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Cornerstones of patient blood management in surgery

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SUMMARY

Pre-operative anaemia and perioperative red blood cell transfusion carry significant consequence when it comes to surgical outcomes. The establishment of patient-centred clinical pathways has been designed to harness and endorse good transfusion practice, termed the three pillars of patient blood management (PBM). These focus on the timely and appropriate management of anaemia, prevention of blood loss and restrictive transfusion where appropriate. This article reviews the current evidence and ongoing research in the field of PBM in surgery. Strategies to implement PBM have shown significant benefits in appropriate transfusion practice, reduced costs and improved length of hospital stay. Recently published national quality standards have recognised the features of the PBM blueprint such as the consideration of alternatives to red blood cell transfusion, the active measures to reduce perioperative blood loss and the appropriate management of post-operative anaemia. Adopting PBM in surgical patients should be paramount to reduce the risks posed by perioperative anaemia and blood transfusions. The principles of PBM help structure the interventions and decisions relating to anaemia and blood transfusion, but, more importantly, represent a paradigm shift towards a more considered approach to blood transfusion, acknowledging its risks, preventatives and alternatives.

Key words: bleeding, iron deficiency, patient blood management, preoperative anaemia, surgery.

WHY IS PRE-OPERATIVE ANAEMIA A PROBLEM?

Pre-operative anaemia carries significant consequence when it comes to surgical outcomes. In the hospital setting, one-third of elective surgical patients are admitted with co-existing anaemia, which alone is an established risk factor for a number of adverse outcomes. Although anaemia increases the need for red blood cell (RBC) transfusion, anaemia is associated with increased morbidity and mortality correlating with the degree of anaemia.

In the last few years, there has been a stepwise increment in the quantity of publications, revealing high-quality evidence of the independent association with worse outcomes in patients who have pre-operative anaemia across most surgical specialties, such as orthopaedics, upper/lower GI, hepatobiliary and gynaecology (Carson *et al.,* 1996; Musallam *et al.,* 2011; Jans *et al.,* 2013; Baron *et al.,* 2014; Fowler *et al.,* 2015). The prevalence of pre-operative anaemia in the surgical population, when both genders are involved, is approximately 30% (Munoz *et al.,* 2015). In a secondary analysis of 39 309 patients undergoing non-cardiac surgery in the European Surgical Outcomes Study (EuSOS), multivariable analysis revealed that patients with severe or moderate anaemia had a higher in-hospital mortality than those with normal pre-operative haemoglobin concentration: OR 2·28 (95% CI 2·06 to 3·85) and OR 1·99 (95% CI 1·67 to 2·37), respectively (Ferraris *et al.,* 2012).

Pre-operative anaemia is the strongest indicator for perioperative blood transfusion. The emphasis placed on recognising at-risk patients and managing accordingly is supported by the association of anaesthetists of the UK and Ireland (AAGBI, 2016), NHS Blood and Transplant (NHSBT, 2013), British Society of Haematology (BSH; Kotzé *et al.,* 2015) and National Institute for Health and Care Excellence (NICE Guideline 24; NICE, 2015). However, the current standard of care for anaemic patients during surgical admission is the management by a RBC transfusion.

The establishment of patient-centred clinical pathways has been designed to harness and endorse good transfusion practice, termed the three pillars of patient blood management (PBM). These focus on the timely and appropriate management of anaemia, prevention of blood loss and restrictive transfusion where appropriate. In the surgical setting, these three pillars of PBM align with pre-operative, operative and post-operative care. Several centres globally, including those in Australia, Europe and the United States, have championed the PBM initiative, albeit with expected apprehension among clinicians. This is due to the overriding issues of hospital culture challenging new strategies and the reluctance to implement PBM bundles due to the limited amount of evidence on whether these interventions do have a positive impact on patient outcomes. This review focuses on

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the current evidence for the practical implementation and safety of the three pillars of PBM in surgery and ongoing research in this field.

