



PATIENT BLOOD MANAGEMENT  
GUIDELINES

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**COMPANIONS**





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# ACKNOWLEDGMENT

The NBA has commissioned the development of a suite of patient blood management (PBM) tools by various stakeholders as outlined by the Patient Blood Management Guidelines Implementation Strategy. The tools are intended to be used as a resource for health professionals to use in implementing the recommendations and practice points in the PBM Guidelines.

The companions are set out with a PBM strategy or technique as a separate topic, generally one to two pages short. Each topic starts with key messages, followed by clinical implications, then the detailed information and finally loads of resources.

Acknowledgements with thanks to the Transfusion Practice and Education Team at the Blood Service.

# PATIENT BLOOD MANAGEMENT GUIDELINES: COMPANIONS

## Purpose

The [National Blood Authority \(NBA\) Patient Blood Management \(PBM\) Guidelines](#) provide comprehensive, evidence and consensus based guidance regarding PBM in six modules covering all patient groups and clinical scenarios where transfusion might be required. Patient blood management aims to improve clinical outcomes by avoiding unnecessary exposure to blood components. The companions provide supporting information aimed at improving knowledge and understanding of the guidelines and how they can be used to achieve better patient care and outcomes. If transfusion is clinically indicated, details of risks and benefits to support this process are also outlined in this document.

The important areas of consent and how to best administer a transfusion are not covered in this document – refer to the Australian and New Zealand Society of Blood Transfusion/Australian College of Nursing [Guidelines for the administration of blood products](#), [Flippin' Blood](#), [BloodSafe](#) eLearning and [www.transfusion.com.au](http://www.transfusion.com.au) for guidance.

## Who should use these companions?

Healthcare professionals wanting or needing to become involved in PBM strategies, or experienced clinicians who would like to expand their PBM toolkit.

## Recommendations and practice points

The PBM guidelines recommendations and practice points are frequently referred to throughout the companions. The recommendations are based on evidence from systematic reviews and the practice points are based on consensus decision-making (where insufficient high-quality data was available). To distinguish the recommendations and practice points for the different modules the following terms have been used:

- CBMT – PBM Guidelines: Module 1 - Critical Bleeding Massive Transfusion
- PO - PBM Guidelines: Module 2 - Perioperative
- MED - PBM Guidelines: Module 3 - Medical
- CC - PBM Guidelines: Module 4 - Critical Care
- R# - Recommendation
- PP# - Practice point

For example CBMT-R1 refers to recommendation 1 in the Critical Bleeding Massive Transfusion module.

## Resources

In order to incorporate a PBM strategy or technique into routine practice, the use of clinical practice improvement methodology is recommended (See Appendix 1).

Resources for implementation may also be found on the NBA, Australian Commission on Safety and Quality in Health Care, Australian Red Cross Blood Service and jurisdictional program websites:

- [Australian Commission on Safety and Quality in Healthcare](#)
  - [National Safety and Quality Health Service Standard 7: Blood and Blood Products](#)
  - [Standard 7: Blood and Blood Products Safety and Quality Improvement Guide](#)
- [National Blood Authority](#)
- [Australian Red Cross Blood Service](#)
- [Blood Matters](#)
- [BloodSafe](#)
- [Clinical Excellence Commission – Blood Watch](#)
- [Queensland Blood Management Program](#)
- [WA Department of Health Patient Blood Management Program](#)

# 1. PATIENT BLOOD MANAGEMENT

Patient Blood Management (PBM) is the timely application of evidence-based medical and surgical concepts designed to maintain haemoglobin concentration, optimise haemostasis and minimise blood loss in an effort to improve patient outcomes.<sup>1</sup>

## Key messages

- PBM focuses on effective management and conservation of a patient's own blood rather than being reliant on donor blood.<sup>2</sup>
- Strategies and techniques can be beneficial for all patient groups and clinical scenarios as outlined in the six modules (Obstetrics and Paediatric/ Neonates yet to be released).
- PBM is based on three principles commonly referred to as the three pillars:
  - ♦ optimising the patient's own blood elements including red cell mass
  - ♦ minimising the patient's blood loss and bleeding
  - ♦ optimising the tolerance of anaemia.<sup>3</sup>
- Use of PBM strategies and techniques has been associated with improved patient outcomes, patient satisfaction and healthcare costs savings.<sup>4</sup>

## Clinical implications

- 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.

## Background

PBM is a key area of focus for both the Australian and international healthcare sector. Significant work is being undertaken to further refine and review the appropriateness and indications for transfusion. Locally the National Blood Authority has funded and managed the development of six patient focused evidence-based, PBM Guidelines:

- Critical Bleeding Massive Transfusion
- Perioperative
- Medical
- Critical Care
- Obstetrics and Maternity
- Paediatric/Neonatal

An increasing focus on PBM has been driven by a number of factors:

- the risks associated with blood transfusion - with increasing evidence of higher risk of morbidity and mortality and increased length of stay;
- rising costs, both direct and indirect, associated with provision and transfusion of allogeneic blood;
- challenges of maintaining an adequate blood supply in the face of increased demand due to an ageing population.<sup>4</sup>

The “three pillars” concept arose from the results of the Austrian Benchmark Study of blood use in adult patients undergoing elective surgery, which showed that >90% of transfusions in this group of patients were attributable to 3 main predictors.<sup>5</sup> Table 1 highlights the relationship between the predictors of red blood cell transfusion and the three pillars of patient blood management.<sup>2</sup>

**Table 1 Relationship between the predictors of red blood cell transfusion and the three pillars of patient blood management<sup>2</sup>**

Predictors for red blood cell transfusions	Pillars of PBM
Prevalence of preoperative anaemia	Optimisation of blood volume and red cell mass
Perioperative blood loss	Minimisation of blood loss
Failure to adopt a more restrictive threshold for transfusion	Optimisation of the patient’s tolerance of anaemia

Whilst originally based on a surgical population, this concept is relevant to all patient groups and clinical scenarios, with the ultimate goal of improving patient outcomes. Considering the promising benefits of PBM strategies for patients and the healthcare system, it is hoped that PBM is increasingly viewed and adopted as a standard of care for all patients who may be at risk of being transfused at any time during their care.<sup>6</sup>

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#### Additional resources

- National Blood Authority. [Patient Blood Management Guidelines and Quick Reference Guides](#).



# 2. SUMMARY OF PBM MODULES RECOMMENDATIONS AND PRACTICE POINTS

PBM strategy/technique	Critically bleeding patient	Perioperative patient	Medical patient	Critical care patient
R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>PBM Guidelines:</b> Module 1	<b>PBM Guidelines:</b> Module 2	<b>PBM Guidelines:</b> Module 3	<b>PBM Guidelines:</b> Module 4
<b>Pillar one – optimise blood volume, especially red cell mass (anaemia management)</b>				
Identify, evaluate and manage anaemia	✓ Assess as early as possible prior to surgery (R2, R3, PP1, PP4, PP5)	✓ Assess as early as possible prior to surgery (R2, R3, PP1, PP4, PP5) ✓ If iron deficient; or suboptimal iron stores; or with ESAs (R4, R5, PP6, PP7) ✗ Oral iron not for use in immediate post-op period (R6)	✓ Reversible causes in cancer patients (PP8)	
Iron therapy	✓ If iron deficient; or suboptimal iron stores; or with ESAs (R4, R5, PP6, PP7) ✗ Oral iron not for use in immediate post-op period (R6)	✓ If iron deficient; or with ESAs; or in absolute and functional iron deficiency in patients with CHF; (R3, PP4, PP12, PP14) ✓ IV iron may be required in IBD (PP15)	✓ If iron deficient; or with ESAs; or in absolute and functional iron deficiency in patients with CHF; (R3, PP4, PP12, PP14) ✓ IV iron may be required in IBD (PP15)	
Erythropoiesis stimulating agents (ESAs)	✓ May be indicated in anaemia of chronic disease (PP7) ✓ Where ESAs are indicated, they must be combined with iron therapy (R5)	✓ May be indicated in anaemia of chronic disease (PP7) ✓ Where ESAs are indicated, they must be combined with iron therapy (R5)	✓ In anaemic patients with CKD (R4, R5, R6, R7, PP13, PP14) ✗ Not for routine use in cancer patients (R2)	✗ Not for routine use in critically ill (R2)
Preoperative autologous donation (PAD)	✗ Routine use not recommended (R11)	✗ Routine use not recommended (R11)		

CHF = chronic heart failure      CKD = chronic kidney disease      IBD = inflammatory bowel disease

<b>PBM strategy/technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>Critically bleeding patient</b> <b>PBM Guidelines:</b> Module 1	<b>Perioperative patient</b> <b>PBM Guidelines:</b> Module 2	<b>Medical patient</b> <b>PBM Guidelines:</b> Module 3	<b>Critical care patient</b> <b>PBM Guidelines:</b> Module 4
<b>Pillar two – minimise blood loss (haemostasis management and blood conservation modalities)</b>				
Assess bleeding risk	Values suggestive of physiological derangement: PLT < 50 x 10 <sup>9</sup> /L PT > 1.5 x normal INR > 1.5 APTT > 1.5 x normal fibrinogen < 1.0 g/L	✓ In general, can undergo invasive procedures with PLT ≥50x10 <sup>9</sup> /L or INR ≤ 2 (PP17) ✓ Seek haematology advice as per PP18		
Manage medications inhibiting coagulation e.g. aspirin, warfarin, NSAIDs, SSRIs, complementary medicines (continue/cease/bridge)		✓ Refer to module for guidance on if, how, when to cease: Clopidogrel (R7, PP9) Aspirin (R8, PP8) NSAIDs (R9) Warfarin (R10, PP10)		
Consider medications enhancing coagulation Tranexamic acid (TXA) Desmopressin Aprotinin ε –aminocaproic acid (ε-ACA)	✓TXA ( CRASH 2 trial)	✓TXA in cardiac surgery (R17) ✓TXA in non-cardiac surgery (R18) ✗Desmopressin – routine use not supported (PP16) Note: evidence of beneficial effects of aprotinin and ε-ACA, but aprotinin withdrawn, and ε-ACA not marketed in Australia and New Zealand (PP14, R19, PP15)		✓Within 3 hours of injury (R3,PP14, PP15) ✓Upper GI bleeding (R4, PP15)

