ONTraC

ontario transfusion coordinators

Patient Blood Management

An ONTraC Toolkit Guide for Hospitals

Revised 2020

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With considerable assistance from materials from the Society for Advancement of Blood Management (SABM), the Society of Hospital Medicine (SHM), and the Australian National Blood Authority

*** The ONTraC program is a network of Patient Blood Management Coordinators in 25 Ontario hospitals; the program has been funded since 2002 by the Ontario Ministry of Health and Long-Term Care**

Patient Blood Management - a great resource

A toolkit guide to Patient Blood Management (PBM)

Blood transfusion is a lot like marriage.
It should not be entered into lightly,
unadvisedly or wantonly,
or more often
than is absolutely necessary.

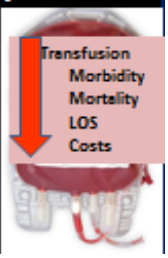
[Beal RW: Aust N Z J Surg 46:309, 1976]

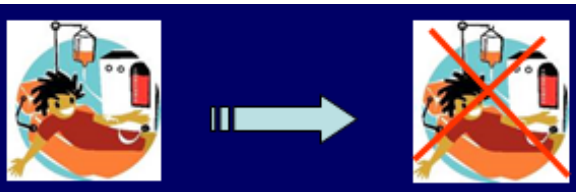
PBM is one of the few areas of medicine where you can:

- **Improve outcomes**
- **Reduce risks**
- **Save costs**

All at the same time

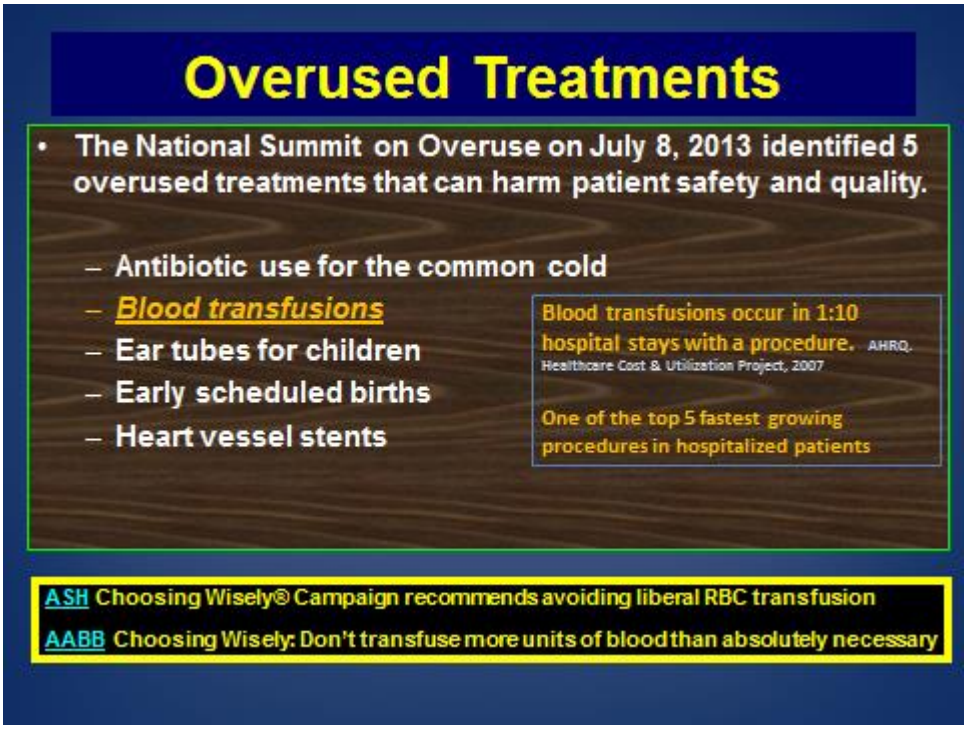
www.sabm.org





Blood Conservation = Patient Blood management (PBM)

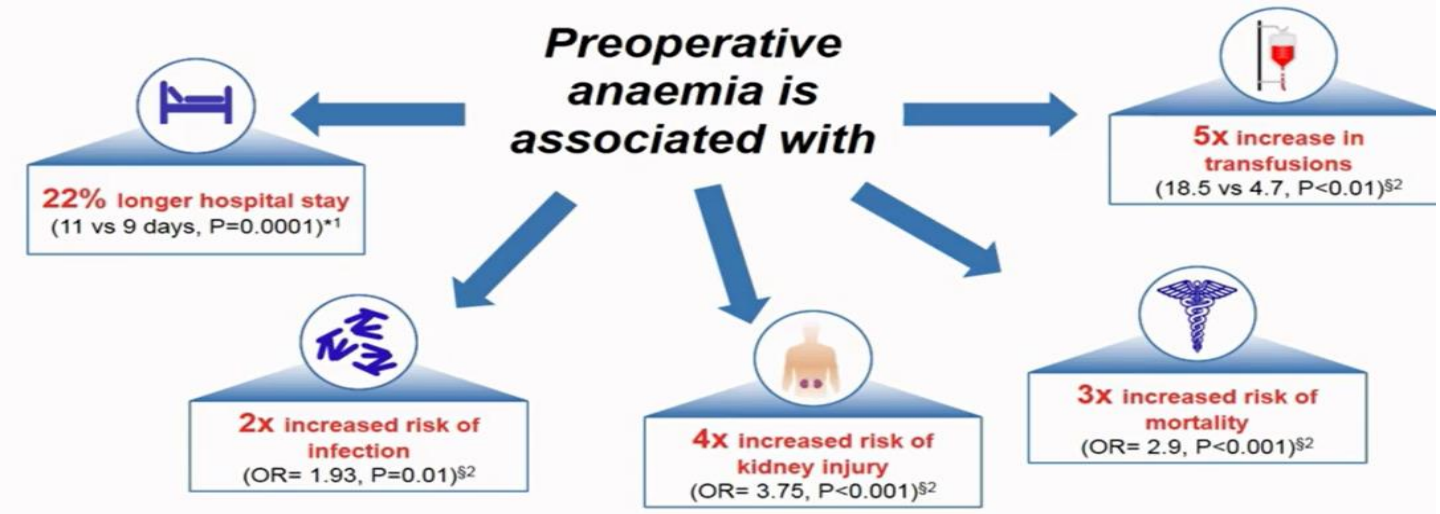
- ***Patient Blood Management (PBM) is the timely multidisciplinary application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize haemostasis and minimize blood loss in an effort to improve patient outcome.***



In 1997, the Krever Commission Report on 'tainted blood' in Canada stated that 'blood components and blood products will never be without risk. The best way to reduce that risk is to reduce their use'

Despite important advances to reduce transfusion risks, this statement remains true today

- **30-70%** of patients come to surgery anemic
- Long tradition of accepting anemia as a relatively harmless problem easily corrected with transfusion
- **BUT** anemia is an independent risk of morbidity & mortality (2.5-fold ↑ in mortality for each gram ↓ in Hb)



Beattie WS et al. Anesthesiology. 2009;110:574–81; 2. Fowler AJ et al. Br J Surg. 2015;102:1314–24; 3. Musallam KM et al. Lancet. 2011;378:1396–1407

EXECUTIVE SUMMARY

"Improve patient outcomes! Conserve limited resources! Identify cost-saving opportunities!" These goals are on the to-do list of every health administrator. One initiative could simultaneously advance each of these important goals.

In the presence of clinical uncertainty, the default position has been to administer a blood transfusion; this is not usually the case with other therapies. Blood transfusion is inherently hazardous and costly and should only be prescribed when there is evidence that patient benefit would outweigh the potential for harm. In 1997, the Krever Commission Report stated that ***"blood components and blood products will never be without risk. The best way to reduce that risk is to reduce their use".*** Despite important advances to reduce transfusion risks, this statement remains true today.

Patient Blood Management (PBM) is the timely multidisciplinary application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome.

Why Patient Blood Management (PBM; Blood Conservation)?

1) Conserving a limited resource:
- Supply of blood is an increasing challenge; while 40% of the population is eligible to donate, only ~ 4% do.
- Changing demographics results in fewer donors and more usage.
- The CBS addresses the supply side of this equation, but it is up to us to decrease unnecessary demand.
- A "minimum of 40%, possibly as high as 60% of transfusions are administered to stable non-bleeding patients." (International Consensus Conference on Transfusion Outcomes: www.eurekalert.org/pub_releases/2009-04/hp-bta042209.php)

2) Improving patient outcomes:
- Evidence is unequivocal that patient outcomes are better when transfusion policies are restricted.
- Trials (e.g. ABC, TRICC, CRIT) have shown lower infection rates, lower mortality and shorter length of stay (LOS), with reduced transfusion.

3) Financial impact:
- The true costs of transfusing blood products is only recently being understood.
- Previous studies generally fell short of capturing the multiple activities involved in this complex process.
- A recent conference of international experts put the average cost of delivering one unit of red blood cells at $1200-1400 a unit (Shander et al, Transfusion 50:753-765, 2010). Patients may receive many units.
- Established PBM programs may have a 50-75% reduction in blood use in orthopedic and cardiac surgery.

In 2002, the Ontario Ministry of Health and Long Term Care (MOHLTC) took the lead and began a unique provincial blood conservation program. The Ontario Nurse Transfusion Conservation Coordinators (ONTraC) Program enhances transfusion practice by promoting alternatives to allogeneic transfusion and by improving patient outcomes and well-being through optimal blood management/conservation in a cost-effective manner through the placement of 28 Blood Conservation Coordinators in 25 Ontario hospitals.

The ONTraC program has been highly successful in achieving these aims. The transfusion rates in Ontario have been markedly reduced: e.g. in knee surgery the provincial transfusion rate has decreased from 25% to 0.7%, and in cardiac bypass surgery from 60% to 23%. This has been achieved in large measure by preoperative raising of the patients' hemoglobin levels by the ONTraC blood conservation coordinators. Relevant patient outcomes have shown a consequent significant reduction in length-of-stay, and in infection rates, and cost savings to the health care system of greater than $45 million per year (over $15 million for cost of red cells alone) compared to baseline. The success of this program's network approach has led to its being emulated in other countries e.g. Australia. This paradigm shift in Transfusion Medicine from product-oriented to patient-oriented needs to be sustained.

Patient Blood Management - a great resource

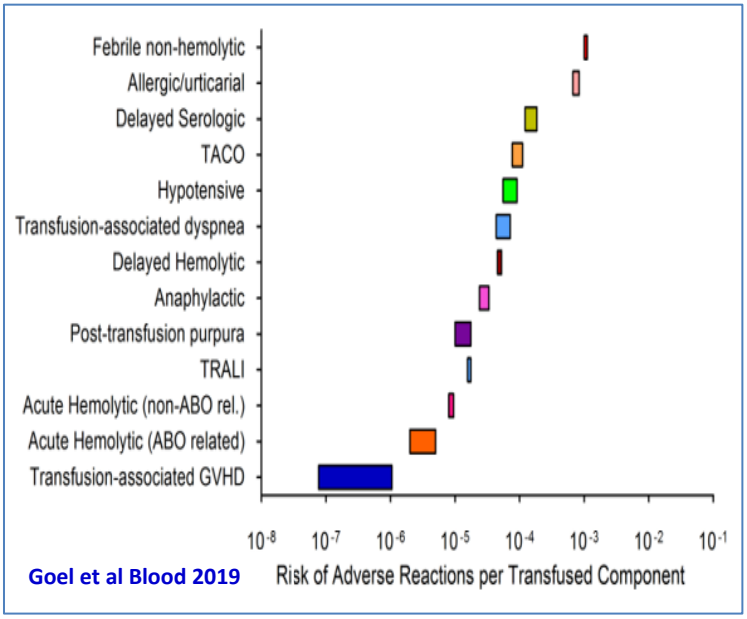
Background:

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: there for when surgery doesn't quite go according to plan, and patients need a little 'top-up'. They are also a lifeline for people with inherited blood disorders, certain rare diseases or who are undergoing chemotherapy. But the field of transfusion medicine is changing. Instead of being viewed as an inert recharging of fluid, we are now appreciating that a blood transfusion is essentially a liquid organ transplant, and like any other organ transplant, it has its risks.

Whilst Canada has one of the safest blood supplies in the world, 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 same level of research scrutiny – at least on the patient outcomes side of things – that other treatments are subjected to. Over the past 25 years, studies have increasingly shown that blood transfusions carry more risks than had long been thought. It has become apparent that the mere fact you received a blood transfusion was a risk factor and could be associated with poorer outcomes in terms of increased length of stay in hospital, certain post-operative infections, etc. Studies of restrictive transfusion have essentially all shown that a restrictive policy did not leave the patients any worse off and there is some evidence that they were better off. Jehovah's Witnesses are one group that have inadvertently served as a sort of test case for non-transfusions -- they did better, because of a better standard of care: they were being prepared better for surgery, with correction of anemia before surgery, the greater care taken by surgeons at surgery to avoid or reduce bleeding, and changed surgical technique, particularly in cardiac surgery.

The downsides of blood transfusions

A challenge in assessing the negative consequences of a blood transfusion is that if someone is considered sick enough to need a transfusion, there's a good chance they're already in a bad way physically. This makes it difficult to say with any degree of certainty that someone's multi-organ failure or sepsis is caused by the blood transfusion or is the result of the illness and trauma that led to them receiving the blood transfusion.



What we do know is that many (and increasing) observational and experimental studies have pointed to an immunosuppressive effect of transfusion resulting in increased time spent in hospital, an increased risk of infections after operations, increased likelihood of needing artificial ventilation, and an increased risk of multi-organ failure leading to ICU admission and/or death. Even one unit of blood is enough to cause problems and the effects are dose-dependent.

Risks higher than most believe: Many studies have shown that transfusions are associated with

- Increased morbidity
- Increased mortality
- Increased infection rates
- Increased length of ICU and hospital stay

Precautionary principle for transfusions

It used to be thought that if a patient needed a unit of blood, you might as well give them two, but that paradigm has changed. This shift has had significant consequences for surgery and intensive care, and anesthetists and intensivists are increasingly driving this focus on what we call Patient Blood Management, which is aimed at using blood transfusion in the most optimum way.

One important change has been to address any underlying anemia before any elective surgery. This reduces the likelihood of that a person's hemoglobin will drop to dangerous levels during or after surgery. As well, surgeons are working to minimize blood loss during surgery by using different surgical techniques. In some hospitals, there is also a procedure known as 'cell salvage' in which the patient's own lost blood is carefully collected during surgery, filtered, and transfused back into them. In addition, pharmacologics (such as antifibrinolytics like tranexamic acid) and fibrin glues and sealants can play important roles in reducing blood loss at surgery.

To transfuse, or not to transfuse?

While there are still unanswered questions on how, when and why blood transfusions are carried out, there are medical situations in which a blood transfusion is the only option. And in these situations, it can make the difference between life and death and it is important that we don't lose sight of the fact that blood transfusions are still life-saving. The message is that while we don't want to scare people, there is a need for a precautionary approach. You shouldn't be doing something to a patient if there is no evidence of benefit. ***Primum non nocere***.

A recent review (Hare GMT, Cazorla-Bak MP, Ku M, et al: When to transfuse your acute care patient? A narrative review of the risk of anemia and red blood cell transfusion based on clinical trial outcomes. Can J Anesth, 7 Aug 2020, https://doi.org/10.1007/s12630-020-01763-9) emphasizes that the decision to transfuse RBCs is complex and depends on the interaction between multiple factors including the balance between the risk of anemia and the risk of RBC transfusion, existing patient comorbidities, and medical and surgical exposures. The transfusion thresholds recommended by current guidelines vary for medical and surgical patient populations. Guidelines suggesting specific transfusion thresholds for different patient groups (see page 31) should be viewed as a starting point for making informed decisions. Alternatives to transfusion (i.e. patient blood management), as outlined in this guide, should always be considered when considering the need for transfusion in the perioperative period.

Although blood transfusion may be essential, even life-saving, despite improvements in safety measures in blood procurement and manufacturing, donated blood has various risks with potential serious adverse events. In addition, it is a limited and expensive resource. PBM can help 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 thereby conserving limited donor blood for patients with the greatest need.

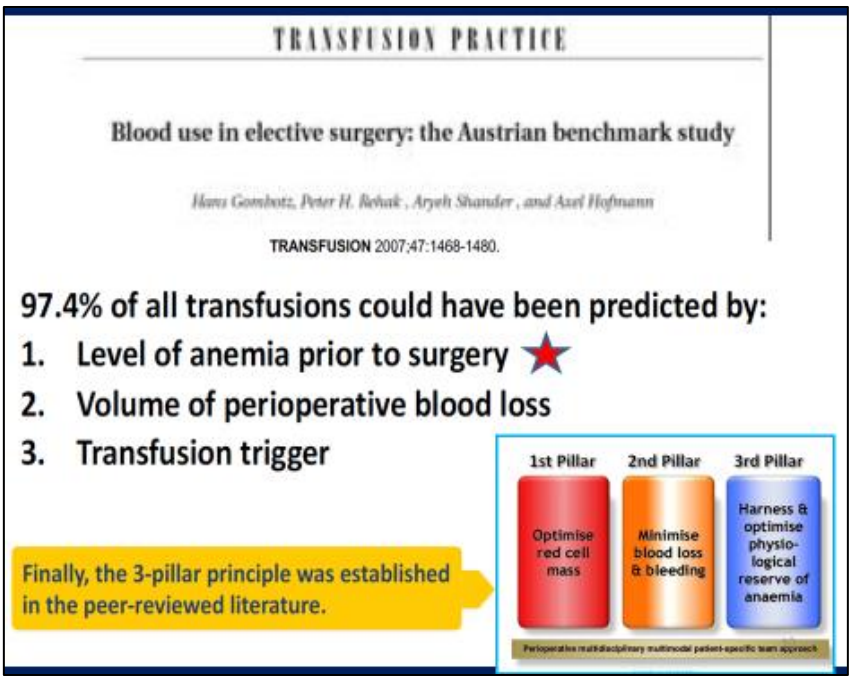
What is Patient Blood Management (PBM)?

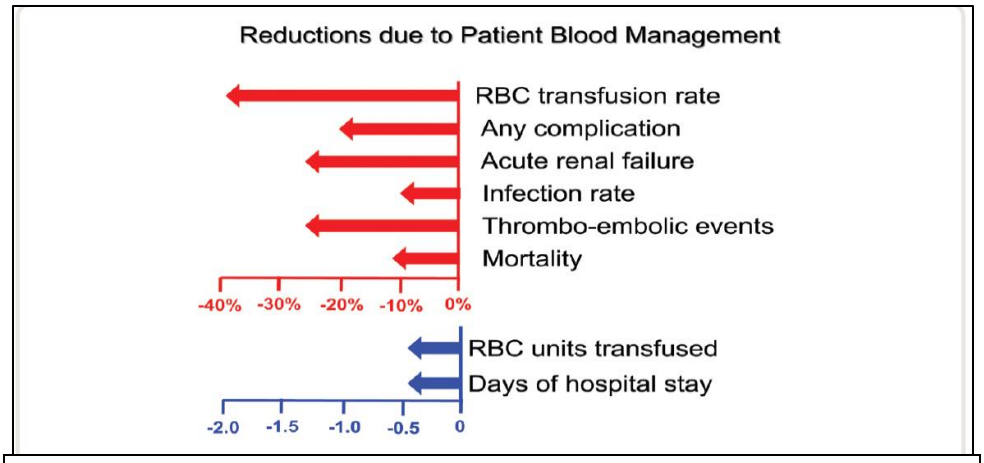
Patient Blood Management (PBM; also known as Blood Conservation or Bloodless Medicine/Surgery) is an evidence-based, multidisciplinary approach aimed at optimizing the care of patients who might need transfusion.[1-5] It puts the patient at the heart of decisions made around blood transfusion, promoting appropriate use of blood and blood components and the timely use of alternatives where available. PBM represents an international initiative in best practice for transfusion medicine.

In elective surgery, the principles of PBM have been described as the so called '3 pillars', namely:

- **Optimizing the patient's own blood (e.g. pre-operative optimization of hemoglobin and hemostasis)**
- **Minimizing surgical blood loss**
- **Optimizing the patient's physiological reserve in relation to anemia (including use of restrictive transfusion triggers)**

Comprehensive utilization of effective perioperative PBM includes, but is not limited to, meticulous surgical technique, perioperative cell salvage, acute normovolemic hemodilution (ANH), appropriate fluid management, and minimization of iatrogenic blood loss, and, importantly, management of anemia. There should be continuous postoperative assessment for development of bleeding, coagulopathy and anemia. The PBM model of care should include education and involvement of medical professionals, patients and their families. A clinical focus review of the effectiveness and future potential of PBM by Spahn DR et al can be found at Anesthesiology, 123:212-222, 2020.





In Spahn et al, Anesthesiology 133:212, 2020; from Althoff et al, Ann Surg 2019; 269:794-804.

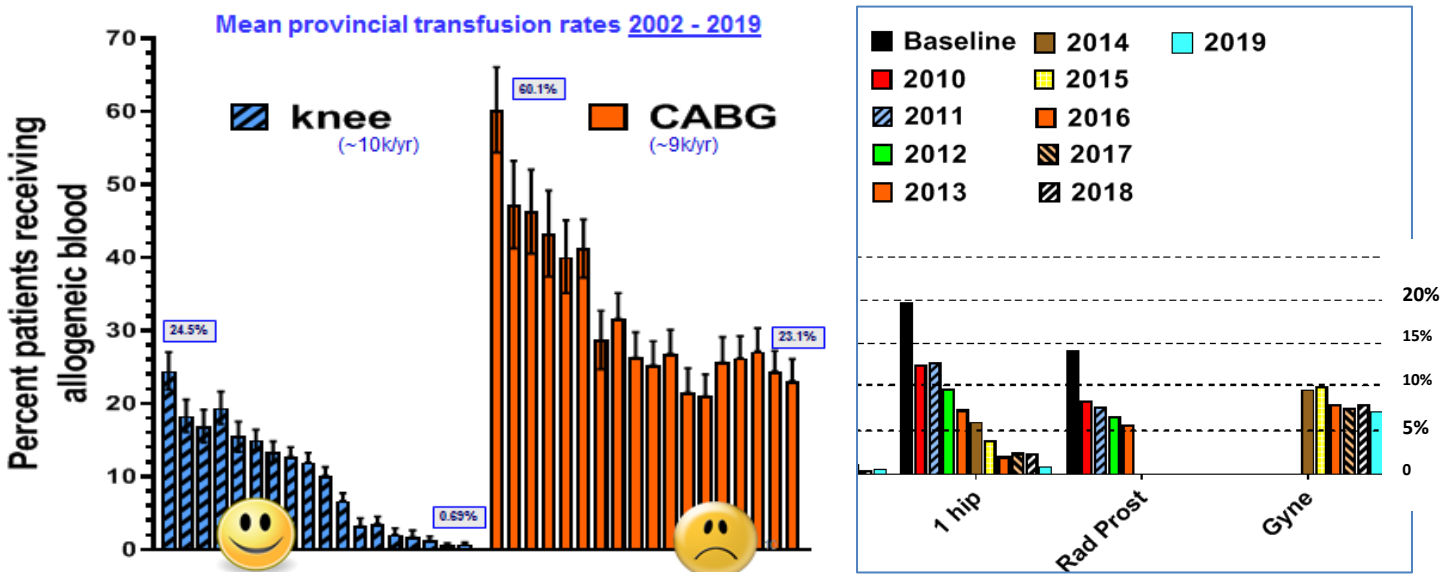
PBM practices are well known, until recently they have not been integrated into a universal standard of care. They are now, however, being increasingly recognized as the 'standard of care', particularly in the surgical setting. However the key principles of PBM apply not just to surgery, but to all patients who may need a blood transfusion (medical, obstetric, pediatrics), and to both elective and emergency clinical settings. The overall use of red cells is decreasing in many countries but large audits still show much inappropriate use. Greater scrutiny is also needed in relation to appropriate use of platelet and plasma transfusion. 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. By reducing the need for allogeneic blood transfusions and minimizing risks and unnecessary work, PBM can also reduce health-care costs.

The principles of PBM apply to **all** patients who may need transfusion!

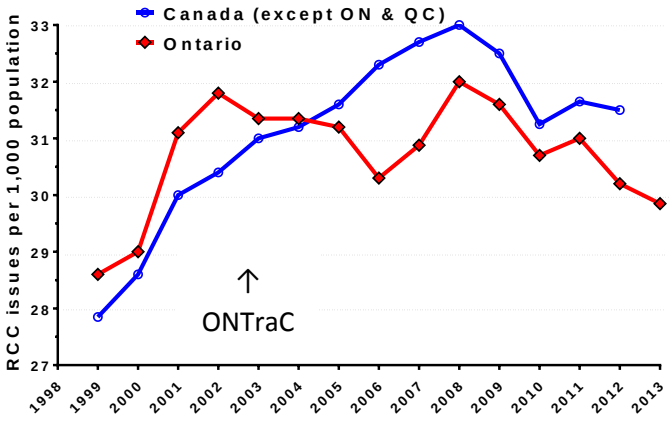
This guide focuses on red blood cell (RBC) transfusions.

Does PBM work?

Figure 1 below shows the reduction in provincial transfusion rates in Ontario in knee surgery and coronary artery bypass graft (CABG) surgery in the decade over which PBM has been implemented in 25 Ontario hospitals (ONTraC)[2-4]: Not only has there been a significant reduction in patients transfused, but those who are transfused are receiving less blood. Furthermore the initial marked inter-institutional variability has flattened out (not shown).



The Figure below shows the reduction in RBC use per thousand population in Ontario versus the rest of the country (excluding Quebec). Some of this effect was due, in part at least, to the PBM programs put in place since 2002.



