Patient Blood Management is not about blood transfusion:
it is about patients' outcomes

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Patient Blood Management (PBM) is "the timely application of evidence-based medical and surgical concepts designed to maintain haemoglobin concentration, optimize haemostasis and minimize blood loss in an effort to improve patient outcome". The definition presented by the Society for the Advancement of Blood Management (SABM), as well as several other definitions of PBM, have moved away from placing the focus on reducing the use of blood components to the development of a multidisciplinary and multimodal strategy centred on patients' outcome. Reducing transfusions might be a means, but it is certainly not an end. Thus, PBM has moved from a product-centred approach to a patient-centred approach.

Based on a growing body of evidence published over the years, clinicians have learnt to use the therapeutic options presented in the three pillars of PBM: optimising haematopoiesis, minimising bleeding and blood loss, and harnessing and optimising physiological tolerance of anaemia while it is treated appropriately. This has resulted in a tailored approach toward the clinical use of blood components, a limited resource that should be reserved for those patients who really need them. Using this strategy, the harm associated with inappropriate transfusions is avoided. Several clinical societies and scientific associations have published guidelines on the performance and content of PBM bundles for different populations of patients, such as those published by NATA, the Network for the Advancement of patient blood management, haemostasis and thrombosis in paediatric cardiac surgery and obstetrics or by SABM.

It is in this evolving context that Mueller et al. recently reported on the results of the Frankfurt Consensus Conference on PBM. The authors presented the conference as a multidisciplinary and multinational event with "188 participants representing more than 10 clinical disciplines from 33 different countries and 5 continents". Furthermore, the extensive description of a strict methodology, opinion polls and voting among participants appear to imply that the "evidence-based" recommendations were constructed in an objective and neutral manner.

The conference produced ten clinical recommendations and twelve research statements relating to pre-operative anaemia, red blood cell transfusion thresholds and implementation of PBM programmes. Regarding pre-operative anaemia, the authors recommended the detection and management of pre-operative anaemia early enough prior to major elective surgery to maximise the clinical response to treatment. They also recommended the use of iron supplementation in adult patients with iron deficiency anaemia "to reduce rate of red blood cell transfusion". The panel made a weak recommendation not to use erythropoiesis-stimulating agents routinely, but to consider such agents in anaemic adults undergoing major orthopaedic surgery. The panel did not address the actual indications for the use of erythropoiesis-stimulating agents, namely anaemia of inflammation or chronic disease that is independent of the type of surgery to be performed. Recommendations 5 to 8 dealt with restrictive transfusion thresholds, proven non-inferior to liberal transfusion thresholds in a number of randomised controlled trials (RCT). Finally, the panel recommended implementation of PBM programmes to improve appropriate red blood cell utilisation and recommended computerised or electronic decision-support systems to improve appropriate red blood cell utilisation.

We can only agree with some of the recommendations put forward by the 2018 Frankfurt Consensus Conference, but we feel that a true consensus between blood bankers, clinicians well-versed in the management of patients undergoing major surgery at risk of bleeding and researchers in the field would have sent a stronger and more relevant message in favour of PBM. Unfortunately, in our opinion, this was not the case here, at least not entirely.

To cast light on the context, the blood transfusion network in Germany is producer-driven and located in donation centres, housed predominantly outside hospitals. In several other countries, blood transfusion
centres are hospital-based services and are in charge of supporting and monitoring the appropriateness of blood utilisation. The collection of blood and component production may or may not be hospital-based, depending on countries. We have sincere concerns that the organisers of the conference (i.e., blood establishments) might not be in the best position to publish recommendations for the use of their “products” free of conflicts of interest.

The way the organisation and content of the consensus recommendations have been presented raises doubts regarding the authors’ intentions to produce clinically relevant recommendations on PBM. The described methodology falls short on important aspects. Prior to the opening plenary session (convention methodology 1), the questions and topics were determined before the conference by a well-selected elite without transparency and without the greater involvement of clinicians. Although described correctly, decisions were made by panels of invited experts, chairs, and rapporteurs in closed sessions while excluding clinicians (convention methodology 2). Thus, the representatives of clinical associations and even some authors of the article were not allowed to vote on decisions. The so-called “consensus” was not one that involved the majority of physicians worldwide who are in charge of prescribing and performing blood transfusion, nor those who manage PBM programmes in their institutions.