PATIENT BLOOD MANAGEMENT IN SURGERY

Patient blood management is a globally recognised and WHO-endorsed concept (WHA63.12) that aims to manage the issues of pre-operative anaemia and blood transfusion by addressing the quality and safety of transfusion practice. Strategies to implement PBM have shown significant benefits in appropriate transfusion practice, reduced costs and improved length of hospital stay (Moskowitz *et al.,* 2010; Goodnough *et al.,* 2014; Theusinger *et al.,* 2014; Gross *et al.,* 2015; Meybohm *et al.,* 2016b). This was best highlighted in the summary report from the Western Australian PBM initiative; a six-year educational jurisdiction-wide programme of PBM introduction was associated with a reduction in pre-operative anaemia rates, reduced blood transfusion and overall utilisation of blood products with associated reduction in length of hospital stay and improved patient outcomes (Leahy *et al.,* 2017).

PBM guidelines and standards have developed from Australian leading professional associations. They provide the detailed evidence-based information and recommendations on PBM in Australia, in the United States, and in several European nations (Kozek-Langenecker *et al.,* 2013b; Society for the Advancement of Blood Management (SABM), 2014; Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee, 2014; American Society of Anesthesiologists, 2015; Hunt *et al.,* 2015; Klein *et al.,* 2016). A recent paper by Meybohm and his colleagues provided comprehensive bundles of PBM components encompassing more than 100 different PBM measures to facilitate a stepwise implementation process of the most feasible measures (Meybohm *et al.,* 2017). Practical recommendations targeting elective surgery are summarised in Table 1 and will be described further in this review.

Recently published NICE quality standards for blood transfusion have also incorporated many features of the PBM blueprint including the consideration of alternatives to red blood cell transfusion, the active measures to reduce perioperative blood loss and the appropriate management of post-operative anaemia (Table 2) (NICE, 2016).

PILLAR 1 – MANAGING PRE-OPERATIVE ANAEMIA IN SURGICAL PATIENTS

Despite the multiple guidelines and opinion documents on the management of pre-operative anaemia or mandates such as those developed by NICE, few provide pragmatic guidance or strong evidence-based platforms for the underlying determinant of anaemia in surgical patients.

The cause of anaemia in pre-operative patients can often be complex and multifactorial. Nutritional deficiencies (e.g. iron, vitamin B_{12} and folate) and chronic inflammatory states are the major contributors. The issue for the diagnosis of iron deficiency anaemia (IDA) is inconsistency in the awareness and evidence surrounding the mechanisms of ID in surgical patients. Additionally, there remains the absence of clear pathways and clinics in place to assist in the diagnosis and treatment of IDA.

It is recommended that in elective surgical patients undergoing a major surgical procedure, with an expected blood loss of >500 mL or a high probability of a RBC transfusion requirement, they have a full blood count (FBC), which is reviewed, at least two weeks prior to surgery (Muñoz *et al.,* 2017). If the patients are found to have unexpected pre-operative anaemia or suboptimal haemoglobin (Hb), surgery should be delayed in the elective surgical setting (characteristically for arthroplasty surgery) until satisfactory review and management are completed (Goodnough *et al.,* 2011). Additionally, screening for common nutritional deficiencies, such as ferritin, vitamin B_{12} and folate, should be a standard practice, in order to direct care and achieve patient optimisation appropriately. Several diagnostic algorithms have been published with regard to this (Goodnough & Schrier, 2014; Muñoz *et al.,* 2017). Unfortunately, these recommendations have faced many hurdles, often revealing the disengagement between primary and tertiary health care. In addition, several centres have emphasised the need to fast-track patients and provide the same-day admission, contradicting the principles of PBM of pre-operative patient optimisation. Surgical trials focusing on this aspect of PBM are ongoing with the aim to provide more evidence surrounding the effectiveness of the management of pre-operative anaemia (Richards *et al.,* 2015; Spahn, 2016; Bemelman, 2016).