Establishing and implementing a PBM strategy

PBM builds on strategies for good clinical transfusion practice and lessons from hemovigilance. It can be helpful to use established practice improvement frameworks, where these exist, and build on them to establish a PBM strategy. The World Health Organization (WHO) supports PBM and has identified a number of priorities for action at international, national and hospital level.[6] 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, and

active participation by patients. Active participation of patients in the planning, implementation and evaluation of PBM programs may be useful. At an operational level, the cornerstone of a PBM program is the multidisciplinary team.

General practitioners, surgeons, anesthetists, nurses, hematology/transfusion medicine 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.

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 information technology available to support PBM to collect blood usage data, support audit, computerized physician order entry (CPOE) systems
6. Audit and data collection – consider benchmarking internally and externally; feedback data to all relevant teams

How to implement and sustain a PBM program at your hospital

Develop a common vision which will determine the scope of the undertaking and should be tailored to the needs/capabilities of your organization. For example, you may be focusing on specific areas or on multiple areas such as decreasing overuse of RBC transfusions, improving preoperative anemia management, decreasing unnecessary phlebotomy, etc. It is important to gauge the priorities and concerns of individuals. Establishing common interests and a shared need for change is essential. 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 RBC transfusion
- The mortality associated with untreated anemic patients going for surgery (although you certainly do not want to send the message that transfusion is the desired treatment)
- The potential harm associated with iatrogenic anemia

Institutional support is critical to project success, as it provides access to the resources required to change current hospital culture and practices. Efforts should align with the hospital's mission and vision, while addressing issues identified as care delivery and operational priorities. The clinical rationale for improving anemia prevention and management is presented later in this Guide. A compelling business case can be made for improved anemia prevention and management that can help secure "buy-in" from the hospital's senior leadership.

PBM Healthcare issues that Impact both Cost and Quality

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 was the most frequently performed therapeutic

procedure in 2004[7] and it has been shown that a significant proportion of transfusions are inappropriate. In spite of the very high cost of transfusion (more than $200 M for Ontario for labile products), there is wide variation in practice that is not explained by patient characteristics, and it has been estimated that greater than 50% of all transfusions may be inappropriate.[8] Given this evidence of overuse and the associated cost in terms of both dollars and potential harm, regulators and professional societies have taken notice.

Effective practices targeting anemia prevention and management are increasingly seen as indicators of quality care. More recently, multiple societies have endorsed recommendations from the Choosing Wisely Campaigns that are directed at better anemia prevention and management. These include avoiding transfusions of red blood cells for arbitrary hemoglobin or hematocrit 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. Similar recommendations have come from the Canadian Choosing Wisely campaigns which have been endorsed by the Canadian Hematology Society and the Canadian Society of Transfusion medicine (CSTM). As healthcare financing becomes increasingly focused on paying for value, the business case for reducing costs by addressing overuse (e.g., transfusion, phlebotomy) becomes more compelling. A recent cost-benefit analysis of PBM by Meybohm P et al. Vox Sang, 115:182-188, 2020, shows significant savings with PBM.

Potential Impact on Hospital length-of-stay (LOS)

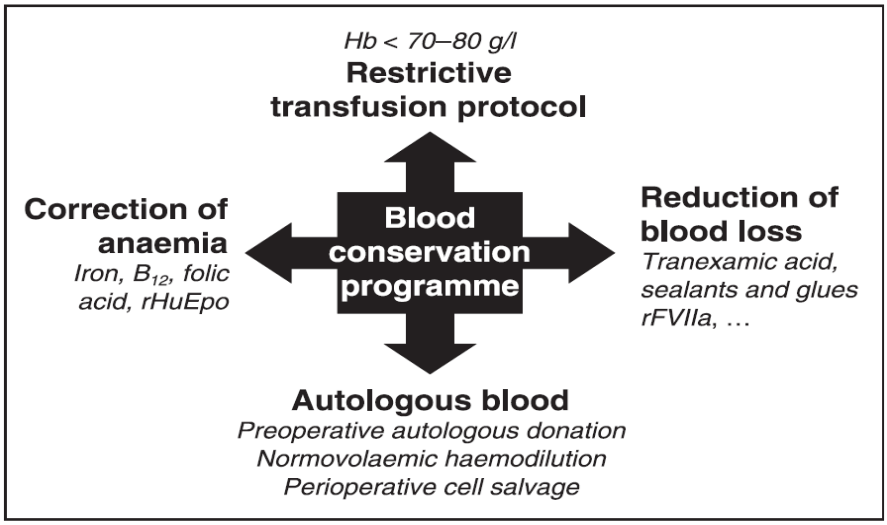
It is worth noting that both anemia and transfusion have been associated with increased LOS and that better prevention and management of anemia concomitant with decreasing transfusion may favorably impact LOS, which in turn may enhance patient turnover and increase the revenue per day for the organization. Although this might be a useful bullet point in a formal presentation, it should not be a primary selling point as it may be hard to deliver a measurable impact that is attributable to your efforts. The major impact is on patient risk management.

Opportunities for Expense Reductions — Decreasing Use of Red Blood Cell Transfusions

The direct cost of a unit of RBC has been estimated in an ORBCoN evaluation at about $450. But 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. A recent multicenter study estimated the cost of a transfusion at about $1100.[9] 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.

PBM offers an opportunity to, at the same time, enhance patient care, reduce costs, and conserve a valuable and scarce resource.

How can we do it? There may be many ways to achieve these ends:



While one PBM modality is beneficial, the use of multiple modalities in the patient confers significantly better effect.

Multimodal BC

	knee (N=1296)		hip (N=1216)	
	% Txed	(% in group)	% Txed	(% in group)
Any BC X 0	16.1%	(9.6)	18.9%	(14.1)
Any BC X 1	11.4%	(53.6)	15.4%	(49.0)
Any BC X 2	7.3%	(26.7)	6.6%	(26.4)
Any BC X ≥3	3.1%	(10.0)	7.9%	(10.6)

BC = a blood conservation measure

Pre-operative:

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

PAD

The use of PAD has diminished and it is rarely used today as the drawn blood is usually not used, it may render the patient anemic, and it is an unnecessary expense.[10] Rather let the patient serve as his/her own blood bank.

Anemia management

It is now clear that anemia is not just an innocent bystander [1]. In the critically ill, low hemoglobin (Hb) concentration, independent of red blood cell (RBC) transfusion, is associated with higher mortality and increase in length of stay [2].

Preoperative anemia evaluation and readiness for surgery

Anemia should be viewed as a serious and treatable medical condition, rather than simply an abnormal laboratory value, an 'innocent bystander' which can be easily managed with transfusion. Preoperative anemia, even when mild, is an independent risk factor that can increase perioperative morbidity and mortality. Anemia is an

independent risk factor for several unfavorable outcomes, including increased risk of hospitalization or readmission, prolonged hospital length of stay (LOS), loss of function, diminished quality of life and increased risk of morbidity and mortality.[11,12] It can also exacerbate the underlying chronic condition in a positive feedback loop that further increases patients' negative outcomes. Unfavorable outcomes independently linked to anemia include increased risk of surgical complications, infection, acute myocardial infarction, kidney injury, cancer progression and recurrence, stroke, mortality, and higher risk of subsequent admission to critical care unit.[12a] Finally, anemia is a leading (yet modifiable) risk factor for allogeneic blood transfusion and evidence of the harmful effects of unwarranted allogeneic blood is indisputable. 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 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, chronic gastrointestinal or genitourinary blood loss. Particular attention should be paid to anticoagulant and antiplatelet medications with a concrete plan of how to modify these therapies in the few days before surgery.

Laboratory testing with detection of anemia should include tests to determine its cause, in order to institute appropriate treatment. Common causes include iron deficiency, B12 deficiency, chronic kidney disease and anemia of chronic inflammation. Treatment may involve administration of oral or intravenous iron, erythropoiesis stimulating agents (ESAs), folate or vitamin B12. Referral to a specialist such as a hematologist or gastroenterologist may be necessary for patients with moderate to severe anemia or anemia of unclear etiology. For these patients, it is prudent to consider deferral of a truly elective surgical procedure to a later date, in agreement with the surgeon, until the patient is appropriately optimized.

In the absence of overt anemia, laboratory tests to evaluate iron stores can play an important role in patients with co-morbidities that are known to be 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. Optimization of iron storage may help to avoid post-operative anemia and/or the need for transfusions.

The results of preoperative anemia screening and the management plan should be communicated to the primary care practitioner and referring surgeon in a timely manner and patients who are treated for preoperative anemia should be followed in the postoperative period to ensure continued management of the anemia as appropriate.

Assessing the Risks of Anemia

Over the last three decades, RBC transfusion practice has come under more scrutiny and there has been an increased interest in the "tolerability" or risk of anemia. Anemia is common in critical illness and is independently associated with worse clinical outcomes. Similarly, in the general hospitalized population, individuals who develop either moderate (hemoglobin 9-11 g/dL) or severe (Hb <9 g/dL) hospital-acquired anemia have an increase in mortality (moderate OR 1.51; severe OR 3.28).[13] Carson et al[14] studied the risk of death and morbidity in Jehovah's Witness patients undergoing non-cardiac surgical procedures: they observed that even mild anemia was associated with increased mortality risk and this was substantially higher for individuals with cardiovascular disease. In a recent study of non-cardiac surgery, the adjusted 30-day mortality and morbidity was increased even in patients with mild anemia (hematocrit of 29-39% in men or 29-36% in women).

On the other hand, there is considerable evidence that low levels of hemoglobin can be tolerated in healthy subjects. Hematocrits of 10-20% have been achieved in animals using normovolemic hemodilution without untoward effects.[15,16] Similarly, studies in individuals with preserved left ventricular function undergoing coronary artery bypass grafting demonstrated that hemodilution to a target hematocrit of 15% was well tolerated.[17] Weiskopf et al induced normovolemic hemodilutional anemia to a hemoglobin concentration of 5 g/dL in healthy individuals prior to surgery as well as normal volunteers and found no evidence of reduced oxygen delivery associated with this acute anemia.[18] Similar data regarding the impact of anemia on surgical outcome comes from patients who refuse RBC transfusion: in these, patients, it has been observed that it is not until nadir hemoglobin concentration falls below 5 to 6 g/dL (50 to 60 g/L) that morbidity and mortality increases substantially.[19,20]

Assessing the tolerability or risk of anemia, either acute or chronic, has been made more difficult because recent clinical studies have focused on the risks and benefits of RBC transfusion and other interventions in anemic patients rather than risk of the anemia per se. While RBC transfusions may not be beneficial when the hemoglobin concentration is 7-8 g/dL, it is also clear that even mild degrees of anemia are associated with increase in risk across a broad range of clinical situations.

Preoperative optimization of hemoglobin

Anemia is defined by the World Health Organization as a hemoglobin level below 120 g/L in women and 130 g/L in men. Specific thresholds apply to pregnant women and children. A surgical procedure with a moderate or high blood loss will further aggravate the anemia and deplete iron stores. Early screening for preoperative anemia is necessary to allow time for diagnostic workup and for treatment to raise the hemoglobin concentration and reduce perioperative transfusion; this may be done by the surgeon or family physician as soon as prospective surgery is contemplated. The anemia should be classified and underlying cause identified and treated, if possible. Iron deficiency anemia is the most frequent type e.g. caused by bleeding, diet or malabsorption. Anemia of chronic inflammation (disease) is also frequent e.g. due to autoimmune disease or cancer, and is often seen in combination with iron deficiency. Other causes of anemia are hematologic disease, kidney failure, B-vitamin deficiency and hemolytic conditions, and some of these will be more amenable to treatment than others.

Patients with multiple preoperative risks, such as anemia in combination with anticoagulant treatment and a major surgical procedure may be at risk for intraoperative organ ischemia and/or massive transfusion and a complicated postoperative period. Patients, in whom anemia diagnosis reveals severe disease, may have to have their surgery postponed or cancelled. In other cases, performing the surgery quickly may be imperative, and further anemia management may have to be postponed. Therefore, a complete PBM plan should always include an individual risk assessment. Even though PBM should be tailored to the patient, algorithms for anemia management prior to specific procedures such as cardiac or orthopedic surgery are useful. See example algorithm below (page 21).

Summary of evidence base:

According to WHO limits, anemia prevalence increases with age to 10% of the general population above 65 years of age and >20% of above 85 years of age.[21] In the middle-aged population, anemia is associated with cancer, heart and kidney disease, and with increased long-term mortality,[22] even at hemoglobin concentrations well above WHO anemia definition. In the preoperative setting, 30% of patients undergoing major non-cardiac surgery are anemic. The prevalence of anemia in hospitalized patients ranges from what is normally seen in the general population to much

higher numbers, 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 substantially higher, with elderly patients and those with chronic conditions at increased risk. Also, 74% of hospitalized patients will develop a hospital-acquired anemia[13] with 95% of patients admitted to the intensive care unit (ICU) developing anemia by the third ICU day.

Hospital-Acquired Anemia (HAA)[12a]:

The etiology of HAA is complex and may include blood loss, shortened RBC life span and decreased RBC production. Decreased RBC production and anemia of inflammation is particularly important, characterized by hypoferremia and iron deficient erythropoiesis and involves elevated hepcidin and decreased erythropoietin levels.[12a] Another major component of HAA is iatrogenic, a direct result of diagnostic phlebotomy. Phlebotomy for diagnostic testing is common in the hospitalized patient and can result in iatrogenic anemia and RBC transfusion. This was highlighted almost 30 year ago with the coining of the term "Medical Vampires". In a study of critically ill patients, almost half of the variation in the amount of blood transfused was accounted for by diagnostic phlebotomy.

Forty years ago, Rosenzweig argued that the practice of blood draws in modern medicine should be called out for its similarities with the ancient ritual of blood-letting and its purported effects on cleansing and purifying the body.[12a] He observed that upon admission at his hospital, patients were automatically subjected to over 30 mL of blood draw for complete blood count (CBC) and serologic tests and laboratory tests were ordered daily even when no clinical changes were occurring. He noted that while clinicians appeared to have little interest in the relatively large amount of blood wasted through unnecessary laboratory testing, they would have aggressively intervened upon spotting much smaller amounts of bleeding from a patient's mouth or rectum.

Two separate studies have noted the average daily blood sampling volume in ICU was 41mL.[24,25] In one study this represented 17% of total blood loss in those admitted to ICU for more than three days. The use of micro sampling in ICU has been shown to reduce the volume of blood loss by 37 - 47%,[26] and can be associated with a significant reduction in blood transfusion.

Traditionally, when drawing blood from indwelling devices (such as arterial or central venous catheters), the initial sample used to clear the line is discarded. Having a process and device to re-infuse the initial blood taken to 'clear the line' (drawback blood) has been associated with a 50% reduction in diagnostic blood loss.[27]

A variety of approaches have been taken to reduce phlebotomy blood loss:

- Reduction of unnecessary blood testing has been identified as a Choosing Wisely recommendation. Only order essential blood tests and minimize the volume of blood drawn.
- An educational intervention focusing on unnecessary phlebotomy modestly reduced laboratory testing.
- Reduction of discarded blood volume using blood conservation devices can reduce blood loss as well as RBC transfusion; having a process and device to re-infuse initial blood loss from indwelling devices has been associated with a 50% reduction in diagnostic blood loss.
- The introduction of point-of-care testing could further reduce the volume of samples drawn.
- Noninvasive hemoglobin monitoring is now becoming more available and may be useful in decreasing blood loss for patients requiring frequent hemoglobin monitoring.
- The use of microsampling has been shown to significantly reduce the volume of blood loss and has been associated with a significant reduction in blood transfusion.

Implementing strategies to reduce iatrogenic blood loss in an organization requires strategic planning, communication and implementation with relevant stakeholders such as medical staff, laboratory and nursing staff.

Laboratory assessment of anemia

You need to establish if and when hemoglobin is measured (how many days or weeks before surgery). If anemia is systematically investigated weeks prior to surgery, you can go on to measure the effect of anemia treatment by checking hemoglobin levels immediately prior to surgery and the effect on perioperative blood transfusion.

TABLE 3. Surrogate Markers of Importance for Assessing Anemia Due to Either Possible Coexisting Iron Deficiency (IDA), Chronic Disease (ACD), or Both (IDA + ACD)

	Values Compared With Normal Range			
Laboratory Test	IDA	ACD	IDA + ACD	Comments
Iron	Low	Low	Low	
Transferrin	High	Low to normal	Low	
Ferritin	Low	Normal to high	Normal to high	<30 ng/mL quiescent disease; >30 ng/mL active disease
TSAT	Low	Low	Low	<16–20%; observe circadian variation
sTfR/log ferritin	>2	<1	>2	
MCV/MHC	Low	Low to normal	Low to normal	
Reticulocyte Hb content (CHr)	Low	Normal	Low	
Vitamins (folate, B_{12}, D)	Normal	Low to normal	Low to normal	
Acute-phase proteins	Normal	Normal to high	Normal to high	
Hepcidin	Low*	High	Low to high	*Might be undetectable in true iron deficiency even in the presence of inflammation

CHr = reticulocyte hemoglobin content; MCV = erythrocyte mean cell volume; MHC = mean cell hemoglobin concentration; sTfR = soluble transferrin receptor; TSAT = transferrin saturation.

If hepcidin testing is available, a high level may identify patients who will not respond to oral iron.

However, it is important to recognize that a patient may have iron deficiency without overt anemia and it may be useful to consider avoiding using hemoglobin to evaluate patients for iron deficiency in susceptible populations. Instead, use ferritin. Iron depletion is a progressive process with anemia as the final phase. Thus, screening for iron deficiency using hemoglobin (Hb) will only identify the most severe cases. Moreover, Hb is not specific for iron deficiency or iron deficiency anemia.

Serum ferritin is a measure of iron stores and is the most sensitive biomarker to test for early stages of iron deficiency as well as iron deficiency anemia. Sensitivity of ferritin test is 89% for diagnosis of iron depletion compared to hemoglobin, which is only 26%. Moreover, a ferritin cut off of ≤30 ng/mL provides 92% sensitivity and 98% specificity for iron deficiency anemia and is the best screening test for this disorder (American Society for Clinical Laboratory Science, June 10, 2020).

Evaluating patients for iron deficiency with ferritin will identify early stage iron deficiency and will potentially result in iron therapy, preventing iron deficiency anemia.

Ferritin is an acute phase reactant, and occasionally in inflammatory conditions, ferritin levels may be normal or elevated even in the presence of iron deficiency. Additional laboratory tests such as reticulocyte hemoglobin content (CHR or Ret-He), mean corpuscular volume (MCV), red cell distribution width (RDW), and additional iron studies such as percent transferrin saturation and total iron binding capacity, accompanying clinical correlation are also helpful to determine iron deficiency. C-reactive protein levels may help in diagnosing anemia of chronic disease/inflammation.

In some cases, other causes of anemia may also need to be ruled out e.g. hemoglobinopathy, vitamin B12 deficiency, etc.

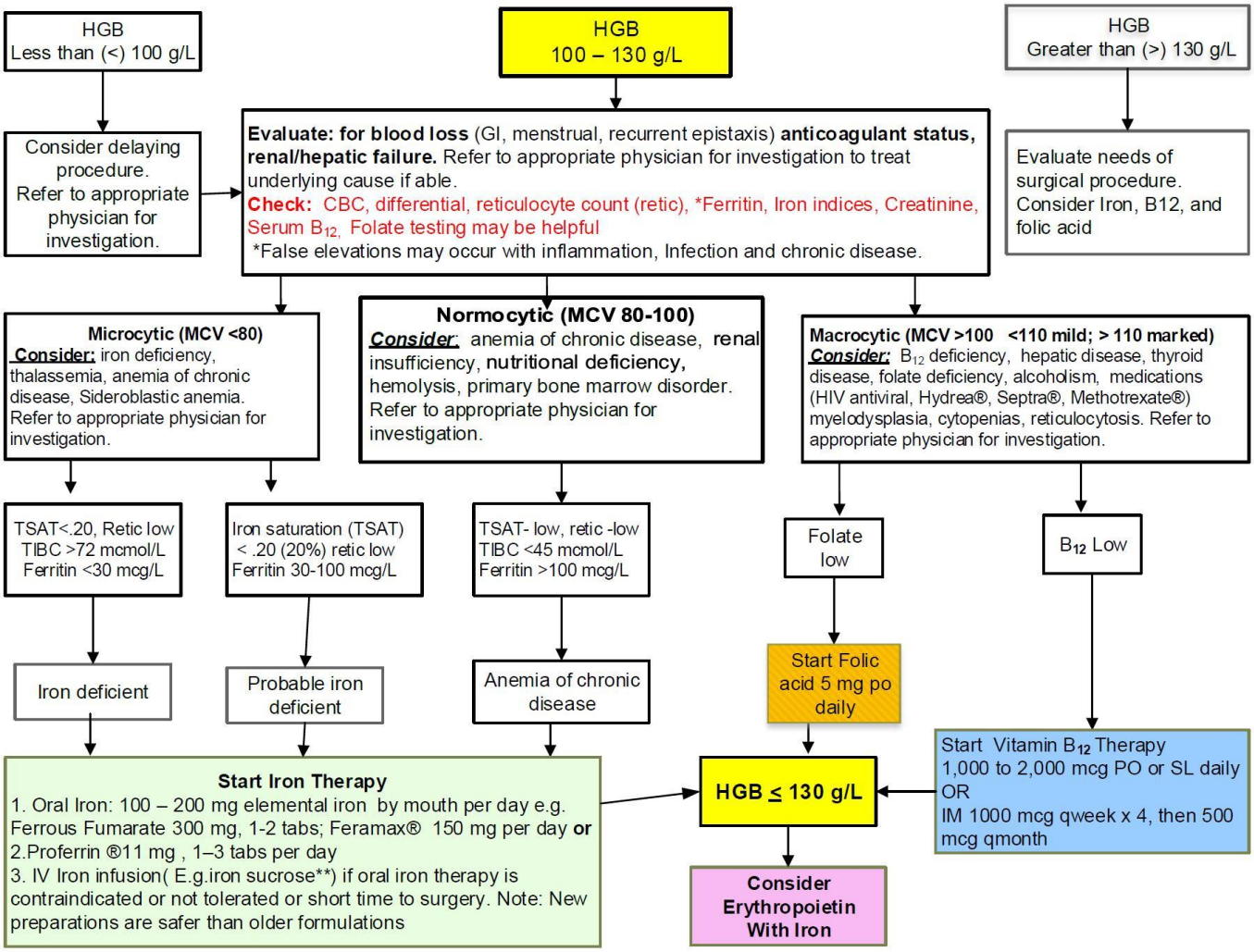
Preoperative Hemoglobin Optimization and Anemia Management

Goal: Transfusion avoidance in adult surgical patients

Risk Factors for Transfusion: Hemoglobin (HGB) less than (<) 130 g/L, weight less than 65 Kg, elderly, female, complex or repeat surgical procedure, renal insufficiency (creatinine clearance <40 ml/min), antiplatelet agents, anticoagulants, some supplements

Transfusion Avoidance Strategies: Early assessment (28 days before surgery) and evidence based, coordinated interventions as required.

Interventions must take into consideration age, gender, anticipated surgical blood loss and pre-existing medical conditions.



Epoetin Alfa (Erythropoietin)** HGB optimization using erythropoietin: **USUAL** target is HGB 130 g/L, **MAXIMUM** target in renal and oncology patients to less than 120g/L. Patients with pre-existing thrombotic events should be monitored closely.

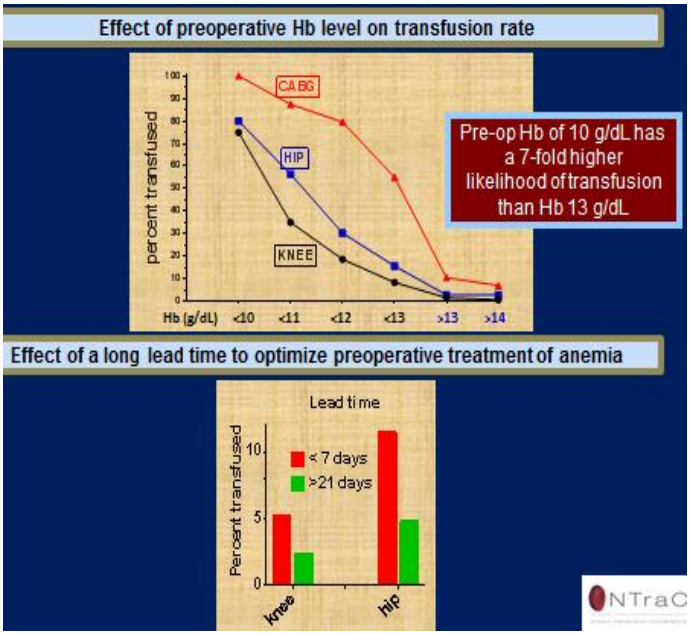
Standard Dosing: Epoetin Alfa 20,000 – 40,000 units subcutaneously (600 units/kg) weekly to a maximum of 4 doses depending on presenting hemoglobin and time to surgery.

Short dosing schedule is available for urgent cases: Epoetin Alfa 300 IU/kg given for 10 consecutive days prior to surgery, on the day of surgery, and for four days immediately thereafter.

