

## Transfusion Medicine: Time for a Change: Patient Blood Management and the Ontario ONTraC Program

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### Abstract

Despite increasing recognition of the potential adverse effects of blood transfusion there is evidence that the procedure is over-utilized and often inappropriately and unnecessarily administered. Patient Blood Management (PBM) is a recent world-wide initiative to optimize transfusion therapy by employing preoperative and perioperative maneuvers and alternatives to avoid unnecessary blood transfusion. These approaches are, however, not restricted to the surgical setting, but may be applied whenever transfusion is contemplated. A key component of PBM is the appropriate management of anemia, a prime determinant of transfusion. Another is tolerance of anemia through the use of restrictive transfusion thresholds for transfusion and of a single unit at a time policy. Among a number of options at surgery, antifibrinolytics have proven effective at reducing blood loss and transfusion. Burgeoning literature demonstrates that PBM (also known as Blood Conservation or as 'Bloodless Medicine/Surgery') is cost-effective while improving patient outcomes and conserving the blood supply. Data from the ONTraC program in Ontario are described herein to illustrate the effectiveness of PBM approaches.

**Keywords:** Blood transfusion; Patient blood management; PBM; Blood conservation; ONTraC; Anemia

### Key messages

- Patient Blood Management (PBM) focuses on effective management and conservation of a patient's own blood rather than being reliant on donor blood.
- PBM is based on three principles commonly referred to as 'the three pillars':
  - optimizing the patient's own blood elements including red cell mass
  - minimizing the patient's blood loss and bleeding
  - optimizing the tolerance of anemia.
- PBM Strategies and techniques can be beneficial for all patient groups and clinical scenarios.
- PBM requires early identification and intervention for patients at high risk for transfusion.
- Techniques may involve pharmaceutical agents and medical devices.
- As demonstrated in the ONTraC program the use of PBM strategies is associated with significant reduction in transfusion rates, improved patient outcomes, and healthcare costs savings.

### Introduction

Countless lives have been saved over the many years that people have been receiving blood transfusions. Transfusions replenish blood lost through trauma, illness or surgery. They are a medical safety net. But the field of transfusion medicine is changing. Instead of being viewed as an inert recharging of fluid, we now appreciate that a blood

transfusion is essentially a liquid organ transplant, and like any other organ transplant, it has its risks.

While we often hear that transfusion is safer than it has ever been, that doesn't mean blood transfusion is 100% safe. Blood occupies a somewhat privileged position in modern medicine, in that it has evolved as a treatment option without the equivalent research scrutiny – at least on patient outcomes – that other treatments are subjected to. Studies over the past 25 years have shown that simply receiving a transfusion is a risk factor and may be associated with poorer outcomes in terms of increased length of stay in hospital, post-operative infections, and risk of multi-organ failure leading to ICU admission and/or death [1-6]. Red blood cell (RBC) transfusion is associated with a risk-adjusted increased risk for every postoperative morbid event: mortality, renal failure, prolonged ventilator support, serious infection, cardiac complications and neurologic events [2] and even one unit of blood is enough to cause problems [5,6] and the effects are dose-dependent [5-7]. While there are still unanswered questions on how, when and why blood transfusions are administered, there are situations in which a transfusion is the only option and can make the difference between life and death. But known risks should outweigh perceived benefits every time. There is a need for a precautionary approach—nothing should be done to a patient if there is no evidence of benefit. *Primum non nocere*.

There is a growing body of evidence that RBC transfusion is overused and incurs avoidable costs to healthcare organizations and avoidable harm to patients. Blood transfusion has been said to be one of five most overused procedures in medicine and the most frequently performed therapeutic procedure [8-10]. While the overall use of red cells is decreasing in many countries, large audits show much inappropriate use (up to 50%) [11] and considerable inter-institutional variability (ranging from 7.5 to 98 percent transfusion rates in cardiac surgery) [12]. Recently, multiple societies have endorsed recommendations from the Choosing Wisely Campaigns [13-16] that

include avoiding transfusion for arbitrary hemoglobin (Hb) thresholds in the absence of symptoms of active coronary disease, heart failure or stroke, and not performing repetitive CBC and chemistry testing in the face of clinical and lab stability.

## What is Patient Blood Management (PBM)?

PBM (also known as Blood Conservation or Bloodless Medicine/Surgery) is an evidence-based, multidisciplinary approach aimed at optimizing the care of patients who might need transfusion [17-19]. PBM represents an international initiative to improve patient outcomes by promoting the use of transfusion of blood and components only when clearly required. This minimizes unnecessary transfusion, reducing the risk of adverse events and conserving limited donor blood for patients with the greatest need. The principles of PBM have been described as the so called '3 pillars' namely: (i) Optimizing the patient's own blood (e.g. pre-operative optimization of hemoglobin (Hb) and hemostasis), (ii) Minimizing surgical blood loss, and (iii) Optimizing the patient's physiological reserve in relation to anemia (including use of restrictive transfusion triggers). The key principles of PBM apply not just to surgery, but to all patients who may need a blood transfusion in both elective and emergency clinical settings. Accordingly, PBM covers all aspects of decision-making in transfusion therapy, including patient evaluation and clinical management with use of appropriate indications and triggers, minimization of blood loss and optimization of the patient's own red cell mass. Anesthetists, transfusionists and intensivists are increasingly driving this focus aimed at using blood transfusion in the most optimum way. By reducing the need for allogeneic blood transfusions and minimizing risks and unnecessary work, PBM can also reduce health-care costs.

## Effect of PBM on Costs

PBM can reduce costs both at the blood supply and the hospital levels. The business case for reducing costs by addressing overuse is compelling. Transfusion is expensive. In addition to production, testing and shipping costs, there are further costs associated with transfusion: hospital Transfusion Service type and screen, crossmatch, storage and disbursement, nurse administration and monitoring of the transfused patient, increased LOS and infections in transfused patients. Recent studies have estimated the cost of a transfusion at about USD \$1100 [7,20]. There are, however, proven strategies (e.g. a restrictive approach to RBC transfusion, a one-unit dose in non-bleeding patients, and avoiding "routine" daily lab testing in hospitalized patients) and proven tools (e.g. order sets and decision support) that can be used to reduce unnecessary and inappropriate transfusions [21-23] and reduce transfusion costs [7,24-26].