TREATMENT STRATEGIES FOR IRON DEFICIENCY ANAEMIA

The proposed treatment of pre-operative IDA in surgical patients with IV iron has been of particular focus over the past few years as an approach to managing what we now recognise as an often complex, multifactorial condition.

The British Society of Gastroenterology and NICE guidelines for the management of pre-operative IDA state that all patients should have iron supplementation to correct anaemia and replenish body stores, and the option of parenteral iron should be considered when oral preparations are not tolerated or ineffective (NICE, 2015; Ponikowski *et al.,* 2015). Although this may be effective in raising the [Hb] in this setting, there remains a significant paucity in the evidence as to whether using intravenous iron in the pre-operative setting has any patient benefits and equipoise remains.

Oral iron remains the first-line, low-cost recommendation for IDA. The total body stores of iron are 3000–4000 mg in healthy individuals with a normal turnover/loss of 2 mg per day. A systematic review has demonstrated that oral iron may reduce the proportion of patients requiring blood transfusion (Goddard *et al.,* 2011). However, enteral iron is absorbed at a rate of 2–16 mg per day, and 3–6 months of treatment is required to provide 1000–2000 mg to replenish the physiological

Table 1. Implementing PBM in elective surgery

Pillar 1. Management of anaemia

Pre-operative	Intra-operative	Post-operative
• Diagnosis of anaemia (ideally two weeks prior to planned surgery).	• Optimising cardiovascular and pulmonary tolerance.	• Manage post-operative anaemia (whether developed as a consequence of surgery or pre-existing).

• Identification of the underlying cause of anaemia: perform full blood count (FBC).
  • Performed by GP as a part of referral process or initial surgical outpatients.
  • Educate surgical/perioperative teams which procedures are most likely to require anaemia screening, e.g. *major* open abdominal surgery.
• Diagnosis of IDA and vitamin B_{12}/folate deficiency.
• Extended diagnosis of anaemia, e.g. further referral to gastroenterology, endoscopy and haematology.
• Treatment of anaemia.
  • IV iron, vitamin B_{12}/folate and EPO.
	• Haemodynamic monitoring in high-risk procedures/patients.	• IV iron/EPO.
		• Avoidance of unnecessary 'top-up' transfusions.

Pillar 2. Managing perioperative bleeding

Pre-operative	Intra-operative	Post-operative
• Identifying at-risk patients (surgical outpatients/pre-operative assessment).	• Ensuring physiological management and optimal conditions for haemostasis (e.g. normothermia, pH >7·2).	• Monitor and manage ongoing bleeding, e.g. cell salvage.
• Including full medical and pharmaceutical review.	• Point-of-care testing (e.g. viscoelastic testing).	• Maintain physiological conditions.
	• Cell salvage.	• Minimise unnecessary phlebotomy.
	• Surgical technique.	• Haemostasis/anticoagulation management.

Pillar 3. Managing post-operative anaemia

Pre-operative	Intra-operative	Post-operative
• Patient-focused care – identifying and optimising patient's physiological reserve.	• Cell salvage.	• Evidence-based transfusion thresholds. • Manage IDA with IV iron.

reserve of iron as the bioavailability of ferrous iron is only 10–15%. This is further reduced by poor absorption resulting from the down-regulation of duodenal absorption by inflammation, infection and chronic disease. A reduced uptake is one of the main reasons why oral iron may often fail to ameliorate anaemia in the surgical cohort. Furthermore, compliance can also be poor owing to the common side effects associated with oral iron salts, including abdominal pain, diarrhoea and constipation. A meta-analysis has shown that oral iron salts have an OR of 2·32 (95% CI 1·74 to 3·08; $P < 0{\cdot}001$) compared to placebo for gastrointestinal side effects (Clevenger *et al.,* 2016).