NSAIDs = Non-steroidal anti-inflammatory

GI = gastrointestinal

SSRIs = selective serotonin reuptake inhibitor



<b>PBM strategy/technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>Critically bleeding patient</b> PBM Guidelines: Module 1	<b>Perioperative patient</b> PBM Guidelines: Module 2	<b>Medical patient</b> PBM Guidelines: Module 3	<b>Critical care patient</b> PBM Guidelines: Module 4
<b>Pillar two – minimise blood loss (haemostasis management and blood conservation modalities)</b>				
rFVIIa	✗ Routine use not recommended (R2) ✓ MTP to include advice on administration of rFVIIa (note: not licensed for this use) (PP8,9)	✗ Prophylactic or routine use not recommended (R22) ✓ Consider in life threatening haemorrhage (PP20)		
Prevention of hypothermia	✓ Aim for temperature > 35°C (PP1,2)	✓ Measures should be used (R12)		
Appropriate patient positioning		✓ Avoid excessive venous pressure at surgery site (PP11)		
Deliberate induced hypotension		✓ Radical prostatectomy or major joint replacement (R13)		
Acute normovolaemic haemodilution		✓ Surgery where substantial blood loss anticipated (R14, PP12)		
Cell Salvage – intraoperative		✓ Surgery where substantial blood loss anticipated (R15, PP13)		✓ Critically ill trauma patients (PP13) ✓ Patients undergoing emergency AAA surgery (PP13)

11 MTP = massive transfusion protocol

AAA= abdominal aortic aneurysm

<b>PBM strategy/ technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>Critically bleeding patient</b> PBM Guidelines: Module 1	<b>Perioperative patient</b> PBM Guidelines: Module 2	<b>Medical patient</b> PBM Guidelines: Module 3	<b>Critical care patient</b> PBM Guidelines: Module 4
<b>Pillar two – minimise blood loss (haemostasis management and blood conservation modalities)</b>				
Cell Salvage post-operative		✓ Cardiac surgery or total knee arthroplasty (R20)		
Surgical technique		✓ Refer <a href="#">Box 3.1 Surgical haemostasis options</a>		
Haemostasis analysis		✓ TEG in patients undergoing cardiac surgery (R16)		
Blood products to manage coagulopathy FFP, platelets, fibrinogen, cryoprecipitate	✗ Insufficient evidence to support or refute the use of specific ratios of RBCs to components (PP4) ✗ Suggested doses in MTP: FFP: 15 mL/kg Platelets: 1 adult dose Cryo: 3-4 g			
Red Blood Cells (RBCs)	✓ Use of RBCs can be lifesaving, however increased volumes may be independently associated with increased mortality and ARDS (PP6) ✓ Use MTP to facilitate timely and appropriate use (PP7)	✓ Red Cell transfusion based on patient's clinical status, applying a restrictive transfusion strategy, using a single unit followed by reassessment to determine if further unit required (PP2-PP3)	✓ Red Cell transfusion based on patient's clinical status, applying a restrictive transfusion strategy, using a single unit followed by reassessment to determine if further unit required (PP1, PP2).	✓ Red Cell transfusion based on patient's clinical status, applying a restrictive transfusion strategy, using a single unit followed by reassessment to determine if further unit required (PP1, PP2).
Fresh frozen plasma (FFP)		✗ Prophylactic use of FFP in cardiac surgery not recommended (R21)	✓ Refer to guidelines for use of FFP in specific patient groups (PP17) ✗ Routine use of FFP in medical patients with coagulopathy not supported (PP16)	✗ Routine use of FFP in critically ill not advised (PP5, PP6, PP7)

TEG = thromboelastography

ARDS = adult respiratory distress syndrome

MTP = massive transfusion protocol



<b>PBM strategy/technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>Critically bleeding patient</b> PBM Guidelines: Module 1	<b>Perioperative patient</b> PBM Guidelines: Module 2	<b>Medical patient</b> PBM Guidelines: Module 3	<b>Critical care patient</b> PBM Guidelines: Module 4
<b>Pillar two – minimise blood loss (haemostasis management and blood conservation modalities)</b>				
Platelets (PLT)		<ul style="list-style-type: none"> <li>✓ Prophylactic PLT use after cardiac surgery not supported (PP19)</li> <li>✓ In general, can undergo invasive procedures with PLT <math>\geq 50 \times 10^9 / L</math> or INR <math>\leq 2</math> (PP17)</li> <li>✓ Seek haematology advice as per (PP18)</li> </ul>	<ul style="list-style-type: none"> <li>✓ Prophylactic PLT transfusion for patients undergoing chemotherapy and haematopoietic stem cell transplant at: <math>&lt; 10 \times 10^9 / L</math> in absence of risk factors; <math>&lt; 20 \times 10^9 / L</math> in presence of risk factors (R8)</li> <li>✓ PLT transfusions may be indicated for prevention of haemorrhage in patients with thrombocytopenia or PLT function defects (PP20)</li> <li>✓ Patients with chronic failure of PLT production are best managed with expert opinion (PP21)</li> <li>✗ PLT transfusions are not indicated in all causes of thrombocytopenia and may be contraindicated in certain conditions (e.g. TTP and HIT) (PP20)</li> </ul>	<ul style="list-style-type: none"> <li>✓ PLT transfusion may be appropriate if PLT <math>&lt; 20 \times 10^9 / L</math> (PP10, PP11, PP12)</li> </ul>

TTP = thrombotic thrombocytopenic purpura      HIT = heparin-induced thrombocytopenia

<b>PBM strategy/technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	Critically bleeding patient PBM Guidelines: Module 1	Perioperative patient PBM Guidelines: Module 2	Medical patient PBM Guidelines: Module 3	Critical care patient PBM Guidelines: Module 4
<b>Pillar two – minimise blood loss (haemostasis management and blood conservation modalities)</b>				
Platelets (PLT) continued from previous page			✗ In patients undergoing chemotherapy and HSCT, there is no evidence to support a lower trigger for prophylactic PLT transfusion for patients with risk factors; or for therapeutic-only PLT transfusions (PP22)	
Fibrinogen, cryoprecipitate			✓ Refer to guidelines for use of cryoprecipitate or fibrinogen in specific patient groups (PP19) ✓ Specialist opinion advised for DIC (PP18) ✗ Routine use of cryoprecipitate or fibrinogen in medical patients with coagulopathy not supported (PP18)	✗ Routine use of cryoprecipitate and fibrinogen in critically ill not advised (PP8, PP9)

HSCT = haematopoietic stem cell transplantation



<b>PBM strategy/technique</b> R = Recommendation PP = Practice point ✓ = recommended or suggested strategy ✗ = NOT recommended or suggested	<b>Critically bleeding patient</b> PBM Guidelines: Module 1	<b>Perioperative patient</b> PBM Guidelines: Module 2	<b>Medical patient</b> PBM Guidelines: Module 3	<b>Critical care patient</b> PBM Guidelines: Module 4
<b>Pillar three – optimise tolerance of anaemia</b>				
Single unit (RBC) transfusion policy	✓ Single unit policy (PP3)	✓ Single unit policy (PP2)	✓ Single unit policy (PP2)	✓ Single unit policy (PP2)
Restrictive transfusion thresholds  (See document for Hb triggers)	✓ Restrictive transfusion strategy (PP2, PP3)	✓ Restrictive transfusion strategy (R1, PP1, PP3, PP5, PP6, PP7, PP9, PP10, PP21) ✓ Special care with ACS (R1) and CHF (PP7) ✗ In patients with thalassaemia, the evidence does not support a change to the current practice of maintaining a pretransfusion Hb 90–100 g/L (PP23) ✗ In patients with myelodysplasia who are regularly and chronically transfused, there is no evidence to guide particular Hb thresholds. (PP24) Note: New evidence indicates that a restrictive transfusion strategy (threshold 7 g/L, target 7–9 g/L) significantly improves outcomes in patients with acute upper GI bleeding (Villanueva et al, NEJM 2013)	✓ Restrictive transfusion strategy (R1, PP1, PP3) ✓ Restrictive transfusion strategy (R1, PP1, PP3)	✓ Restrictive transfusion strategy (R1, PP1, PP3)

GI = gastrointestinal



# 3. IDENTIFY, EVALUATE AND MANAGE ANAEMIA

Identifying, evaluating and managing anaemia is a key strategy for optimising red blood cell (RBC) mass in all patient groups (PBM Pillar 1).