## How is PBM Done?

There may be many ways to achieve PBM. One important change has been to address underlying anemia before any elective surgery. Also important is tolerance of anemia: studies of restrictive transfusion have essentially shown that a restrictive policy did not adversely affect patient outcomes. While it used to be thought that if a patient needed a unit of blood, you might as well give them two, that paradigm has changed. At surgery, a variety of techniques and approaches can be employed to minimize blood loss. In some hospitals, there is also a procedure known as 'cell salvage' in which the patient's own lost blood is collected during surgery, filtered and transfused back.

Pharmacologics (such as antifibrinolytics like tranexamic acid) and fibrin glues and sealants can play important roles in reducing blood loss at surgery. And good surgical technique remains critical.

## Pre-operative/perioperative

- Pre-operative autologous donation (PAD)
- Anemia management
- Restrictive transfusion trigger

## PAD

Advantages of PAD may include prevention of disease transmission, of red cell alloimmunization and of some adverse reactions. PAD may also supplement the blood supply, allow provision of blood to patients with alloantibodies, and provide reassurance to patients about blood risks. On the other hand, PAD does not affect the risk of bacterial contamination or the risk of ABO incompatibility due to clerical error, and may be associated with donor reactions e.g. vasovagal reactions, while being more costly than allogeneic blood. Furthermore, PAD may contribute to perioperative anemia and increased likelihood of transfusion. Consequently, the use of PAD has diminished and it is rarely employed today as the drawn blood is usually not administered and it is an unnecessary expense [27]. Rather let the patient serve as their own 'blood bank'. But, when judiciously used, PAD may avoid allogeneic transfusion.

## Preoperative anemia evaluation and readiness for surgery

Anemia should be considered a serious and treatable medical condition rather than simply an abnormal laboratory value. Preoperative anemia, even when mild, is an independent risk factor that can increase perioperative mortality and morbidity, including increased risk of hospitalization or readmission, prolonged hospital LOS), loss of function, diminished quality of life [28,29]. Despite clear evidence of the harmful effects of unwarranted allogeneic blood, anemia is a major, but modifiable, risk factor for allogeneic blood transfusion.

Anemia is defined by the World Health Organization as a Hb below 120 g/L in women and 130 g/L in men. Specific thresholds apply to pregnant women and children. Anemia prevalence increases with age to 10% of the general population above 65 years of age and >20% of above 85 years of age [30,31]. In the literature, anemia rates in pre-surgical patients range from 5 to 75 percent, depending on the procedure. For example, a large review of 31,857 patients undergoing elective vascular surgery identified 47% as having preoperative anemia [32]. The prevalence of anemia in hospitalized patients ranges from that in the general population to much higher, depending on the reason for admission, co-morbidities and patient factors such as age and gender; the reported prevalence is at least 25-50% and may be higher, with the elderly and those with chronic conditions at increased risk [33,34]. Also, 74% of hospitalized patients will develop a hospital-acquired anemia [35] with 95% of patients admitted to the intensive care unit (ICU) developing anemia by the third ICU day [36]. A surgical procedure with a moderate or high blood loss will further aggravate the anemia and deplete iron stores.

Early screening for preoperative anemia will allow for diagnostic workup and treatment; this may be done by the surgeon or family physician as soon as prospective surgery is contemplated.