Intravenous iron has been demonstrated as an alternative treatment for correcting IDA in surgical patients. Several intravenous iron preparations, including iron polymaltose, ferumoxytol, ferric carboxymaltose, iron sucrose and iron isomaltoside, are available (Tolkien *et al.,* 2015). Historically, parenteral iron preparations were associated with high rates of adverse effects including anaphylaxis, but these reactions were related to historical dextran-containing preparations. Modern carbohydrate preparations have a significantly improved safety profile with an overall anaphylaxis rate comparable to that of IV penicillin (Wang *et al.,* 2015), about 3–10 per 100 000. Overall, the severe adverse event rate of modern IV iron is about 3–4 times less than that of a unit of blood. There is good evidence for their safety and efficacy in a range of conditions, including the perioperative setting (Auerbach *et al.,* 2013).

A systematic review of patients with anaemia undergoing surgery (including orthopaedics, colorectal, gynaecology, spinal, cardiac, upper GI and head and neck) demonstrated an increase in the haemoglobin concentration and reduced

Table 2. NICE quality standards (NICE, 2016)

Standards	
Statement 1	People with iron deficiency anaemia who are undergoing surgery are offered iron supplementation before and after surgery.
Statement 2	Adults who are undergoing surgery and expected to have moderate blood loss are offered tranexamic acid.
Statement 3	People are clinically reassessed and have their haemoglobin levels checked after each unit of red blood cells they receive, unless they are bleeding or are on a chronic transfusion programme.
Statement 4	People who may need or who have had a transfusion are given verbal and written information about blood transfusion.

risk of RBC transfusion [relative risk (RR) 0·74; 95% CI 0·62 to 0·88] with intravenous iron, especially when used with erythropoiesis-stimulating agents (ESAs) or in patients with lower ferritin concentration, without significant difference in mortality or severe adverse events (Lin *et al.*, 2013).

Two recent surgical trials involving the use of IV iron to treat pre-operative anaemia in patients undergoing colorectal and unspecified abdominal surgeries have shown conflicting responses in terms of transfusion outcomes (Froessler *et al.,* 2016; Keeler *et al.,* 2017). A trial by Froessler and his colleagues shows a significant reduction in RBC transfusion use by 60% in patients treated with IV iron pre-operatively (Froessler *et al.,* 2016). No difference was observed in secondary outcomes in terms of morbidity, mortality and quality of life, which is likely due to small sample size. A study by Keeler *et al.* showed that IV iron that is more effective in increasing Hb compared to oral iron made no difference in terms of RBC transfusion use for colorectal surgery patients (Keeler *et al.,* 2017). Both trials, small in population, have only identified primary outcomes in terms of RBC transfusion use, indicating the need for the continuation of larger ongoing trials and development of new studies investigating more insightful primary patient outcomes with a focus on functional performance and quality of life (Richards *et al.,* 2015; Spahn, 2016; Bemelman, 2016).

PILLAR 2 – MANAGEMENT OF INTRA-OPERATIVE BLEEDING

Risk stratification of the surgical patient is important. Bleeding history must be included as a part of the pre-operative assessment, including a medication review, focusing on the use of anticoagulants. Intra-operative bleeding may be impacted by surgical techniques, anaesthetic blood loss reduction strategies, such as point-of-care testing and cell salvage, and pharmacological management.

In current practices, the key factor is the increasing number of patients continued on anticoagulants and antiplatelets well into the perioperative period. Annually, approximately 10% of patients on any long-term oral anticoagulation will undergo surgery or other invasive procedures (Douketis *et al.,* 2012). Anticoagulants are commonly prescribed agents for the prevention and treatment of a number of cardiovascular conditions. The BRIDGE study showed that patients on warfarin undergoing elective invasive procedure, foregoing bridging anticoagulation, exhibited no difference in terms of reducing arterial thromboembolism and demonstrated reduced bleeding risk (Douketis *et al.,* 2015).