## Key messages

- Anaemia is an independent risk factor for morbidity and mortality in both medical and surgical patients.<sup>1,2</sup>
- RBC transfusion in medical patients has been associated with mortality and morbidity in some patient groups.<sup>2</sup>
- Preoperative anaemia is predictive for RBC transfusion which is associated with increased morbidity, mortality, ICU length of stay and hospital length of stay.<sup>1</sup>

## Clinical implications

- Preoperative anaemia requires identification, assessment and management in order to optimise haemoglobin and iron stores before elective surgery is scheduled.<sup>1</sup>
- Treatment of the underlying condition and pharmacological treatment of anaemia is preferable to transfusion.
- Use the [preoperative haemoglobin assessment and optimisation template](#) to guide practice for patients undergoing procedures in which substantial blood loss is anticipated. The template can be adapted for local use.<sup>1</sup>
- Iron therapy, erythropoiesis stimulating agents ESAs and RBC transfusion are possible treatments for anaemia.
- In patients with iron deficiency anaemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated.<sup>2</sup>

## Background

Anaemia is defined by the World Health Organization (WHO) as a haemoglobin level of <130 g/L in males and <120 g/L in females.<sup>3</sup> Anaemia occurs when there is insufficient production of red blood cells, or excessive loss or destruction of red blood cells. Common causes include iron or vitamin deficiencies, anaemia of chronic disease and bone marrow disorders.

Anaemia is common in the community and incidence increases with age. Prevalence rates from a large population based study in the US found rates of approximately 10% in adults over age 65; more than doubling to 23% at age ≥85 years.<sup>4</sup>

Anaemia is independently associated with an increased risk of morbidity and mortality and with an increased likelihood of RBC transfusion.<sup>1,5</sup>



Anaemia is an independent risk factor for mortality and adverse cardiovascular outcomes in medical patients.<sup>2</sup> In medical patients including those with cancer, the aetiology of anaemia is often multifactorial; where appropriate, reversible causes should be identified and treated.<sup>2</sup> (MED-PP8)

Preoperative anaemia is common in elective surgical patients. The prevalence ranges widely from 5% to 76%<sup>6</sup> depending on age, co-morbidities and the nature of the underlying condition requiring surgery. Examples of reported prevalence rates include:

- 24 ± 9% in hip or knee arthroplasty<sup>7</sup>
- 44 ± 9% in hip fracture repair<sup>7</sup>
- 26% ± 4% in cardiac surgery<sup>8</sup>
- 31 to 75% in colorectal surgery<sup>9</sup>

Preoperative anaemia is associated with an increased risk of adverse outcomes including increased morbidity, such as cardiac events, pneumonia and postoperative delirium; and up to an almost 5-fold increase in mortality.<sup>1-2,10-16</sup>

Preoperative anaemia has also been shown to be predictive for perioperative transfusion of allogeneic blood products such as red blood cells, which itself carries a significant risk of morbidity, mortality, ICU length of stay and hospital length of stay (PO-R2,R3).<sup>4,14-16</sup>

Preoperative anaemia requires identification, assessment and management in order to optimise haemoglobin and iron stores prior to elective surgery (PO-R1, PP1, PP4, PP5).<sup>1</sup> The PBM guidelines: Module 2 – Perioperative contain a [preoperative haemoglobin assessment and optimisation template](#) to guide practice for patients undergoing procedures in which substantial blood loss is anticipated, such as cardiac surgery, major orthopaedic, vascular and general surgery. Specific details, including reference ranges and therapies, may need adaptation for local needs, expertise or patient groups.<sup>1</sup>

A [case study](#) has been developed to guide clinicians to implement preoperative anaemia assessment within their health care organisations. <http://www.blood.gov.au/preoperative-anaemia-identification-assessment-and-management-case-study>

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#### Additional resources

- Preoperative anaemia identification, assessment and management case study available, <http://www.blood.gov.au/preoperative-anaemia-identification-assessment-and-management-case-study>





# 4. IRON THERAPY

Iron can be given in oral or intravenous forms for patients with iron deficiency.

## Key messages

- Iron therapy is an important tool for optimising red blood cell mass (PBM Pillar 1).
- Iron therapy may be used as a primary treatment for anaemic or non-anaemic iron deficiency (including sub-optimal iron stores prior to surgery), or to augment the response to ESAs.<sup>1,2</sup>
- The underlying cause of the iron deficiency should be identified and managed.

## Clinical implications

- In medical patients with iron deficiency anaemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated.<sup>2</sup>
- Iron therapy is recommended for patients with or at risk of iron deficiency and for those with suboptimal iron stores.<sup>1,2</sup>
- Oral iron therapy is suitable and effective in most patients.<sup>3</sup>
- Intravenous iron should be considered for patients whose surgery cannot be delayed, or if oral iron is contraindicated or not tolerated.<sup>1,3</sup>
- Newer preparations of intravenous iron are safe, easy to administer and well tolerated.<sup>3,4</sup>
- Patients should be provided with information brochures about oral or intravenous iron therapy.
- Oral iron therapy is not recommended in the early postoperative period as it is not clinically effective.<sup>1</sup>

## Background

Iron therapy may be used as a primary treatment for anaemic or non-anaemic iron deficiency, or to augment the response to ESAs. When administered with ESAs, iron therapy prevents both absolute and functional iron deficiency and minimises the dose of ESA needed to achieve target Hb concentrations.<sup>1,2</sup> In Australia, ESAs are only indicated for the "treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g/L, where intrinsic renal disease, as assessed by a nephrologist, is the primary cause of the anaemia".<sup>5</sup> (See ESA companion)

In medical patients with iron deficiency anaemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated (MED-PP4).<sup>2</sup> 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 (MED-R3).<sup>2,6</sup> In patients with cancer, the aetiology of anaemia is often multifactorial; and where appropriate, reversible causes should be identified and treated (MED-PP8).<sup>2</sup>

The WA Health PBM Program has developed a [list of surgical patients who will benefit from preoperative iron/RBC assessment](#).

In surgical patients, iron therapy is recommended for patients with or at risk of iron deficiency (PO-R4,PP7); and for those with suboptimal iron stores (PO-PP6).<sup>2</sup> Most studies report that preoperative oral iron supplementation is effective in raising haemoglobin concentration, and decreases perioperative transfusion by 50-82%.<sup>4</sup> Oral iron is 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 (PO-R6).<sup>2</sup>

Although oral iron supplementation may be suitable for a high proportion of patients, there are some in whom intravenous iron should be considered, e.g. for patients whose surgery cannot be delayed, or if oral iron is contraindicated or not tolerated, usually due to gastrointestinal side effects.<sup>3,4</sup>

Two studies of intravenous iron sucrose, administered preoperatively to patients scheduled for major surgery, have shown a significant increase in haemoglobin concentration, resolving anaemia in up to 58% of patients in one study.<sup>4</sup> Preoperative intravenous iron can reduce transfusion among patients undergoing surgery for trochanteric hip fracture by 33%.<sup>4</sup>

However, in contrast to these results, a randomised controlled trial performed in 60 patients undergoing colorectal cancer resection reported that intravenous iron administered 14 days before surgery had no impact on haemoglobin concentration in comparison with placebo, and no impact on transfusion rates.<sup>4</sup>

Intravenous iron may provide a greater increase in haemoglobin concentration than oral iron. In a randomised, prospective study, women with anaemia caused by menorrhagia were treated with intravenous iron sucrose or oral iron protein succinylate daily.<sup>4</sup> Treatment was administered during the 3 weeks before elective surgery, and a significantly greater increase in haemoglobin concentration was observed in the intravenous group (3.0 vs. 0.8 g/dL). One study in gynaecological cancer showed a 64% reduction in RBC transfusion in patients treated with IV iron compared to those who received oral iron.<sup>2,4</sup>

Intravenous iron is well tolerated. Older preparations of iron for intravenous administration (e.g. iron dextran) were associated with a risk of anaphylactic reactions.<sup>4</sup> However, a number of studies performed in recent years have reported favourable tolerability. Currently available intravenous iron preparations are much safer than previous preparations, although the possibility of adverse events such as hypotension, arthralgia, abdominal discomfort and back pain remains. There is no prospective data to confirm association with bacteraemia and intravenous iron.<sup>4</sup>

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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
2. National Blood Authority. [Patient Blood Management Guidelines: Module 3 – Medical](#). Australia, 2012.
3. Pasricha SR, Flecknoe-Brown SC, Allen KJ, Gibson PR, McMahon LP, Olynyk JK, et al. [Diagnosis and management of iron deficiency anaemia: a clinical update](#). MJA 2010;193:525–532.
4. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#). Eur J Anaesthesiol. 2013;30:270–382.
5. The Schedule of Pharmaceutical Benefits. Accessed 10 September 2013. Available at: <http://www.pbs.gov.au/pbs/home>
6. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand (Chronic Heart Failure Guidelines Expert Writing Panel). [Guidelines for the prevention, detection and management of chronic heart failure in Australia](#). Updated July 2011.

# 5. ERYTHROPOIESIS STIMULATING AGENTS

Erythropoiesis stimulating agents (ESAs) boost the production of red blood cells and as such may play a role in optimising red cell mass (PBM Pillar 1) in specific groups of patients.

## Key messages

- ESAs are a method of optimising red cell mass (PBM Pillar 1)
- ESAs are an Authority item on the Pharmaceutical Benefits Scheme (PBS) with a limited indication.<sup>1</sup>
- ESAs have FDA prescribed Boxed Warnings for Chronic Kidney Disease (CKD), cancer and perisurgical use.<sup>2,3</sup>

## Clinical implications

- Routine use of ESAs are not recommended for cancer patients<sup>4</sup> or in the critically ill.<sup>5</sup>
- ESAs have been recommended or suggested in:
  - patients with Chronic Kidney Disease (CKD) and anaemia to avoid transfusion and relieve fatigue.<sup>4,7</sup>
  - surgical patients with anaemia of chronic disease.<sup>6,7</sup>
- Where an ESA is used, it must be combined with iron therapy.<sup>6</sup>
- In patients with CKD, ESAs to target a haemoglobin 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.<sup>4</sup>
- If ESA therapy is prescribed outside the PBS indication, 'Individual Patient Approval' may be required.
- If ESA therapy is made locally available for management of patients with anaemia in the perioperative setting, a [local clinical guideline](#)<sup>6</sup> which includes indications, dosage, administration and monitoring should be developed.