****May be Accessed in Ontario through** Third party provider or Ontario Drug Benefits Plan (Exceptional Access Program, Trillium)

Developed by Ontario Transfusion Coordinators (ONTraC), the Patient Blood Management initiative funded by the Ministry of Health and Long Term Care of Ontario 2007, Revised 2012, 2013, 2016

www.ontracprogram.com



Anemia management

Anemia is often ignored or inappropriately treated with transfusion, but it can be treated effectively; it is a modifiable and preventable risk factor. Early detection and treatment can reduce or eliminate anemia-related risks. Strategies span a wide array of approaches, including various hematinics, management of underlying causes and preventive measures, such as minimization of blood loss, which could be as conspicuous as surgical hemorrhage, or as mundane as unnecessary phlebotomy.

As shown in the Figure to the left, data from ONTraC shows that the likelihood of receiving a transfusion increases exponentially when the hemoglobin falls below 13 g/dL (130g/L). 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 hemoglobin level, the less likely the patient is to receive a transfusion. Lead time is necessary for the anemia treatment. The Figure also shows that a longer lead time (green bars) results in fewer transfusions. We try to get to see the patient at least 3-4 weeks prior to surgery. Family physicians can play an important role in anemia management (see our Family Physician initiative on page 72-75).

One Swiss approach to anemia management is shown below.

Table 2. Anemia Management Algorithm of the University Hospital of Zurich, Switzerland

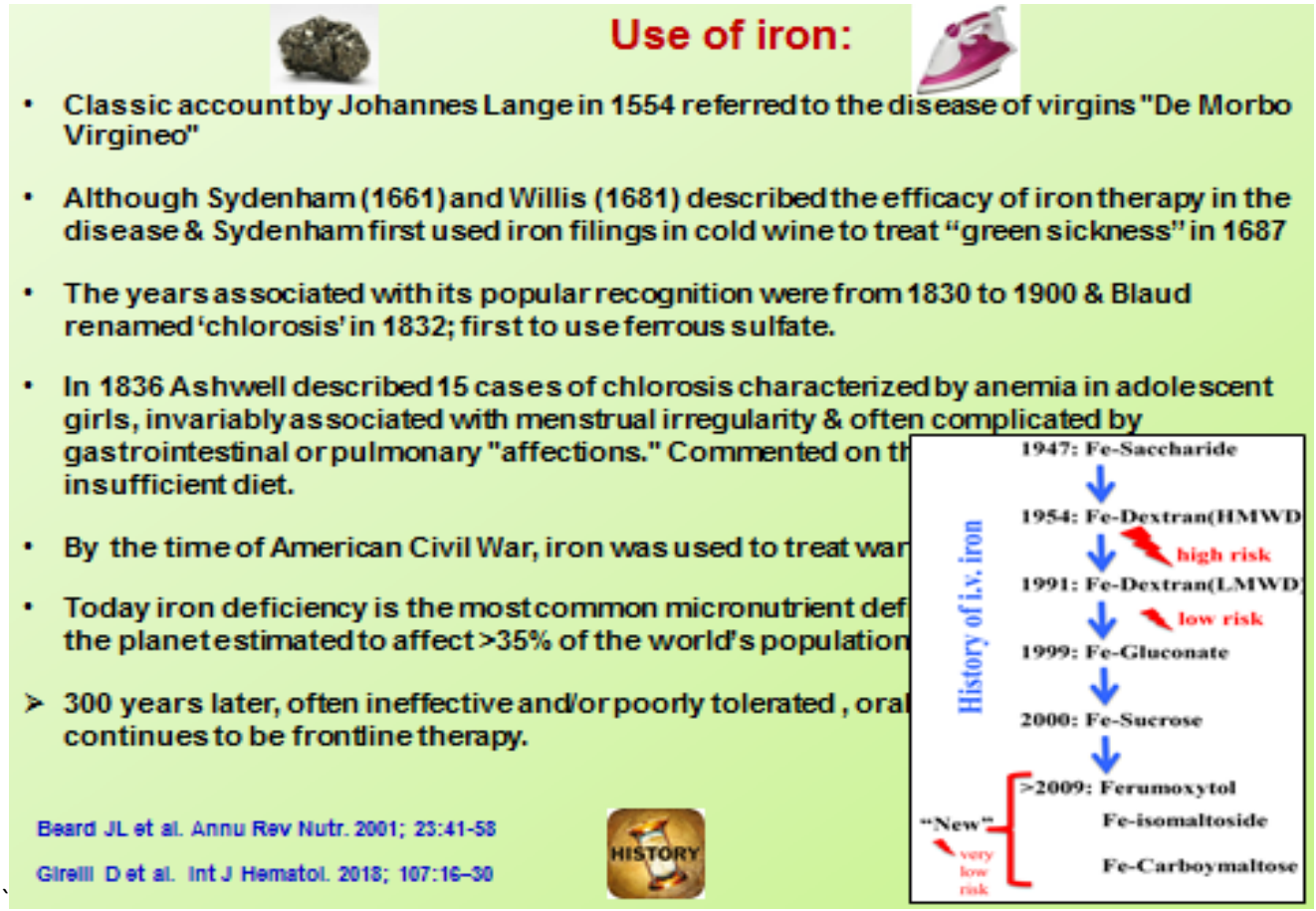
Condition						
Hb*	**Ferritin**		**TSAT**	**CCL**	**CRP**	**Treatment**
Hb < 130 g/l	< 100 ng/ml	or	< 20%	≥ 50 ml/min		IV iron: 20 mg/kg†‡ SC vitamin B12: 1 mg§ PO folic acid: 5 mg‖
Hb < 130 g/l	≥ 100 ng/ml	and	≥ 20%	< 50 ml/min		SC epoetin alpha 600 U/kg BW# IV iron: 20 mg/kg† SC vitamin B12: 1 mg§ PO folic acid: 5 mg‖
Hb < 130 g/l	≥ 100 ng/ml	and	≥ 20%		> 5 mg/l	SC epoetin alpha 600 U/kg BW# IV iron: 20 mg/kg† SC vitamin B12: 1 mg§ PO folic acid: 5 mg‖
Hb ≥ 130 g/l	< 100 ng/ml	or	< 20%			IV iron 20 mg/kg†

*Applies to women and men. †With some IV iron preparations maximum dose limitations need to be respected. ‡If time to surgery is less than or equal to 5 days, add SC epoetin alpha 600 U/kg BW. §Indicates some vitamin B12 formulations may be administered intramuscularly. ‖Indicates until day of surgery. #Usually, total dose is limited to 40,000 U.

BW, body weight; CCL, creatinine clearance; CRP, C-reactive protein; Hb, hemoglobin; IV, intravenous; PO, by mouth; SC, subcutaneous; TSAT, transferrin saturation.

Spahn DR et al. Anesthesiology 133:212-222, 2020.

Iron therapy



The purpose of anemia treatment is to raise the hemoglobin concentration before surgery. Treatment should be directed against the cause of the anemia. In iron deficiency anemia and in functional iron deficiency, hemoglobin can be raised with iron alone or in combination with erythropoiesis-stimulating agents. Iron can be administered orally, which is cheap but takes time to work. Between 10-30% of the patients on oral iron have gastrointestinal side effects, which may reduce compliance with treatment. Inflammation inhibits gastrointestinal absorption and reticuloendothelial release of iron for erythropoiesis, so tablets may not be useful in anemia of chronic disease.

Iron therapy may be used as a primary treatment for anemic or non-anemic iron deficiency (including sub-optimal iron stores prior to surgery), or to augment the response to ESAs. Iron can be given in oral or intravenous forms (see Tables below).

Intravenous iron is more expensive but may increase hemoglobin levels in 2-4 weeks, depending on the pre-treatment hemoglobin level. Intravenous iron bypasses gastrointestinal absorption and may increase hemoglobin levels in patients with anemia of chronic disease, even as a sole therapy. Side effects are few and generally mild, but rare cases of anaphylaxis are seen, although the newer preparations have fewer significant adverse effects. Older preparations of iron for intravenous administration (e.g. high molecular weight iron dextran) were associated with a risk of anaphylactic reactions. However, studies performed in recent years with newer preparations have reported favorable tolerability. While currently available intravenous iron preparations are much safer than previous, the possibility of adverse events such as hypotension, arthralgia, abdominal discomfort and back pain remains. One meta-analysis suggested an increase in infection rates with intravenous iron,[28] but there are no prospective data to confirm this.

Intravenous iron may provide a greater increase in hemoglobin concentration than oral iron. In a randomized, prospective study,[29] women with anemia caused by menorrhagia were treated with intravenous iron sucrose or oral iron protein succinylate daily. Treatment was administered during the 3 weeks before elective surgery, and a significantly greater increase in hemoglobin concentration was observed in the intravenous group (3.0 vs. 0.8 g/dL). One study in gynecological cancer showed a 64% reduction in RBC transfusion in patients treated with IV iron compared to those who received oral iron.[30]

In surgical patients, iron therapy is recommended for patients with or at risk of iron deficiency and for those with suboptimal iron stores. In patients with iron deficiency anemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated. Iron therapy is recommended for patients with or at risk of iron deficiency and for those with suboptimal iron stores. When dosing iron, the expected surgical blood loss should be included in the dose calculation. Oral iron therapy may be suitable and effective in many patients. Studies have reported that preoperative oral iron supplementation is effective in raising hemoglobin concentration, and decreases perioperative transfusion by 50-82%.[31] Intravenous iron should be considered for patients whose surgery cannot be delayed, or if oral iron is contraindicated or not tolerated. Studies of intravenous iron sucrose, administered preoperatively to patients scheduled for major surgery, have shown a significant increase in hemoglobin concentration, resolving anemia in up to 58% of patients in one study.[31] Preoperative intravenous iron can reduce transfusion among patients undergoing surgery for trochanteric hip fracture by 33%.[31] However, in contrast, a randomized controlled trial in patients undergoing colorectal cancer resection reported that intravenous iron administered 14 days before surgery had no impact on hemoglobin concentration in comparison with placebo, and no impact on transfusion rates.[31] Oral iron therapy is generally not recommended in the early postoperative period as it is not clinically effective due to reduced absorption associated with the acute inflammatory response post-surgery.

In medical patients with iron deficiency anemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated. In patients with chronic heart failure (CHF), identification and treatment of iron deficiency (functional and absolute) has been shown to reduce symptoms and improve submaximal exercise tolerance and quality of life. In patients with cancer, the etiology of anemia is often multifactorial, and appropriate reversible causes should be identified and treated. It should be noted that iron deficiency and iron deficiency anemia are major public health problems worldwide, especially in young women – a recent review of the latter is “Oral iron supplementation in iron- deficient women: how much and how often” by Stoffel et al, Molecular Aspects of Medicine, in press 2020, https://doi.org/10.1016/j.mam.2020.100865

In addition to primary treatment for anemic or non-anemic iron deficiency, adjunctive iron is necessary to augment the response to ESAs. When administered with ESAs, iron therapy prevents both absolute and functional iron deficiency and minimizes the dose of ESA needed to achieve target Hb concentrations.

Patients should be provided with information brochures about oral or intravenous iron therapy.

Iron deficiency treatment should be considered when:

- Microcytic hypochromic RBCs on blood film; low mcv, mch, mchc (although other etiologies may apply)
- Transferrin saturation less than 20% in the setting of a patient with malignancy
- In patients with total iron deficit greater than 1 gram, if the ferritin is less than 100 ng/ml and the transferrin saturation less than 20% (NOTE that transferrin is an acute phase reactant and may be increased in inflammatory conditions)

- For iron deficiency as demonstrated by a decreased transferrin saturation and/or ferritin in pregnancy and within 8 weeks after delivery
- Any patient being treated with an ESA
- Patients with obesity and post-bariatric surgery

When choosing an iron supplement, instead of looking at the overall strength (or weight), look at the amount of elemental iron. Elemental iron is the amount of iron available for absorption. For example, an iron supplement may read "300 mg" on the container, but only contain 60 mg of elemental iron.

To ensure the body absorbs as much iron from the supplement as possible it should be taken on an empty stomach (if tolerated) or with foods that are high in vitamin C, which has been found to enhance iron absorption (this is not necessary, however, when taking an iron supplement formulated with polysaccharide-iron complex or heme iron polypeptide).

TABLES OF ORAL AND OF INTRAVENOUS IRON PREPARATIONS

Oral iron therapies:

Oral Iron	Strength per Capsule/Tablet	Elemental Iron per Capsule/Tablet	Heme Iron/Non-Heme Iron	Ionic/Non-Ionic
Polysaccharide-Iron Complex (eg. FeraMAX® 150)	150 mg	150 mg	Non-heme	Non-Ionic
Ferrous fumarate (eg. Palafer® & generics available)	300 mg	100 mg	Non-heme	Ionic
Ferrous sulphate (generics available)	300 mg	60 mg	Non-heme	Ionic
Ferrous sulphate dried sustained-release (eg. Slow-Fe®)	160 mg	50 mg	Non-heme	Ionic
Ferrous gluconate (generics available)	300 mg	35 mg	Non-heme	Ionic
Heme-Iron Polypeptide (eg. Proferrin®)	11 mg	11 mg	Heme	N/A

Anemia Guidelines for Family Medicine, 3rd Edition, 2014 (page 8)

New alternative oral iron preparations appear frequently on the market (e.g. Optifer, Ferrous Ascorbate Iron EBMfer) and individual preferences and costs should be considered.

Note: Recent evidence suggests that alternate day treatment with oral irons may result in better absorption than daily administration.

Some characteristics of intravenous iron preparations:

	Non-Dextran				Dextran/Modified Dextran	
	Monoferric (iron isomaltoside)	**Injectafer** (ferric carboxymaltose)	**Venofer** (iron sucrose)	**Ferrlicit** (Na ferric gluconate complex)	**INFeD** (iron dextran)	**Feraheme** (ferumoxytol)
Single dose	Usually 1000 mg Comes as 100 mg/mL in 1, 5, 10 mL vials	750 mg (2 doses separated by at least 7 days)	100-400 mg depending on indication	Maximum dose should not exceed 125 mg per dose	Individual doses of 100 mg or less may be given on a daily basis	Initial 510 mg dose followed by 510 mg 3 to 8 days later
Recommended cumulative dose	1000 to 2000 mg dependent on Hb and body weight – see product monograph	Total cumulative dose not to exceed 1500 mg of iron per course	Usual total treatment course is 1000 mg	Most patients may require cumulative dose of 1000 mg	Ranges based on the calculated iron requirement for each patient	1020 mg
IV infusion rate	Over 20 minutes – see product monograph	Over at least 15 min	Over 15 min to 2.5 hrs, depending on dose	Over 1 hr	NA	Over at least 15 min
Test dose required	No	No	No	No	Yes	No
MRI interference	?	No	No	No	No	Yes (for up to 3 mos)

The product monographs should be consulted before using IV irons. Note transient hypophosphatemia may occur.

Erythropoiesis stimulating agents (ESAs)

Erythropoiesis stimulating agents (ESAs; e.g. Eprex, Darbopoietin) boost the production of red blood cells and as such may play a role in optimizing red cell mass in specific groups of patients. Routine use of ESAs is not recommended for cancer patients or in the critically ill.

ESAs have been recommended or suggested in:

- patients with Chronic Kidney Disease (CKD) and anemia to avoid transfusion and relieve fatigue. In patients with CKD, ESAs to target a hemoglobin level of greater than 110 g/L increases the risk of serious adverse cardiovascular events and has not been shown to provide additional patient benefit.
- surgical patients with anemia of chronic disease (Eprex is the preferred - and more effective - product for PBM)
- anemia of HIV/AIDS

Where an ESA is used, it must be combined with iron therapy. Patients should receive antithrombotic therapy post-op.

In 2011, the U.S. Food and Drug Administration (FDA) and Health Canada informed healthcare professionals of modified recommendations for more conservative dosing of ESAs in patients with CKD to improve the safe use of these drugs. This was because of data showing increased risks of cardiovascular events (stroke, thrombosis and death) with ESAs in this patient population. WARNING: ESAs MAY INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE. Prior warnings existed for use in cancer patients and in the perisurgical setting. However, flaws in the studies responsible for the warnings have been pointed out and the extensive use of Eprex in the perisurgical setting has not in general been associated with an increase in adverse events.

Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a hemoglobin level of greater than 110 g/L.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- In anemic patients with CKD, ESA therapy to a low to intermediate Hb target may be used to avoid RBC transfusion , and/or to relieve fatigue, after consideration of risks and benefits for the individual patient. A target Hb >130 g/L is not recommended because of increased morbidity. While a Hb target between 100-115 g/L has been recommended, the FDA warning advises that using ESAs to target a hemoglobin level of greater than 110 g/L increases the risk of serious adverse cardiovascular events and has not been shown to provide additional patient benefit.
- In anemic patients with non-dialysis dependent CKD, type 2 diabetes and a history of malignancy, the routine use of ESAs is not recommended because of the increased risk of cancer-related mortality.
- Use the lowest ESA dose sufficient to reduce the need for RBC transfusions.

Cancer:

- ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.
- Because of these risks, prescribers and hospitals should enroll in and comply with a required ESA protocol.
- In cancer patients with anemia, the routine use of ESAs is controversial because of the increased risks of mortality and thromboembolic events. If ESAs are used, iron status should be evaluated to guide adjuvant iron therapy
- To decrease risks use the lowest dose needed to avoid RBC transfusions.
- Use ESAs only for anemia from myelosuppressive chemotherapy.
- Discontinue following the completion of a chemotherapy course.

Perisurgery (Eprex/Procrit only):

- In surgical patients with anemia of chronic disease (also known as anemia of inflammation), ESAs may be indicated.
- Where indicated, it must be combined with iron therapy.
- International guidelines recommend ESAs for orthopedic surgery patients with anemia, in whom nutritional deficiencies are absent or have been corrected.
- FDA Boxed Warnings and local Product Information advise use of DVT prophylaxis in the peri-surgical setting.
- Target Hb should not exceed >130 g/L.
- A common dosing schedule is 40,000 IU weekly X 3-4. An alternative is administration of Eprex daily X 10.
- Eprex is somewhat costly at about $500 per dose. While some patients are able/willing to pay for this, many in Ontario have private insurance which will cover the costs. For patients over the age of 65, application can be made to the Ontario special access to drugs program -- note that all required information MUST be provided and the process may be sometimes protracted, so early application is recommended. The same may apply for intravenous iron therapy. The Trillium program may pay for the drug for patients that qualify.
- A local clinical guideline for indications, dosage, administration and monitoring would be useful.

ESAs in chronic heart failure

- There is some evidence of reduced mortality with ESA therapy in a group of patients with diabetes and congestive cardiac failure. In a systematic review the incidence of thromboembolic events, mortality and heart failure-related hospitalizations were not affected by ESAs[32] but there was a significant improvement in exercise tolerance.

ESAs in critically ill patients

- ESAs should not be routinely used in critically ill anemic patients. This recommendation is based on the lack of effect of ESAs on mortality in a heterogeneous population of critically ill patients.

Suggested dosing of EPO (Proceedings from the SABM Annual Meeting 2017: Management dilemmas of the surgical patient when blood is not an option. Tan GM, Guinn NR, Frank SM, Shander A.)

Etiology of anemia	Elective surgery > 3 weeks	Elective surgery < 3 weeks
ACD with normal iron stores (ferritin > 100 ng/mL, iron sat >20%)	EPO 600 U/Kg SC weekly starting 21 d before surgery; oral iron	EPO 300 U/Kg SC daily starting 10d before surgery and up to 4 d postop; oral (or IV) iron
ACD with low iron stores (ferritin > 100 ng/mL, iron sat >20%)	EPO 600 U/Kg SC + IV iron weekly starting 21d before surgery	EPO 300 U/Kg SC daily + IV iron starting 10d before surgery and up to 4 d postop
Iron deficiency anemia (ferritin < 20 ng/mL)	IV iron 1000 mg	IV iron 1000 mg

Recent potentially useful references on anemia management include Shander A, Kaufman M, Goodnough LT: How I treat anemia in the perisurgical setting. Blood 13 August 2020, 136:814-822; Gilreath JA, Rodgers GM: How I treat cancer-associated anemia. Blood 13 August 2020, 136:801-813; Mistry R, Upchurch C, Locantore-Ford P: Hemoglobin optimization prior to cardiac surgery results in improved patient outcomes. Blood 134(Suppl 1):4989, November 13, 2019.

Family physician initiative

Treatment of anemia should be implemented as early as possible. To this end, we have recently implemented an initiative to involve Family Physicians/General Practioners in the early diagnosis of anemia when surgery is first contemplated, offering referral to the ONTraC transfusion nurse (see pages 72-75)

Restrictive transfusion approach

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. PBM Guidelines support restrictive transfusion and a single unit transfusion guideline 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 RBC transfusion should be an independent clinical decision based on the risk, benefits and alternatives. Transfuse to alleviate patient signs and symptoms of anemia. Where transfusion is indicated, a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. This reassessment will also guide the decision on whether to retest the hemoglobin level. Each unit of RBCs will raise the hemoglobin concentration in an average sized adult by approximately 10 g/L.

Why single-unit RBC transfusion:

Transfusion is a live tissue transplant. Risks associated with transfusion are dose dependent.[2,33,34] Studies in coronary artery bypass graft patients have shown that RBC transfusion was 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. Each unit of RBCs transfused was associated with incrementally increased risk for adverse outcome. The Transfusion Requirements After Cardiac Surgery (TRACS) study showed that the number of transfused red blood cell units was an independent risk factor for clinical complications including respiratory, cardiac, renal and infectious complications and for death at 30 days.[35] Berger and colleagues[36] changed from a double to a single-unit red blood cell transfusion policy in patients with hematologic malignancies receiving intensive chemotherapy or hematopoietic stem cell transplantation resulting in a 25% reduction in RBC usage, equating to 2.7 RBC units, per therapy cycle; overall survival was similar in both cohorts. Ma et al used retrospective data to examine the impact of using single unit transfusions in an institution with a high rate of at least 2-unit RBC transfusions and estimated that RBC savings of between 0.21 and 0.82 RBC units per transfused patient.[37]

- Single-unit dosing has been proven safe when applied together with a restrictive transfusion trigger in a number of randomized controlled trials. Transfusion of one unit should be followed by a clinical or laboratory assessment of the patient to review if transfusion therapy is adequate or more units are needed.
- Transfusion of two or more RBC units in succession is associated with an increased risk of pulmonary edema or transfusion-associated circulatory overload (TACO), especially in the elderly, females and patients with heart or kidney failure, or a positive fluid balance.
- 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.
- If one unit of RBC is given to an anemic and otherwise stable patient, this is a single-unit transfusion provided that no further units are given until seeing a post-transfusion hemoglobin, or stating a new clinical transfusion indication, or within 24 hours after transfusing the first RBC unit.
- RBC transfusion is inappropriate therapy for iron deficiency anemia unless there is acute bleeding or symptoms of acute physiological stress due to compromised oxygen delivery.

- For patients who are chronically transfused with RBC, there are no randomized studies to guide threshold or dosing scheme. Transfusion treatment should be tailored individually, based on a clinical decision and the patient's response to previous transfusions.

Single-unit RBC transfusion was standard care in the majority of RCTs comparing liberal to restrictive transfusion in circulatory-stable patients with anemia. These studies form the evidence base for RBC transfusion in these patient populations, and therefore when translating these findings into daily practice, both hemoglobin trigger and RBC dose should be followed. Moreover, some of the RCT studies and meta-analysis of RCT data have shown that even with a single-unit dose, liberal transfusion is still associated with higher frequency of pulmonary edema or TACO, compared with the restrictive regime. This indicates that either the higher number of units transfused to patients in the liberal arm or the higher hemoglobin level reached in this way increases the risk for Transfusion Associated Circulatory Overload (TACO). TACO is among the highest risks associated with RBC transfusion, estimated at up to 1 in 100 per unit transfused; this is of particular concern in patients with chronic heart failure.[38,39] Observational studies have found that the risk of TACO increases with every RBC unit transfused, that passive reporting greatly underestimates the frequency of TACO, and that TACO may increase morbidity and mortality. Accordingly the introduction of a single-unit regime is generally encouraged to avoid TACO, and, in patients with cancer or hematological malignancy, a single-unit regime has not been associated with adverse effects (non-randomized studies).

Transfusion therapy in severely bleeding patients should follow separate guidelines/evidence.

Platelets and plasma single-unit transfusion

- The principle of avoiding over-transfusion through routinely ordering more than one unit in the non-bleeding patient also applies to platelets and plasma. However there is limited evidence to support a fixed number of units, as platelets and coagulation factors may be removed or consumed in various non-bleeding clinical conditions, e.g. in the presence of platelet antibodies, sepsis or disseminated intravascular coagulation.
- Platelet transfusion should be guided by the clinical indication, platelet count and functional platelet tests, as recommended by guidelines for specific patient populations.
- Plasma transfusion should be guided by clinical indication and pre- and post-transfusion coagulation tests and/or point-of-care whole blood functional assays according to evidence and guidelines.