POINT-OF-CARE TESTING

The guided management of coagulopathy through the use of point-of-care testing has shown to be a valuable tool. Unlike the conventional means of coagulation analysis, which is prolonged and often inaccurate, the development of viscoelastic testing (this allows changes in the blood clot tensile strength to be measured over time) now provides real-time and rapid analysis of the dynamics of clot formation. In recent years, an increase in the worldwide use of viscoelastic testing such as thromboelastography (TEG®, Haemonetics, Braintree, MA, USA) and rotational thromboelastography (ROTEM®, Tem International, Basel, Switzerland), which give a rapid description of the cell-based model of coagulation together with both cellular and humeral contributions to coagulation. The administration of fresh frozen plasma, platelets, cryoprecipitate, factor concentrates and antifibrinolytic drugs can be guided by specific patterns of viscoelastic testing measurements. Currently, NICE guidelines only recommend the use of viscoelastic testing in cardiac surgery (NICE, 2014). However, a recent meta-analysis despite showing the potential to reduce the requirement of blood products and mortality demonstrates that the trials of evidence these guidelines are based on are low quality, low power and high bias (Wikkelsø *et al.,* 2017). Trials for guided therapy in specialty areas such as trauma and obstetrics are ongoing.

CELL SALVAGE

If anticipated blood loss is greater than 500 mL, the use of intra-operative cell salvage is recommended (Klein *et al.,* 2016). It is a commonly used technique in cardiac surgery but less so in other areas, for no good reason. Cell salvage is carried out with the use of a double-lumen suction device to collect blood. Blood is stored within a reservoir with added anticoagulants. Once the enough blood is collected, RBCs are washed, filtered, suspended in saline and re-infused back into the patient. As recommended by NICE, the efficacy of cell salvage is improved with the use of antifibrinolytic drugs and tranexamic acid (TXA) (NICE, 2015). A Cochrane review found that the use of cell salvage reduced the rate of allogeneic RBC transfusion by 38% (RR 0·62; 95% CI 0·55 to 0·70), leading to an average saving of 0·68 unit of RBCs per patient (weighted mean difference −0·68; 95% CI −0·88 to

−0·49) (Carless *et al.,* 2010). In disciplines such as orthopaedic surgery, the risk reduction was 55%.

Concerns have been raised surrounding the issues of retransfused blood and the potential harmful reintroduction of substances aspirated from the surgical field, including bacteria and malignant cells. Studies have shown that despite the aspiration of microbiologically contaminated blood, no increase in positive cultures or post-operative infection is observed, even though the washing phase is unable to eliminate all bacteria (Bowley *et al.,* 2006; Feltracco *et al.,* 2007). Furthermore, a recent systematic review emphasising the use of leucocyte depletion filters to eliminate tumour cells should be used and demonstrated no association with an increased risk of tumour dissemination or metastases (Kumar *et al.,* 2014). Guidelines by the European Society of Anaesthesiology suggest that the decision to use salvaged blood potentially contaminated with bacteria or malignant cells should be made on an individual basis (Kozek-Langenecker *et al.,* 2013b). Reviews have demonstrated that cell salvage does not increase outcomes in terms of mortality, reoperation for bleeding, infection, wound complication, non-fatal myocardial infarction, thrombosis, stroke and length of hospital stay. (Carless *et al.,* 2010; Meybohm *et al.,* 2016b). Up-to-date meta-analyses on randomised controlled trials focusing on washed cell salvage in all surgical groups demonstrated a reduced rate of infection (Meybohm *et al.,* 2016a).

ANTIFIBRINOLYTICS

Perioperative bleeding is a major indicator for RBC transfusions (Levy *et al.,* 2006). To reduce blood loss, a number of pharmacological agents, including antifibrinolytic agents, TXA and ε-aminocaproic acid (EACA), are used. These are synthetic lysine analogues that act to inhibit fibrinolysis by their action at the active sites on plasminogen, inhibiting the activation of plasmin. Tranexamic acid should be used prophylactically in major surgery where perioperative blood loss is predicted to be high and has been shown to significantly reduce perioperative blood loss.