## Background

ESAs include recombinant human erythropoietin (EPO) derivatives: epoetin alfa (Eprex®), epoetin beta (Neorecormon®), and epoetin lambda (Novicrit®); and chemically modified forms of EPO such as methoxy polyethylene glycol-epoetin beta (Mircera®) and darbepoetin alfa (Aranesp®).

In Australia, ESAs are available on the PBS as an Authority item for the "treatment of anaemia requiring transfusion, defined as a haemoglobin level of less than 100 g/L, where intrinsic renal disease, as assessed by a nephrologist, is the primary cause of the anaemia".<sup>1</sup> 'Individual Patient Approval' may be required if patients fall outside these guidelines.



In June 2011, the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modified recommendations for more conservative dosing of ESAs in patients with CKD to improve the safe use of these drugs. FDA has made these recommendations because of data showing increased risks of cardiovascular events (stroke, thrombosis and death) with ESAs in this patient population.<sup>2</sup> Previous warnings exist for use in cancer patients and in the perisurgical setting.<sup>3</sup>

## FDA Boxed Warnings for ESAs:

### **WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE**

#### **Chronic Kidney Disease:**

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- Use the lowest ESA dose sufficient to reduce the need for red blood cell (RBC) transfusions *[see Warnings and Precautions]*.

#### **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 *[see Warnings and Precautions]*.
- Because of these risks, prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology program to prescribe and/or dispense ESA to patients with cancer. To enroll in the ESA APPRISE Oncology Program, visit [www.esa-apprise.com](http://www.esa-apprise.com) or call 1-866-284-8089 for further assistance *[see Warnings and Precautions]*.
- To decrease these risks, as well as the risk of serious cardiovascular and thromboembolic reactions, use the lowest dose needed to avoid RBC transfusions *[see Dosage and Administration]*.
- Use ESAs only for anemia from myelosuppressive chemotherapy *[see Indications and Usage]*.
- ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure *[see Indications and Usage]*.
- Discontinue following the completion of a chemotherapy course *[see Dosage and Administration]*.

#### **Perisurgery (EPOGEN/PROCRIT only):**

- Due to increased risk of Deep Venous Thrombosis (DVT), DVT prophylaxis is recommended *[see Dosage and Administration and Warnings and Precautions]*.

## ESAs in cancer

In cancer patients with anaemia, the routine use of ESAs is not recommended because of the increased risks of mortality and thromboembolic events (MED-R2). If ESAs are used, iron status should be evaluated to guide adjuvant iron therapy (MED-PP12). ESAs are not currently listed on the PBS for reimbursement for patients with cancer.<sup>3</sup>

## ESAs in chronic heart failure

At the time of the systematic reviews for the PBM guidelines: Module 3 – Medical, there was evidence of reduced mortality with ESA therapy in a group of patients, including a large subset with diabetes and congestive cardiac failure.<sup>3</sup> In a separate systematic review the incidence of thromboembolic events, mortality and heart failure-related hospitalisations were not affected by ESAs<sup>4</sup> but there was a significant improvement in exercise tolerance. ESAs are not currently listed on the PBS for reimbursement for patients with cardiac failure.

## ESAs in chronic kidney disease

In anaemic patients with CKD, ESA therapy to a low to intermediate Hb target may be used to avoid RBC transfusion (MED-R4), and/or to relieve fatigue (MED-R5), after consideration of risks and benefits for the individual patient.<sup>4</sup> However a target Hb >130 g/L is not recommended because of increased morbidity (MED-R6). The CARL guidelines recommend a Hb target between 100–115 g/L.<sup>8</sup> The FDA warning advises that using ESAs to target a haemoglobin 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.<sup>2</sup> In anaemic 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 (MED-R7).<sup>4</sup> ESA use is less effective in patients with chronic renal failure who have absolute or functional iron deficiency (MED-PP13).<sup>4</sup> For comprehensive information about ESA and iron therapy in patients with CKD, refer to [CARL iron guidelines](#) (MED-PP14).<sup>4</sup> Refer also to the [FDA warnings](#).<sup>2,3</sup>

## ESAs in critically ill patients

ESAs should not be routinely used in critically ill anaemic patients (CC-R2)<sup>4</sup>. This recommendation is based on the lack of effect of ESAs on mortality in a heterogeneous population of critically ill patients.<sup>4</sup>

## ESAs in perioperative patients

In surgical patients with anaemia of chronic disease (also known as anaemia of inflammation), ESAs may be indicated (PO-PP7).<sup>5</sup> Where indicated, it must be combined with iron therapy (PO-R5).<sup>5</sup> International guidelines recommend ESAs for orthopaedic surgery patients with anaemia, in whom nutritional deficiencies are absent or have been corrected.<sup>6</sup> FDA Boxed Warnings and local Product Information advise use of DVT prophylaxis in the perisurgical setting. However they are not currently listed on the PBS for this indication in Australia.

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### References

1. The Schedule of Pharmaceutical Benefits. Accessed 10 September 2013. Available at: <http://www.pbs.gov.au/pbs/home>
2. FDA Drug Safety Communication: [Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents \(ESAs\) in chronic kidney disease](#).
3. Important Prescribing Information. [Updated Aranesp® \(darbepoetin alfa\) and EPOGEN®/PROCRIT® \(epoetin alfa\) United States Prescribing Information \(USPI\)](#). Accessed 14 October 2013.
4. National Blood Authority. [Patient Blood Management Guidelines: Module 3 – Medical](#). Australia, 2012.

5. National Blood Authority. [Patient Blood Management Guidelines: Module 4 – Critical Care](#). Australia, 2012.
6. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
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8. McMahon LP, MacGinley R. KHA-CARI guideline: [biochemical and haematological targets: haemoglobin concentrations in patients using erythropoietin-stimulating agents](#). Nephrology 2012; 17(1):17-9.
9. WA Health. Patient Blood Management Program. [Erythropoietic Stimulating Agents: general guidelines \(PDF 157KB\)](#)

#### Additional Resources

- Council of Australian Therapeutic Advisory Groups (CATAC): Guiding Principles for the quality use of off-label medicines. Nov 2013 <http://www.catag.org.au/rethinking-medicines-decision-making/>

# 6. PREOPERATIVE AUTOLOGOUS DONATION (PAD)

Preoperative autologous blood donation (PAD) is the process of collecting a person's blood for their own use in the lead up to planned surgery. Routine use of this intervention is not supported by the evidence based PBM guidelines.

## Key messages

- PAD results in lower preoperative haemoglobin.
- PAD is associated with higher transfusion rates.
- Autologous blood is not without risk.

## Clinical implications

- The routine use of PAD is not recommended.<sup>1</sup>
- PAD collection should only be undertaken in exceptional circumstances, such as patient with a rare blood group or multiple red cell antibodies whose transfusion requirements cannot be met with allogeneic blood and are fit for donation<sup>2,3</sup>.

## Background

PAD has previously been adopted in the belief that it is a safer alternative to allogeneic blood. However, patients who have undergone preoperative autologous collection have been shown to have significantly lower preoperative haemoglobin levels, resulting in an increased likelihood (24%) of requiring a transfusion (autologous or allogeneic).<sup>1</sup> PAD is associated with risks in relation to collection (adverse events such as vasovagal reactions), storage and handling, and transfusion. Many of these are similar to those for allogeneic transfusions, such as bacterial contamination, and clerical error resulting in transfusion of the wrong blood to the patient.<sup>4,5</sup> Many studies highlight the low cost-benefit ratio and significant wastage (up to 50% of units) that occurs with PAD.<sup>4-7</sup> Routine preoperative autologous blood donation is no longer recommended (PO-R11).<sup>1</sup>

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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
2. Boulton FE, James V. Guidelines for policies on alternatives to allogeneic blood transfusion. 1. [Predeposit autologous blood donation and transfusion](#). *Transfus Med* 2007;17:354–65.
3. Australian Red Cross Blood Service. Requirements for autologous blood collection, <http://www.transfusion.com.au/node/554>.
4. Yazer MH, Waters JH. [How do I implement a hospital-based patient blood management program](#). *Transfusion* 2012;52:1640–1645.



5. Woodfield G, Davis KG, Francis A, Hudson P, Liew YW, Roper T, Theakston E. [Topics in Transfusion Medicine Special Edition: Guidelines for Autologous Blood.](#)
6. Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, Snyder-Ramos SA et al. [Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery.](#) Circulation 2007;116:471–479.
7. Brecher ME, Goodnough LT. [The rise and fall of preoperative autologous blood donation.](#) Transfusion 2001;41:1459–1462.

# 7. ASSESS BLEEDING RISK

Assessment of bleeding risk is a key component of PBM strategies to minimise blood loss (PBM Pillar 2).

