Author's response to reviews

Title: Trial design: Computer guided normal-low versus normal-high potassium control in critically ill patients: Rationale of the GRIP-COMPASS study.

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Author's response to reviews: see over
Dear Dr Aldcroft,

We appreciate the opportunity to submit our revised paper on the study design of the GRIP-COMPASS trial to BMC Anesthesiology. In this study we compare two normal-range potassium targets levels in 1200 critical ill patients using a computerized decision support system. We wish to address the reviewer’s comments on a point-by-point basis. Furthermore a number of requested changes and a number of minor corrections in the text were made, all highlighted with color in the revised manuscript.

The reviewer notes that it is highly interesting to compare the effects of "low normal" to "high normal" potassium levels, but the reviewer doubts the usefulness of publishing the trial design in its current form. He also recommends that the protocol should be posted on ClinicalTrials.gov.

With regard to the latter remark, the trial was already posted on ClinicalTrials.gov (NCT01085071), but this website is focused only the key features of the study design with little room for the rationale and computer-technology behind it. In our experience, publishing a separate paper devoted to rationale and trial design allows a more focused and coherent manuscript, especially when unusual trial elements are involved and need justification.

In the case of GRIP-COMPASS there are several arguments that we think justify a separate paper:

- Potassium targets have never been compared (in sharp contrast to glucose for example).
- A prospective study that compares two therapies with targets that are both considered "normal" is highly unusual.
- The central role of a computer algorithm that is executing potassium regulation for both trial arms.
- The methodological and ethical consequences of such a study.
- ClinicalTrials.gov does not allow elaboration on the rationale behind a particular trial design.
- Since more prospective trials that compare computer guided strategies will surely follow, the current paper may have relevance beyond potassium control.

In summary, we feel that in the case of the GRIP-COMPASS trial it is justified to write a separate paper that highlights and explains its unique rationale and consequent design.
We hope that the manuscript in its revised form will now be considered suitable for publication in *BMC Anesthesiology*.

Yours Sincerely,
On behalf of all co-authors,

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