Restrictive transfusion: threshold/trigger

Restrictive transfusion thresholds (triggers) are an effective method of reducing and conserving RBC use.[40] RBC transfusion should not be dictated by a hemoglobin 'trigger' alone, but rather based on assessment of the patient's clinical status. Where indicated, transfusion of a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. While PBM Guidelines provide guidance on Hb 'triggers' this should always be in the context of the patient's clinical status.[41]

Supporting evidence for a restrictive transfusion practice

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. In a systematic review of 45 observational studies with 272,596 participants,[42] RBC transfusion was associated with increased morbidity and mortality. A Cochrane systematic review[43] compared "high" versus "low" hemoglobin thresholds in 19 prospective, randomized trials involving 6,264 patients. The authors found that "low" hemoglobin thresholds were well-tolerated and that RBC transfusions were reduced by 34%, with a mean reduction of 1.2 RBC units in the "low" hemoglobin cohort. A subsequent meta-analysis from trials with 2,364 participants found that a restrictive RBC transfusion strategy (targeting a Hb transfusion trigger <7 g/dL) was accompanied by reduced cardiac events, re-

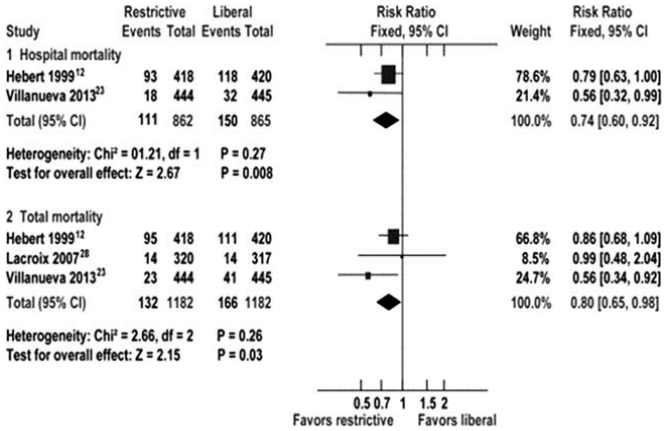
bleeding, bacterial infections and mortality.[44] When 19 trials from the primary (Hb <7 g/dL) and secondary (Hb >7 g/dL) analyses for restrictive transfusion strategies were pooled together, the restrictive strategy was still associated with a significant reduction in hospital mortality, 30-day mortality, pulmonary edema, bacterial infections and re-bleeding.[44]

Important relevant studies supporting restrictive transfusion strategies include: TRICC, a large multicentre randomized, controlled trial comparing a restrictive (Hb < 70 g/L) to a liberal (< 100 g/L) RBC transfusion strategy in ICU patients found no difference in 30-day mortality regardless of the Hb threshold employed.[45] TRACS, a large single unit, prospective, non-inferiority, randomized, controlled trial comparing a restrictive (HCT ≥ 24%) to a liberal (≥ 30%) RBC transfusion strategy in cardiac surgery patients found non-inferior rates of the combined 30-day all-cause mortality and severe morbidity in the restrictive group.[46] FOCUS, a large, randomized, controlled trial comparing a restrictive (Hb < 80 g/L) to a liberal (< 100 g/L) RBC transfusion strategy in hip fracture surgery patients found that a liberal transfusion strategy did not reduce rates of death or inability to walk independently on 60-day follow-up or reduce in-hospital morbidity in elderly patients at high cardiovascular risk.[47,48] A large randomized controlled trial comparing restrictive (Hb < 70 g/L) to a liberal (Hb < 90 g/L) RBC transfusion strategy in patients admitted with gastrointestinal bleeding, found that a restrictive strategy significantly improved patient outcomes, including significantly lower mortality at 45 days, lower risk of death in some patient subgroups (e.g. cirrhosis, peptic ulcer), lower rates of further bleeding, lower rates of rescue therapy, lower overall complication rates, and shorter length of hospital stay. 51% of patients in the restrictive strategy group did not receive a transfusion, compared with 14% in the liberal group; the mean number of units transfused was significantly lower in the restrictive group.[49] The Cochrane review, found that restrictive transfusion strategies reduced the risk of receiving a RBC transfusion by 39%, reduced the volume of RBCs received, did not impact on the rate of adverse events or reduce functional recovery, hospital or ICU length of stay, and were associated with a statistically significant reduction in hospital mortality (but not 30-day mortality).[43] The TRICSIII trial (Mazer CD et al, NEJM 2017; 377:2133) similarly showed in patients undergoing cardiac surgery at moderate-to-high risk for death, a restrictive strategy was noninferior to a liberal strategy with respect to the composite outcome of death from any cause, myocardial infarction, stroke, or new-onset renal failure with dialysis, with less blood transfused.

Systematic reviews and meta-analyses of mortality and transfusion thresholds by Trentino KM et al can be found at BMC Medicine 18:154-168, 2020 and in Kashani et al, Can J Anesth 67, 577–587, 2020.

Some key clinical trials in adults [53]

Clinical setting (ref)	Hemoglobin threshold (g/L)	Percent patients transfused
Intensive care[45]	70 100	67 99
Cardiothoracic surgery[46]	80 100	47 78
Hip fracture repair[47,48]	80 10	41 97
Acute upper GI bleeding[49]	70 90	49 86
Symptomatic coronary disease[50]	80 100	28g NA
Septic shock[51]	70 90	64 99
Cardiac surgery[52]	75 90	53 92



Restrictive transfusion strategy and mortality.
A restrictive (Hb trigger <7 g/dl) was associated with reduced in-hospital mortality and total mortality, compared with a liberal transfusion strategy. From Salpeter S et al. Am J Med 127:124–131, 2014.[44]

A recent review for the non-inferiority of the restrictive approach in cardiac surgery may be found in Shehata N, Mistry N, da Costa BR, Pereira TV, Whitlock R, et al. Restrictive compared with liberal red cell transfusion strategies in cardiac surgery: a meta-analysis. Eur Heart J. 2019; 40:1081–1088.

As an example, below are **Practice Points for Hb 'triggers' taken from the Australian PBM Guidelines[54]:**

Perioperative:

- In the absence of acute myocardial or cerebrovascular ischemia, postoperative transfusion may be inappropriate for patients with a Hb level of >80 g/L. NOTE: other Guidelines suggest a Hb level of 70 g/L. Some hospitals 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. with cardiovascular or cerebrovascular disease.
- Patients should not receive a transfusion when the Hb level is ≥100 g/L.
- In postoperative patients with acute myocardial or cerebrovascular ischemia and a Hb level of 70-100 g/L, transfusion of a single unit of RBC, followed by reassessment of clinical efficacy, may be appropriate.

Medical: Direct evidence is not available in general medical patients. Evidence from other patient groups suggests:

- Hb <70g/L, RBC transfusion may be associated with reduced mortality and may be appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.
- Hb 70–100g/L, RBC transfusion is not associated with reduced mortality.
- The decision to transfuse patients (with a single unit followed by reassessment) should be based on the need to relieve clinical signs and symptoms of anemia, and the patient's response to previous transfusions. No evidence to warrant a different approach for patients who are elderly or who have respiratory or cerebrovascular disease.
- Hb > 100g/L, RBC transfusion is likely to be unnecessary and is usually inappropriate.

In Acute Coronary Syndrome (ACS) patients with:

- Hb <80 g/L, RBC transfusion may be associated with reduced mortality and is likely to be appropriate.
- Hb 80-100 g/L, the effect of RBC transfusion on mortality is uncertain and may be associated with an increased risk of recurrence of MI.
- Hb >100 g/L, RBC transfusion is not advisable because of an association with increased mortality.

Thalassemia:

- The evidence does not support any change to the current practice of maintaining a pretransfusion Hb of 90-100 g/L, with transfusions at about monthly intervals.

Myelodysplasia:

- For patients who are regularly and chronically transfused, there is no evidence to guide particular Hb thresholds. Individualize decisions around appropriate triggers & frequency of transfusion considering anemia-related symptoms, functional status, and the patient's response to previous transfusions.

Critically ill patients:

- Hb <70 g/L, RBC transfusion is likely to be appropriate; however, transfusion may not be required in well-compensated patients or where other specific therapy is available.
- Hb 70-90 g/L, RBC transfusion is not associated with reduced mortality. Decision to transfuse (with a single unit followed by reassessment) should be based on the need to relieve clinical signs and symptoms of anemia.
- Hb >90 g/L, RBC transfusion is generally unnecessary.

Key messages:

Use of a restrictive transfusion protocol can be regarded as an important blood saving and cost-saving strategy. Restrictive transfusion does not lead to adverse events when compared to liberal transfusion strategies in the non-high risk patient (regarding mortality, cardiac events, myocardial infarction, stroke, pneumonia and thromboembolism). Effects of restrictive transfusion triggers in high risk groups such as acute coronary syndrome need to be tested in further large clinical trials. In 1988 the NIH published consensus guidelines for RBC transfusion. Since then, a large number of guidelines have been published, recommending that a range of Hb levels between 60 and 100 g/L can be used, depending on the presence of serious co-morbidity. The number of published clinical practice guidelines for RBC transfusions attest to the increasing attention paid to transfusion practices by professional societies. The selection of a discrete hemoglobin as a 'trigger' for RBC transfusion has been controversial and instead a full clinical assessment of the patient is recommended, along with transfusion of only one RBC unit per transfusion event, with re-assessment of the patient in between transfusion events. It is generally agreed that transfusion is not of benefit when the hemoglobin is greater than 10 g/dL, but may be beneficial when the hemoglobin is less than 60-80 g/L (6-8 g/dL).

It is also 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. Recent editorials have summarized the implications of the trials and meta-analyses by identifying a "new normal" Hb level of 7 g/dL (or even suggesting that "6 g/dL could be the new 7 g/dL",[55]) to be used for making transfusion decisions. However, another stated "it is no longer acceptable to recommend that we transfuse using vague approaches such as clinical judgment or in the hope of alleviating symptoms';[56] this approach advocates the use of a laboratory number, to the exclusion of clinical assessment for variables that are relevant for making transfusion decisions. However, this risks over-interpreting the available evidence for a 'transfusion trigger' by underestimating the heterogeneity of anemias (e.g. acute versus chronic) and the heterogeneity of patients (e.g. comorbidities such as age), especially considering the suboptimal participation rate (less than 60% in three of seven trials) of patients who were eligible for some of these trials. Nevertheless, many clinicians mainly use hemoglobin values to guide transfusion decisions.

Despite the fact that the appropriate transfusion threshold in a given clinical setting may be unclear, there is increasing evidence that RBC transfusions are often ineffective and possibly harmful in many of the clinical settings in which they are administered. Thus, the guiding principle for RBC transfusion therapy should be that less is more. In the American Board of Internal Medicine's Choosing Wisely campaign, the American Association of Blood Banks (AABB) recommended that single-unit RBC transfusions be administered for non-bleeding hospitalized patients, echoing recommendations originally published more than 20 years ago by the American College of Physicians. Additional RBC units should be prescribed only after reassessment of the patient between RBC transfusion events.

Physician compliance with clinical practice guidelines is 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.[86,87] This tool uses a Hb threshold number in a smart Best Practices Alert (BPA) at physician order entry, in order to trigger a concurrent utilization self-review for whether blood transfusion therapy is appropriate. Development and initiation of a best practice program for RBC transfusion can involve several steps: forming a multidisciplinary team to develop an accepted institutional transfusion guideline that is accepted, incorporating the RBC guidelines into a computer order set with best practices alerts (BPAs) for RBC transfusions outside the clinical practice guideline, an educational program starting prior to initiation of the effort and continuing post-implementation ongoing evaluation post-implementation with provider feedback.

Reducing perioperative blood loss:

A variety of approaches have been employed to reduce perioperative blood loss.[e.g.57-59] The development of protocols involves multidisciplinary collaboration between surgeons, anesthesiologists, hematologists, transfusion medicine, perfusionists and pharmacy. The approach may vary depending on surgical procedure.

- Reversal of antithrombotic medications
- Point of care testing/thromboelastography, to assess coagulation and guide blood product use
- Topical hemostatic agents (fibrin glue/sealant)
- Hemostatic drugs ---- Procoagulant; Antifibrinolytics
- Perioperative blood salvage

Assessing bleeding risk[60-62]

- Preoperative assessment of bleeding risk by clinical interview in all patients and coagulation tests in select patients will improve patient outcomes.

- Bleeding risk should be assessed by structured patient interview, physical examination, assessment of comorbidities and medication history. This should include personal or family bleeding history, previous excessive post-traumatic or postsurgical bleeding and detailed information on the patient's medication including complementary medications.

Physical examination should be performed, focusing on signs of bleeding and diseases which may cause hemostatic failure (e.g. liver disease). Gender, body mass index and comorbidities including arterial hypertension, diabetes mellitus and renal dysfunction are independent risk factors for bleeding and transfusion.

- Routine coagulation testing to predict bleeding risk is not recommended. Coagulation tests may suggest increased bleeding risk, but they are poor predictors of intraoperative or postoperative bleeding.

- Comprehensive assessment, specialist guidelines or hematology advice may be required in at risk patients, particularly if undergoing certain types of procedures. Advice should be sought for at risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy, whether acquired, associated with medication or with systemic, metabolic or endocrine comorbidities.

Cessation of medications affecting coagulation

Numerous medications and complementary therapies affect hemostasis. Cessation or bridging therapy may be required in order to minimize blood loss.

- Specialist guidelines or advice may be required.

- The management of antiplatelet agents including non-steroidal anti-inflammatory agents, aspirin and clopidogrel and anticoagulant therapy including warfarin, heparin and the new oral anticoagulants (NOAC/DOAC) will need to be tailored for each patient to balance the risk of bleeding and thrombotic events, taking into consideration the indications for the medications, and the nature of the procedure and its risk of bleeding.

- A multidisciplinary team approach, involving surgeon, anesthetist, cardiologist and hematologist, may be necessary to develop a management plan appropriate for the patient.

- In patients undergoing coronary artery bypass graft (CABG) surgery , clopidogrel therapy should be stopped, where possible, at least 5 days before surgery. In patients receiving clopidogrel who are scheduled for elective noncardiac surgery or other invasive procedures, a multidisciplinary approach should be used to decide whether to cease therapy or defer surgery, balancing the risk of bleeding and thrombotic events.

- Data suggests that perioperative bridging anticoagulation may not be necessary for patients receiving warfarin for atrial fibrillation (Douketis JD, NEJM 2015; 373:823-833).

Tranexamic acid (TXA)[63-65]

Antifibrinolytic drugs are widely used, particularly in orthopedic and cardiac surgery (andObstet/Gynecol), and they have been found to be effective in reducing blood loss, the need for transfusion, and the need for re-operation due to continued or recurrent bleeding. Three formulas of antifibrinolytic drugs are in use: aprotinin, tranexamic acid (TXA) and epsilon aminocaproic acid (EACA). TXA is about eight times more active than its analogue EACA. Aprotinin has proven to be effective in reducing blood transfusions in cardiac surgery, but there are some concerns about its side effects and this is no longer in general use. Therefore the most studied antifibrinolytic drug for a variety of surgical and medical indications has been TXA. TXA is a synthetic lysine analogue antifibrinolytic agent. It is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin, by binding to specific sites of both plasminogen and plasmin, a molecule responsible for the degradation of fibrin. TXA has been in clinical use for many years and has important health and economic implications. TXA has been available for more than 30 years and its costs are small.

Indications for TXA:

- **Oral Surgery:**

TXA can be used topical (gauze saturated with TXA) or systemic in oral surgery. Whether topical is as effective (or even better) as systemic use of TXA has yet to be proven.

- **Urinary Tract Surgery**

Surgery of urinary tracts leads to increasing urokinase challenging hemostasis. A recent meta-analysis investigated the effect of lysine analogues in pelvic surgery including urinary tract surgery and showed a significant reduction of blood loss and blood transfusion during pelvic surgery. More data will be required to definitively assess adverse events.

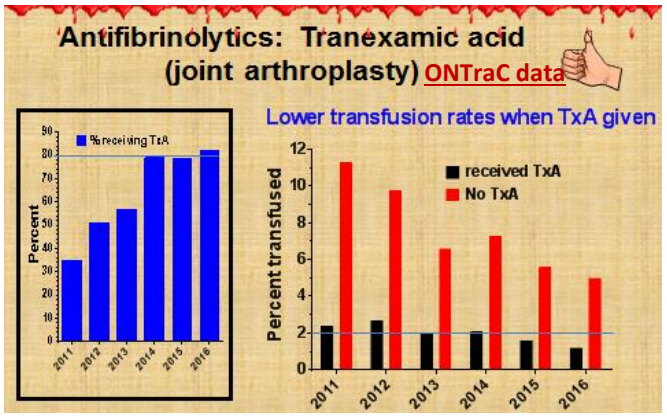
- **Hepatic Surgery**

During liver surgery hyperfibrinolysis may exist either due to underlying disease or due to the operation itself for which TXA can be administered, but in end-stage liver disease there is increasing evidence of a prothrombotic tendency, warranting care with the administering TXA.

- **Orthopedic Surgery**

Most studies with regard to TXA have been done in total hip and total knee replacement and spinal surgery. Two meta-analyses of TXA in total hip replacement both showed a statistically significant reduction in intraoperative, postoperative, and total blood loss as well as a significant reduction in allogeneic blood transfusion requirements in the TXA group compared to the control group. Meta-analyses of use of TXA in unilateral knee replacement also showed that

TXA significantly reduced postoperative drainage, total blood loss, and blood transfusion requirements. VTE as an adverse event of TXA use was addressed both in total hip and knee replacement, but could not be commented upon due to the design of the investigated studies. Furthermore there are discussions whether TXA should be used intravenously, topically or both. A recent meta-analysis[65] of use of TXA in spinal surgery showed reduced blood loss and less transfusion when TXA was used; however, the studies were not powered to evaluate safety. Nonetheless, use of TXA in orthopedic surgery has increased markedly over recent years e.g. Pavenski K, Ward S, Hare GMT, Freedman J, Pulendrarajah R, et al: A rationale for universal Tranexamic Acid in major joint arthroplasty: overall efficacy and impact of risk factors for transfusion. Transfusion, 59:207-216, 2019



- **Hematology**

Although there is insufficient evidence from large randomized controlled trials, for patients with hemophilia, Von Willebrand disease and Glanzmann thrombasthenia, TXA (topically or systematically) often has positive effects.

- **Trauma**

In trauma patients the effect of TXA was studied in the CRASH-2 trial (Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage).[66] All-cause mortality was significantly reduced with TXA, and the risk of death due to bleeding was also significantly reduced. A Cochrane analysis showed that TXA safely reduces mortality in trauma patients with bleeding without increasing the risk of adverse events.[67] The ongoing CRASH-3 study which is conducted in patients with isolated traumatic brain injury should resolve remaining uncertainties with regard to effect of TXA in those patients.[68] For non-traumatic subarachnoidal bleeding (SAB), the Dutch ULTRA study will assess whether there is effect of adding TXA to standard care of SAB (to prevent recurrent bleeding from the aneurysm) with regard to functional outcome.[69] In trauma patients with, or at risk of, significant hemorrhage, TXA (loading dose 1 g over 10 minutes, followed by infusion of 1 g over 8 hours) is recommended by the CRASH 2 trial. In acutely bleeding critically ill trauma patients, TXA should be administered within 3 hours of injury. In critically ill patients with upper GI bleeding, consider the use of TXA. Late administration of TXA is less effective and may be harmful.

- **Cardiac Surgery**

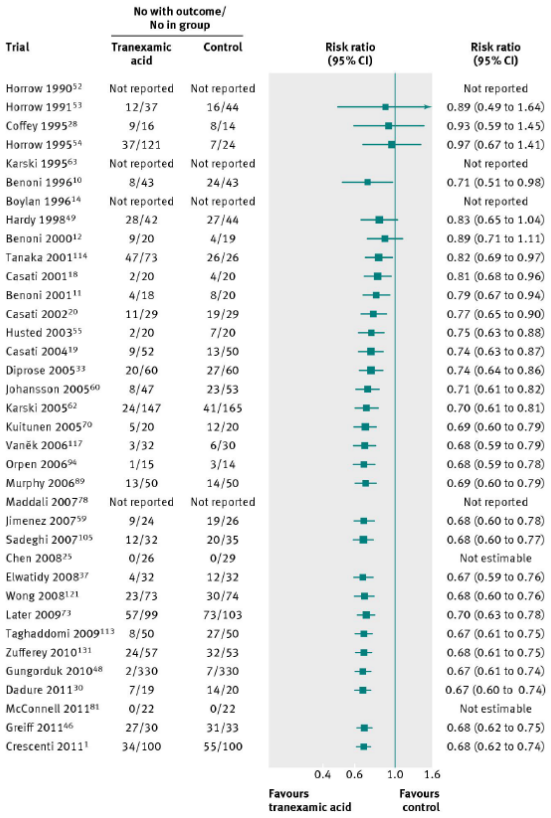
Many studies with TXA have been conducted in cardiopulmonary bypass operations and its benefit is clear. The optimum dose of TXA has been discussed widely, with regard to antifibrinolytic effectiveness, prevention of blood loss and side effects (especially convulsive seizures). A consensus meeting recommended not to exceed a maximum TXA total dose of 100 mg/kg in patients over 50 years of age undergoing pump surgery in open heart procedures.

- **Bleeding patients who are on Direct Oral Anticoagulants (DOAC)**

TXA has been recommended for mildly and moderately bleeding patients on DOACs (in addition to local management of bleeding site and withdrawal of drug), although evidence of its effect is low.

- **Gynecology and Obstetrics**

The use of TXA has been studied in pregnant women both in post-partum hemorrhage and elective Cesarian section. A recent meta-analysis on treatments for primary post-partum hemorrhage recommended further studies to assess the effect of TXA. The WOMAN trial (World Maternal Antifibrinolytic Trial; Lancet 2017 389:2105-2116), showed that TXA reduces death due to bleeding in women with post-partum hemorrhage with no adverse effects; when used as a treatment for postpartum hemorrhage, TXA should be given as soon as possible after bleeding onset. A positive effect of TXA on blood loss in elective Caesarian section has also been shown.[70] For menstruating women, TXA can reduce menstrual blood loss and quality of life,[71] as well as for women with a congenital bleeding disorder. For benign and oncological surgery meta-analyses show (some) advantage of TXA use.



Trial	No with outcome / No in group: Tranexamic acid	Control	Risk ratio (95% CI)	Risk ratio (95% CI)
Horrow 1990[52]	Not reported	Not reported		Not reported
Horrow 1991[53]	12/37	16/44		0.89 (0.49 to 1.64)
Coffey 1995[28]	9/16	8/14		0.93 (0.59 to 1.45)
Horrow 1995[54]	37/121	7/24		0.97 (0.67 to 1.41)
Karski 1995[63]	Not reported	Not reported		Not reported
Benoni 1996[10]	8/43	24/43		0.71 (0.51 to 0.98)
Boylan 1996[14]	Not reported	Not reported		Not reported
Hardy 1998[49]	28/42	27/44		0.83 (0.65 to 1.04)
Benoni 2000[12]	9/20	4/19		0.89 (0.71 to 1.11)
Tanaka 2001[114]	47/73	26/26		0.82 (0.69 to 0.97)
Casati 2001[18]	2/20	4/20		0.81 (0.68 to 0.96)
Benoni 2001[11]	4/18	8/20		0.79 (0.67 to 0.94)
Casati 2002[20]	11/29	19/29		0.77 (0.65 to 0.90)
Husted 2003[55]	2/20	7/20		0.75 (0.63 to 0.88)
Casati 2004[19]	9/52	13/50		0.74 (0.63 to 0.87)
Diprose 2005[33]	20/60	27/60		0.74 (0.64 to 0.86)
Johansson 2005[60]	8/47	23/53		0.71 (0.61 to 0.82)
Karski 2005[62]	24/147	41/165		0.70 (0.61 to 0.81)
Kuitunen 2005[70]	5/20	12/20		0.69 (0.60 to 0.79)
Vaněk 2006[117]	3/32	6/30		0.68 (0.59 to 0.79)
Orpen 2006[96]	1/15	3/14		0.68 (0.59 to 0.78)
Murphy 2006[89]	13/50	14/50		0.69 (0.60 to 0.79)
Maddali 2007[78]	Not reported	Not reported		Not reported
Jimenez 2007[59]	9/24	19/26		0.68 (0.60 to 0.78)
Sadeghi 2007[105]	12/32	20/35		0.68 (0.60 to 0.77)
Chen 2008[25]	0/26	0/29		Not estimable
Elwatidy 2008[37]	4/32	12/32		0.67 (0.59 to 0.76)
Wong 2008[121]	23/73	30/74		0.68 (0.60 to 0.76)
Later 2009[73]	57/99	73/103		0.70 (0.63 to 0.78)
Taghaddomi 2009[113]	8/50	27/50		0.67 (0.61 to 0.75)
Zufferey 2010[131]	24/57	32/53		0.68 (0.61 to 0.75)
Gungorduk 2010[48]	2/330	7/330		0.67 (0.61 to 0.74)
Dadure 2011[30]	7/19	14/20		0.67 (0.60 to 0.74)
McConnell 2011[81]	0/22	0/22		Not estimable
Greiff 2011[46]	27/30	31/33		0.68 (0.62 to 0.75)
Crescenti 2011[1]	34/100	55/100		0.68 (0.62 to 0.74)

Every trial has shown a reduction in transfusion rate when TXA is used

Ker K et al: BMJ 2012 344:e3054[67]

Dosing of Tranexamic Acid (Cyklokapron ®)

Intravenous	Solution 100mg/ml, ampul (vial) 5 ml
Topical	Solution 50 mg/ml
Oral	Tablet 500 mg (it can be divided into two)

Adverse events (most common):

GI upset; Allergic reactions; Seizures (high doses)

The effect of tranexamic acid on thromboembolic events and mortality remains uncertain.

Contra-indications:

Patients with or at elevated risk for thrombosis
Hematuria
Fibrinolytic conditions following consumption coagulopathy
History of convulsion
Renal failure (dose adjustment)
Pregnancy (only use in strict conditions)

Other medications which might minimize bleeding:

Desmopressin

Desmopressin is a synthetic analogue of the antidiuretic hormone arginine vasopressin that produces a transient increase in factor VIII and von Willebrand factor in plasma. This therapy has been used for the treatment of mild haemophilia and von Willebrand disease (type 1), but clinical experience has expanded its use to other potential

indications. However, the evidence for the efficacy of desmopressin in reducing blood loss is weak and the increased risk of cardiovascular complications should be considered. In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anemia that would require therapy) is anticipated, the routine use of desmopressin is not supported, due to uncertainty about the risk of stroke and mortality.

