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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Dear Ladies and Gentlemen of the Editorial Board of *BMC Health Services Research*,

The World Health Organization (WHO) encourages all member states to implement patient blood management (PBM) programs employing multiple combined strategies to minimize unnecessary exposure to blood products as a new standard of care [1]. Early detection and appropriate treatment of anemia, multidisciplinary concepts designed to maintain hemoglobin concentration, to optimize hemostasis, and to minimize blood loss shall be thrived for in an effort to improve patient outcome [2]. Several public-based PBM initiatives are underway for instance in Australia to optimize red blood cell concentrates utilization [3]. However, none of these initiatives are designed to provide scientific data in terms of safety issues. Thus, a large study with robust and relevant clinical endpoints is required and we hereby submit our study design paper termed

**SAFETY AND EFFECTIVENESS OF A PATIENT BLOOD MANAGEMENT (PBM) PROGRAM IN SURGICAL PATIENTS**

The study design for a multi-centre prospective epidemiologic non-inferiority trial

This study is the first prospective multi-centre controlled trial to demonstrate that the implementation of a simple PBM program is safe. Using an epidemiologic non-inferiority trial design, approximately 100,000 patients undergoing surgical procedures will be included. A patient-focused and evidence-based PBM program will be implemented in the four German University Hospitals in Frankfurt, Kiel, Bonn and Münster. Different time slots for control, implementation and study phases according to a non-randomized stepped wedge trial design are allocated [4]: The control phase in Frankfurt already started in January 2013. The implementation phases will be carried out hospital-wise starting with the University Hospital Frankfurt in July 2013, followed by the University Hospital Bonn in October 2013, the University Hospital Kiel in January 2014, and the University Hospital Münster in April 2014 and will last three months. The intervention phase (PBM) will start after the implementation phase has been completed, respectively, and last until April 2015.

Primary efficacy endpoint is a composite outcome comprising in-hospital myocardial infarction, stroke, acute renal failure, death of any cause, pneumonia and sepsis until discharge from hospital in
patients before and after implementation of PBM program. The efficacy endpoints will be monitored by means of the hospital-information system Agfa ORBIS, where the relevant diagnoses are encoded based on the German Diagnosis Related Groups (G-DRG) system. All patient-related data will be analyzed electronically and pseudonymized. The follow-up will last until discharge from the hospital. Secondary endpoints are length of stay on the intensive care unit, total hospital stay, and quantitative utilization of allogeneic red blood cell units, platelet concentrates, other blood products (e.g. fresh frozen (therapeutic) plasma), coagulations factors, and cell saver systems during hospital stay.

In conclusion, this prospective, multi-centre trial intends to determine whether or not the implementation of a PBM program is safe and effective in about 100.000 hospitalized patients undergoing surgery.

The manuscript has been seen and approved by all authors, it is not under active consideration for publication, has not been accepted for publication, nor has it been published, in full or in part.

We would like to thank you in advance for the consideration of this work to be published in the section “Study Protocols”.

Sincerely yours,

Dania Fischer

References