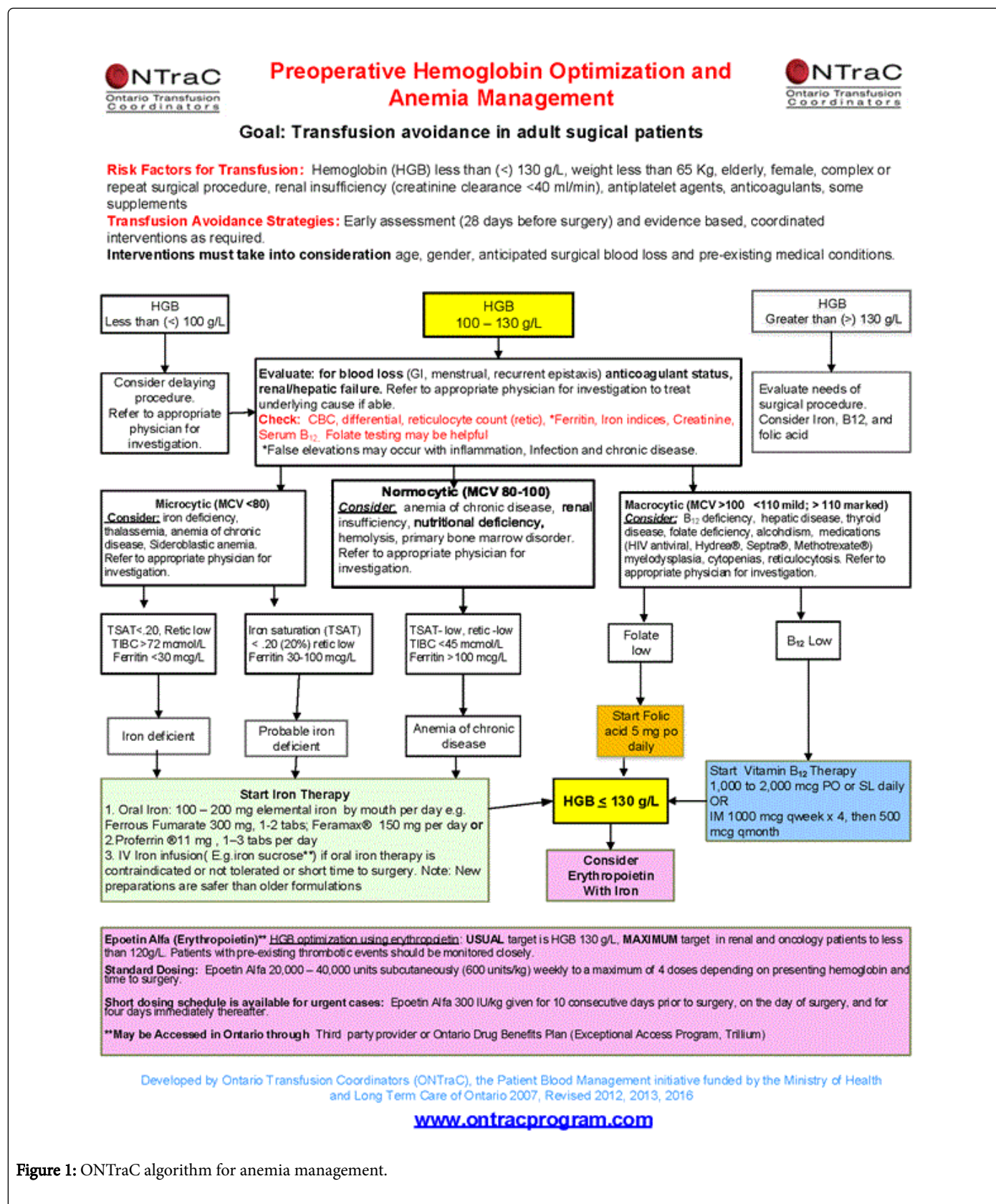


Figure 1: ONTraC algorithm for anemia management.

In the absence of overt anemia, laboratory tests to evaluate iron stores may be done in patients with co-morbidities associated with

depletion of iron stores, such as chronic heart failure, chronic renal failure, rheumatoid arthritis, inflammatory bowel disease or chronic genitourinary and gastrointestinal blood loss.

A standardized approach for the detection, evaluation and management of anemia in the preoperative setting is an important aspect of an effective PBM program. A complete PBM plan should always include an individual risk assessment but algorithms for anemia management may be useful.

Figure 1 is an example algorithm. A time frame of at least three to four weeks prior to surgery is recommended to allow sufficient time to diagnose and optimize treatment of anemia based on the identified cause. A comprehensive history and physical examination should be performed with attention to important risk factors for anemia such as advanced age, small body size, female gender, chronic renal, hepatic or connective tissue diseases, and sources of blood loss. Particular attention should be paid to anticoagulant and antiplatelet medications with a clear plan of how to modify these therapies in the few days before surgery, as well as to laboratory testing to determine the cause of the anemia, in order to institute appropriate treatment. Treatment may involve administration of oral or intravenous iron, erythropoiesis-stimulating agents (ESAs), folate or vitamin B12. It is important to note that while oral iron is effective in treating iron deficiency, this takes time and often the time is insufficient in the pre-surgical setting and intravenous iron is preferred. Referral to a specialist such as a hematologist or gastroenterologist may be necessary and for some patients it may be prudent to consider deferral of a truly elective surgical procedure to when the patient is appropriately optimized.

Patients with preoperative anemia should be followed in the postoperative period to ensure appropriate continued management of the anemia.

### Restrictive transfusion approach

As transfusion practice has come under more scrutiny, there has been increased interest in the “tolerability” or risk of anemia. For example, Carson et al. [37] showed that even mild anemia was associated with increased mortality risk and this was higher for individuals with cardiovascular disease. On the other hand, there is considerable evidence that low levels of Hb can be tolerated in healthy subjects. Hematocrits (Hct) of 10-20% have been achieved in animals and humans using normovolemic hemodilution without untoward effects [38,39]. It has been observed that it is not until the Hb concentration falls below 50 to 60 g/L that morbidity and mortality increases substantially [40].

With recognition that less, or no, transfusion can be associated with improved patient outcomes (e.g. shorter length-of-stay and fewer infections than in transfused patients) and with an increasing acceptance of tolerating lower Hb levels in patients, restrictive transfusion practices are being increasingly applied. These consist primarily of (1) a single unit at a time policy and (2) accepting a lower Hb trigger for transfusion. Use of a restrictive transfusion protocol can be regarded as an important blood-saving and cost-saving strategy which does not lead to adverse events in the non-high risk patient and can readily be achieved at no additional cost.

### Single unit transfusions

Single unit RBC transfusion is the practice of prescribing only one unit at a time, with clinical reassessment of the patient prior to prescribing a subsequent unit, in patients who are not critically

bleeding. Traditionally, single-unit RBC transfusions were believed to be insufficient to treat anemia, but recent data suggest that they lead to a safe reduction of transfusion requirements. Each transfusion should be an independent clinical decision based on the risk, benefits and alternatives and transfusion should be to alleviate patient signs and symptoms of anemia. A single unit of RBC will often relieve acute symptoms of anemia and/or raise hemoglobin level in a stable patient to a level above the guideline trigger, in which case transfusion may be unnecessary or can be postponed or replaced by other anemia treatment. A single unit policy may have the added advantages of conserving the blood supply and of reducing the risk of Transfusion Associated Circulatory Overload (TACO) which is among the highest risks associated with RBC transfusion, of particular concern in the elderly, females and patients with heart or kidney failure, or a positive fluid balance [41,42]. Hence, where transfusion is indicated, a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. Transfusion therapy in severely bleeding patients may require separate guidelines.

### Restrictive transfusion threshold/trigger

Restrictive transfusion thresholds (triggers) are an effective method of reducing and conserving RBC use and improving patient outcomes [43]. RBC transfusion should not, however, be dictated by a Hb ‘trigger’ alone, but rather based on assessment of the patient’s clinical status. While PBM Guidelines provide guidance on Hb ‘triggers’ this should always be in the context of the patient’s clinical condition. The threshold for RBC transfusion in both medical settings and in the postoperative surgical period has evolved over the years. A number of large, randomized clinical trials and prospective observational studies have assessed the effectiveness of allogeneic RBC transfusion and demonstrated that restrictive RBC transfusion practices result in at least equivalent patient outcomes as liberal approaches, and may actually reduce morbidity and mortality rates in some patients. Figure 2 shows some of the randomized prospective trials demonstrating the reduction in transfusion rates when a restrictive trigger is employed [44-49].