- Apart from mild hemophilia or von Willebrand's disease, routine use of desmopressin is not supported.

rFVIIa

Recombinant Factor VIIa (rFVIIa) is a manufactured form of activated Factor VIIa, a central protein in the initiation of coagulation. The use of rFVIIa is generally reserved for life threatening hemorrhage where conventional measures have failed.

rFVIIa is indicated for the control of bleeding and surgical prophylaxis in patients:

- with inhibitors to coagulation Factors VIII or IX;
- with congenital FVII deficiency;
- with Glanzmann's Thrombasthenia, who have antibodies to GPIIb-IIIa and/or HLA, and with past or present refractoriness to platelet transfusions.

The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not supported. The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality and variable effect on morbidity. rFVIIa may have a role in controlling massive bleeding when conventional measures have failed, but the routine or prophylactic use of rFVIIa in perioperative patients is not supported and is not recommended because concerns remain about its safety profile, particularly thrombotic adverse events. If used, an initial rFVIIa dose of 90 µg/kg is reasonable in massive transfusion.

Preventing hypothermia[72,73]

Anesthetic-induced hypothermia can reduce platelet function and impair enzymes of the coagulation cascade. When the surgical patient's body temperature drops, the number of circulating platelets reduce and the function of remaining platelets is affected, with a 2 degree drop in temperature producing a 100% increase in bleeding time.[73]

- Mild hypothermia (<1 degree) significantly increases blood loss by approximately 16% and increases the risk of transfusion by 22%.[72] Conversely, maintenance of normothermia during the perioperative period reduces blood loss and transfusion requirement by clinically significant amounts.[72]
- In the critically bleeding patient mortality is highest when acidosis and hypothermia occur with coagulopathy. To improve patient survival and outcomes, management strategies should be directed to avoiding or reducing the extent of these complications.
- Maintenance of normothermia during the perioperative period assists in reducing blood loss.
- Hypothermia prevention strategies result in significant reductions in transfusion incidence and blood loss.
- The risk of morbid cardiac events and wound infections have been found to be significantly reduced when hypothermia prevention strategies are used.
- In the critically bleeding patient, survival rates are improved when actions are taken to prevent or reduce the extent of hypothermia.
- Measures to prevent hypothermia should also be used in patients with critical bleeding/massive transfusion scenario.

Patient positioning

Excessive venous pressure at the site of surgery should be avoided by appropriate patient positioning, both during and after the procedure. Patient positioning during surgery has important cardiac physiological consequences that can impact on perioperative bleeding. Evidence from three of four RCTs examining the effect of patient positioning during surgery demonstrated that lateral, reverse Trendelenburg, or appropriate prone positioning reduced blood

loss.[74,75] A further study by Ong was able to demonstrate a 25% reduction in blood loss in total knee replacement with elevation of the leg at 35 degrees from the hip with the knee extended.[76]

- Intraoperative patient positioning requires balancing the need for the best surgical access while minimizing potential risks for the patient.
- Use lateral, reverse Trendelenburg, or appropriate prone positioning, to reduce blood loss.
- Excessive venous pressure at the site of surgery should be avoided by appropriate patient positioning, both during and after the procedure.

Surgical technique

Meticulous surgical technique is the cornerstone of intraoperative blood conservation !!!

Choice of surgical technique or access influences the amount of blood loss and transfusion requirements.

Close communication between the surgeon, anesthetists and other members of the PBM team is essential to plan the approach, and when needed, adapt the strategy to conditions arising intraoperatively. Minimally invasive arthroplasty has been shown to reduce bleeding, but not to a clinically significant extent and computer-assisted knee arthroplasty shows a greater reduction in surgical intervention but no significant influence on transfusion rate. Nevertheless, such techniques contribute in a multimodal approach to reduction of blood loss and improved patient care. Minimally invasive procedures have been shown to be effective in cardiac surgery[59] as has robotic surgery in radical prostatectomy. Surgical hemostasis options should be considered and utilized where appropriate. Options include but are not limited to:

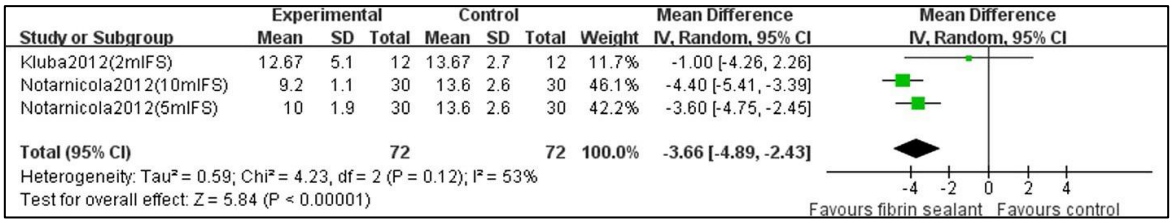
- Vascular conserving anatomical operative approaches,
- Minimally invasive surgery,
- Limb exsanguination before the application of a tourniquet,
- Use of a surgical tourniquet at correct limb occlusion pressure to enable surgeons to work in a bloodless operative field,
- Electrosurgical diathermy & harmonic scalpel techniques (e.g. argon beam cavitational ultrasonic surgical aspirator),
- Use of topical hemostatic agents.
- Techniques including preventing hypothermia, patient positioning, and cell salvage should also be considered.

Topical hemostatics

Topical hemostat, fibrin sealant and adhesive components of the surgical toolbox continue to evolve and enter clinical practice at a rapid rate. The main components of the sealant are fibrinogen, factor XIII, thrombin, and antifibrinolytic agents, such as aprotinin or tranexamic acid. Fibrin sealants achieve their local hemostatic effects by reproducing the last step of the coagulation cascade, thereby facilitating formation of a stable fibrin clot and subsequent hemostasis.

Studies in patients undergoing cardiac (and other) surgeries have shown that the use of topical hemostatics/fibrin sealants can result in less blood loss and fewer transfusions with reduced LOS (Forest plots below). A number of systematic reviews have examined the efficacy and safety in cardiac surgery,[77] thoracic surgery,[78] plastic and re- constructive surgery[79] and orthopedic surgery settings.[80]

Wang H, Shan L, Zeng H et al: Is fibrin sealant effective and safe in total knee arthroplasty? A meta-analysis of randomized trials. J Orthpaed Surg Res 2014, 9:36.



Forest plot for **length of hospital stay** in TKA.

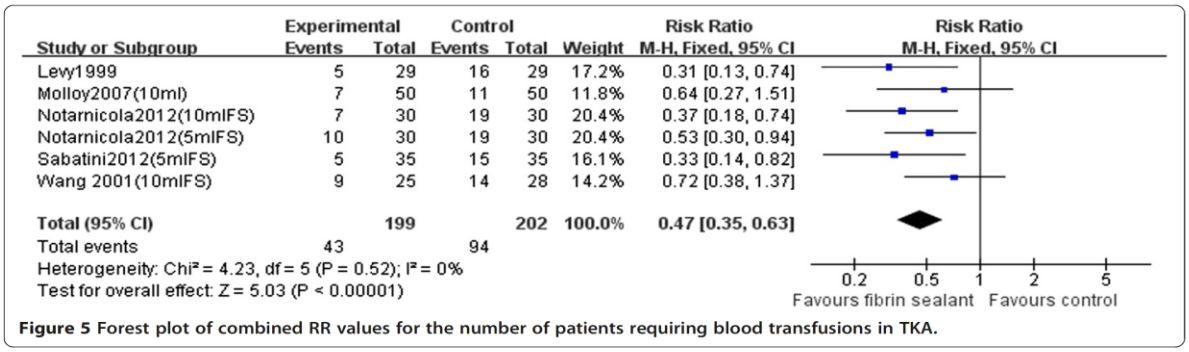


Figure 5 Forest plot of combined RR values for the number of patients requiring blood transfusions in TKA.

Types of hemostatic agents: (Kindly provided by Alanna Harrison, Medical Science Liaison, Surgery & Anesthesia, Baxter Corporation)

Category per Health Canada indication	**Hemostatic agent Single component**	**Hemostatic agent Combination/Dual component**			**Sealants**		**Adhesives**
Type	**Single component**	**Advanced Pad**	**Flowable**	**Human fibrin**	**Human fibrin**	**Synthetic**	**Glues**
Component	**Cellulose Gelatin Collagen Polysaccharide**	**Collagen+PEG+FD&C #1 blue dye Collagen+fibrin sealant**	**Gelatin+Thrombin +/- Patient's plasma**	**Fibrinogen+Thrombin +/- Fibrinolysis inhibitor**	**Fibrinogen+Thrombin +/- Fibrinolysis inhibitor**	**PEG +/- FD&C#1 blue dye**	**Gluteraldehyde+BSA Cyanoacrylate+BLCA**
Mechanism of action	**Contact activation Platelet aggregation**	**Contact activation Platelet aggregation Tissue adherence**	**Contact activation + Fibrinogen converted to fibrin**	**Replicates final stage of clotting cascade**	**Replicates final stage of clotting cascade Adheres tissue and grafts**	**Covalently and mechanically bonds to tissue and synthetic grafts**	**Chemical bonding to tissue**
Field conditions	**Wet**	**Wet**	**Wet**	**Dry**	**Dry**	**Dry**	**Dry**
Pressure tolerance	**N/A**	**N/A**	**N/A**	**Low**	**Low**	**High**	**High**
Patient coagulation status	**Intact**	**Intact through coagulopathic**	**Intact through coagulopathic**	**Independent of coagulation cascade**	**Independent of coagulation cascade**	**Independent of coagulation cascade**	**Independent of coagulation cascade**
Use	**Capillary, small venous, arteriolar**	**Capillary, small venous, arteriolar**	**Capillary to arterial oozing to spurting**	**Capillary, small venous, arteriolar**	**Low pressure sealing Graft adhesipn**	**High pressure sealing**	**Repair of large vessels and soft tissue**
Products	**Surgicel family (Original, NU-Kit, Fibrillar, Snow) Gelfoam Surgifoam Surgiflo Avitene/Ultrafoam Arista Hemostase MPH Quickclot**	**Hemopatch Tachosil**	**Floseal Surgiflo with thrombin**	**Tisseel Evicel**	**Tisseel Artiss**	**Coseal Duraseal**	**Bioglue Omnex**
Refer to product monographs for complete indications for use, preparation guides, contraindications and safety warnings							

Emergency radiological/surgical interventions to reduce blood loss

The European Society of Anaesthesiology guidelines[31] suggest that endovascular embolization is a safe alternative to open surgical intervention after failed endoscopic treatment for upper gastrointestinal bleeding; super-selective embolization as primary therapy for treatment of angiogram-positive lower gastrointestinal bleeding; and embolization as first-line therapy for arterial complications in pancreatitis.

Anesthetic technique

Anesthetic agents and techniques can impact on perioperative blood loss.

Anesthesiologists have a key role in PBM from preoperative optimization of red cell mass and coagulation status, to minimization of perioperative blood loss, to appropriate management of postoperative anemia. Anesthetists should be aware of the contribution that strategies such as volatile (inhalational) versus total intravenous anesthesia, regional versus general anesthesia, and spontaneous versus positive pressure ventilation, have on blood loss. Propofol-based total intravenous anesthesia (TIVA) has been associated with reduced blood loss in several settings e.g. spinal surgery, endoscopic surgery and first trimester pregnancy termination. Neuraxial anesthesia has been shown to reduce blood loss by 25-30% and reduce transfusion rates from 33% (with general anesthesia) to 12% in total hip arthroplasty.[81]

Although there is less evidence for choice of anesthesia having a significant effect on perioperative bleeding in other types of surgery, anesthetists should be aware of the possible benefits of regional anesthesia, TIVA and spontaneous ventilation in reducing blood loss. Anesthetic techniques to reduce blood loss should be considered and utilized where appropriate. Some options include but are not limited to:

- Propofol-based total intravenous anesthesia (TIVA) has been associated with reduced blood loss in several settings,
- Neuraxial block has been found to reduce blood loss and transfusion requirements,
- Positive pressure ventilation has been associated with increased intraoperative blood loss compared to spontaneous ventilation in total hip replacement surgery under general anesthesia.
- Choice of anesthesia technique for total hip arthroplasty should take account of the potential benefit of regional techniques with regard to blood conservation,
- Acute normovolemic hemodilution (ANH), cell salvage and point of care testing may also be considered.

Cell salvage

Cell salvage is an autologous blood conservation technique for minimizing blood loss in the surgical setting. It can be performed during the intra- and/or postoperative periods.

- Cell salvage has been demonstrated to be safe and effective at reducing allogeneic blood transfusions particularly in adult elective cardiac and orthopedic surgery.[82,83]
- Cell salvage can be cost-effective.
- Intraoperative cell salvage requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it.
- Intraoperative cell salvage may be recommended in adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anemia that would require therapy) is anticipated,
- Postoperative cell salvage may be used in adult patients undergoing cardiac surgery or total joint arthroplasty, in whom significant postoperative blood loss is anticipated, but recent literature has questioned the efficacy and cost-efficiency of its use in knee arthroplasty.
- The use of cell salvage may be considered in critically ill trauma patients and patients undergoing emergency surgery for ruptured abdominal aortic aneurysm.

A systematic Cochrane review[82] reported that use of cell salvage reduced the rate of exposure to allogeneic RBC transfusion by 38%, and resulted in an average saving of 0.68 units of allogeneic blood per patient. It did not appear to impact adversely on clinical outcomes and found reduced rates of infection and length of hospital stay.

Intraoperative cell salvage (ICS)

Intraoperative cell salvage begins by aspiration of blood shed into the surgical field or wound and collected into a sterile collection reservoir. During collection blood is anticoagulated and filtered to remove large particulate debris. The salvaged blood is centrifuged and washed with normal saline, with the remaining red blood cells resuspended in saline to a hematocrit of 50-80% for subsequent reinfusion to the patient. Cell salvage is recommended in adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anemia that would require therapy) is anticipated. In addition to cardiac surgery, it may also be beneficial in revision or bilateral joint replacement.

The major advantage of intraoperative cell salvage is the reduction in exposure to allogeneic blood transfusion and all its associated risks. In particular, clerical errors and immune-modulatory effects are mitigated. It has been shown to be cost-effective and associated with minimal complications.[81] There are few contraindications, but intraoperative cell salvage is not recommended when bowel content or infected material is present in the surgical field and its use in malignancy is controversial, requiring additional procedures.

Intraoperative cell salvage requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it.

Post-operative cell salvage (PCS)

Postoperative cell salvage involves collecting blood that is lost from the wound post-operatively into special autologous wound drains where it is filtered before being re-infused to the patient. Postoperative cell salvage may be considered in adult patients undergoing cardiac surgery or joint arthroplasty, in whom significant postoperative blood loss is anticipated. The cost-effectiveness of this approach has, however, been controversial.

Point of care testing

Point of care (POC) testing devices provide rapid bedside monitoring to aid the clinician in directing appropriate targeted therapy.[84,85, 85a]

- The use of transfusion algorithms in conjunction with POC testing has been shown to reduce both transfusion requirements and blood loss in cardiac surgery.
- In adults undergoing cardiac surgery, the use of thromboelastography (TEG) or ROTEM should be considered.
- Patients undergoing cardiac surgery are vulnerable to platelet defects which can be either pre- existing defects, drug-induced, as well as anti-platelet effects from cardiopulmonary bypass (CPB). It is therefore important monitor platelet function during cardiac surgery.

Currently there is limited evidence for the effect of POC testing other than TEG. However thromboelastometry (ROTEM) is becoming more widely used and is considered equivalent by international guidelines. TEG/ROTEM analysis reflects hemostasis in vivo, including clot development, stabilization and dissolution. A meta-analysis found that the use of a TEG-based transfusion algorithm resulted in a significant reduction in the incidence of transfusion with fresh frozen plasma (FFP) and platelets, and may have reduced the incidence of RBC transfusion, compared with the use of a transfusion protocol that was not TEG based.

Role of Transfusion Practitioner

The Transfusion Practitioner (TP) or equivalent (e.g. PBM Practitioner/Nurse/Coordinator, etc - herein referred to as TP) has a critical role to play in developing a Patient Blood Management (PBM) culture within healthcare establishments. Although only one part of the team needed to develop and implement the required PBM strategies, they have a multifaceted role to play in engaging with both scientific, laboratory and clinical colleagues, as well as patients. PBM requires a multi-disciplinary approach and a primary role of the TP is to promote safe and appropriate use of blood to clinical colleagues within and outside of the laboratory. Very often the TP is the conduit for information pulling together available resources both financial and personnel, reviewing activities undertaken by transfusion colleagues in other centres, collecting audit data and evaluating how these activities might be beneficial within their own healthcare establishment.

TPs have made a significant contribution in helping to improve transfusion practice at a local, regional and national level by promoting safe transfusion practice. It is widely understood that the TP has a very valuable role to play within PBM. To do this, information must be taken to clinical colleagues to engage with them and plan strategies. The many different elements that make up 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 blood and blood components. The TP should not lead these projects as it would seem best practice that they are owned and managed at a local level by the users of blood, but the TP can have the essential role of having a 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. It was expected this role would work as part of the Hospital Transfusion Team, made up with the Transfusion Laboratory Manager and Consultant in charge of blood transfusion. Over the intervening years most UK Trusts have appointed to the Transfusion Practitioner role, employing experienced staff with a Nursing, Midwifery or Biomedical Science background. Ontario has, since 2002, developed the network of Transfusion or PBM Coordinators in 25 hospitals throughout the province i.e. ONTraC[2-4] – further information on this program can be found (along with much information on PBM, including patient pamphlets) at www.ontracprogram.com and at pages 58-77 of this guide. As shown earlier in this Guide, the Ontario ONTraC program has proven to be very effective and cost-efficient.

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. The ONTraC TPs are expected to spend 50% of their time on PBM practices, 25% on staff and patient education, and 25% on data collection.[2,3] A book by the 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-centre-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.

Patient-centered decision making

When patients are asked to consent to RBC transfusion, they rarely decline, unless they have religious objections to transfusion. However, the discussion is often cursory. In a study from Sunnybrook Hospital in Toronto (Cheung et al, Transfus Med 2014; 24:269-273) patients experienced a variable informed consent process prior to blood transfusion; although a video improved their understanding of risks, it did not improve patient comfort towards giving consent for transfusion, as, in this study, the level of comfort was already high.

Shared decision-making is a collaborative process that allows patients and physicians to make treatment decisions, taking into account patients' values and preferences as well as scientific evidence. The current RBC transfusion consent process does not necessarily meet this goal. Patients and physicians often place different values on potential outcomes, and patients often change their decisions when presented with more detailed information. In many, particularly non-emergency, circumstances, RBC transfusion can be viewed as "preference-sensitive" care, meaning that how a patient values the benefit versus harm will impact choice. The value of shared decision-making has been shown in a variety of clinical situations and is facilitated by the development of decision aids that outline the details of the clinical choice. An ideal consent process would use decision support tools to better inform patient decisions. For example, if the transfusion consent process reviewed your institution's indications for transfusion, or permitted patients to specify under which conditions they would accept blood, the consent process could serve to educate both doctors and patients about appropriate indications.

Choose metrics and develop a data collection plan

To avoid inappropriate and potentially injurious transfusion practices, agencies such as the Society for Advancement of Blood Management (SABM) the AABB and The Joint Commission (TJC) have promoted initiatives in patient blood management (PBM). PBM, as defined by SABM refers to "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome." Considerable information on PBM, including Standards, can be found on the SABM website, www.sabm.org, and guidance about relevant metrics for PBM initiatives can be found.

Many employed measures are process measures, while demonstration of meaningful improvement with outcome measures would be ideal. One should implement and evaluate more proactive anemia management and use of pharmacologic alternatives to transfusion.

Transfusion Rates: The RBC transfusion rate can be assessed as total RBCs transfused per patient, expressed per 100 patient-days, or admissions, or discharges, depending on the data available. You may want to exclude transfusions given perioperatively or for bleeding, or at least analyze them separately. Data may be extractable by type of procedure and physician or service, as well as specific clinical unit. Other key metrics include the percent of RBC transfusions given above a specific hemoglobin threshold, according to an institutional protocol, and the percent of transfusions with a dose of two or more units. Examining this information by service or clinical unit can sometimes uncover major differences in transfusion practices. While global hospital data can be collected, it is useful to examine homogenous patient populations, to allow comparison with other local, national or international evaluations.

However you obtain data, you also want to know if reliable information can be obtained electronically (e.g. accurate identification of all transfusions given for hemoglobin >7g/dL) or whether additional chart review will be required (e.g. identify bleeding or instability not captured by coding data, but which justified transfusion) — and decide if you need added help to do this review. Avoid designing a project your data acquisition capabilities cannot support.

You also need to plan data analysis. Collect data that you will be able to analyze in a meaningful way. Instead of tables of numbers, or aggregate "before and after" rates, data may be best presented in the form of a control chart

(either P-chart or U-chart) that allows evaluation of performance over time, and easy recognition of whether you've achieved statistically significant improvement.

It is important to obtain current performance both to generate leadership support and to identify initial areas for the project's focus. Do not embark on a complex, time-consuming project without a clear understanding of the room for improvement and the potential return on investment at your institution. The necessary performance data will initially depend upon the specific project(s) you're planning, and the data available. At a minimum, global institutional performance data should be obtained (e.g. RBC transfusion rates). The more data can be focused down to specific units or services or providers the more helpful it will be in identifying outliers — this can help you decide if an institution-wide change or service-specific education makes the most sense.

Benchmarking

Internal benchmarking is done to identify variations in blood product use and potential opportunities for improvement. For example, different surgical services can be compared to identify practice variations and stimulate discussions about best practices. If volume is sufficient, individual physician prescribing patterns can be compared for similar lessons.

External benchmarking establishes how a hospital compares to other institutions. One good source of information for surgical specialties may be the data from the US National Surgical Quality Improvement Program (NSQIP). Other benchmarks are available as well: in data from a 2011 AABB survey of 506 hospitals, the average pre-transfusion hemoglobin was 7.9 g/dL with a range of 6-12 g/dL. In a large analysis of blood transfusion practices (464 hospitals and 7.4 million discharges from April 2011-March 2012), substantial variation was noted — representing an opportunity to save 800,000 units of blood and $165 million annually. You can also look at your use of blood products per adjusted discharge, taking into account factors such as whether your hospital has special populations, like a bone marrow transplantation service.

Potential Initial Metrics for Transfusion Projects

Good performance measures share attributes of being correlated to patient outcomes, validity and feasibility (particularly in terms of time and effort required for data collection). Based on these principles, you may consider the following initial metrics (can analyze data by service or physician adjusted by volume):

For stable, non-bleeding patients:

- Total RBC units per patient days at risk
- Percent RBC units transfused with Hb level ≥ 8 g/dL (AABB)
- Hb level at transfusion
- Percent single-unit transfusions in non-bleeding patients (ACP, AABB)
- Hb level after transfusion (OB or trauma) or at discharge (look for over-transfusion)
- Reason for transfusion if Hb ≥8 g/dL (in non-bleeding patient).
- Percent of transfused patients with a discharge Hb level greater than 100 g/L (possible overtransfusion).

For elective OR cases that have blood requested on a surgical schedule:

- Percent patients transfused
- Percent cases with preoperative Hb <12 g/dL (SABM, NATA)
- Percent cases with no Type & Screen before day of surgery (TJC: The Joint Commission)
- Compliance with patient safety checklist
- Percent of transfused patients with a discharge Hb level greater than 100 g/L (possible overtransfusion).

You may also be able to measure transfusion-related complications by reviewing adverse event reports, but you may not be able to show a decline in these relatively rare events.

Define Data Collection Strategies

The main decision point regarding data extraction for anemia and transfusion QI relates to the availability of electronic medical records (EMRs) within your facility and the extent to which these systems contain data elements of interest that can be collected without manual chart review. For data elements that can be extracted electronically, a 100% case sampling approach should be used; coordinate with your IT team members to make sure that if or when CPOE changes are built to consider how data will be collected from the new process.

For data requiring manual extraction, a random sampling approach (10 charts a month may be adequate for a given unit or hospital) is a cost-conscious and well-accepted approach for process performance measurement. Make sure that your plan collects all necessary information but that it is as easy to use as possible. For example, if you would refer off-protocol transfusions for peer review, you would probably want to check the chart for evidence of a specific rationale/special circumstance for transfusion, but if you are only using the information as a metric to track progress, collecting that level of detail would likely be unnecessary and onerous. Depending on your interventions, you may be able to measure your processes and intervene at the same time. For example, if indications will be confirmed by blood bank staff, they can simultaneously gather indication data for 100 percent of transfusions.

Implementing Your Protocol

After you have identified your PBM performance metrics and determined your baseline performance on those metrics, your QI team will need to develop solutions and intervention strategies for various points of the patient encounter. This section will provide possible strategies to improve the prevention, assessment and management of PBM and anemia in both the preoperative clinic and inpatient settings. Because the clinic and inpatient settings are so different, and because anemia has diverse causes (and therefore diverse prevention and treatment strategies), you cannot tackle them all. You will need to select one or a few key strategies to start with, depending on factors such as your baseline performance, resources and stakeholder engagement.

