Author's response to reviews

Title: Safety and Effectiveness of a Patient Blood Management (PBM) Program in Surgical Patients - The study design for a multi-center prospective epidemiologic non-inferiority trial

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Author's response to reviews: see over
Dear Ladies and Gentlemen of the Editorial Board of *BMC Health Services Research*,

thank you very much for the opportunity to revise our manuscript “Safety and Effectiveness of a Patient Blood Management (PBM) Program in Surgical Patients - The study design for a multi-center prospective epidemiologic non-inferiority trial” (MS: 9020630121239504). We have undertaken extensive redrafting. Please find below our point-by-point reply to the comments:

**Referee 1:**

*This is a concise description of a highly interesting and important study.*

**Major comments**

> Hb intervention thresholds: Why were real low Hb intervention thresholds used (Hb<11 g/dL in men and Hb<10 g/dL in women)? The WHO clearly defines anemia in men as a Hb<13 g/dL and in women as a Hb<12 g/dL, and Musallam et al. have clearly shown in 2011 (Lancet 378: 1396) that already mild anemia is associated with increased mortality (+40%) and increases morbidity (+30%). This discrepancy needs to be discussed.

We have been realising this as well and changed the Hb thresholds for preoperative screening, diagnosis and treatment of anaemia to WHO-definition.

**Minor comments**

2. **Title page - Affiliations: Superscripts are a, b, e. Affiliations are a – k. This requires some fine-tuning.**

3. **References in the manuscript: Different formats were used within the text. Please unify.**

Thank you for these remarks – we corrected the affiliations and unified the formats.

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**Editorial Requests**

*We included the Email addresses of all co-authors on the title page and changed “Conflict of Interest to “Competing Interests. We changed “sources of support” to “Acknowledgments”.*

> **Statistics**

*Please include a power calculation in the 'Methods' section of the manuscript.*

We included a Sample size and Power calculation:

According to preliminary data, the composite endpoint has an approximate incidence of 10%. A difference of 0,5% is set as the non-inferiority margin as this can be seen as the natural standard deviation. The level of significance of non-inferiority is determined be $\alpha=2.5\%$. This is consistent with a two-sided 95 % confidence range of $1+\alpha=95\%$ for the difference in the composite endpoint. A power of $1+\beta=80\%$ is sought. As the number of patients treated in each of the four university hospitals vary, an exact sample size calculation is not possible to this date. However, we expect approximately 100.000 participating patients.

> **Reporting standards**

*Please indicate whether the study adhered to TREND guidelines.*

The study adheres to the TREND guidelines.

We would like to thank you in advance for the further consideration of this work regarding its suitability for publication!

Sincerely yours,

Dania Fischer