A significant reduction in the risk of death from haemorrhage with the early use of TXA in the trauma setting has been demonstrated. The clinical randomisation of an antifibrinolytic agent in significant haemorrhage (CRASH-2 trial) highlighted the benefit of early therapy with TXA (1 g followed by a 1-g infusion over 8 h), significantly reducing the risk of death from haemorrhage and all-cause mortality in traumatic bleeding (Collaborators CT, 2010). This evidence has been extrapolated in other major intra-operative scenarios with the possibility of blood loss. The recent ATACAS trial demonstrated that in cardiac surgery patients receiving TXA, there was a significantly lower risk of bleeding complications and transfusion requirements and also reduction in reoperation compared to placebo (Myles *et al.,* 2017). No difference was observed in composite primary outcomes of mortality and thrombotic event within 30 days of index surgery between TXA and placebo (RR 0·92; 95% CI 0·81 to 1·05).

Aprotinin is a potent, nonspecific serine protease inhibitor, derived from bovine lung, with antifibrinolytic properties to directly inhibit plasmin. It was used in cardiac procedures until it was withdrawn from the clinical use after the blood conservation using antifibrinolytics. BART randomised trial showed an increase risk of death with its use (Fergusson *et al.,* 2008). The results of that trial have been disputed, and subsequently, aprotinin has been relicensed for use in myocardial revascularisation surgery (McMullan & Alston, 2013). In terms of efficacy, a Cochrane systematic review by Henry and his colleagues concluded that the use of antifibrinolytics significantly reduced the requirement of perioperative RBC transfusion by 32%, which is similar for both aprotinin and TXA (Henry *et al.,* 2011).

PILLAR 3 – POST-OPERATIVE PERIOD

Continued effort to reduce blood loss should be ongoing during the post-operative period. Simple interventions to decrease iatrogenic blood loss reduce the incidence of anaemia. Reducing the frequency and volume of phlebotomy, particularly in critical care, can have a significant impact. Additional strategies include a reduction in the sample volume with the use of paediatric blood tubes, using continuous sampling lines with small dead space volumes (for arterial line samples) and evaluation of the requirement for each blood test according to the clinical needs (Raad *et al.,* 2016). Blood loss into drains is another area of interest. In orthopaedic surgery, the use of drain has been shown to increase blood transfusion requirements (Parker *et al.,* 2004). In keeping with many enhanced recovery programmes, the use of post-operative surgical drain is decreasing. Cell salvage can also be used after operation, with retransfusion of blood from drains, particularly in major orthopaedic surgery (Ashworth & Klein, 2010).

The surgical stress response, inflammation and infection may lead to functional iron deficiency, in a manner similar to that of chronic disease. This may contribute to the development of or further worsen a pre-existing IDA. This may impede recovery and rehabilitation and lead to further post-operative complications including readmission or re-operation. It is unclear whether the implementation of restrictive transfusion practices may have a significant impact on optimal patient outcomes. Limited research has focused on the area of post-operative care and the role of IV iron. Recent randomised controlled trials involving, in general, elective and orthopaedic surgery (Khalafallah *et al.,* 2016) and post-gastrectomy (Kim *et al.,* 2017) show that patients receiving IV iron post-operatively had a significant increase in Hb values four and twelve weeks after index surgery. Khalafallah and his colleagues also showed a significant reduction in the blood transfusion requirements in patients administered IV iron compared to a standard care (incidence rate ratio 0·10; 95% CI 0·01 – 0·85). This is in contrast to an earlier smaller study comparing IV iron vs. oral iron in orthopaedic surgery patients, showing no difference in blood transfusion requirements (Bisbe *et al.,* 2014). These studies exhibit significant heterogeneity, warranting further larger studies in this field.