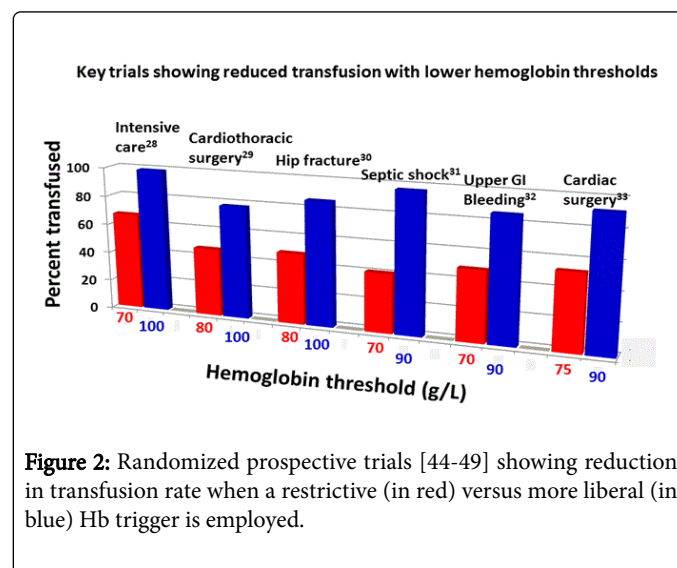


Figure 2: Randomized prospective trials [44-49] showing reduction in transfusion rate when a restrictive (in red) versus more liberal (in blue) Hb trigger is employed.

Meta-analyses of 19 trials showed that restrictive transfusion strategies were associated with a significant reduction in hospital mortality, 30-day mortality, pulmonary edema, bacterial infections and re-bleeding [50]. In the absence of acute myocardial or cerebrovascular

ischemia, postoperative transfusion may be inappropriate for patients with a Hb level of >80 g/L; other Guidelines suggest a Hb level of 70 g/L [51]. Some use a trigger of 70 g/L for most patients and a trigger of 80 g/L for patients with evidence of potential added oxygen need e.g. those with cardiovascular or cerebrovascular disease.

It is important to recognize that the Hb level selected should be viewed as a threshold rather than a trigger; if the Hb is below the threshold level, a transfusion may be considered but is not mandatory. Nevertheless, many clinicians mainly use Hb values to guide transfusion decisions. Physician compliance with clinical practice guidelines is, however, often incomplete, as multiple barriers limit guideline adherence. However, recently programs utilizing clinical decision support (CDS) directed toward more appropriate RBC transfusion practice have been successfully implemented and have been effective in reducing RBC utilization with equivalent or improved patient outcomes [22].

### Reducing perioperative blood loss

A variety of approaches have been employed to reduce perioperative blood loss [52-67]. The development of protocols involves multidisciplinary collaboration between surgeons, anesthesiologists,

hematologists, transfusion medicine and pharmacy. The approach may vary depending on surgical procedure, but useful considerations include reversal of antithrombotic medications, point-of-care testing to assess coagulation and guide blood product use, topical hemostatic agents (fibrin glue/sealants), hemostatic drugs (antifibrinolytics), and perioperative blood salvage. Other considerations in the PBM program include patient positioning and anesthetic [68] considerations, and good surgical technique remains paramount.

### PBM at the hospital level

Establishing a PBM strategy needs leadership and support at all levels, from policymakers and managers, to executive management and health professionals from various clinical disciplines within hospitals. Patient input on achieving patient acceptance and participation is often useful. At an operational level, the cornerstone of a PBM program is the multidisciplinary team. General practitioners, surgeons, anesthesiologists, nurses, hematology/transfusion medicine, pharmacy and laboratory staff all have important roles to play in surgical PBM and should be engaged in the development and implementation of the PBM strategy. PBM strategies also apply in the non-surgical setting. Table 1 shows key elements of a PBM program at the hospital level.

At the hospital level key elements include:
1. A hospital PBM policy based on national/regional guidance supported by the Hospital Transfusion Committee with senior medical/ nursing/ management support
2. Hospital-wide awareness and education
· Medical, nursing, laboratory staff, in all clinical areas that administer blood and components
· Identifications of clinical champions in key disciplines
· Inclusion in induction for new staff
· Clear messages: posters, intranet, newsletter
3. Guidelines promoting appropriate use of blood and components and alternatives
4. Informing and involving patients
5. Reviewing available information technology to support PBM data collection (including computerized physician order entry (CPOE))

**Table 1:** Key elements of a hospital PBM program.

Institutional support is critical to project success, as it provides access to the resources required to change current hospital culture and practices. Examples of areas that people may rally around include the financial costs of RBC overuse to the organization, the potential impact on LOS and hospital-acquired infections associated with transfusion, the costs and mortality associated with untreated anemic patients, or the potential harm associated with iatrogenic anemia. Although useful, these arguments should not necessarily be the primary selling point -- the major impact is on managing patient risks for patient safety.

### Role of Transfusion Practitioner

The Transfusion Practitioner (TP) [69] or equivalent (e.g. PBM Practitioner/Nurse/Coordinator) has a critical role to play in developing a PBM culture within healthcare establishments. Although only one part of the team developing and implementing the required PBM strategies, they have a multifaceted role in engaging with scientific, laboratory and clinical colleagues, as well as, importantly, the

patients. Very often the TP is the conduit for information, pulling together available resources, reviewing activities undertaken by transfusion colleagues in other centers, collecting audit data and evaluating the benefit of activities.

Tps have made a significant contribution in helping to improve transfusion practice at a local, regional and national level by promoting safe transfusion practice. To do this, information must be provided to clinical colleagues to engage with them and plan strategies. The many different elements that constitute PBM can be tailored for the different clinical specialties that use blood transfusion services and, through good clinical leadership, the TP can coordinate a number of initiatives and work streams such as pre-surgery optimization, medical management in iron deficient anemia, or electronic solutions for blood ordering and prescribing. The TP may not lead these projects as they are owned and managed at a local level by the users of blood, but the TP can have the global view of PBM and the benefits it brings.

Currently there is a lack of definitive evidence on the role of the TP within PBM and much of the information is anecdotal. It is acknowledged that a greater focus of the role of the TP in PBM is needed within the printed material and resources available. In the UK the TP role was recommended as part of the Department of Health Better Blood Transfusion strategy. Over the years many UK Trusts have appointed to the TP role, employing experienced staff with a Nursing, Midwifery or Biomedical Science background. TPs also play a major role within Hospital Transfusion Committees (HTCs) and hospitals may also have a separate PBM Committee. HTCs should play a key role in blood conservation and evidence does exist for improved use of blood components due to interventions such as transfusion policies, clinical audits, education of clinicians.

