluded sentence to “Although the acceleration over time was significantly related to an increasing number of studies (particularly substudies) being launched over time, the dynamics of the acceleration of enrollment were more complex.”

3. As suggested, we have estimated, in addition to the absolute difference between predicted and observed, also the relative magnitude of the discrepancy between these two figures (percentage above or below the observed enrollment). The Methods now state that “both the absolute and proportional” differences were calculated. These figures are provided next to the absolute numbers in the end of the Results: “When all studies were considered, the prediction missed the actual observed accrual by over 30% in 5 quarters and the average relative deviation from the observed accrual was
24.7%. At the largest deviation, the predicted deviation was double than the observed accrual. Excluding substudies, the prediction also missed the actual observed accrual by over 30% in 5 quarters and the average relative deviation from the observed accrual was 20.8%. At the largest deviation, the predicted accrual was 69% larger than the observed accrual.”

**Minor comments**

1. As suggested, we have corrected: “there are anecdotal beliefs…”
2. As suggested, we have added in Methods and Materials under Databases: “The analyses excluding substudies may be more robust, because by definition substudies typically included only subsets of the same patients as the main studies”.
3. Adequate and satisfactory forecasting ability may be subjectively interpreted. We prefer to provide the exact numerical data, instead of setting an arbitrary definition. However, to account for this interesting comment, we acknowledge the following in a new 4th paragraph of the Discussion: “Although we deem that the overall predictive performance of the developed models was satisfactory, of course we should acknowledge that the adequacy of the forecasting ability depends also on a subjective interpretation of the results. Under different settings, it may be necessary to achieve even tighter predictions for the performance of a model to be satisfactory for operational use by a multicenter clinical trials group.”

We thank you again for the quality of the peer-review process. We hope that our revised manuscript would now be acceptable for publication at BMC Medical Research Methodology in its current form.

Sincerely,

Anna-Bettina Haidich, MSc

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