

Dear eLife editor,

With pleasure I submit the fruits of our project on estimating data manipulation in the DECREASE clinical trials on beta-blockade and the effect on patient mortality rates in the perioperative period. We address this piece towards both more statistically oriented researchers (estimating the extent of data manipulation) and practitioners (expanding on the problematic aspects we discovered in this project with respect to this type of beta-blockade research).

The last six years in the medical field, with respect to the use of beta-blockade, has been disturbed by the Poldermans case of scientific misconduct. As a result, the question of whether beta-blockade decreases or increases mortality in non-cardiac surgeries has become quite unclear. The original studies are not retracted, despite the findings of scientific misconduct. A meta-analysis that disentangles problematic and non-problematic trials shows beta-blockade increases mortality. Scientific misconduct here could have a very real effect and can harm humans all around the world, which concerns us as scientists and human beings.

Some insightful discussion has already taken place in the literature with respect to type of beta blockade, but the extent of the problems in the DECREASE trials has not been further investigated. Moreover, we found out there are some missing aspects to the debate, namely that the DECREASE trials appear to maintain a wholly different paradigm with respect to beta-blockade in light of non-cardiac surgeries. Our investigation taught us much about this field and we hope this report contributes to progress in this area by highlighting from various disciplines how the problems with state of what we think we know about the effectiveness of beta-blockade. Our insights were the consequence of combining reflections from various fields: statistics, pharmacology, and anaesthesiology.

Our report is primarily aimed at estimating the extent of manipulation based on summary statistics (which our model shows is present for one of the DECREASE trials). Previously, the scientific integrity reports said statistical evaluation of these trials was not feasible, because those investigations looked at separate trials in isolation. We took a different approach, aimed at comparing trials that supposedly investigate the same effect. By doing this, we extended their original investigation and according to our model, data manipulation did occur but the degree could vary.

We have not been able to achieve any new insights with respect to the effectiveness of beta-blockade itself, because we use already existing data. However, we feel that the variation between the non-DECREASE trials is substantial and provides attention points for new trials moving into the future.

We eagerly await your response to our submission, and hope you see the value of it regardless of your decision for the eLife journal.

Yours sincerely,
Chris Hartgerink