TPs add value with regards to training and education, transfusion safety and clinical practice. However, the role and responsibility of the TP varies widely and has changed significantly for some since it was introduced. There is significant variation in how TPs spend their time. A book by the American Association of Blood Banks (AABB), 'Transfusion Medicine's Emerging Positions: Transfusion Safety Officers and Patient Blood Management Coordinators', provides some guidance on such positions (whether hospital-based or blood-center-based), the professionals who make good candidates, the scope of their responsibilities, their key role in improving patient outcomes and the influence they have on various hospital departments.

### The Ontario experience

In Ontario (population approx. 13,000,000), the ONTraC (Ontario Transfusion Coordinators) network program funded by the Ontario Ministry of Health and Long-term Care has placed PBM coordinators in 25 community and teaching hospital throughout the province [7,70,71]. These hospitals account for about 75% of the blood used in the province and the intent is to educate physicians, nurses and patients about best transfusion practices and alternatives to transfusion. The ONTraC TPs are expected to spend 50% of their time on implementing PBM practices, 25% on staff and patient education, and 25% on data collection [7]. Figure 3 shows the reduction in annual provincial transfusion rates in Ontario in knee arthroplasty and coronary artery bypass graft (CABG) surgery since initiation of the program in 2002. Not only has there been a significant reduction in proportion of patients transfused, but those who are transfused are receiving less blood (for example, CABG patients who were transfused in 2002 received a mean of 3.3 units RBC; in 2015 transfused patients received a mean of 2.5 units). Overall, in the initial four ONTraC targeted surgical procedures (knee, hip, CABG and radical prostatectomy) transfusions have decreased between 60 and 90% from baseline, and many additional diagnoses and surgeries (e.g. gynecologic and obstetric procedures, heart valves, spine and colon surgery) have been added. In 2015, RBC usage in Ontario was 27.4 units per thousand population, among the lowest internationally [72]; by contrast, data collected in an AABB survey showed that RBC usage in 2013 in the USA was 40.3 units per thousand population [73].

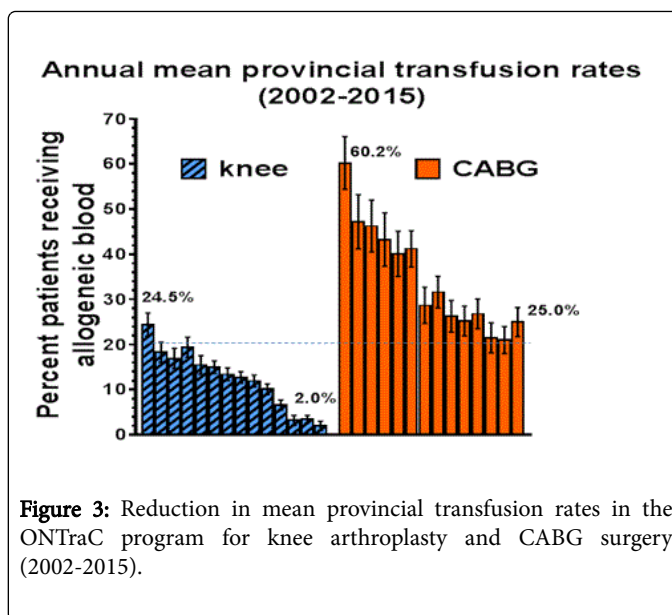


Figure 3: Reduction in mean provincial transfusion rates in the ONTraC program for knee arthroplasty and CABG surgery (2002-2015).

In the ONTraC program there is a focus on correction of preoperative anemia. Data from ONTraC shows that the likelihood of receiving a transfusion increases exponentially when the preoperative Hb level is below 130 g/L (Figure 4). Similar results have been reported by others. Hence we try to achieve this level if possible in the preoperative management of anemia. Whilst not always possible, the higher we are able to get the Hb level, the less likely the patient is to receive a transfusion. Lead time is necessary for the anemia treatment. A longer lead time results in fewer transfusions: for example, in 2014 knee arthroplasty patients who had a lead time of <7 days had a transfusion rate of 5.5%, versus those with a lead time of 7-15 days of 4.7%, 15-21 days of 3.7% and >21 days of 1.8%. We try to get to see the patient at least 3-4 weeks prior to surgery. Family physicians can play an important role in the management of the anemia.

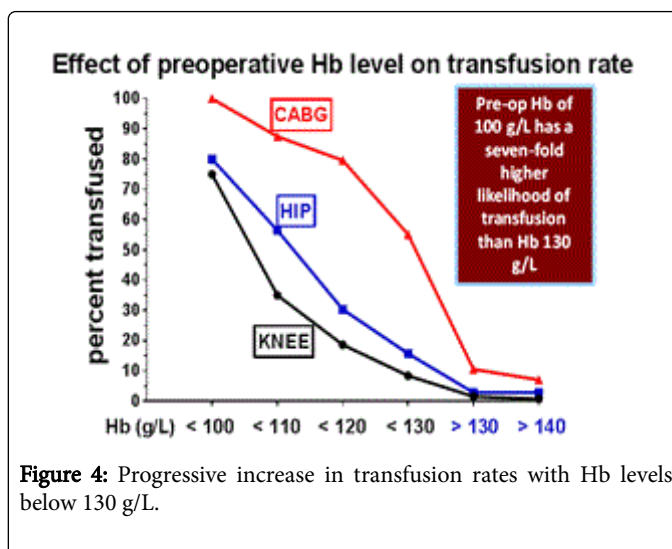


Figure 4: Progressive increase in transfusion rates with Hb levels below 130 g/L.

The ONTraC TPs also emphasize the need for tolerance of anemia and 'restrictive' transfusion thresholds when appropriate and, in Ontario, for knee arthroplasty for example, whereas in 2002 the mean nadir Hb (transfusion trigger surrogate) was 84 g/L, it has decreased to 72 g/L.