## Key messages

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

## Clinical implications

- Bleeding risk should be assessed by structured patient interview, physical examination, assessment of comorbidities and medication history.<sup>1,2</sup>
- Routine coagulation testing to predict bleeding risk is not recommended.<sup>1,2</sup>
- Comprehensive assessment, specialist guidelines or haematology advice may be required in at risk patients, particularly if undergoing certain types of procedures.<sup>3</sup>

## Background

The use of a structured patient interview or questionnaire before surgery or invasive procedures to assess bleeding risk has been recommended in international guidelines.<sup>1,2</sup> 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.<sup>1,2</sup>

Physical examination should be performed as a second step, focusing on signs of bleeding and diseases which may cause haemostatic failure (e.g. liver disease).<sup>2</sup> Gender, body mass index and comorbidities including arterial hypertension, diabetes mellitus and renal dysfunction are independent risk factors for bleeding and transfusion.<sup>2</sup>

Routine coagulation testing to predict perioperative bleeding risk in unselected patients prior to surgery or other invasive procedures is not recommended.<sup>1,2</sup> Coagulation tests may suggest increased bleeding risk, but they are poor predictors of intraoperative or postoperative bleeding.<sup>2</sup>

A patient with a positive bleeding history or clinical signs of a bleeding tendency needs further assessment with coagulation testing and haematology review.

Specialist guidelines or haematology advice should be sought for at risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy (PO-PP18),<sup>3</sup> whether acquired, associated with medication or with systemic, metabolic or endocrine comorbidities.<sup>2</sup> The management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology provide recommendations and suggestions for perioperative management of patients with haemostatic derangements resulting from comorbidities, congenital bleeding disorders, and medications.<sup>2</sup> The Australasian Society of Thrombosis and Haemostasis provide guidance on perioperative management of patients on new oral anticoagulants (NOAC) undergoing elective surgery or procedures.<sup>4</sup>

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## References

1. Y. L. Chee, J. C. Crawford, H. G. Watson and M. Greaves. [Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures](#). British Committee for Standards in Haematology. British Journal of Haematology, 2008;140:496–504.
2. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#). Eur J Anaesthesiol. 2013;30:270-382.
3. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
4. Tran H, Joseph J, Young L, McRae S, Curnow J, et al. [New oral anticoagulants – a practical guide on prescription, laboratory testing and peri-procedural/bleeding management](#). Internal Medicine Journal, 2014;44:525-536

## Additional Resources

- Bleeding risk assessment and intervention guide – currently under development by the Blood Service and the NBA

# 8. CESSATION OF MEDICATIONS AFFECTING COAGULATION

Numerous medications and complementary therapies affect haemostasis. Cessation or bridging therapy may be required in order to minimise blood loss (PBM Pillar 2).

## Key messages

- Numerous medications and complementary therapies may affect haemostasis.

## Clinical implications

- The management of antiplatelet agents and anticoagulant therapy needs 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.
- The PBM guidelines: Module 2 – Perioperative provide some evidence and consensus based guidance.<sup>1</sup>

Specialist guidelines or advice may be required.

## Background

Numerous medications and complementary therapies may affect haemostasis so a comprehensive list of what the patient is taking is 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) 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, anaesthetist, cardiologist and haematologist, may be necessary to develop a management plan appropriate for the patient.

Some guidance regarding management of patients on anticoagulant and antiplatelet agents is provided in the PBM guidelines: Module 2 – Perioperative as outlined below.<sup>1</sup>

In patients undergoing coronary artery bypass graft (CABG) surgery either (with or without cardiopulmonary bypass off-pump coronary artery bypass), clopidogrel therapy should be stopped, where possible, at least 5 days before surgery (PO-R7).<sup>1</sup> 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.



Specific evaluation is required for patients who have had a recent stroke, or received a drug-eluting stent within the last 12 months or a bare metal stent within the last 6 weeks. If a decision is made to cease therapy preoperatively, this should occur 7–10 days before surgery (PO-PP9).<sup>1</sup>

In patients undergoing noncardiac surgery, it is reasonable to continue low dose aspirin therapy. This may require specific evaluation in neurosurgery and intraocular surgery. (PO-R8) For those undergoing cardiac surgery, aspirin may be continued until the time of surgery (PO-PP8).<sup>1</sup>

In patients undergoing elective orthopaedic surgery, NSAID therapy should be ceased preoperatively to reduce blood loss and transfusion. The timing of the cessation should reflect the agent's pharmacology (PO-R9).<sup>1</sup>

In patients undergoing minor dental procedures, arthrocentesis, cataract surgery, upper gastrointestinal endoscopy without biopsy or colonoscopy without biopsy, warfarin may be continued (PO-R10).<sup>1</sup> In patients receiving warfarin who are scheduled for elective noncardiac surgery or other invasive procedures (excluding minor procedures - see PO-R10); specific management according to current guidelines is required (e.g. guidelines from the American College of Chest Physicians and the Australasian Society of Thrombosis and Haemostasis) (PO-PP10).<sup>1</sup>

Additional sources to assist management include: [New oral anticoagulants - a practical guide](#),<sup>2</sup> [Consensus guidelines for warfarin reversal](#): Australasian Society of Thrombosis and Haemostasis;<sup>2</sup> [The perioperative management of antithrombotic therapy](#): American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8<sup>th</sup> Edition);<sup>3</sup> [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#);<sup>4</sup> and [Guideline on the management of bleeding in patients on antithrombotic agents](#): British Committee for Standards in Haematology.<sup>5</sup>

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1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
2. Tran H, Joseph J, Young L, McRae S, Curnow J, et al. [New oral anticoagulants – a practical guide on prescription, laboratory testing and peri-procedural/bleeding management](#). Internal Medicine Journal, 2014;44:525-536
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5. Chee YL, Crawford JC, Watson HG, Greaves M. [Guideline on the management of bleeding in patients on antithrombotic agents](#): British Committee for Standards in Haematology. British Journal of Haematology, 2008;140:496-504.

## Additional Resources

- Case study Point of Care Coagulation Testing National Blood Authority <http://blood.gov.au/point-care-coagulation-testing-case-study-prince-charles-hospital-brisbane>

# 9. ANTIFIBRINOLYTICS

The use of antifibrinolytic agents is an important component of therapy to minimise transfusion in some patients (PBM Pillar 2).

## Key messages

- Antifibrinolytic therapy has been shown to significantly reduce blood loss and transfusion rates for some patients.<sup>1</sup>

## Clinical implications

- Antifibrinolytic agents include tranexamic acid (TXA), aprotinin and  $\epsilon$ -aminocaproic acid, however only TXA is currently available in Australia.<sup>1</sup>
- TXA is recommended in adult patients undergoing cardiac and non-cardiac surgery and in acutely bleeding, critically ill trauma patients.<sup>1,2</sup>
- TXA should be considered in critically ill patients with upper GI bleeding.<sup>2</sup>
- TXA must be given within 3 hours of injury.<sup>2</sup>

## Background

Antifibrinolytics work by blocking the binding sites of plasminogen, displacing plasminogen from the fibrin surface which results in inhibition of fibrinolysis and stabilisation of clots, with subsequent reduction in blood loss. Antifibrinolytic agents include tranexamic acid (TXA), aprotinin and  $\epsilon$ -aminocaproic acid, however only TXA is currently available in Australia. In adult patients undergoing cardiac surgery (PO- R17); and in those undergoing noncardiac surgery, if substantial blood loss is anticipated (PO-R18), the use of intravenous TXA is recommended.<sup>1</sup>

In trauma patients with, or at risk of, significant haemorrhage, TXA (loading dose 1 g over 10 minutes, followed by infusion of 1 g over 8 hours) is recommended by the CRASH 2 trial. The CRASH 2 trial was published on 14 June 2010 after the cut-off date of the systematic review for PBM guidelines: Module 1 – Critical Bleeding/Massive Transfusion.<sup>3</sup> Note that due to concerns regarding generalizability of these findings, clinical trials are underway to further investigate this strategy in Australia.

In acutely bleeding critically ill trauma patients, TXA should be administered within 3 hours of injury (CC-R3).<sup>2</sup> In critically ill patients with upper GI bleeding, consider the use of TXA (CC-R4). Late administration of TXA is less effective and may be harmful (CC-PP14).<sup>2</sup>

There is evidence for the beneficial effect of intravenous aprotinin on incidence and volume of transfusion, blood loss, and the risk of reoperation for bleeding. However, the drug has been withdrawn due to concerns that it is less safe than alternative therapies (PO-PP14).<sup>1</sup>

There is evidence for the beneficial effect of intravenous  $\epsilon$ -aminocaproic acid on reduction of perioperative blood loss and volume of transfusion (PO-PP15) and it is recommended in adult patients undergoing cardiac surgery (PO-R19), however, the drug is not marketed in Australia and New Zealand.<sup>1</sup>

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## References

1. National Blood Authority, [Patient Blood Management Guidelines: Module 2 Perioperative](#). Australia, 2012.
2. National Blood Authority [Patient Blood Management Guidelines: Module 4 – Critical Care](#). Australia, 2013.
3. National Blood Authority. [Patient Blood Management Guidelines: Module 1 Critical Bleeding Massive Transfusion](#). Australia 2011.

## Additional Resources

- CRASH-2 trial collaborators (Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *The Lancet* 376(9734):23–32.  
[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(10\)60835-5/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60835-5/fulltext)

# 10. OTHER MEDICATIONS WHICH MAY MINIMISE BLEEDING

## Desmopressin

Desmopressin (DDAVP) stimulates a rise in endogenous Factor VIII and von Willebrand's Factor (vWF). It has been used to minimise intraoperative bleeding (PBM Pillar 2).