EFFICACY AND SAFETY OF IMPLEMENTING PBM IN SURGERY

Red blood cell transfusion is a reliable and life-saving intervention that is effective in replacing blood loss, but in the non-bleeding patient, although it may 'top-up' haemoglobin (Hb) levels, it does not address the underlying cause of anaemia. Increasing evidence accumulated over the past few years shows that transfusion is independently associated with increased morbidity, mortality, quality of life and length of hospital stay across various surgical populations (Hofmann *et al.,* 2012; Kotzé *et al.,* 2012; Keeler *et al.,* 2016; Papageorge *et al.,* 2017). There are concerns surrounding the increased risk of transfusion-associated circulatory overload (TACO), as well as sepsis, and cancer recurrence in oncology patients. The implementation of PBM has highlighted the best practice to restrict the use of red blood cell transfusion and ensure that every blood transfusion is appropriate.

Timely identification and appropriate management of pre-operative anaemia as indicated in PBM mandates have been shown to reduce the need for perioperative blood transfusions, even with modest rises in Hb levels (Papageorge *et al.,* 2017). In a systematic review of above 20 000 patients with colorectal cancer, Acheson and his colleagues found that 58·8% of patients received blood transfusions (Acheson *et al.*, 2012). Blood transfusion was associated with an increased all-cause mortality (OR 1·72; 95% CI 1·55 to 1·91; $P < 0{\cdot}001$) and an increased OR of cancer-related mortality, combined recurrence–metastasis–death, post-operative infection and surgical re-intervention, with a mean duration of observation of 62·8 [standard deviation (SD) 28·8] months in the analysed studies (Acheson *et al.*, 2016).

A recent Cochrane review on the impact of liberal transfusion strategies (typical transfusion trigger Hb 90–100 g L^{-1}) with more restrictive strategies (typically transfusion trigger 70–80 g L^{-1}) demonstrated that of the 31 trials involving 12 587 participants, no evidence of difference in patient outcomes was observed (Carson *et al.,* 2016). Many trials exploring the effectiveness and safety of restrictive transfusion practices often rely on the Hb value, regardless of whether there is active bleeding. The trials analysed involve inclusion of patients with a broad range of clinical indications, not only inclusive of elective surgery, such as septic patients in critical care, where the transfusion indications and end-goal of treatment varies. Additionally, it must be made aware that Hb may be an unreliable biomarker, in terms of active bleeding where it can remain falsely elevated in due to inadequate fluid resuscitation or fall due to haemodilution intra-operatively (Klein *et al.,* 2016).

Although blood transfusions can be a life-saving therapy for some, each transfusion brings a small risk of serious reactions. In particular, severe cardiopulmonary complications, including transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO), have been identified as the leading cause of transfusion-associated death (Bolton-Maggs *et al.,* 2017). In a recent multicentre, retrospective analysis of almost 5000 transfusion episodes, 1·1% were associated with TACO and 0·08% with TRALI (Hendrickson *et al.,* 2016). Other transfusion risks include anaphylaxis and hypotensive episodes and milder events, including febrile non-haemolytic, minor allergic and delayed serological reactions.

CONCLUSION

Adopting PBM in surgical patients should be paramount to reduce the risks posed by perioperative anaemia in red blood cell transfusion. The programme of PBM recently addressed in national blood transfusion guidelines and its active implementation has demonstrated both patient and health economic benefits. The decision to transfuse red blood cells should not be a reflex reaction to a laboratory-defined value, as it was often done in past practice but a considered risk–benefit decision taken on an individual basis. The principles of PBM help structure the interventions and decisions relating to anaemia and blood transfusion, but, more importantly, represent a paradigm shift towards a more considered approach to blood transfusion, acknowledging its risks, preventatives and alternatives.

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