Another focus has been on the use of the antifibrinolytic drug, tranexamic acid. Whilst this was extensively used in cardiac surgery, despite increasing literature advocating its use in orthopedic surgery, it was relatively infrequently employed in the latter. Table 2 shows the effectiveness in the ONTraC program of tranexamic acid in decreasing transfusion in knee arthroplasty.

	2011	2012	2013	2014	2015
N	5878	5314	5409	4175	5373
% receiving TXA	34.9	51	56.9	79	78.5
% transfused of patients receiving TXA	2.4	2.7	2	2.1	1.6
% transfused of patients NOT receiving TXA	11.3	9.8	6.6	7.3	5.6

**Table 2:** Effect of tranexamic acid (TXA) use on provincial transfusion rates in knee arthroplasty.

The annual cost savings potentially attributed to the ONTraC program for the four initial targeted procedures only compared to baseline are over CAD 15 million in purchase of RBCs and over CAD 45 million in savings to the healthcare system overall [70]. The cost of the program is approximately CAD 3 million. Hence, in addition to catering to patients' preferences, the program reduces risks, improves outcome and is cost-effective and cost-efficient.

Further information on the ONTraC program can be found (along with much information on PBM, including patient pamphlets) at [www.ontracprogram.com](http://www.ontracprogram.com).

## Conclusion

Pathways supporting PBM are simple in design, labor costs relatively low, capital investments small, quality and outcomes gains high, savings for the organization large, and the greater public good is served. So why is it not more extensively practiced? This is in large part because of physician training and 'traditional' practices, i.e., transfusion was the default position for anemia, and, secondly, the belief that blood is safe – risks have decreased with improved HIV and hepatitis testing. We need to replace the 'Traditional Concept' that blood products are an effective therapeutic intervention with the 'New Concept' that transfusion of blood products is rather an undesirable outcome. We have learned that transfusion rates are not patient-dependent, but are institution (geography) dependent and while 30% of the variation may be surgeon dependent, 70% is hospital specific and that there are 'high-transfusion' hospitals and 'low transfusion' hospitals [74,75] – so we need to change the 'culture' in hospitals, although this is often not easy.

We have recognized that although hazardous, anemia is frequently ignored, exacerbated by wasteful practices such as excess phlebotomy, or inappropriately treated with inappropriate transfusion. However, anemia is easily treated, and effective protocols have been developed to guide physicians in their care of anemic patients. Improving the management of anemia therefore represents a great opportunity to improve patient outcomes and reduce costs and adverse events. In the operative period, the benefits of appropriate use of antifibrinolytics, of cell salvage and of topical hemostats, among other approaches, have been shown. The principles of PBM extend beyond surgery and are multidisciplinary, best applied by a team approach involving a large

variety of health care personnel and patients. There are challenges in embarking on a PBM project, given the scope and complexity of the issue, but a systematic approach to the process (including forming a multidisciplinary team, obtaining institutional support, assessing baseline performance, thoughtful design and implementation of interventions, and careful monitoring) increases the chance of success. PBM is cost-effective and presents an opportunity to improve outcomes, reduce risks and save costs all at the same time.

It is interesting to note that recognition of the risks of transfusion is not new. A letter to the *Lancet* in 1949 [76] stated: "blood transfusion ... a mass produced remedy which daily presents fresh problems. In the hands of experts it is virtually safe, and very valuable; but there is little doubt that ... many deaths supposed to have occurred 'in spite of transfusion' have really been caused by it. In fact there are few risks when the doctor fails to insert a needle ... into the vein; they begin to mount once he succeeds." And in the 'immortal words of Dr. Beal in 1976 [77]: "Blood transfusion is a lot like marriage. It should not be entered into lightly, unadvisedly or wantonly, or more often than is absolutely necessary."

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## References

1. Hill GE, Frawley WH, Griffith KE, Forestner JE, Minei JP (2003) Allogeneic blood transfusion increases the risk of postoperative bacterial infection: A meta-analysis. *J Trauma* 54: 908-914.
2. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, et al. (2006) Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med* 34: 1608-1616.
3. Ranucci M, Aronson S, Dietrich W, Dyke CM, Hofmann A, et al. (2011) Patient blood management during cardiac surgery: Do we have enough evidence for clinical practice? *J Thorac Cardiovasc Surg* 142: 249.e1-32.
4. Surgenor SD, Kramer RS, Olmstead EM, Ross CS, Sellke FW, et al. (2009) The association of perioperative red blood cell transfusions and decreased long-term survival after cardiac surgery. *Anesth Analg* 108: 1741-1746.
5. Karkouti K, Wijesundera DN, Yau TM, Beattie WS, Abdelnaem E, et al. (2004) The independent association of massive blood loss with mortality in cardiac surgery. *Transfusion* 44: 1453-1462.
6. Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, et al. (2006) Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. *Ann Thorac Surg* 81: 1650-1657.
7. Freedman J, Luke K, Escobar M, Vernich L, Chiavetta JA (2008) Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). *Transfusion* 48: 237-250.
8. Morton J, Anastasopoulos KP, Patel ST, Lerner JH, Ryan KJ, et al. (2010) Frequency and outcomes of blood products transfusion across procedures and clinical conditions warranting inpatient care: an analysis of the 2004 healthcare cost and utilization project nationwide inpatient sample database. *Am J Med Qual* 25: 289-296.
9. [https://www.jointcommission.org/overuse\\_summit/](https://www.jointcommission.org/overuse_summit/)
10. Shander A, Fink A, Javidroozi M, Erhard J, Farmer SL, et al. (2011) Appropriateness of allogeneic red blood cell transfusion: The international consensus conference on transfusion outcomes. *Transfus Med Rev* 25: 232-246.