### Key messages

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

### Clinical implications

- In adult patients undergoing surgery in which substantial blood loss is anticipated, the routine use of desmopressin is not supported, due to uncertainty about the risk of stroke and mortality (PO-PP16).<sup>1</sup>

## Background

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.<sup>2</sup> In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, the routine use of desmopressin is not supported, due to uncertainty about the risk of stroke and mortality (PO-PP16).<sup>2</sup>

## rFVIIa

Recombinant Factor VIIa (rFVIIa) is a manufactured form of activated Factor VIIa, a central protein in the initiation of coagulation.

### Key messages

- The use of rFVIIa is generally reserved for life threatening haemorrhage 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.<sup>3</sup>



## Clinical implications

The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not supported.

rFVIIa may have a role in controlling massive bleeding when conventional measures have failed.

The routine or prophylactic use of rFVIIa in perioperative patients is not supported.

## Background

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 (CBMT-R2).<sup>4</sup>

A massive transfusion protocol (MTP) should include advice on the administration of rFVIIa when conventional measures – including surgical or interventional radiological haemostasis and component therapy – have failed to control critical bleeding (CBMT-PP8, PO-PP20).<sup>3</sup> Note that rFVIIa is not licensed for this use. Its use should only be considered in exceptional circumstances where survival is considered a credible outcome (see Template MTP example).

An initial rFVIIa dose of 90 µg/kg is reasonable in massive transfusion (CBMT-PP9).<sup>3</sup>

The routine therapeutic use of rFVIIa is not recommended because concerns remain about its safety profile, particularly thrombotic adverse events (PO-R22).<sup>1</sup>

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### References

1. National Blood authority, Patient Blood Management Guidelines: Module 2 Perioperative. Australia, 2012.
2. Bisbe E, Molto L. Pillar 2: Minimising bleeding and blood loss. Best Practice & Research Clinical Anaesthesiology. 2013;27:99-110.
3. [NovoSeven® RT Product Information](#): Novo Nordisk Pharmaceuticals Pty Ltd NSW, Date of most recent amendment 4 January 2012
4. National Blood Authority. [Patient Blood Management Guidelines: Module 1 Critical Bleeding Massive Transfusion](#). Australia, 2011.

# 11. PREVENTING HYPOTHERMIA

Maintenance of normothermia during the perioperative period assists in reducing blood loss (PBM pillar 2).

## Key messages

- Hypothermia prevention strategies result in significant reductions in transfusion incidence and blood loss.<sup>1</sup>
- The risk of morbid cardiac events and wound infections have been found to be significantly reduced when hypothermia prevention strategies are used.<sup>1</sup>
- In the critically bleeding patient, survival rates are improved when actions are taken to prevent or reduce the extent of hypothermia.<sup>2</sup>

## Clinical implications

- Measures to prevent hypothermia should be used in patients undergoing surgery (PO-R12).<sup>1</sup>
- Measures to prevent hypothermia should be used in patients in the critical bleeding/massive transfusion scenario.<sup>2</sup>

## Background

Anaesthetic induced hypothermia is known to reduce platelet function and impair enzymes of the coagulation cascade.<sup>3</sup> When the surgical patient's body temperature drops, the number of circulating platelets reduce and the function of remaining platelets are affected, with a 2 degree drop in temperature producing a 100% increase in bleeding time.<sup>4</sup> Mild hypothermia (<1 degree) significantly increases blood loss by approximately 16% and increases the risk of transfusion by 22%.<sup>3</sup> Conversely, maintenance of normothermia during the perioperative period reduces blood loss and transfusion requirement by clinically significant amounts.<sup>3</sup> Specific guidance on the management of perioperative hypothermia is available from the National Institute for Health and Clinical Excellence (United Kingdom)<sup>5</sup>.

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.<sup>2</sup>

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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
2. National Blood Authority. [Patient Blood Management Guidelines: Module 1 Critical Bleeding Massive Transfusion. Australia](#) 2011.
3. Rajagopalan S, Mascha E, Na J, Sessler D. [The Effects of Mild Perioperative Hypothermia on Blood Loss and Transfusion Requirement](#). *Anesthesiology* 2008;108:71-77.

4. Mahoney, CB, Odom J. [Maintaining intraoperative normothermia: A meta-analysis of outcomes with costs](#). AANA Journal 1999;67;155-164.
5. National Institute for Health and Clinical Excellence. [CG65 Perioperative hypothermia \(inadvertent\): NICE guideline](#). UK. 2008.

# 12. PATIENT POSITIONING

Patient positioning during surgery has important cardiovascular physiological consequences that can impact on perioperative bleeding<sup>1</sup> (PBM pillar 2).

## Key messages

- Intraoperative patient positioning requires balancing the need for the best surgical access while minimising potential risks for the patient.
- Use lateral, reverse Trendelenburg, or appropriate prone positioning to reduce blood loss.<sup>2</sup>

## Clinical implications

- Excessive venous pressure at the site of surgery should be avoided by appropriate patient positioning, both during and after the procedure.<sup>1</sup>

## Background

Excessive venous pressure at the site of surgery should be avoided by appropriate patient positioning, both during and after the procedure (PO-PP11).<sup>1</sup> Patient positioning during surgery has important cardiac physiological consequences that can impact on perioperative bleeding.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup>

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## References

1. Network for the Advancement Transfusion Alternatives, [Anesthetic techniques to reduce blood loss](#).
2. National Blood Authority. [Technical report on perioperative patient blood management- Volume 1b](#). Australia, 2012.
3. Ong SM and Taylor GJSC (2003). [Can knee position save blood following total knee replacement?](#) Knee Surgery 10(1):81-85





# 13. DELIBERATE INDUCED HYPOTENSION

Deliberate induced hypotension (DIH) is the controlled decrease of mean arterial pressure (MAP) to reduce surgical blood loss (PBM pillar 2).

## Key Messages

- DIH is used to reduce surgical blood loss and improve visibility in the surgical field.
- Hypotension must be closely monitored and controlled to ensure adequate perfusion of vital organs.<sup>1</sup>

## Clinical Implications

- In patients undergoing radical prostatectomy or major joint replacement, if substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, deliberate induced hypotension (MAP 50-60mmHg) should be considered, balancing the risk of blood loss and the preservation of vital organ perfusion (PO – R13).<sup>2</sup>

## Background

There are a number of techniques used to control hypotension, such as inhaled anaesthetic agents, vasodilators, beta blockers, and/or alpha adrenergic receptors, combined with mechanical manoeuvres to potentiate the action of hypotensive agents. In patients undergoing radical prostatectomy or major joint replacement, DIH was associated with a significant reduction in operative blood loss. DIH also significantly reduced the volume of blood transfusion with 55.8% of the hypotensive groups receiving a transfusion, compared to 78.7% in the control groups.<sup>3</sup>

A meta-analysis of randomised controlled trials found that DIH reduces blood loss most effectively for.<sup>3</sup>

- hip arthroplasty (503ml reduction)
- spine fusion (318ml reduction)
- orthognathic surgery (147ml reduction)

The clinical significance of DIH is dependent on patient co-morbidity and the specific surgical procedure.<sup>3</sup>

DIH should not be confused with the concept of permissive hypotension as described in the Patient Blood Management Guidelines: Module 1 - Critical Bleeding/Massive Transfusion section 3.4.<sup>4</sup>

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## References

1. Bisbe, E., Molto, L., [Pillar 2: Minimising bleeding and blood loss](#). Best Practice & Research Clinical Anaesthesiology 27, 99-110 (2013)

2. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative. Australia 2011](#)
3. Paul J., Ling, E. Lalonde, C. and Thabane L., [Deliberate hypotension in orthopaedic surgery reduces blood loss and transfusion requirements: A meta-analysis of randomized controlled trials](#). Canadian Journal of Anaesthesia 54 (10): 799-810. (2007)
4. National Blood Authority. [Patient Blood Management Guidelines: Module 1 – Critical Bleeding/Massive Transfusion](#). Australia, 2011.

# 14. ACUTE NORMOVOLAEMIC HAEMODILUTION

Acute normovolaemic haemodilution (ANH) is a blood conservation technique which may be considered for patients undergoing surgery in which substantial blood loss is anticipated. (PBM Pillar 2)

## Key messages

- ANH removes whole blood from a patient at the start of surgery, which is reinfused at the conclusion of surgery. It may minimise red cell loss.
- ANH may reduce the incidence and volume of allogeneic blood transfusion.<sup>1</sup>

## Clinical implications

- In adult patients undergoing surgery in which substantial blood loss is anticipated, the use of ANH should be considered (PO-R14).<sup>1</sup>
- ANH requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion (PO-PP12).<sup>1</sup>
- ANH can be used alone or in combination with other patient blood management strategies.
- Surgical procedures where a benefit for ANH has been demonstrated include: radical prostatectomy, hip and knee arthroplasty, cardiothoracic surgery, vascular and spinal surgery.<sup>2</sup>

## Background

ANH is performed immediately prior to surgery and involves the removal of whole blood from a patient and replacement of circulating blood volume with colloid and/or crystalloid solutions. The harvested blood, containing functional platelets and clotting factors, may be reinfused when a transfusion is indicated during or after the procedure.