For most sites, a multi-pronged effort to improve transfusion practices (involving education and a transfusion protocol with guidance at the point of care) will be the best initial strategy. However, you may find significant opportunities to intervene on preoperative surgical patients with anemia, or to reduce phlebotomy-related blood loss. Layering multiple interventions usually improves results compared to a single intervention (e.g. education + a transfusion protocol + audit and feedback). However, avoid tackling every potential intervention at once and add things stepwise. As you evaluate opportunities for systems change, remember these key patient safety principles:

- Reduce reliance on memory.
- Education alone is unlikely to produce major changes, although education is an important strategy to prepare your clinicians for changes to their workflow and secure their engagement with the other strategies you employ.
- Provide guidance at the point of care.
- In contrast to lectures, posters or policies that are separate in space and time from clinical decisions, concise decision support embedded in order sets (or hyperlinked from the order set) puts information in the clinician's hands at the optimal moment, and serves as ongoing reinforcement of best practices.[86,87]
- By using methods that automate key steps or using hard stops to require clinician attention, you will have better success than if you rely on clinicians to remember to do something or use an "opt-in" approach that clinicians can skip. However, make sure that any hard stops or electronic alerts are truly necessary and do not disrupt the clinical workflow.

- Default the best choice. Some institutions find old protocols still in use that reinforce outdated practices. For example, a hematology service admit order set that allows clinicians to opt for transfusions whenever the hemoglobin drops below 8, 9 or 10 g/dL encourages bad practice and gives the impression the hospital endorses those thresholds. Defaulting the threshold to 7 g/dL should promptly improve practice, and clinicians can take the extra steps to change the default to higher values in the rare patients for whom this is appropriate. Defaulting the transfusion dose to one unit is another good example.
- Standardize and simplify processes. Criteria should be as consistent across different services and environments as possible, as well as simple and easy to remember. Clinicians will more likely accept processes that are simple, easy to use and avoid redundancy. One example would be best practice alerts that pop up only when an order appears off-protocol and provides the relevant lab values so clinicians don't have to look for them.

While data is necessary for quality improvement, it is not sufficient on its own. QI is a team effort that relies on collaboration and sharing. A key success factor is the creation of a network focusing on peer-to-peer support.

Audit

Audits are an important component of a PBM strategy. In general, an audit involves checking a process, a structure, or even an outcome itself, to ensure that it conforms to an expectation of performance. The audit will reveal whether the process is doing what is desired , and in an efficient manner. Audits of transfusion practice can occur both in the blood bank itself and on the hospital wards and operation rooms; audits of the latter are generally performed to ensure that clinicians are following the institutional directives or guidelines for transfusion practice. Simply by starting to look at a process, potential areas for improvement can be found. Below are audit topics both inside and outside the transfusion service, and includes some examples that can be adapted for use at your institution.

Outside of the transfusion service

Audits outside of the transfusion service are an essential part of PBM, and can help to focus novel PBM initiatives on wasteful practice. A example of a simple audit that can be performed under the auspice of the hospital's transfusion committee is to regularly monitor the crossmatch:transfusion (C:T) ratio of individual blood product prescribers or entire services. The C:T ratio is a measure of the clinician's acumen in using the RBCs that they had crossmatched. Again, the ideal ratio is 1 as this would represent a clinician who uses every unit that they had ordered to be crossmatched. However, as clinical situations can change rapidly, it is not always realistic to expect that a clinician will use every RBC unit that was crossmatched, so a C:T ratio of 2:1 is often accepted as the standard. Ratios significantly in excess of 2:1 reflect a clinical service that overestimates the number of RBC units that they will ultimately transfuse.

Computerized physician order entry as an audit tool

Thus far, this section has described audits that have been performed at the level of a hospital or clinical service. Audits can also be performed at the level of the individual clinician or blood product prescriber. In order to be able to be this specific, the transfusion service or hospital's information technology must be able to identify specific prescribers of blood products. One way of obtaining this information is by employing a computerized physician order entry (CPOE) system whereby the blood product prescriber must personally log in to the computerized blood product order entry system before they can order the desired component. [86,87] This allows specific feedback to the clinician about their blood product use in relation to that of their colleagues (anonymously) who perform the same procedures. These reports are very useful in identifying outlying practices so that specific interventions can be initiated at the level of an entire service or with specific providers.

Audits can require extensive use of information technology in terms of generating the required data, mining it, and producing an output that can be used to determine if the process is functioning optimally or if it needs to be adjusted. However, even if the technological resources are not available to conduct the types of audits described above,

much simpler audits can be carried out by manually measuring. Simply by starting to look at a process, potential areas for improvement can be found.

Some suggested interventions:[53]

Intervention 1: Focus on Provider Education[53]

As previously mentioned, current evidence indicates that many transfusions are unnecessary, that these transfusions have important negative consequences and costs, and that anemia and common anemia drivers like phlebotomy are underappreciated. A significant contributor to this quality gap is a clinician knowledge gap in assessing the risks and benefits of transfusion, and lack of attention to prevention and treatment strategies for anemia.

The first step in a successful initiative is to ensure that you have educated all providers at your institution on the rationale for your initiative as well as any changes to clinician workflow, such as any new or revised protocols and forms. Your QI team should engage providers on the importance of the intervention(s) you have selected. Make sure you conduct adequate education and stakeholder consultation before you implement your protocol, or you may generate substantial resistance from clinicians who resent workflow and practices changes being thrust on them. Some approaches to address the knowledge gap include:

- Development of educational programs on restrictive transfusion practices for events such as grand rounds, noon conferences or division meetings. Review your project in a concise and memorable way.
- Distribution of educational materials (e.g., pocket cards or ID badge attachments with evidence-based transfusion indications; one-page handouts)
- Guidance at the point of care. You can place links to educational materials within order sets in the EMR environment. Concise messages may fit in a paper or computer order set e.g, “Whenever restrictive and liberal transfusion practices were compared, the lower Hb target was equal or better.”
- Posters, signs and project boards, displayed throughout your institution. These can range from large displays on clinical units to one-page fliers posted in bathrooms.
- A nurse education campaign. By including education for all members of the healthcare team, you create advocates for restrictive transfusion who can speak up during interdisciplinary rounds or in one-on-one discussions about transfusion orders for individual patients.
- Development of conference-delivered or Web-based educational programs. Clinicians can be incentivized by provision of CME credit.
- Dissemination of information about your project at medical staff meetings.

Education will be a necessary component of your PBM project, correcting knowledge deficits and contributing to culture change at your institution. Clinicians may begin viewing transfusion as a risk-conferring procedure that requires clear justification, beyond physician unease with hemoglobin numbers; they may recognize that daily “morning labs” are uncomfortable and costly, disrupt sleep and contribute to anemia, and are not benign, routine or required. However, other interventions will need to be layered into your QI project for best results.

Intervention 2: Development of a Transfusion Protocol[53]

Having developed a list of acceptable indications for transfusion at your hospital, your challenge now is to develop an order set based on those indications which 1) educates providers at the point of care, 2) encourages best practices, 3) allows for protocol deviations in special circumstances, 4) accomplishes these goals without creating additional work for your clinicians — or if possible, makes their work easier, faster and more pleasant. This is likely to be your most powerful intervention i.e. a properly designed order set — emphasizing a lower transfusion threshold and single-unit dose — can significantly reduce off-protocol transfusions. Institution-wide protocols have obvious

advantages, but if consensus across an entire hospital cannot be reached, a protocol can also be implemented by a specific service e.g. cardiothoracic surgery.

- Your order set should ask for a transfusion indication, usually via boxes to check on a paper form or buttons to click on a CPOE order set
- If your team has decided on thresholds that vary by hemoglobin value (e.g. <7g/dL, except in the setting of stroke or myocardial ischemia), special circumstances can be listed among the options. Alternatively, your EMR may have the capacity to vary the options displayed according to the patient's most recent hemoglobin value.
- To improve adherence, default the best choice: since single units are the best choice in most situations, design your order set to emphasize this preference. Consider adding requirements such as physician certification of rapid bleeding for exceptions to this rule, but make sure these certifications are as easy as possible to complete (e.g., a box to click, instead of a blank to fill out).
- Do not forget standardization across your institution. There may be several service- or provider- specific transfusion protocols embedded in admission order sets or as stand-alone protocols at your institution, and working with those stakeholders to ensure they are replaced with the updated version will be necessary for maximum impact.

You may recognize other opportunities for improvement as you review your existing order sets.

When designing your order set, you will have to balance idealism and pragmatism. For example, you might want to make it quite difficult to order transfusions off-protocol. However, providers determined to transfuse their patients might find "work-arounds" to the protocol such as misidentifying the indication for transfusion. If you define your success as an improved percentage of RBC transfusions for Hb <7 in non-bleeding patients, providers identify patients as bleeding to speed through your protocol, and your data may become unreliable. An educational program, and dialog with providers who do off-protocol transfusions, will be more effective than trying to force them to change their practices with an order set.

Intervention 3: Real-Time Decision Support for Transfusion[53]

If your institution has low rates of off-protocol transfusions, but you want to aim for near perfect compliance with your protocol, real-time expert consultation is one potential solution. With this intervention, non-emergency blood product requests would require approval from a designated blood bank staff member. Such a strong intervention and significant change to workflow requires considerable institutional will, stakeholder agreement and staff education. However, it sends a powerful message: blood is a "liquid transplant" that carries serious risks, and this scarce and expensive resource should not be used without clear justifications.

If a requirement for approval would not be acceptable to your stakeholders, a softer version of this approach could be used: bedside clinicians would retain ultimate decision-making authority, but the blood "czar" would contact ordering providers about off-protocol transfusions to confirm orders, allowing a moment for education about relevant clinical trials, or discussion of alternatives (e.g., waiting for thresholds to be reached intra- or post-operatively instead of transfusing prophylactically; tolerating asymptomatic anemia; treating underlying causes). If you lack full-time staffing for such a position, partial implementation would still allow you to reach some providers for real-time support while collecting information about their concerns and intentions that could help you revise your protocol.

Intervention 4: Identify and Treat Anemia in the Preoperative Setting[53]

Sites that have successfully implemented transfusion protocols, achieving low rates of off-protocol transfusions, may identify opportunities for improvement in the area of prevention — e.g. can anything be done to prevent or reduce anemia in elective surgery patients, avoiding transfusion?

- First, identify any additional team members you would need to involve to change how anemia is managed

before elective surgery, and confirm that stakeholders and the institution support your effort.

- Second, to assess your baseline performance, ask clinical staff from key surgical specialties how anemia is managed in preoperative patients. Acquire data by searching for elective surgery patients who required transfusion, or whose last pre-hospitalization tests revealed anemia, and reviewing some of their charts to see if anemia was recognized, diagnosed and treated before surgery was scheduled.
- Third, decide on best practices for preoperative anemia intervention (this may include a flowchart defining anemia evaluation and when to refer), and choose metrics and a data collection plan around these practices (e.g. process measures like % of eligible patients who have preoperative CBCs, or percent of patients with Hb values below a threshold who receive an intervention before surgery, or outcome measures, like % of elective surgery patients [or % of those who were anemic on preoperative testing] who require transfusion).
- Fourth, consider clinic workflows and design an intervention. Options could include a checklist, CPOE best practice alerts or templated preoperative evaluation notes or paper forms that prompt anemia evaluations. You will likely want to focus on a well-defined population with a common preoperative workflow and an anticipated blood loss of 500 mL or more, e.g. elective major joint arthroplasty. Once your intervention has been vetted by stakeholders and piloted on a small scale, proceed with full implementation and monitor the results. Then consider applying your protocol to other surgical populations with a high anticipated blood loss.

Intervention 5: Reduce Blood Loss Due to Phlebotomy[53]

As with preoperative anemia management, your team may identify opportunities to improve phlebotomy practices, reducing the incidence of anemia requiring transfusion and other harms, such as non-severe anemia, exhaustion of veins for phlebotomy/need for central access, pain, sleep disruption and increased costs. As with preoperative anemia, reducing excess phlebotomy would be its own QI project.

A phlebotomy project can be approached with the same framework used throughout this Guide, but there are some unique aspects and challenges. For example, it is hard to define "excess" phlebotomy. Choosing Wisely® recommendations include avoiding "repetitive CBC and chemistry testing in the face of clinical stability," but stability is subjective, and studies that define the optimal frequency of lab tests for diverse patient populations are lacking. Also, lab ordering is so frequent, any changes to the process could be onerous. Thus, your phlebotomy reduction project will need to be less proscriptive than your transfusion protocol. Possible strategies include:

- Educational initiatives at shifting lab-ordering culture from a morning default to mindful consideration of need.
- Eliminating or limiting the ability to order daily labs within your EHR.
- Considering a switch to low volume collection tubes so less blood is removed for standard tests/tubes. (This does not necessarily mean pediatric tubes, which can have implications for compatibility with lab equipment; there are adult tubes designed to collect less blood.)
- CPOE modifications that suggest using add-on testing if the lab has a suitable sample, notify the provider if the requested test has already been obtained within predefined intervals, eliminate the option to order ongoing repetitive tests or notify providers about lab costs. Such changes can reduce phlebotomy by 20%.
- Individual or service-specific feedback on performance, or financial incentives.
- Reconfiguring workflows in which multiple tubes are drawn "prophylactically," so that samples are available for any conceivable test. Changing sample collection tubes so less blood is drawn per stick.

Demonstrating a clear relationship between this effort and improved hemoglobin values or reduced transfusion rates may be challenging given the numerous causes of inpatient anemia. However, you could demonstrate reductions in lab costs or draws, or calculate how much blood you saved — all worthwhile measures of success.

Intervention 6: Diagnose and Treat Inpatient Anemia[53]

There are likely patients at your institution with anemia due to iron or vitamin deficiencies, chronic kidney disease (CKD) or inflammation, who are at risk for anemia progression or transfusion, but who do not receive proper evaluation and/or treatment. Anemia in inpatients is so common it can be perceived as normal, and clinicians may be focused on more acute problems.

There may be ways to search your EMR for patients with anemia of a certain severity, rate of progression or diagnosis that may benefit from intervention (e.g., transfusion recipients with a low MCV, or elevated creatinine). If you are able to identify a treatment population, you might consider intervention with triggered consultation, or a best-practice alert on the EMR recommending action or referring providers to an anemia evaluation protocol. You could develop a protocolized approach to anemia in CKD patients, and work with nephrologists to address anemia in their consultation work.

While such strategies would be appropriate and evidence-based, the target population is large, the diagnoses and interventions are diverse, and published experience with anemia QI interventions that changed important clinical outcomes is lacking. However, if you have addressed "lower hanging fruit" already, your team may have enough bandwidth or EMR capability to attempt an anemia intervention — or you may be able to change the practice of a focused set of clinicians (e.g. the nephrologists in the example above, or gastroenterology consultants who see iron deficiency often) without expending much time or money.

Intervention 7: Patient Education[53]

Most of your interventions will focus on improving the decisions made by clinicians. However, patient knowledge about anemia and its treatment can affect transfusion rates, and creative approaches to the consent process could improve the success of a restrictive transfusion protocol.

If you investigate the blood consent process at your institution, you are likely to find that it involves a decision by the clinician that a transfusion is required (often without rigorous evidence) followed by a brief warning about uncommon complications of transfusion and the acquisition of permission to proceed. These discussions may not be meaningful: the clinician feels that blood is needed, the patient is expected to agree and the consent form is a formality. However, consent could be reframed as a review of options with their own rationales, risks and benefits.

- First, the consent form could be redesigned to reflect your institutional best practices, such that the clinician must identify the evidence-based indication for transfusion (or in the case of preemptive consents, under which circumstances blood will actually be transfused). When the indication is a hemoglobin threshold, the consent form can reinforce the patient-centered option of waiting for anemia symptoms — treating the patient, not the number. Such a change could increase patient engagement and knowledge, and serve to reinforce the education to clinicians, who could be required to check off boxes indicating they discussed which indication (or that their choice was off-protocol) was present, the alternatives and risks, and that they reviewed the preference for single units. A form previously used to document consent for blood can be transformed into a form that records a discussion of options, including no transfusion. A brief video with examples of poorly and properly obtained consents could make a powerful tool to educate clinicians on this change.
- Second, patients at high risk for needing transfusion (such as those in preoperative clinics, or oncology patients) could be given easy-to-understand educational materials like handouts or videos that emphasize your institution's list of indications for transfusion and advise them of the risks of blood. This can facilitate true "informed" consent rather than acquiescence to a clinician's decisions.
- Third, patients could be provided with information regarding signs and symptoms of anemia, prompting visit to their family physician for early management.

Intervention 8: Feedback of Performance to Providers[53]

Feedback to providers regarding the progress in achieving your project outcomes can be an effective method to support the change process. Reports detailing outcomes can be hospital- , unit-, service- or provider-specific. In addition, the results can be provided in real-time, or after retrospective audits. To provide real-time feedback, your EMR would have to track processes like recent CBC results or completion of an anemia evaluation in preoperative clinic, or perhaps whether key anemia diagnostic tests were obtained in patients with hemoglobins below a certain threshold. To reduce unnecessary phlebotomy, providers could be notified that a lab they are ordering has already been obtained within a pre-specified time frame (e.g. hemoglobin A1c within three months) or seems appropriate to be batched with other labs or added on to existing samples.

Real-time outcomes information is actionable and can improve your results. For example, a real- time report could identify all the patients who have ongoing daily labs ordered, allowing a clinician to reconsider their lab ordering practices. Other information, however, can be collected retrospectively.

Transfusion decisions should be enhanced and assisted at the point of care; once transfusions have been given, immediate feedback won't change outcomes. However, a retrospective review of off-protocol transfusions can provide valuable information to the QI team (e.g. which services and providers order the most off-protocol blood and why, permitting targeted education and other interventions). Retrospective data about transfusion practices can be stratified by service and distributed to service leaders, allowing comparisons of different services and possibly creating some healthy competition for improvement. Data can also be stratified at the physician level, providing feedback to individuals; clinicians who give blood without documenting sufficient justification could be sent reminders about the protocol or referred for peer review. This can motivate low performers and allow you to recognize the highest performers. Exactly what feedback is provided to whom depends on your institution's norms and culture, and your data collection capabilities.

Intervention 9: Hospital-Based Policy and Incentives[53]

An important aspect of change management is the formation of hospital policy that supports the processes developed within your QI project. For example, to ensure that restrictive transfusion practices are followed, a hospital may develop policies requiring the use of a protocol with identification of an approved transfusion indication or documentation of special circumstances. In addition, the hospital might have external financial incentives based on achievement of transfusion performance goals, and could reward the highest-performing groups or physicians with recognition or actual financial incentives.

Intervention 10: Monitoring the Effect of Your Interventions[53]

Tracking and trending data over time is important to monitor the progress of your QI project. Robust data collection strategies will be needed to track your performance over time through the EMR or by random sample abstraction of paper charts. Your QI team may choose to track a variety of different outcomes, such as rates of transfusion for hemoglobin levels above target thresholds, or phlebotomy rates. It may be helpful to track your measures by hospital unit, service or individual providers.

The duration and frequency of evaluation will need to be determined by your QI team.

Graphs and run charts may enhance your ability to understand and communicate your results.

Analysis of inappropriate transfusions or other deviations from protocols can illustrate the changes needed for your next improvement cycle.

Intervention 11: Sustainability[53]

The team must consider how its efforts can be made sustainable. Without this essential step, any improvements can be lost when a planned intervention period ends or when busy individuals are inevitably required to move on to other projects. There are two main strategies for sustainability.

The first and easier strategy is the use of hardwired changes and redesigned workflows. As one obvious example, a CPOE change (e.g. that reminds providers that one-unit doses and a transfusion trigger not higher than 7-8 g/dL are preferred) will continue to yield results with almost no further effort (any care protocol requires occasional edits as new clinical evidence becomes available). Having a team member contact individuals with off-protocol prescribing habits, however, is labor intensive and unlikely to be sustainable, although this strategy can be helpful at the beginning of a project to spread the word and gather clinician feedback. Similarly, automated data collection is vastly preferable to collection by chart review; if manual collection cannot be avoided, then obtaining the minimum essential information at designated intervals rather than continuously may be helpful. For example, you could check on total blood usage per admission relatively easily, and do periodic spot checks to see if pre-transfusion Hbs are appropriate.

The second major strategy for sustainability is culture change. The need for culture change in maintaining sustainability cannot be overemphasized. The importance of culture can be illustrated by considering how often clinicians ignore multiple hand hygiene stations on their way to providing patient care despite knowing how important hand hygiene is. Similarly, an intern ordered to order two units of blood for a target Hb of 9-10 g/dL by an attending who has always done it that way is likely to comply no matter what your order set says. You can attempt to shift culture by employing respected local leaders to drive change, making moral/emotional pleas by using patient vignettes along with facts, using incentives to reward change (e.g. recognition, prizes or financial incentives), Involvement of the hospital risk-management team can be very useful. However, culture change can be a long, difficult process and you may also want to leverage your executive sponsor to obtain a top-down message that cooperation with institutional anemia protocols is expected.

Even if you have a project ideally designed for sustainability and you have achieved your goals, anticipate doing some periodic maintenance. For example, you may want to educate new clinicians to the protocol, particularly if you are an academic center and you receive an influx of interns every July. You will also want to spot-check on your transfusion rates or other processes, and investigate any signal that practice has regressed toward old habits.

Intervention 12: Improve Transitions of Care for Patients with Anemia[53]

This focuses on optimizing the care transition at discharge from the hospital. Much of the advice is not specific or unique to anemia management. One of the challenges is that anemia is often a secondary diagnosis and may get lost in the transition where the focus is likely to be on CHF, pneumonia, AKI or whatever the primary problem may be.

Although patients with newly prescribed anemia therapies should be educated about multiple aspects of medication management such as drug-drug interactions (e.g. PPIs and oral iron) and new dietary restrictions (e.g. dairy products and oral iron), the most important items to stress at discharge are:

- Follow-up that assesses response to treatment (e.g. a repeat hemoglobin after discharge)
- Follow-up to pursue further investigations to determine etiology (e.g. colonoscopy to evaluate for source of blood loss in iron deficiency)

Studies indicate that up to 40-80% of medical information that patients receive is forgotten immediately and that nearly half of the information retained is incorrect. Clinicians have a duty to provide information in simple, clear and plain language and to check that patients have understood the information. The Teach Back method is one effective way to ensure that the information you provided was understood. Teach Back means that the clinician educates the patient,

then asks the patient to repeat, in his or her own words, what the patient needs to know or do. Teach Back is not a test of the patient but of how well the clinician has explained the information. It is also a chance to check for understanding and, if necessary, to re-teach the information. Finally, Teach Back creates the opportunity for dialog in which the provider gives information, and then asks the patient to respond and confirm understanding before adding any new information. Despite recent research showing the benefits of Teach Back, surprisingly few providers actually use it every day. Clinicians may not be familiar with the method or may find it difficult to change their communication style. Teach Back is not time consuming and only takes a minute or two, but this technique may require a little practice to master. Proper understanding of the need for follow-up and medication management may lead to better adherence.

At the time of discharge, it is also important to consider the direct and indirect costs for anemia treatment options. Ideally, insurance coverage should be checked and an estimate of out-of-pocket costs provided to the patient. If intravenous iron or therapy with an erythropoiesis-stimulating agent is recommended, it is appropriate to verify that the patient has access to an infusion center, insurance coverage for proposed treatments and any prior authorizations that may be required.

Patients should be educated about their anemia and the implications for both therapy and further diagnostics. For example, patients with iron deficiency anemia should be able to teach back that they will need follow-up and further evaluation for a source of blood loss (e.g. colonoscopy) if the source of blood loss remains unclear at discharge. Similarly, patients should receive education about new medications for anemia. If patients are being prescribed oral iron, they should be educated about the possible side effects (e.g. nausea, constipation, black stools) along with potential mitigation strategies such as stool softeners, anti-emetics and ultimately the possibility of transitioning to IV iron if they cannot tolerate (or do not respond to) oral iron. Reliable attention to patient education at the point of discharge from an acute care hospitalization may increase the likelihood of patient compliance and decrease the likelihood of readmission.

CONCLUSIONS:

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 an undesirable outcome. We have learned[88-90] 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 – 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, most often 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 TXA and of cell salvage 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.

ONTraC hopes you found this Guide to be a useful compendium of information regarding how to improve the management of transfusions and other anemia-related care processes at your hospital. There are challenges facing a QI team that has embarked on a PBM project, given the scope and complexity of the problem, 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.

This Guide should assist your hospital in achieving success in implementing PBM strategies, but there is much to be learned about PBM and safer improved optimal transfusion processes, therefore hospitals are encouraged to publish their improvement experiences, and to share any novel tools or strategies. Members of ONTraC would be happy to be contacted for advice and support.[91]

Key messages

- PBM focuses on effective management and conservation of a patient's own blood rather than being reliant on donor blood. Strategies and techniques can be beneficial for all patient groups and clinical scenarios.
- 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.
- Use of PBM strategies and techniques has been associated with improved patient outcomes, patient satisfaction and healthcare costs savings.
- PBM incorporates proactive treatment regimens which are tailored to suit individual patients integrating a multidisciplinary team approach.
- PBM requires early identification and intervention for patients at high risk for transfusion.
- Techniques may involve the use of pharmaceutical agents and medical devices which reduce the need for allogeneic blood transfusion.

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Appendix: --- the Ontario Blood Conservation Coordinators (ONTraC) Program

STRATEGIC VISION

The following outlines ONTraC goals and objectives:

Implementation of Patient Blood Management or PBM (also known as Blood Conservation) in clinical practice:

- Increase recognition that change in PBM practice is important; heighten awareness of healthcare personnel/administrators of the importance of patient blood management
- Establish a well-organized educational program for patient blood management
- Strengthen guidelines, tools and evaluative information for those engaged in patient blood management
- Increase information available to elective surgery (and other) patients regarding patient blood management options

Become a source of knowledge in Patient Blood Management:

- Decrease the gap in evidence-based information and knowledge of PBM among medical students, interns, residents, staff physicians, healthcare providers and other key stakeholders
- Increase access to evidence-based information and knowledge of PBM
- Change government understanding, attitudes and policies related to PBM
- Increase public awareness of transfusion options and scientific progress in the area of PBM
- Increase visibility among medical societies of the value of intelligent patient blood management at all levels – safety, cost, outcomes, etc.