11. Shander A, Fink A, Javidroozi, Erhard J, Farmer SL, et al. (2011) International consensus conference on transfusion outcomes group. Appropriateness of allogeneic red blood cell transfusion: The international consensus conference on transfusion outcomes. *Transfus Med Rev* 25: 232-246.e53.
12. Bennett-Guerrero E, Zhao Y, O'Brien SM, Ferguson TB Jr, Peterson ED, et al. (2010) Variation in use of blood transfusion in coronary artery bypass graft surgery. *JAMA* 304: 1568-1575.
13. Halpern SD, Becker D, Curtis JR, Fowler R, Hyzyet R, et al. (2014) An official American Thoracic Society/American Association of Critical-Care Nurses/American College of Chest Physicians/Society of Critical Care Medicine policy statement: The Choosing Wisely top five list in Critical Care Medicine. *Am J Respir Crit Care Med* 190: 818-826.
14. Callum JL, Waters JH, Shaz BH, Sloan SR, Murphy MF (2014) The AABB recommendations for the Choosing Wisely campaign of the American Board of Internal Medicine. *Transfusion* 54: 2344-2352.
15. Hicks LK, Bering H, Carson KR, Kleinerman J, Kukreti V, et al. (2013) The ASH Choosing Wisely campaign: five hematologic tests and treatments to question. *Blood* 122: 3879-3883.
16. Onuoha OC, Arkoosh VA, Fleisher LA (2014) Choosing wisely in anesthesiology: The gap between evidence and practice. *JAMA Intern Med* 174: 1391-1395.
17. Goodnough LT, Shander A (2012) Patient blood management. *Anesthesiology* 116: 1367-1376.
18. Shander A, Javidroozi M (2015) Blood conservation strategies and the management of perioperative anaemia. *Curr Opin Anaesthesiol* 28: 356-363.
19. Murphy MF, Goodnough LT (2015) The scientific basis for patient blood management. *Transfus Clin Biol* 22: 90-96.
20. Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, et al. (2010) Activity-based costs of blood transfusions in surgical patients at four hospitals. *Transfusion* 50: 753-765.
21. Goodnough LT, Shah NK (2015) Is there a 'magic' hemoglobin number? Clinical decision support promoting restrictive transfusion practices. *Am J Hematol* 90: 927-933.
22. Zuckerberg GS, Scott AV, Wasey JO, Wick EC, Pawlik TM, et al. (2015) Efficacy of education followed by computerized provider order entry with clinician decision support to reduce red blood cell utilization. *Transfusion* 55: 1628-1636.
23. Farmer SL, Trentino KM, Hofmann A, Semmens JB, Mukhtar SA, et al. (2015) A programmatic approach to patient blood management - reducing transfusions and improving patient outcomes. *Open Anesthesiol J* 9: 1-11.
24. LaPar DJ, Crosby IK, Ailawadi G, Ad N, Choi E, et al. (2013) Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery. *J Thorac Cardiovasc Surg* 145: 796-803.
25. Leahy MF, Mukhtar SA (2012) From blood transfusion to patient blood management: A new paradigm for patient care and cost assessment of blood transfusion practice. *Intern Med J* 42: 332-338.
26. Trentino KM, Farmer SL, Swain SG, Burrows SA, et al. (2015) Increased hospital costs associated with red blood cell transfusion. *Transfusion* 55: 1082-1089.
27. Vassallo R, Goldman M, Germain M, Lozano M; BEST Collaborative (2015) Preoperative autologous blood donation: Waning indications in an era of improved blood safety. *Transfus Med Rev* 29: 268-275.
28. Shander A, Javidroozi M, Ozawa S, Hare GM (2011) What is really dangerous: Anaemia or transfusion? *Br J Anaesth* 107 Suppl 1: i41-59.
29. Hare GM, Freedman J, David Mazer C (2013) Review article: Risks of anemia and related management strategies: Can perioperative blood management improve patient safety? *Can J Anaesth* 60: 168-175.
30. Zilinski J, Zillmann R, Becker I, Benzing T, Schulz RJ, et al. (2014) Prevalence of anemia among elderly inpatients and its association with multidimensional loss of function. *Ann Hematol* 93: 1645-1654.
31. Patel KV (2008) Epidemiology of anemia in older adults. *Semin Hematol* 45: 210-217.
32. Gupta PK, Sundaram A, Mactaggart JN, Johanning JM, Gupta H, et al. (2013) Preoperative anemia is an independent predictor of postoperative mortality and adverse cardiac events in elderly patients undergoing elective vascular operations. *Ann Surg* 258: 1096-1102.
33. Migone De Amicis M, Poggiali E, Motta I, Minonzio F, Fabio G, et al. (2015) Anemia in elderly hospitalized patients: prevalence and clinical impact. *Intern Emerg Med* 10: 581-586.
34. Shander A, Goodnough LT, Javidroozi M, Auerbach M, Carson J, et al. (2014) Iron deficiency anemia--bridging the knowledge and practice gap. *Transfus Med Rev* 28: 156-166.
35. Koch CG, Li L, Sun Z, Hixson ED, Tang A, et al. (2013) Hospital-acquired anemia: Prevalence, outcomes, and healthcare implications. *J Hosp Med* 8: 506-512.
36. Corwin HL, Gettinger A, Pearl RG, Fink MP, Levy MM, et al. (2004) The CRIT Study: Anemia and blood transfusion in the critically ill--current clinical practice in the United States. *Crit Care Med* 32: 39-52.
37. Carson JL, Duff A, Poses RM, Berlin JA, Spence RK, et al. (1996) Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. *Lancet* 348: 1055-1060.
38. Geha AS (1976) Coronary and cardiovascular dynamics and oxygen availability during acute normovolemic anemia. *Surgery* 80: 47-53.
39. Weiskopf RB, Viele MK, Feiner J, Kelley S, Lieberman J, et al. (1998) Human cardiovascular and metabolic response to acute, severe isovolemic anemia. *JAMA* 279: 217-221.
40. Shander A, Javidroozi M, Naqvi S, Aregbeyen O, Caylan M, et al. (2014) An update on mortality and morbidity in patients with very low postoperative hemoglobin levels who decline blood transfusion (CME). *Transfusion* 54: 2688-2695.
41. Popovsky M (2008) Transfusion-associated circulatory overload. *ISBT Science Series* 3: 166-169.
42. Roback JD (2011) Non-infectious complications of blood transfusion. *AABB Technical Manual*, Bethesda.
43. Goodnough LT, Maggio P, Hadhazy E, Shieh L, Hernandez-Boussard T, et al. (2014) Restrictive blood transfusion practices are associated with improved patient outcomes. *Transfusion* 54: 2753-2759.
44. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, et al. (1999) A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med* 340: 409-417.
45. Hajjar LA, Vincent JL, Galas FR, Nakamura RE, Silva CM, et al. (2010) Transfusion requirements after cardiac surgery: The TRACS randomized controlled trial. *JAMA* 304: 1559-1567.
46. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, et al. (2011) Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 365: 2453-2462.
47. Holst LB, Petersen MW, Haase N, Perner A, Wetterslev J (2015) Restrictive versus liberal transfusion strategy for red blood cell transfusion: Systematic review of randomised trials with meta-analysis and trial sequential analysis. *BMJ* 350: h1354.
48. Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, et al. (2013) Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med* 368: 11-21.
49. Murphy GJ, Pike K, Rogers CA, Wordsworth S, Stokes EA, et al. (2015) Liberal or restrictive transfusion after cardiac surgery. *N Engl J Med* 372: 997-1008.
50. Salpeter SR, Buckley JS, Chatterjee S (2014) Impact of more restrictive blood transfusion strategies on clinical outcomes: A meta-analysis and systematic review. *Am J Med* 127: 124-131.
51. Hébert PC, Carson JL (2014) Transfusion threshold of 7 g per deciliter--the new normal. *N Engl J Med* 371: 1459-1461.
52. Ferraris VA, Ferraris SP, Saha SP, Hessel EA, Haan CK, et al. (2007) Perioperative blood transfusion and blood conservation in cardiac surgery: The Society of Thoracic Surgeons and the Society of