[Further information and suggested guidelines for acute normovolaemic haemodilution](#) are available from the WA Health PBM Program<sup>2</sup> and [ANH: A practical approach](#) is available from the Network for Advancement of Transfusion Alternatives (NATA).<sup>3</sup>

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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
2. Government of Western Australia, Department of Health, [Patient Blood Management Program. Acute Normovolemic Haemodilution \(ANH\) – Information and Suggested Guidelines](#).
3. Network for Advancement of Transfusion Alternatives (NATA). [Acute Normovolaemic Haemodilution \(ANH\): A Practical Approach](#)



# 15. SURGICAL TECHNIQUE

Meticulous surgical technique is the cornerstone of intraoperative blood conservation (PBM pillar 2).<sup>1</sup>

## Key Messages

- Choice of surgical technique or access influences the amount of blood loss and transfusion requirements.<sup>2</sup>

## Clinical implications

- Surgical haemostasis options should be considered and utilised where appropriate. Some 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 and harmonic scalpel techniques (e.g. argon beam cavitation ultrasonic surgical aspirator [CUSA]),
  - ♦ Use of topical haemostatic agents.<sup>1</sup>
- Techniques including preventing hypothermia, patient positioning, and cell salvage should also be considered.

## Background

Meticulous surgical technique is the cornerstone of intraoperative blood conservation. Close communication between the surgeon, anaesthetists 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.<sup>3</sup>

The haemostat, sealant and adhesive components of the surgical toolbox continue to evolve and enter clinical practice at a rapid rate.<sup>3</sup> A controlled study in patients undergoing cardiac surgery has shown that the use of topical haemostatics can result in less blood loss and fewer transfusions.<sup>4,5</sup>

### *Emergency radiological/surgical interventions to reduce blood loss*

The European Society of Anaesthesiology guidelines suggest that endovascular embolisation is a safe alternative to open surgical intervention after failed endoscopic treatment for upper gastrointestinal bleeding; super-selective embolisation as primary therapy for treatment of angiogram positive lower gastrointestinal bleeding; and embolisation as first-line therapy for arterial complications in pancreatitis.<sup>6</sup>



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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia 2012.
2. Seeber, P. Shander, A. Basics of Blood Management. Blackwell Publishing, USA, 2007. Chapter 13 pg 174.
3. Bisbe E, Molto L. [Pillar 2: Minimising bleeding and blood loss](#). Best Practice & Research Clinical Anaesthesiology. 2013;27:99-110.
4. Spotnitz WD, Burks S. [Hemostats, sealants, and adhesives III: a new update as well as cost and regulatory considerations for components of the surgical toolbox](#). Transfusion 2012;52:2243-55.
5. Nasso G, Piancone F, Bonifazi R, Romano V, Visicchio G et al. [Prospective, randomized clinical trial of the FloSeal matrix sealant in cardiac surgery](#). Ann Thorac Surg. 2009;88: 1520-6.
6. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#). Eur J Anaesthesiol. 2013;30:270-382.

# 16. ANAESTHETIC TECHNIQUE

Anaesthetic agents and techniques can impact on perioperative blood loss (PBM pillar 2).

## Key Messages

- Anaesthetists play a key role in PBM strategies across the three pillars.

## Clinical Implications

- Anaesthetic techniques to reduce blood loss should be considered and utilised where appropriate. Some options include but are not limited to:
  - ♦ Propofol-based total intravenous anaesthesia (TIVA) has been associated with reduced blood loss in several settings<sup>1</sup>
  - ♦ Neuraxial block has been found to reduce blood loss and transfusion requirements<sup>1,2</sup>.
  - ♦ Positive pressure ventilation has been associated with increased intraoperative blood loss compared to spontaneous ventilation in total hip replacement surgery under general anaesthesia<sup>1</sup>.
  - ♦ Choice of anaesthesia technique for total hip arthroplasty should take account of the potential benefit of regional techniques with regard to blood conservation<sup>1</sup>.
- Deliberate induced hypotension, acute normovolaemic haemodilution, cell salvage and point of care testing should also be considered.

## Background

Anaesthetists have a key role in PBM from preoperative optimisation of red cell mass and coagulation status, to minimisation of perioperative blood loss, to appropriate management of postoperative anaemia. Anaesthetists should be aware of the contribution that strategies such as volatile (inhalational) versus total intravenous anaesthesia; regional versus general anaesthesia; and spontaneous versus positive pressure ventilation have on blood loss. Propofol-based TIVA has been associated with reduced blood loss in several settings such as spinal surgery, endoscopic surgery and first trimester pregnancy termination. Neuraxial anaesthesia has been shown to reduce blood loss by 25-30% and reduce transfusion rates from 33% (with general anaesthesia) to 12% in total hip arthroplasty.<sup>1</sup> Although there is less evidence for the choice of anaesthesia having a significant effect on perioperative bleeding in other types of surgery, anaesthetists should be aware of the possible benefits of regional anaesthesia, TIVA and spontaneous ventilation in reducing blood loss<sup>1</sup>.

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## References

1. National Blood Authority. [Patient Blood Management Guidelines: Module 2 - Perioperative](#). Australia 2011
2. Mauermann WJ, Shilling AM and Zuo Z. [A comparison of neuraxial block versus general anaesthesia for elective total hip replacement: a meta-analysis](#). *Anesth Analg* 103(4): 1018-1025



# 17. REDUCE IATROGENIC BLOOD LOSS

Strategies and techniques to minimise iatrogenic anaemia will result in reduced blood loss (PBM pillar 2).

## Key messages

- Diagnostic testing is an important cause of blood loss in critically ill patients<sup>1</sup>.
- 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.<sup>1</sup>
- The introduction of point-of-care testing could further reduce the volume of samples drawn.

## Clinical implications

- Implementing strategies to reduce iatrogenic blood loss in an organisation requires strategic planning, communication and implementation with relevant stakeholders such as medical staff, laboratory scientist and nursing staff.
- Having a process and device to reinfuse initial blood loss from indwelling devices has been associated with a 50% reduction in diagnostic blood loss.<sup>2</sup>
- Only order essential blood tests and minimise the volume of blood drawn.<sup>3</sup>

## Background

Iatrogenic anaemia is a term applied to the anaemia that results from blood loss due to repeated venepunctures for the purposes of obtaining specimens for laboratory testing. Strategies to reduce iatrogenic blood loss include altering of test ordering behaviour (limiting the number of tests ordered), micro-sampling, reinfusion of blood drawn from indwelling devices and point of care microanalysis.<sup>1,2,4,5</sup>

Micro sampling is when small (paediatric) volumes of blood are withdrawn from the patient rather than the larger quantities routinely drawn for laboratory sampling. Two separate studies have noted the average daily blood sampling volume in ICU was 41mL.<sup>4,5</sup> In one study this represented 17% of total blood loss in those admitted to ICU for more than three days.<sup>3</sup> The use of micro sampling in ICU has been shown to reduce the volume of blood loss by 37% - 47%,<sup>1</sup> and in one study was associated with a significant reduction in blood transfusion.<sup>1</sup>

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 reinfuse the initial blood taken to 'clear the line' (drawback blood) has been associated with a 50% reduction in diagnostic blood loss.<sup>2</sup> The Western Australian Patient Blood Management Program has two examples of Blood Conservation in-line device policies available at: <http://www.health.wa.gov.au/bloodmanagement/professionals/tools.cfm>.

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## References

1. Tinmouth, A, McIntyre, L, Fowler, R. [Blood conservation strategies to reduce the need for red cell transfusion in critically ill patients](#), CMAJ 2008;178:49-57.
2. Gleason E, Grossman S, Campbell C. [Minimizing diagnostic blood loss in critically ill patients](#). American Journal of Critical Care 1992;1:85-90
3. AuBuchon J.P, Puca K, Saxena S, Shulman I.A, Waters J.H. Getting Started in Patient Blood Management. AABB, Bethesda, Maryland. 2011.
4. Von Ahsen N, Muller C, Serke S, et al. [Important role of nondiagnostic blood loss and blunted erthropoietic response in the anaemia of medical intensive care patients](#). Crit Care Med 1999;27:2630-9.
5. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, et al [Anemia and blood transfusion in critically ill patients](#). JAMA 2002;288:1499-507.



# 18. CELL SALVAGE

Cell salvage is an autologous blood conservation technique for minimising blood loss in the surgical setting (PBM Pillar 2). It can be performed during the intra- and/or postoperative periods.

## Key messages

- Cell salvage can help minimise blood loss in the surgical setting.
- Cell salvage has been demonstrated to be safe and effective at reducing allogeneic blood transfusions particularly in adult elective cardiac and orthopaedic surgery.<sup>1</sup>
- Cell salvage can be cost-effective.<sup>2</sup>

## Clinical implications

- 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 (PO-PP13).<sup>3</sup>
- Intraoperative cell salvage is recommended in adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated (PO-R15).<sup>3</sup>
- Postoperative cell salvage is recommended in adult patients undergoing cardiac surgery or total knee arthroplasty, in whom significant postoperative blood loss is anticipated (PO-R20).<sup>3</sup>
- The use of cell salvage may be considered in critically ill trauma patients and patients undergoing emergency surgery for ruptured abdominal aortic aneurysm (CC-PP13).<sup>4</sup>

## Background

A systematic Cochrane review 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.<sup>1</sup>

### 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 the blood is anticoagulated and then 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 haematocrit 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 anaemia that would require therapy) is anticipated (PO-R15).<sup>3</sup> The use of cell salvage may be considered in critically ill trauma patients and patients undergoing emergency surgery for ruptured abdominal aortic aneurysm (CC-PP13).<sup>4</sup>

An example of a list of [Surgical Procedures where intra-operative cell salvage presents significant benefit towards the management of peri-operative blood loss](#) is available. (Link to Appendix II of NBA document).