Organizational effectiveness:

- ONTraC will be an effectively managed, well-governed, fiscally sound organization positioned to achieve its vision and objectives.

Become an internationally recognized leader in the integration of evidence & outcome-based PBM in medical care:

- Effect change and improved patient care in PBM in Ontario
- Become the source of future vision in PBM in Canada and internationally
- Be a leading forum to identify and study critical issues in PBM in Ontario
- Be the definitive source of evidence and education in PBM in Ontario through:
    - Database/registry linking patient blood management to patient outcomes
    - Website for interactive information in patient blood management
    - Clinical guidelines regarding patient blood management
- Become the recognized authority in practices and policies of PBM in Ontario
- Be the voice for physicians and healthcare providers of PBM in Ontario and the primary influence on professional organizations and public/governmental policies toward PBM in Ontario and Canada

A. BACKGROUND

What is PBM?

Patient Blood Management (PBM) is a comprehensive, multidisciplinary approach to minimize blood loss and to reduce the need for, or to avoid as much as possible, allogeneic or donor blood transfusions. It incorporates a planned, systematic use of proven alternatives, strategies, and surgical techniques for blood conservation before, during, and after surgery. Blood conservation programs use principles of evidence-based practice and patient-centered care. The scientific basis of these programs is emphasized through clinical trials, outcome studies, and patient follow-up.

There are three stages in the care of elective patients enrolled in the program: a preoperative, an intra-operative and post-operative phase. The fundamental aim of the ONTraC program is to maximize oxygen delivery to the tissues, and maximize the ability of the body to produce red blood cells, and to minimize blood loss. ONTraC incorporates special procedures and medications that help minimize blood loss during surgery or hospitalization and promote recovery. The "bloodless" approach can be applied to numerous types of surgery: cardiovascular surgery, total joint replacement, neurosurgery, urology, gynecology, and cancer surgery to name a few.

The PBM program, by providing alternative approaches to traditional allogeneic donor transfusion allows patients to have a choice. Appropriate options, as dictated by the resources of each institution may include:

- Preoperative strategies such as oral or intravenous iron and/or erythropoietin (EPO)
- Intraoperative alternatives e.g. cell salvage, topical hemostatics, antifibrinolytics, ANH.
- Using minimal hemoglobin trigger levels for transfusion.
- Treatment of postoperative anemia

PBM thus changes the focus in Transfusion Medicine from product-based to patient-based.

Driving Factors:

Prior to ONTraC, there were three hospitals in Canada with defined PBM programs. Ontario has taken the lead in establishing a province-wide PBM program that has been emulated in other countries e.g. Australia.

Risk Mitigation:
In keeping with enhanced patient safety, the primary goal of a PBM program is to reduce patient exposure to allogeneic blood. Such a program will also be beneficial during blood shortages, which may otherwise result in delays/cancellations of elective surgery.

The risks of anemia (low hemoglobin levels) in increased patient morbidity and mortality, and increased hospital costs is well documented. Similarly, there is considerable evidence that allogeneic transfusion is associated with increased length of stay, increased costs, increased morbidity and increased mortality.

Patient Participation/Patient Choice
Operationally, participation in a Perioperative PBM program should be offered to all suitable patients i.e. those who have stable medical status and are undergoing surgery for a designated diagnosis which is likely to require replacement for blood loss.

In keeping with the concept of patient autonomy, patients should have PBM options discussed with them by the surgeon at the time surgery is first discussed. The patient should be informed that they may not automatically qualify for blood conservation alternatives, but will be assessed for suitability. Furthermore, patients must be informed that despite undergoing one or more of these PBM techniques, they may still require allogeneic blood.

Since the 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, one must ask why adoption of PBM has been so slow. This likely relates to 'traditional' physician training and practices where transfusion has been the default position for anemia and/or blood loss management. This has been accentuated by the belief that blood is safe - risks decreased with improved HIV and hepatitis testing. The ONTraC program aims to change this 'culture'.

B. ONTraC PROGRAM OVERVIEW

Objectives:

- To establish a formal Perioperative PBM network, employing various strategies to minimize patient exposure to allogeneic blood transfusion.
- To provide information sharing between medical personnel, hospital administrators & community stakeholders.
- To provide education to patients for the purpose of informed decision-making.
- To change the 'culture' among physicians and health care providers to recognize that the traditional concept that blood products are an effective therapeutic intervention should be replaced by the new concept that transfusion of blood products is in fact an undesirable outcome.

Rationale:

- Potential recipients of blood products have perceptions and misconceptions about risks of transfusion, and are increasingly seeking more information on blood products and alternatives and wishing to participate in decision-making processes about use of these products.
- The Krever Commission of Inquiry into Canada's Blood System recommended establishment of bodies that monitor and rationalize the use of blood products, and urged that patients be informed about alternatives to transfusion.
- There has been increasing support for "bloodless" surgery programs in both the medical literature and in the lay press.
- Patterns of blood utilization in each institution vary widely, with insufficient feedback from the blood transfusion service to end-users. Improved interaction between the blood conservation coordinators and the ordering physicians can help standardize utilization, help implement available guidelines, and modify transfusion practices to the benefit of the transfusion recipient.
- PBM programs can improve patient outcomes and can reduce costs.

Specific Aims and Benefits:

The following are PBM program outcomes and benefits for each of the following target groups.

For Hospital Administrators:

- To monitor changing patterns in use of blood products and alternatives to assess the fiscal impact on the hospital of these changes.
- To facilitate a process whereby Informed Consent is appropriately implemented, as mandated by the Health Canada Standards for Transfusion Z-902-04, and by the Ontario Institute for Quality Management in Healthcare (IQMH) requirements.
- To provide, via the Transfusion Committee, reports of blood and PBM utilization issues in the hospital to the Medical Advisory Committee.
- To ensure each hospital is meeting the increasingly stringent regulations regarding blood product administration.

For Healthcare Professionals:

- To perform continual prospective tracking of utilization of blood, blood products and blood alternatives in each institution (and potentially by individual physicians); the indications for transfusion, its appropriateness, and the clinical outcomes, with the data maintained in a central computerized database.
- To establish policies and procedures aimed at minimizing unnecessary exposure to allogeneic blood and preventing postponements/cancellations of transfusions or surgeries at times of blood shortages.
- To assess new therapies and alternatives relevant to PBM as they become available and recommend their appropriate use, using evidence-based principles and cost - benefit analyses where appropriate.
- To provide ongoing feedback to service chiefs and individual physicians on blood and PBM utilization.
- To provide a forum for review of ethical issues related to transfusion medicine.
- To provide a forum for staff education on transfusion-related issues.

- To facilitate the use of Informed Consent as part of a standard perioperative protocol, which includes education on both blood and alternative options to managing a patient's anemia.

For Patients:

- To acquire appropriate information regarding blood product use, including its safety.
- To acquire alternatives to allogeneic blood products, including avoidance of human blood products on religious, or any other grounds.
- To acquire education on blood and alternatives in sufficient time for informed and viable decisions to be made between the patient and the healthcare professional.

For the Community:

- To establish the ONTraC hospitals as centres of excellence in the perioperative management of patients' anemia.
- To establish a "patient blood management" program at hospitals throughout Ontario.
- To reduce societal costs of transfusion.

For Research:

- To foster an environment for clinical research in transfusion medicine. The perioperative PBM program has the potential to bring together researchers from many disciplines to identify thematic lines of inquiry. This will be of particular relevance to surgical practices, anaesthesia, laboratory and general medicine.
- To be a model for the establishment of similar programs across Canada, and to establish national links for the purposes of benchmarking, standard setting, and multi-centre collaborative research.

ONTraC Program Structure:

Program Management

ONTraC program management reports to the Drug Programs Policy and Strategy Branch, Drugs and Devices Division of the Ministry of Health of Ontario, and is composed of:

- Medical Program Director (MD)
  - Develop, plan and implement directions of the overall program, consistent with the requirements and needs of the Ministry of health and the individual hospitals.
  - Program evaluation: Monitor progress of the program by evaluating reports, performing statistical analyses, and ongoing assessment of the functioning of the program in individual hospitals and overall.
  - Education: Ensure awareness of the program within the hospitals in Ontario and beyond, increase awareness of blood conservation in the public domain, educate relevant physicians through individual visits, lectures and seminars, newspaper and radio, and publications in the scientific literature. Educate the nurse coordinators in best practices in blood conservation and organize twice-yearly symposia for the coordinators to review practice.
  - Clinical: Provide advice on patient management as requested.
  - Financial: To monitor the budget of the program to ensure that funds are spent appropriately at each hospital and in the program itself and that the budget is not exceeded.
  - Reports: Annual or biannual detailed reports to the Ministry of Health on the progress of the program, overview of biannual financial reports to the Ministry of Health, and other reports as requested on an ad hoc basis.
- 1.0 FTE Program Manager (Registered Nurse)
  - In collaboration with the Program Director, provide leadership to the coordinators through communication via various means (e.g. email, telephone, meetings, site visits, etc)
  - Financial: Monitor budget, ensuring funds spent appropriately
  - Reports: annual and bi-annual reports including financial statements
  - Data: monitors data collections completed as per timelines, liaise with coordinators and statistician in cleaning and preparing data for analysis
  - Education: planning meetings, booking speakers, etc; conference attendance as budget allows
  - Liaise with external sources as needed, ministry, software company, statistician

- 0.5 Team Leader (Registered Nurse)
  - Provides leadership in the manager's absence, ensuring succession planning and stability
  - Reviews annual and semi-annual reports
  - Assists with data and educational activities

ONTraC Funded 'Positions'

- Statistician
  - Statistical services including database manipulation, data cleaning and output as required
  - Provides guidance as needed with regards to statistical analysis
- Infinite Media: develop and maintains electronic ONTraC database, website and chat forum
  - Provide technical and administrator support to the program via ONTraC program managment

ONTraC Steering Committee

The initial mandate of the ONTraC Steering Committee was to review and guide the implementation of the KPMG recommendations, which generally have been completed. Steering Committee Terms of reference were developed and have been updated as noted below to reflect the advisory function of the committee:

- To provide input into ONTraC's strategic direction
- To function as an advisory body that reviews program reports which include financial and clinical data, and program outcomes, monitors progress towards annual goals, and provides recommendations.

Membership is composed of:

- OBAC representative(s)
- ONTraC Program Management
  - ONTraC Program DirectorONTraC Program Manager
  - ONTraC Team Leader (0.5 FTE)
- ONTraC Coordinator Representative
- Hospital Personnel (Physician, Nursing, and/or Senior Administration)
- Patient Representative
- BPCO, MOHLTC representative(s) – ex-officio

Sites and Staffing

- 25 ONTraC Hospital sites (Appendix 5) chosen on the basis of blood use and geographic distribution. The institutions are a combination of teaching and community hospitals.
- 28 Blood Conservation Coordinators:
  - 2 sites, London and UHN each have 2.0 FTE coordinators
  - 4 sites, St. Michael's, Sunnybrook, Health Sciences North and Scarborough each have a 1.5 FTE coordinators
  - All other sites have a 1.0 FTE coordinator
  - All Coordinators are Registered Nurses.

PBM Coordinators

See Pages 67-69 for a detailed role profile. The general objectives of the blood conservation coordinators are:

1. Management of a PBM Program
2. Education - to be a hospital-wide educator on PBM
3. Data Management
4. Institutional and Regional Activities

Procedure

All patients (and physicians) must sign the informed transfusion consent and a copy should be placed on the patient's hospital chart.

In a typical program, patients should be sent to the Pre-Admission Clinic (PAC) four weeks (25 to 32 days) prior to the scheduled date of surgery. The patients will be assessed for suitability following prescribed criteria and the appropriate option(s) will be offered and facilitated. A hemoglobin test will be done and literature on transfusion options will again be provided to the patient. If the patient has questions, these will be addressed by the PBM Coordinator, by the Director of Transfusion Medicine, the Anesthesiologist, or by the designated physician.

It may or may not be possible to start preoperative erythropoietin (EPO) at that visit, depending on resource availability. EPO prescriptions will be made by the surgeon, the PAC physician or the Director, Transfusion Medicine. Since EPO is given as an outpatient drug, costs will not accrue to the hospital. The Coordinator will investigate third party coverage and funding via Individual Clinical Review (ICR), and some patients may pay for it themselves. EPO is given only to patients who are anemic and have a likelihood of significant blood loss and need for transfusion.

At present, the program is primarily routinely focused on orthopedic, cardiac surgery and gynecological patients. Other patients are considered on an ad hoc basis. Periodically, the program will be evaluated for effectiveness and designated procedures for routine PBM may be extended to patients with other surgeries.

Database

The data is collected and entered via the web-based database through a secure log-in on the ONTraC website. The data submitted to the ONTraC program is anonymous, identified only by a numeric code, which is linked to a patient only by the hospital coordinator identification (ID) number. No linkage information (e.g. patient name, initials, date of birth, hospital ID number) is sent to the ONTraC database. In accordance with the Privacy Legislation, patient names, date of birth, and medical record numbers are kept in a file owned and maintained by the coordinator on the institution's computer with only the assigned study ID to link the patient to the data being collected. The anonymized ONTraC database is maintained under lock-and-key at Infinite Media and, in accord with statutory requirements will be kept for at least 25 years. The data is housed in a Secret Level B Facility.

There are two separate data collections: **Targeted** (all consecutive patients for a particular procedure/diagnosis within a defined time frame, whether seen by the coordinator or not – provides a 'snapshot' of transfusion practice; same number of patients per site) and **Non-Targeted** (patients specifically referred to the coordinator for PBM – provides information regarding patient demographics, presurgical condition, treatment modalities employed and their effectiveness; variable numbers depending on institutional patterns, but data from different sites are averaged and evaluated both individually and as aggregate). In both types of data collections, at the end of the data collection period, the coordinators have approximately 1-2 months to submit and complete entering their data prior to data cleaning and analysis. Data accuracy is checked by the Program Managers.

The data collected is aggregated (pooled) to evaluate the effectiveness of the program as a whole; in addition, individual institutions may use the data to examine blood utilization and effectiveness of blood conservation measures in their own site. In addition, most coordinators have developed their own extensive site-specific databases to monitor transfusion practices in the targeted procedures

Data Collections:

At specific time periods, baseline data collections and ongoing prospective data collections have been performed on the following elective **targeted** procedures:

- Coronary Artery Bypass Graft (CABG) surgery
- Knee arthroplasty
- Radical Prostatectomy added in 2005 (discontinued as a targeted procedure in 2014)
- Hip Arthroplasty added in 2007
- Abdominal Aortic Aneurysm (AAA) (discontinued as a targeted procedure)
- Open gynecological (myomectomy and hysterectomy) surgeries added in 2015
- Cardiac valves added in 2016

The data from the targeted and also non-targeted patient analysis is used to inform the coordinators and stakeholders on blood utilization, efficacy of methods used, and to encourage the most cost-effective approaches to transfusion consistent with optimal patient care, while promoting a culture of patient blood management at each site. Targeted data collections occur annually, in general from Feb. 1 to July 31st, and non-targeted data collections occur throughout the calendar year.

The ONTraC program is evaluated using quantitative and qualitative performance measures.

1. **Transfusion rates:** Anticipated overall reduction in the allogeneic transfusion rate over each designated time period. These targets are reviewed annually.
2. **Transfusion outcomes** (LOS, infection rate, mortality, adverse effects)
3. **Efficacy of the PBM measures employed**
4. **Blood utilization** (red cells, platelets, plasma)
5. **Site Visits:** Site Visits are a qualitative performance measure tool. Their purpose is to review Coordinator's performance, assess hospital support for the program, highlight successes and address any issues. The program, the individual hospital data and effectiveness are reviewed with the coordinator, their supervisor and relevant administrative and physician personnel. There needs to be clear direction and leadership in host sites. While this has been painstaking, this support and local champions have been increasingly evident in all institutions. Ensuring that the role profile is being followed cannot be overemphasized; some institutions have initially tended to see the funding as "free" money to do with as they wish, which can place the coordinators in a difficult position. These issues, among others, are focused on in the site visits.
6. **Cost Benefit Analysis: T**he program has been very cost-saving. In 2013, the cost savings achieved through this program compared to baseline exceed $14 million for the cost of red cell product alone and over $46 million to the health care system overall (for orthopedic and CABG procedures; many other diagnostic categories are now added). The cost of the program was $3.2 million (currently $3.54 million, 2020).

Lessons learned

There must be a central ONTraC Program management structure for continuity, accountability, providing a clear understanding of the coordinator role and ensuring that the focus is, and remains on, Patient Blood Management. At the individual hospital sites, it requires strong leadership at all levels, including administrative, nursing and physician support for a PBM program to be successful. In addition, the Coordinator must have champion advocates(s). To change practice, comparative supporting data is needed on current transfusion rates and practices. Although there has been a marked overall reduction in allogeneic transfusions in all targeted procedures, there continues to be variability across sites. Even recognizing the differing circumstances and contingencies of the different sites, there is a need to improve uniformities of practice throughout the province. This often requires a 'culture change' which is often difficult. This may be best accomplished by education, sharing and demonstration of comparative data. To achieve these objectives, an individual dedicated to the concept can result in effective PBM. Culture change may be the most difficult aspect of implementing anew PBM program. There are many barriers to evidence-based PBM, as outlined by Delaforce A et al in Implementation Science, 15:6, 2020, but these are variable, mostly overcomable and there is no conclusive evidence from their systematic review to indicate which implementation strategies are most effective. .

Sample Generic Participation Agreement for a hospital site

ONTraC
ontario transfusion coordinators

Ms.
«TitlePosition»
«Hospital_Institution»
«Address_Line_1»
«City», «Province»
«Postal_Code»

RE: ONTraC Participation Agreement, Fiscal Year 2020-2021

Dear (CEO X):

We are pleased to inform you that the Ministry of Health and Long Term Care (MOHLTC) continues to fund and support a provincial Patient Blood Management (formerly Blood Conservation) through the placement of Patient Blood Management Coordinators within Ontario Hospitals.

Your hospital is a participant in this initiative to enhance optimal transfusion practices and provide/facilitate alternatives to blood transfusion where appropriate. The Ontario Transfusion Coordinators (ONTraC) program has, thanks to the efforts in the participating hospitals, been highly successful e.g. mean provincial transfusion rates for knee surgery, have decreased from 22.6% in 2002 to 0.69% in 2019; in CABG surgery from 60.1% in 2002 to 23.1% in 2019. The successes of the program have also been shown by significantly shorter length-of-stays in non-transfused patients and lower infection rates and cost savings to the province in purchasing of red blood cells of over $15 million and to the healthcare system overall of over $40 million.

Below is some of the data collected for your hospital. More complete analyses have been provided to your hospital coordinator, (Coordinator X), and may be obtained from her.

M			Percent patients transfused with red blood cells (and hospital ranking among participating hospitals)									
			2016			2017			2018			
Procedure	Number participating hospitals	Benchmark transfusion rate	Provincial average	Your Hospital transfusion rate	Your Hospital ranking	Provincial average	Your Hospital transfusion rate	Your Hospital ranking	Provincial average	Your Hospital transfusion rate	Your Hospital ranking	Meets benchmark
Knee	**23**	**3%**	**1.2%**	**3.8%**	**20**	**0.57%**	**0**	**Tied for 1st**	**0.69%**	**2.1**	**18**	**Yes**
Hip	**23**	**3%**	**2.5%**	**0%**	**Tied for 1st**	**1.46%**	**3.6%**	**20**	**0.87**	**0**	**Tied for 1st**	**Yes**
CABG	**10**	**25%**	**27.1%**	**26.6%**	**6**	**24.4%**	**31.0%**	**9**	**23.1%**	**20**	**Tied for 3rd**	**Yes**
Valves	**10**	**30%**	**36.5%**	**35.6%**	**5**	**31.4%**	**25.0%**	**3**	**32.4%**	**27.1%**	**4**	**Yes**
CABG+Valve	**10**	**55%**	**56.5%**	**45.8%**	**3**	**52.2%**	**47.6%**	**2**	**45.0%**	**43.9%**	**5**	**Yes**

Based on the terms and conditions of the agreement between the ONTraC Program, administered by Unity Health Toronto and the MOHLTC, (Hospital X) will receive $112,400 in fiscal year 2020-2021 (April 1st, 2020- March 31st, 2021) for salary and benefits related to the Patient Blood Management Program for a 1.0 FTE Registered Nurse Patient Blood Management Coordinator. Any costs incurred above the funding level are the responsibility of the individual institution and will not be covered by the ONTraC program.

These funds are to be used for salary and benefit costs associated with the ONTraC program and in accordance with the description of the Coordinator role profile (Appendix A). If not all the funding is required for salary and benefits, up to a maximum of $2,500 may be utilized for other expenses (non-salary / benefits) related to the ONTraC program including conference costs. Pre-approval is required for any individual expense, within the other expenses category, which exceeds $500. Pre-approval must be obtained in writing from the ONTraC office.

All unspent funds at year-end must be returned to the MOHLTC via the ONTraC program and cannot be carried forward.

(Insert hospital name):

a. Is responsible for submitting quarterly and a fiscal year-end financial statement documenting how the above mentioned funding has been allocated for the past fiscal year.

   Quarterly Reporting:

   1. Will provide a brief report on current and anticipated surpluses to ONTraC after each of the first three quarters (i.e. quarter 1 by July 30th, quarter 2 by October 30th and January 30th respectively) (Appendix D).

   Year-end Reporting:

   2. The year-end financial statement (Appendix E) must be signed by your Chief Financial Officer, no designates please.
   3. The original, signed year-end statement must be mailed to the auditor and received no later than April 30th, 2021. The ONTraC office or SMH Finance will inform all sites of the auditor's mailing address in the fourth quarter.
   4. To facilitate year-end tracking and reporting to the MOHLTC, and no later than April 30th, 2021, a scanned copy of the signed year-end statement is to be emailed to Alanna Howell, Program Manager ONTraC (alanna.howella@unityhealth.to) and to Julie McKendry, Deputy Chief Financial Officer (alanna.howell@unityhealth.to).
   5. FY2020-21 funds remaining at year-end must be returned no later than May 31st, 2021. Surplus cheques are to be made payable to "Unity Health Toronto (ONTraC Program)" and returned to the attention of the ONTraC Program Manager.

b. Is solely liable for any loss or claim connected with the services of the Patient Blood Management Coordinator, and will obtain and maintain in full force and effect during the term of this contract, comprehensive liability insurance in the amount of five million dollars ($5,000,000.00) per occurrence.

c. Is solely responsible for the hiring of the Patient Blood Management Coordinator, all associated employment taxes, benefits, severance, Worker's Compensation and other Human Resource matters as the Patient Blood Management Coordinator is considered an employee of (Hospital X). Your site Coordinator is not an employee of Unity Health Toronto.

d. Will ensure that the Patient Blood Management Coordinator in your hospital functions in accordance with the role profile provided in Appendix A. The Patient Blood Management Coordinator is expected to work closely with the Director of Transfusion Medicine, Anesthesiologists, Surgeons, other Physicians and Nurses, as well as the Pre-Admission Clinic, and other relevant individuals, including patients, to promote patient blood management in your hospital.

e. Will facilitate attendance, as required, of the Patient Blood Management Coordinator as part of the Program, to attend ONTraC related meetings and conferences (as directed by ONTraC), for which expenses will be covered by the Program.

f. Will facilitate a scheduled site visit of the ONTraC Program Manager and/or Director, who will evaluate the progress of the program in your hospital. This will include scheduled meetings with the Coordinator, their supervisor(s), relevant physicians and nurses. Appendix B provides a general overview of the measures employed to evaluate the progress and success of the program in your hospital.

Please do not hesitate to contact the undersigned if further information is required. Adherence to the Hospital Responsibilities as outlined is essential for obtaining continued funding. Please note that this position is not to be used for research purposes or as a Transfusion Safety Officer.

We are asking (Hospital X) to indicate your ongoing commitment and participation in the ONTraC program. Please review and sign the attached Participation Agreement and return to the ONTraC Program Manager by August 14th, 2020.

ONTraC has been extremely successful and we are grateful that the Ministry has recognized your efforts and those involved in your institution.

Sincerely,

John Freedman, MD FRCPC
Program Director, ONTraC
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30 Bond St., Room 2-048 Shuter Wing
Toronto, ON M5B 1W8
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Fax: (416) 864-6063
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Alanna Howell, RN
Program Manager, ONTraC
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CC:
«CC_NAME_Direct_report», «CC_TitleDirect_Report1»
«CCName2», «CCTitlePosition2»
«CCName3», «CCTitlePosition3»
«CCName4», «CCTitlePosition4»
«CCName5», «CCTitlePosition5»
«CCName6»«CCTitlePosition6»«CCNamePBMC», «CCTitlePosition_PBMC»

Attachments/Enclosures
Appendix A: ONTraC Patient Blood Management Coordinator Role Profile
Appendix B: General Conditions and Recommendations for Success
Appendix C: Financial Reporting
Appendix D: Quarterly Financial Report Template
Appendix E: ONTraC Program Year-end Financial Report Template

General Conditions and Recommendations for Success: Hospital Responsibilities

1. The hospital agrees to use the ONTraC funds only for costs associated with the ONTraC program. Recovery of unused funds may occur based on the Ministry of Health and Long-Term Care Transfer Payment Agreement policy.
2. The hospital will hire an appropriate candidate for the position of Blood Conservation Coordinator (Appendix A – Role Profile).
3. The hospital is responsible for the performance of the Blood Conservation Coordinator, and **all** associated costs including employment taxes, benefits, severance, and Worker's Compensation.
4. To ensure a successful program the hospital will designate supporting and reporting mechanisms for the Blood Conservation Coordinator within the hospital.
5. The hospital will support project timelines as required e.g. hiring of new or replacement candidate(s), data collections, etc. as defined by the ONTraC Program
6. The hospital and its medical staff agree to support the ONTraC Coordinator in adhering to the Coordinator Role description (Appendix A) by:
7. Working collaboratively with the Coordinator to promote blood conservation;
8. Working to establish hospital systems that support the pre-surgical assessment and intervention of patients in the identified groups (Cardiovascular, Orthopedic etc).
9. Reviewing new clinical guidelines and best practices related to patient blood management with the goal of adoption and integration into physician practice (e.g. informed consent for blood products)
10. It is expected that the hospital and medical staff will review the blood utilization data on a regular basis to examine trends throughout the year and create solutions to identified concerns in patient blood management and improve overall performance.
11. The hospital administration and representative(s) of the medical staff agree to meet on-site on an annual basis with the ONTraC Program Director and Manager to discuss the ONTraC Coordinator performance, successes and barriers to managing a blood conservation program within your hospital, and to discuss corrective strategies to address any issues.