It is our strong belief and opinion that true consensus requires a mutual agreement in aim, topic and methodology. Clinicians as well as haematologists and blood bankers who actually care for patients at the bedside are responsible for the safety and best quality of their patients’ treatment. Therefore, clinicians might be hesitant to accept PBM recommendations from those responsible for the production of blood components. Their responsibility is to provide clinicians with high-quality and safe products in a timely fashion, not to control their use.

Finally, while the number of RCT vs observational studies might be an important consideration for questions relating to treatment of pre-operative anaemia and red blood cell transfusion thresholds, this is not necessarily the case for questions on PBM implementation. When using the GRADE methodology, RCT are assessed as “high” quality studies while observational studies are considered as “low” quality studies. Accordingly, Mueller et al. rated the level of evidence regarding implementation of PBM programmes to improve appropriate RBC utilisation as “Conditional recommendation, low certainty in the evidence of effects”.

When it comes to the assessment of therapies or strategies, one should keep in mind that not all strategies can be assessed by a RCT. RCT apply to the comparison of therapeutic strategies or drugs using strict inclusion and exclusion criteria, leading to the inclusion of only a small “sanitised” proportion of patients. Due to the complexity of the inclusion and exclusion criteria, as well as the need for prospective recruitment, patients included in RCT are not always representative of the population clinicians are used to deal with in their daily practice. Taking the recent TRICS trial as an example, among the 45,667 patients who underwent cardiac surgery during the study period, 14,702 were considered eligible for inclusion, and only 5,243 were actually randomised to the restrictive vs liberal transfusion strategy. We all understand that patients included (11% of the patients who underwent cardiac surgery) are not truly representative of the cardiac surgical population. One could argue that the patients excluded could have benefited, maybe more, from a better transfusion strategy than the patients actually included in the study. On the other hand, large observational studies include a large proportion (if not all) of patients physicians are taking care of in their clinical practice and use sophisticated statistical methods to reflect the real clinical world better than RCT do. In 2000, Concato et al. compared observational studies and RCT, concluding that the results of well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment as compared with those in RCT on the same topic. They went on to say that “The popular belief that only randomized, controlled trials produce trustworthy results and that all observational studies are misleading does a disservice to patient care, clinical investigation, and the education of health care professionals”.

Considering that PBM is a clinical “bundle” promoting the implementation of a patient-centred and multimodal strategy, it does not lend itself to being studied in the same manner as a single therapy (such as transfusion) does. PBM is not amenable to randomisation because each patient is unique and therapeutic approaches will vary according to the clinical situation. Observational trials, including “before and after” studies, are the best option to obtain data on its effectiveness. Observational studies may not have been judged by Mueller et al. to be the most robust from a methodological standpoint (leading to a conditional, weak recommendation), but the number of patients included to this day and the benefits derived from observational studies on PBM are so compelling that they have convinced clinicians to implement PBM for the benefit of their patients.

In conclusion, PBM is not centred on transfusion of blood components, and certainly not on red blood cells only. PBM is centred on patients, more specifically on those who undergo major surgical or major medical procedures that put them at an increased risk of complications or mortality. PBM is not an offensive
PBM is about patient outcome against producers of blood components. PBM aims to improve the outcomes of patients at risk through the optimisation of the patient's condition before, during and after the procedure and, only when absolutely needed, the implementation of an effective blood transfusion strategy. A reduction in the transfusion of blood components may well be "collateral damage" for blood producers but they must endorse this with open arms in exchange for better outcomes for patients. As we all work together in the endless quest toward improving patients' health, change is inevitable, and if it affects industry, it is the responsibility of the industry to adjust itself to the change.

The Authors declare no conflicts of interest.

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