- Cardiovascular Anesthesiologists clinical practice guidelines. *Ann Thorac Surg* 83: S27-S86.
53. Ferraris VA, Brown JR, Despotis GJ, Hammon JW, Reece TB, et al. (2011) 2011 Update to the society of thoracic surgeons and the society of cardiovascular anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg* 91: 944-992.
54. Menkis A, Martin J, Cheng D, Fitzgerald D, Freedman J, et al. (2011) Drugs, devices, technologies & techniques for blood management in minimally-invasive and conventional cardiothoracic surgery: A consensus statement from the International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS). *Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery. Innovations (Phila)* 7: 229-241.
55. Bisbe E, Moltó L (2013) Pillar 2: Minimising bleeding and blood loss. *Best Pract Res Clin Anaesthesiol* 27: 99-110.
56. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. (2013) Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 30: 270-382.
57. Chee YL, Crawford JC, Watson HG, Greaves M (2008) Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. *British Committee for Standards in Haematology. Br J Haematol* 140: 496-504.
58. Tengborn L, Blombäck M, Berntorp E (2015) Tranexamic acid--an old drug still going strong and making a revival. *Thromb Res* 135: 231-242.
59. Jenkins I, Shander A (2015) Anemia prevention and management program implementation guide. SABM and the Society for Hospital Medicine.
60. Baker JE, Pavenski K, Pirani RA, White A, Kataoka M, et al. (2015) Universal tranexamic acid therapy to minimize transfusion for major joint arthroplasty: A retrospective analysis of protocol implementation. *Can J Anaesthesiol* 62: 1179-1187.
61. Yang B, Li H, Wang D, He X, Zhang C, et al. (2013) Systematic review and meta-analysis of perioperative intravenous tranexamic acid use in spinal surgery. *PLoS One* 8: e55436.
62. Ker K, Roberts I, Shakur H, Coats TJ (2015) Antifibrinolytic drugs for acute traumatic injury. *Cochrane Database Syst Rev* 5: CD004896
63. Rousou JA (2013) Use of fibrin sealants in cardiovascular surgery: A systematic review. *J Card Surg* 28: 238-247.
64. Carless PA, Henry DA (2006) Systematic review and meta-analysis of the use of fibrin sealant to prevent seroma formation after breast cancer surgery. *Br J Surg* 93: 810-819.
65. Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, et al. (2010) Cell salvage for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev* 4: CD001888.
66. Murphy GJ, Rogers CS, Lansdowne WB, Channon I, Alwair H, et al. (2005) Safety, efficacy and cost of intraoperative cell salvage and autotransfusion after off-pump coronary artery bypass surgery: a randomized trial. *J Thorac Cardiovasc Surg* 130: 20-28.
67. Karkouti K, McClusky SA, Callum J, Freedman J, Selby R, et al. (2015) Evaluation of a novel transfusion algorithm employing point-of-care coagulation assays in cardiac surgery. *Anesthesiology* 122: 560-570.
68. Mauermann WJ, Shilling AM, Zuo Z (2006) A comparison of neuraxial block versus general anesthesia for elective total hip replacement: A meta-analysis. *Anesth Analg* 103: 1018-1025.
69. Miller K, Akers C, Davis AK, Wood E, Hennessy C, et al. (2015) The evolving role of the transfusion practitioner. *Transfus Med Rev* 29: 138-144.
70. Freedman J (2014) The ONTraC Ontario program in blood conservation. *Transfus Apher Sci* 50: 32-36.
71. Freedman J, Luke K, Monga N, Lincoln S, Koen R, et al. (2005) A provincial program of blood conservation: The Ontario Transfusion Coordinators (ONTraC). *Transfus Apher Sci* 33: 343-349.
72. Van Hoveen LR, Janssen MP, Rautmann G (2015) The collection, testing and use of blood and blood components in Europe: 2012 EDQM for the Council of Europe.
73. Whitaker B, Rajbhandary S, Kleinman S, Harris A, Kamani N (2016) Trends in United States blood collection and transfusion: Results from the 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey.
74. Qian F, Osler TM, Eaton MP, Dick AW, Hohmann SF, et al. (2013) Variation of blood transfusion in patients undergoing major noncardiac surgery. *Ann Surg* 257: 266-278.
75. Jin R, Zelinka ES, McDonald J, Byrnes T, Grunkemeier GL, et al. (2013) Effect of hospital culture on blood transfusion in cardiac procedures. *Ann Thorac Surg* 95: 1269-1274.
76. Milner H (1949) Foolproof blood-transfusion. *The Lancet* 254: 217.
77. Beal RW (1976) The rational use of blood. *Aust N Z J Surg* 46: 309-313.