12. The hospital will communicate with the ONTraC Program Office any concerns regarding the program or Blood Conservation Coordinator function.

13. The hospital will, if deemed necessary within the hospital policies, provide a copy of the Research Ethics Board approval for the data collection on an annual basis.

14. The hospital will provide to the ONTraC Program Manager a fiscal year-end financial report documenting the costs associated with the program for the past fiscal year, signed by the Chief Financial Officer, within 2 months of March 31st for each fiscal year. These costs should be provided in general categories including: base salary, benefits, supplies, miscellaneous, and other.

15. The hospital understands that ongoing funding in future years is contingent upon meeting the above conditions.

16. NOTE: This is NOT a Transfusion Safety Officer Position.

Blood Conservation Coordinator --- Role Profile

A. PREAMBLE

Recent years have seen a significant change in attitude towards blood transfusion by both physicians and patients. It has become increasingly apparent that the beneficial effects of transfusion must be balanced against the potential hazards that can result from transfusion. Blood Conservation Coordinators will assist in restoring confidence to patients and physicians who are concerned about both infectious (e.g. HIV and Hepatitis) and non-infectious transfusion-related complications. There are risks other than transfusion-transmitted infections that are of concern, including wrong blood, hemolytic reactions, cardiac overload and transfusion-related acute lung injury (TRALI). Considerable evidence links allogeneic transfusion as an independent predictor of postoperative infections, increased length of stay, multi-organ failure and mortality.

Blood is a scarce and expensive commodity. The donor pool continues to shrink (due to restrictions) and it is at times difficult for supply to meet demands. The evidence on appropriate use of red cells for various surgical indications has improved, and there are evidence-based guidelines that need to be promoted. There is increasing evidence around appropriate alternatives to transfusion, such as erythropoietin, intravenous iron, intra-operative cell salvage, antifibrinolytics, volume expanders, and surgical techniques that can also be part of a blood conservation program.

Blood Conservation Coordinators will work collaboratively with physicians, surgeons, nurses and other allied health professionals to develop centers of excellence in blood conservation (also known as patient blood management). In order to reduce allogeneic transfusion, the Blood Conservation Coordinators will perform a variety of activities that will contribute to establishing a Blood Conservation Program, by implementing Blood Conservation algorithms in the perioperative patient population.

B. QUALIFICATIONS

- Evidence of certification with the College of Nurses of Ontario. Meets the current Standards of Practice for the College of Nurses. Baccalaureate in Sciences/Health Sciences preferred.
- Minimum of five years related clinical experience
- Commitment to continuing education and willingness to remain current within a fast changing environment.
- Ability to actively participate in relevant internal and external committees and groups concerned with blood conservation issues.
- Proven leadership capabilities.
- Demonstrated ability to work autonomously.
- Demonstrated excellence in interpersonal and supervisory skills, including verbal, written, and organizational skills.
- Demonstrated organizational skills to assess, plan, design, coordinate, implement, and evaluate adult educational programs.
- Ability to anticipate and resolve problems in a collaborative and/or independent manner, as appropriate.
- Administrative and computer skills essential. Experience preferred in word processing, spreadsheet, Powerpoint and database applications.

C. AREAS OF RESPONSIBILITY

Using advanced knowledge and skills to provide optimal care to patients/families at risk of requiring an allogeneic blood transfusion through the development of a Blood Conservation Program. The following details the Blood Conservation Coordinator's major areas of responsibility. Percentage of workload data is approximate and based on historic trends.

1) Management of a PBM Program (50%)

Provides ongoing support for the Provincial Blood Utilization Strategy by performing a variety of activities that will contribute to establishing a PBM Program within eligible Ontario hospitals.

- Liaises with appropriate personnel in relevant departments (i.e. Anesthesia, Pre-Admission Clinic, Perioperative Services, Transfusion and Laboratory Services).
- Screens and enrolls qualified patients in the appropriate blood conservation programs.
- Facilitates referrals to appropriate services as required, i.e. CBS Autologous Program, Hospital's Autologous Program, *EPREX Assistance Line, etc.
- Liaises with appropriate staff to follow up on type of Blood Conservation strategy employed.
- The coordinator may organize and arrange quarterly meetings of hospital Blood Conservation Committee. Alternatively, the coordinator may participate in meetings and report to the Hospital Transfusion Committee or another appropriate hospital committee tasked with reviewing hospital transfusion practices.
- Identifies and communicates risk management issues to appropriate organizational infrastructure, i.e. the Department of Surgery, Department of Anesthesia, Medical Director of Transfusion Medicine through participation in one of the above mentioned committees.
- Participates in development of hospital blood conservation policies and standard operating procedures through participation in one of the above mentioned committees.
- May monitor informed consent for transfusion, and may perform chart audits to monitor compliance with the hospital policy.
- While the coordinator may monitor nursing transfusion practices e.g. appropriate storage of blood products outside the Transfusion Laboratory, administration of blood products, etc., these activities should comprise only a small percentage of time and the coordinator's functions are not meant to be those of, or to replace, a Transfusion Safety Officer.
- May contact patients by phone, mail, or in person to provide pertinent information to patients once they are accepted for a surgical procedure that may require a transfusion. It is expected that most contacts will be in person.
- The coordinator's focus will be on the designated surgical procedures as defined by the ONTraC Program Director, e.g. CABG, Knee & Hip arthroplasty, Radical Prostatectomy and other areas of focus that may be developed. Full data collection (as defined by the ONTraC program) will be expected on these patients.
- The coordinators may also secondarily see patients not in the targeted groups; full data collection will be expected on these patients too.

2) Patient, Family & Staff Education (25%)

Ensures that patient/family focused support and educational information is provided to those patients who may require a blood/blood product transfusion. Ensures that patients, family, and relevant staff are made aware of, and have access to the information on the current risks of allogeneic transfusion, blood conservation strategies, and alternatives to blood transfusion.

- Provides a forum to promote educational initiatives related to Blood Conservation and Transfusion
- Participates in the education of hospital staff (example, nurses, physicians, surgeons, technologists, pharmacists, etc.) and patients regarding blood conservation.
- Develops patient blood management algorithms appropriate for the hospital
- Relates procedural information as per hospital standards.
- Informs patients and their families of available options, to facilitate patients having procedures completed within recommended waiting time guidelines.

3) Data Management and Analysis (20%)

Ensures maintenance of a current, complete, and accurate database for all patients enrolled in the PBM Program.

- Maintains accurate, up-to-date information, entered regularly or as instructed by the ONTraC management.
- As instructed by ONTraC, the PBM coordinator collects and submits data required for program evaluation.
- Forwards Monthly Activity Reports to the Provincial office as required.
- Provides hospital reports as per policy or as required.
- Ensures data accuracy through ongoing quality assurance at the institutional and provincial levels.

4) Institutional and Regional Activities (5%)

- Participates as a member of the PBM/Blood Conservation Committee and/or the Transfusion Committee, collaborating and communicating with other health care professionals, acting as an advocate for patients.
- Participates in hospital program development and implementation activities using a continuous quality improvement approach.
- Communicates with fellow PBM Coordinators, referring physicians and institutions within the region.
- Participates on regional Provincial PBM/Blood Conservation Committees as required.
- Collaborates with the hospital transfusion service and provides hospital transfusion data upon request
- Participates with appropriate hospital personnel to develop hospital-specific benchmarks for blood conservation
- Participates with ONTraC program management in developing hospital PBM benchmarks for performance evaluation
- Facilitates (with hospital administration) the site visits of the program Manager and Program Director
- Attends ONTraC and other meetings as required by the Program
- No more than 5% of time should be spent on independent research projects.

D. CORE OUTCOMES OR PERFORMANCE INDICATORS

PBM Program

Liaisons developed with hospital staff to customize PBM guidelines and standards to be appropriate to the scope of hospital practice and able to be implemented
Local 'champion(s)' in place
Procedures set up with preadmission facility or alternatives to obtain access to appropriate patients for pre-surgical counseling on anemia management strategies
Patients provided with appropriate information and opportunity to access alternatives
Demonstrated progress in PBM in the hospital in accord with agreed upon criteria from the ONTraC program
Provision of ONTraC recommendations and policies to appropriate hospital staff and departments
Provision of data reports from the ONTraC program to appropriate hospital staff and departments e.g. to relevant individuals in the Departments of Anaesthesia, Surgery, Gynecology, Hematology, Laboratory Services, Hospital Administration, etc

Education

Educational materials on PBM provided to hospital staff
In-hospital PBM algorithm(s) developed and distributed to relevant health care personnel
PBM procedures aligned with hospital procedures
Education provided to patients and families through forums, materials, and/or one-on-one sessions

Data Management

Database set up for required data maintenance
Processes established to implement data collection and entry on patients in the PBM program
Accuracy of data entered
Reports on monthly blood conservation program activities, as required, are timely and complete

Regional participation

Participation as member of hospital PBM Committee and/or Transfusion Review Committee and/or equivalent
Participation in hospital PBM program development and implementation activities (using a continuous improvement approach)
Communication with fellow PBM Coordinators, referring physicians and institutions within the region
Participation on regional Provincial PBM/Blood Conservation Committees as required
Provision of hospital transfusion data upon request to MOHLTC, hospital quality assurance or blood transfusion or blood conservation committees and to the ONTraC program

E. ACCOUNTABILITY

1) The PBM Coordinators actions are governed by:

- Regulated Health Professional's College, College of Nurses; according to the Regulated Health Professional Act (RHPA) Standards of Practice
- Ontario Health Care Consent Act
- Hospital: Vision and Mission Statement, and Policies and Procedures
- Health Canada regulations

- CSA Standards Z902-04
- Adherence to the following voluntary standards is encouraged: Canadian Society for Transfusion Medicine (CSTM), American Association of Blood Banks (AABB), Society for Advancement of Blood Management (SABM).

2) The PBM Coordinator functions in a matrix reporting relationship with various stakeholders within their respective institution and to the Provincial Coordinating Office, including:

- A line reporting relationship within the hospital to the Medical Director of PBM/Blood Conservation Program (example, Medical Director of Transfusion Medicine, Medical Director of Perioperative Services, etc. this is institution specific)
- A line reporting relationship to the Administrative staff at the ONTraC Provincial PBM Office for previously defined deliverables
- General accountability to the physicians and surgeons as applicable in the provision of service as defined above.
- General accountability to any working groups or committees in which the PBM Coordinator may participate.

3) The program as a whole, including financial accountability, is accountable to the Ministry of Health and Long-term Care of Ontario

ONTraC
ontario transfusion coordinators

Patient Blood Management
Preventing post-operative anemia – how family practice clinicians can help

Why should family physicians be involved in preventing post-op anemia?

- 30-70% of patients present to elective surgery with anemia
- Patients with undiagnosed or undertreated anemia have worse outcomes: increased morbidity, mortality and health care costs
- Historically, anemia was thought of as harmless and easily corrected with blood transfusions; but transfusion is inherently hazardous and is also associated with increased morbidity and mortality and is an independent risk factor for increased length of stay (1.5 to 2-fold), and infection rates (1.5 to 2-fold). Furthermore transfusion is costly (purchase cost of a unit of red cells is CAD $420; overall cost of a transfusion to the health care system is $1200 USD -- *Shander A, Best Pract Res Clin Anaesthesiol 21:271, 2007; Shander et al, Transfusion 50:753, 2010; Freedman et al, Transfusion, 48:237-250, 2008*).

Who are candidates for anemia work-up prior to elective surgery?

- All patients going for elective surgery in whom blood loss is expected to be >500 ml e.g. orthopedic, cardiac, gynecologic surgeries.

What can the Family physician do?

- Detect preoperative anemia early, preferably > 30 days before surgery. Waiting until the preadmission clinic which is often within 21 days prior to surgery is too late to diagnose and treat anemia
- At the time of referral to a surgeon for a high blood loss surgery (e.g. orthopedic, cardiac, major vascular surgery, major gynecology or gastrointestinal surgery), or as soon as your office is informed about a patient's surgery date, order a CBC. If the patient has a hemoglobin below 130 g/L, then order a serum ferritin, transferrin saturation (sometimes also ordered as iron saturation depending on the laboratory).

How can patients be treated?

- Although there may be many causes of anemia, the most common cause is iron deficiency anemia (IDA). This is defined as a ferritin < 30 mcg/mL or in the setting of inflammation, a ferritin of < 100 mcg/L with a transferrin saturation of < 20%.
- Treatment of iron deficiency anemia requires identifying the cause of iron deficiency (e.g. identify source of blood loss or malabsorption). Once that is identified, iron supplementation is required.
    - When time to surgery is sufficient (> 6 weeks), oral iron may be considered (Table next page). Oral iron can be started as 40–60 mg elemental iron daily or 80–100 mg every other day.
    - IV iron is indicated if oral iron is poorly tolerated, is ineffective (no increase in Hb after 4 weeks), or if insufficient time until surgery (< 4-6 weeks). IV iron is relatively safe: studies have shown no increased risk of severe adverse events such as infections, cardiovascular, neurological, respiratory, gastrointestinal, thromboembolic and constitutional severe reactions; anaphylaxis is rare and the benefits of IV iron significantly outweigh the risks. However, IV iron administration may be slow (up to 4 h, although with some 15-30 min; and 30 min afterwards), space is needed for infusion, and patients need to be monitored; resuscitation equipment and trained personnel should be available. If you do not have access to IV iron, please see the next section on "who can help?"
- In other cases of preoperative anemia, management depends on the underlying cause and may require a referral.

Who can help?

- There are Patient Blood Management (PBM) nurse coordinators present in 25 Ontario hospitals as part of the ONTraC program. If a patient has preoperative anemia with a planned surgery at one of these hospitals, the patient can be referred to the local PBM nurse coordinator who can then assist with the Hb optimization of the patient (and provide documentation to the referring physician, the surgeon and/or anesthesiologist) – the earlier the coordinator knows about the patient, the more likely a better outcome. A list of coordinators and a simple referral form are appended
-

Key messages for diagnosis and management of iron deficiency

Minck S, Robinson K, Saxon B, Spigiel T, Thomson A: Australian Family Physician 42(5): 291-297, 2013

Investigations

- Iron deficiency is never a final diagnosis in itself and a cause should always be sought
- Upper and lower GI tract in all postmenopausal women and men with IDA unless clear overt evidence of non-GI blood loss
- In premenopausal women, GI investigations should be done in those aged >50 years, those with symptoms suggesting GI disease and those with a strong family history of GI cancer
- Patients with IDA may need assessment for celiac disease

Iron therapy

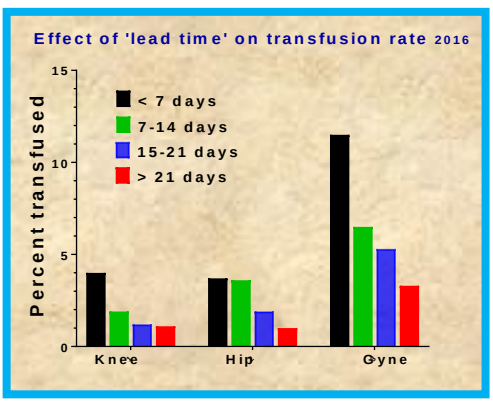
- Increasing dietary iron intake alone is inadequate to treat frank iron deficiency
- Oral iron therapy in appropriate dosing and for sufficient duration is effective first line therapy for most patients
  - After therapeutic doses of oral iron, reticulocytosis should occur within 72 hours and Hb should rise by about 20 g/L every 3 weeks
  - Oral iron should be continued for 3-6 months beyond hemoglobin normalization so that stores are replenished
- IV iron may be considered in those with:
  - Demonstrated intolerance, non-compliance or lack of efficacy with oral iron
  - A clinical need for a rapid response e.g. insufficient time before non-deferrable surgery
  - Intestinal malabsorption
  - Ongoing blood loss that exceeds absorptive capacity
- Blood transfusion should be reserved for patients with or at risk of cardiovascular instability due to their anemia

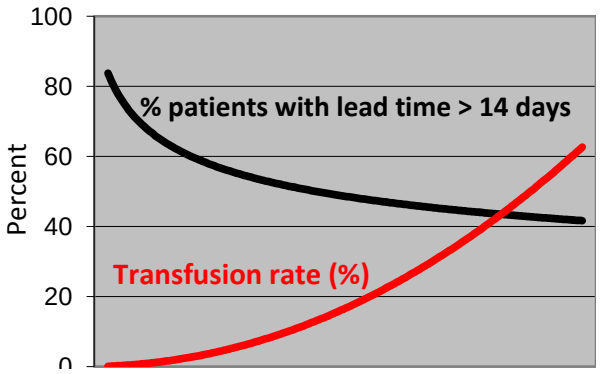
Oral irons (preparations vary in cost)	Strength per capsule/tablet	Elemental iron per capsule/tablet
Ferrous fumarate (e.g. Palafer & generics available)	300 mg	100 mg
Ferrous gluconate (generics available)	300 mg	35 mg
Ferrous sulfate (generics available)	300 mg	60 mg
Ferrous sulfate dried sustained release (Slow-Fe)	160 mg	50 mg
Polysaccharide iron complex (e.g. Feramax)	150 mg	150 mg
Heme-iron polypeptide (e.g. Proferrin, Optifer alpha)	11 mg	11 mg

To ensure best iron absorption, supplement should be taken on an empty stomach (if tolerated) or with foods high in vitamin C, which enhances iron absorption; not necessary, however, when taking polysaccharide-iron complex or heme iron polypeptide. Gastro-intestinal side effects might lead to poor compliance with oral iron therapy; it is important to discuss clearly with the patient the expectations when taking oral iron e.g. black tarry stools, constipation.

An algorithm for diagnosis and management of anemia used by the ONTraC program can be obtained from a Coordinator or by visiting the ONTraC website at www.ontracprogram.com

Seeing patients early allows pre-op planning and decreases transfusion rates (from ONTraC data)

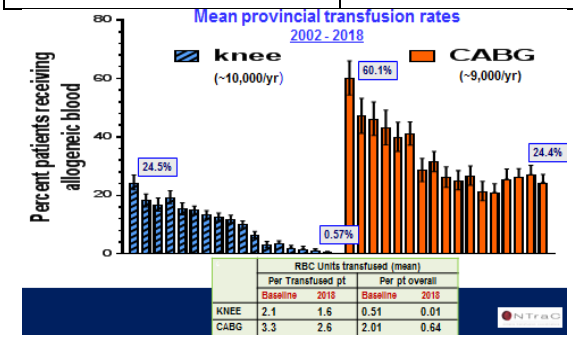




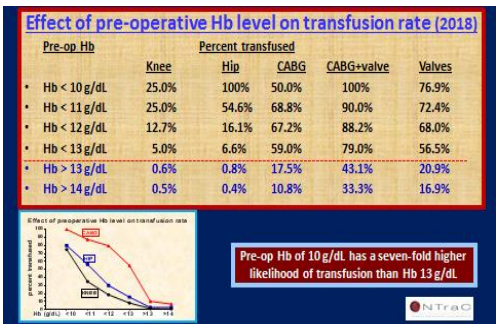
The fewer patients with longer lead times the higher the transfusion rate

ONTraC program PBM Coordinators

Hospital	Coordinator	Phone	FAX	email
Guelph General Hospital	Lucinda Lahey	519-837-6440 x2583	519 837 6779	Llahey@gghorg.ca
Hamilton Health Sciences	Linda Pickrell	905-521-2100 x75836	905 521 5058	Pickrell@hhsc.ca
Health Sciences North (Sudbury)	Carla Delisle	705-523-7100 x8695	705 671 5268	cdelisle@hsnsudbury.ca
Hospital for Sick Children	Nadia Naraine	416-813-6264	416 813 5433	nadia.naraine@sickkids.ca
Humber River Hospital	Krystal-Lyn Harder	416-242-1000 x62023	416 242 1128	KHarder@hrh.ca
Kingston Health Sciences Centre	Karen Letourneau	613-548-1347	613 548 2409	Karen.letourneau@kingstonhsc.ca
Lakeridge Health	Kelly Syer	905-576-8711 x3764	905 721 4855	ksyer@lh.ca
London Health Sciences Centre	a. Christine Cotton b. Lynda Wright	a. 519-685-8500 x32707 b. 519-685-8300 x35659	519 663 3563	Christine.Cotton@lhsc.on.ca Lynda.Wrightr@lhsc.on.ca
Michael Garron (TEGH)	Esther Cabrera	416-469-6580 x2768	416 469 6676	Esther.Cabrera@tehn.ca
Mt Sinai	Amanda Sellers	416-586-4800 x2627	416 586 8830	Amanda.sellers@sinaihealth.ca
Niagara Health System	Barbara Last	905-378-4647 x46570	905 682 9929	barbara.last@niagarahealth.on.ca
North Bay Regional Health System	Nancy Chapin	705-474-8600 x4930	705 495 8130	Nancy.chapin@nbrhc.on.ca
Ottawa Hospital	Donna Touchie	613-737-8899 x71735	613 739 7686	dtouchie@toh.on.ca
Peterborough Regional Health Centre	Kim Devlin	705-743-2121 x3019	705 876 5135	kdevlin@prhc.on.ca
Sault Area Hospital	Currently Vacant			
Scarborough Health Network	Laura McKenzie-Kerr	416-438-2911 x6626	416 431 8245	lmckenzie@shn.ca
Southlake Regional Health Centre	Sheila McCarthy	905-895-4521 x2909	905 830 5965	smccarthy@southlakeregional.org
St Joseph's (Toronto)	Maria Monteiro	416-530-6486 x4286	416 530 6006	Maria.Monteiro@unityhealth.ca
St Mary's General Hospital	Alisa Paneghel	519-749-6578 x1941	519 749 6636	apaneghel@smgh.ca
St Michael's Hospital	a. Anna Nassis b. Yvonne Davis-Read	a. 416-864-6060 x6733 b. 416-864-6060 x3036	416 864 6063	Anna.Nassis@unityhealth.to Yvonne.Davis@unityheaalth.to
Sunnybrook Health Sciences Centre	Saudia Jadunandan Ruby Tano	416-480-6100 x2061	416 480 4128	Saudia.jadunandan@sunnybrook.ca ruby.tano@sunnybrook.ca
Trillium: Credit Valley	Gerry O'Brien	905-813-1100 x5540	905 813 3848	Gerry.OBrien@thp.ca
Trillium: Mississauga	Cecilia Addison	905-848-7580 x2074	905 804 7906	Cecilia.Addison@thp.ca
University Health Network (UHN)	a. Lucia Evans (TWH) b. Sujung Yi (TGH)	a. 416-603-5800 x5164 b. 416-340-4800 x6102	416 603 5622 416 340 3757	Lucia.evans@uhn.ca Sujung.yi@uhn.ca
Windsor Regional Hospital	Currently vacant			
ONTraC Program Manager	Alanna Howell	416-864-6060 x4055	416 864 6063	Alanna.Howella@unityhealth.ca



Annual mean transfusion rates (x axis: years from 2002 to 2018)



The higher the preoperative hemoglobin level, the lower the transfusion rate (marked decrease when hemoglobin ≥ 130 g/L)

REFERRAL TO ONTRAC COORDINATOR FOR ANEMIA MANAGEMENT

PATIENT

Name of patient: _____.

Patient's hospital ID (if known) _____.

Patient age: _____ **Patient sex (please circle):** M F .

Patient contact information: Phone: **Fax:** **Email** _____.

Address if none of above applicable _____.

REFERRING PHYSICIAN **(Can use "stamp" if available)**

Name of referring physician _____.

Contact details of referring physician:

Phone: _____.

FAX: _____ .

Email: _____.

Name of referring physician's secretary/assistant/nurse (if appropriate): _____.

PROCEDURE

Anticipated procedure _____.

Name of surgeon or anesthesiologist (if known) _____.

Name of anticipated hospital for surgery (if known) _____.

Date of anticipated surgery (if known) _____.

LAB RESULTS:

Date of Hemoglobin determination _____ .

Hemoglobin level _____g/L

Ferritin level (if known) _____.

TSAT (if known) _____.

ONTraC COORDINATOR

Referral to ONTRaC Coordinator: **Coordinator's name:** _____ .

Method of referral (please circle): FAX: email: Phone: Letter.

Date of referral: _____.

Special instructions from referring physician to coordinator: _____.

_____.

****

For coordinator use:

Date patient contacted

Date patient seen:

Date report to referring physician:

Date report to surgeon/anesthesiologist:

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