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.<sup>1,2,5</sup> There are few contraindications, however intraoperative cell salvage is not recommended when bowel content or infected material is present in the surgical field.<sup>6</sup>

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 (PO-PP13).<sup>3</sup>

### 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 reinfused to the patient.<sup>6</sup>

Postoperative cell salvage should be considered in adult patients undergoing cardiac surgery or total knee arthroplasty, in whom significant postoperative blood loss is anticipated (PO-R20).<sup>3</sup>

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### References

1. Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA. [Cell salvage for minimising perioperative allogeneic blood transfusion](#). Cochrane database of systematic reviews (Online) [Internet]. 2010;(4):CD001888.
2. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#). Eur J Anaesthesiol. 2013;30:270-382.
3. National Blood Authority [Patient blood management guidelines: Module 2 – Perioperative](#). Australia, 2012.
4. National Blood Authority [Patient blood management guidelines: Module 4 – Critical Care](#). Australia, 2013.
5. Murphy GJ, Rogers CS, Lansdowne WB, Channon I, Alwair H, Cohen A, Caputo M, Angelini GD. [Safety, efficacy, and cost of intraoperative cell salvage and autotransfusion after off-pump coronary artery bypass surgery: a randomized trial](#). [Internet]. The Journal of thoracic and cardiovascular surgery. 2012 p. 20–8.
6. UK Cell Salvage Action Group. [Intraoperative Cell Salvage education workbook](#). 2008.

### Additional Resources

- Guidance for the Provision of Intraoperative Cell Salvage – <http://www.blood.gov.au/ics>

# 19. POINT OF CARE TESTING

Point of care (POC) testing devices provide rapid bedside monitoring to aid the clinician in directing appropriate targeted therapy.<sup>1</sup>

## Key Messages

The use of transfusion algorithms in conjunction with POC testing has been shown to reduce both transfusion requirements and blood loss in cardiac surgery.<sup>1</sup>

## Clinical Implications

In adults undergoing cardiac surgery, the use of thromboelastography (TEG) should be considered (PO- R16).<sup>2</sup>

## Background

Patients undergoing cardiac surgery are vulnerable to platelet defects which can be either pre-existing defects, drug induced and from the anti-platelet effects from cardiopulmonary bypass (CPB).<sup>1</sup> It is therefore important monitor platelet function during cardiac surgery.<sup>1</sup>

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.<sup>3</sup> TEG analysis reflects haemostasis in vivo, including clot development, stabilisation 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.

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## References

1. Enriquez LJ, Shore-Lesserson L. [Point -of-care coagulation testing and transfusion algorithms](#). BJA 2009;103:i4-i22.
2. National Blood Authority. [Patient Blood Management Guidelines: Module 2 - Perioperative](#). Australia 2012.
3. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, et al. [Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology](#). Eur J Anaesthesiol. 2013;30:270-382.

## Additional Resources

- Case study Point of Care Coagulation Testing National Blood Authority <http://blood.gov.au/point-care-coagulation-testing-case-study-prince-charles-hospital-brisbane>



# 20. CLINICAL INDICATIONS FOR RED BLOOD CELL TRANSFUSION

Red blood cell (RBC) transfusion is indicated for the treatment of clinically significant anaemia with symptomatic deficit of oxygen carrying capacity, and for replacement of traumatic or surgical blood loss.<sup>1</sup>

## Key messages

- RBC transfusion may be life-saving.
- RBC transfusion is associated with risks and adverse outcomes including increased morbidity and mortality. Some risks are dose dependent.
- Each RBC transfusion should be an independent clinical decision based on the risk, benefits and alternatives.
- Each unit of RBCs contains enough haemoglobin to raise the haemoglobin concentration in an average sized adult by approximately 10 g/L.<sup>1</sup>

## Clinical implications

- The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions. It should not be dictated by Hb concentration alone.<sup>2,3,4</sup>
- 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 Hb level.<sup>3,4</sup>
- Increasingly evidence is favouring a restrictive transfusion strategy.

## Background

The National Blood Authority Patient Blood Management Guidelines provide guidance on the principles of PBM – the management and preservation of patients' own blood to reduce or avoid the need for transfusion. However, where transfusion is required, the guidelines provide evidence where available, and guidance where evidence is lacking, on appropriate transfusion practices. The guidelines support restrictive transfusion and a single unit transfusion guideline.

Examples of specific guidance include:

- In all patients with heart failure, there is an increased risk of transfusion-associated circulatory overload. This needs to be considered in all transfusion decisions. Where indicated, transfusion should be of a single unit of RBC followed by reassessment of clinical efficacy and fluid status (MED-PP7).<sup>3</sup>



- There is a lack of specific evidence relating to the effects of RBC transfusion in patients with cancer. (MED-PP9).<sup>3</sup>

More information can be found in the Single unit transfusion and Restrictive transfusion threshold companions.

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#### References

1. Australian Red cross Blood Service. [Blood Component Information Circular of Information – An extension of blood component labels](#). Australia 2012.
2. National Blood Authority. [Patient Blood Management Guidelines: Module 2 – Perioperative](#). Australia, 2012.
3. National Blood Authority. [Patient Blood Management Guidelines: Module 3 – Medical](#). Australia, 2012.
4. National Blood Authority. [Patient Blood Management Guidelines: Module 4 – Critical Care](#). Australia, 2012

# 21. TRANSFUSION RISKS AND BENEFITS

Transfusion can be vital and lifesaving therapy but may carry a risk to the patient.

## Key messages

Best transfusion practice means transfusing a patient only when there is an identified clinical need.<sup>1</sup>

Blood transfusion may relieve morbidity and reduce mortality when administered appropriately.<sup>1</sup>

Australia has one of the safest blood supplies in the world in terms of viral safety and risk of transfusion transmissible infections.<sup>2</sup>

Non-infectious risks are higher frequency and carry greater morbidity than infectious risks.<sup>3</sup>

## Clinical implications

The decision to transfuse should take into account the full range of available therapies, and balancing the evidence for efficacy and improved clinical outcome against the potential risks.

The prescribing clinician should gain informed consent from the patient/carer for transfusion.

## Background

As with all healthcare interventions the transfusion of blood components has both potential risks and benefits. Informed consent requires that the patient has a clear understanding of the potential risks, benefits and available alternatives before proceeding with a transfusion.<sup>1</sup> Clear indications include replacing blood that is lost during haemorrhage and providing platelets for patients having chemotherapy.<sup>1</sup> However many purported benefits of transfusion practice have been founded on anecdotal evidence rather than scientific rigor.<sup>4</sup> Some adverse patient outcomes have been linked to transfusion as outlined in Table 1.

**Table 1 Adverse patient outcomes linked to transfusion**

RBC transfusion related adverse outcomes	
Increased morbidity	Significant predictor of infection, including wound infection, sepsis and pneumonia; with dose-dependent effect Significant predictor of cardiac, renal, respiratory and neurologic morbidities; with dose-dependent effect Predictor of development of venous thromboembolism in major vascular surgery
Increased mortality	Significant predictor of short-term mortality in cardiac and non-cardiac surgery; with dose dependent effect Significant predictor of 6-month, 1-year and 5-year mortality
Increased length of stay	Associated with an increase in ICU length of stay in cardiac and non-cardiac surgery Associated with an increase in hospital length of stay in cardiac and non-cardiac surgery
Increased readmission	Associated with increase in hospital readmission in surgery for hip fracture

The Australian blood supply can be referred to as one of the safest blood supplies in the world in terms of viral safety and risk of transfusion transmissible infections, due to the advanced screening, testing and processing techniques used.<sup>2</sup> However, even with the significant advancement in the viral and bacterial safety of blood, newly emerging and unquantifiable risks remain a threat to the blood supply.<sup>4</sup>

The most commonly reported non serious non-infectious risks include headache, mild fever, itching and hives; with the most frequently reported serious events based on international data being transfusion related acute lung injury (TRALI), bacterial sepsis and haemolysis.<sup>4,5</sup> Even though some incidents may be due to human error, such as haemolysis resulting from the transfusion of an ABO incompatible component, others are potentially related to unavoidable risks associated with a transfusion and may be caused by the actual nature of blood products.<sup>4</sup> Taking into account the potential risks of transfusion, growing evidence of adverse outcomes, and lack of evidence for benefit of transfusion in many clinical scenarios, clinicians must consider whether blood transfusion will improve the outcome of their patient.

The section titled “Transfusion risks and Calman chart for explaining transfusion related risks to patients” contains immunological and non-immunological risk estimates for transfusion related adverse events based on international data; and the risks of transfusion-transmissible infection calculated on Blood Service data, with the Calman chart to put into everyday context.

#### References

1. Armstrong B. [Benefits and risks of transfusion](#). ISBT Science Series 2008; 3 : 216–230
2. National Blood Authority. [Patient Blood Management Guidelines: Module 2 Perioperative](#). Australia, 2012
3. Thomson A, Farmer S, Hofmann A, Isbister J, Shander A. [Patient blood management – a new paradigm for transfusion medicine?](#) ISBT Sci Ser 2009;4:423–35
4. Shander A, Waters JH, Gottschall JL. Perioperative Blood Management: A Physician’s Handbook 2nd Edition. AABB; 2009.
5. [BloodSafe The Quick Reference Guide: December 2012 Obtaining Informed Consent for Blood and Blood Products \[pamphlet\]](#). Government of South Australia SA Health and Australian Red Cross Blood Service; 2012.

#### Additional resources

- Hofmann A, Gombotz, H Theusinger O, Spahn D. [Estimating the cost of blood: past, present, and future directions](#). Clinical Anaesthesiology 2007; 21(2) 271–289
- Blood Service clinical website [www.transfusion.com.au/adverse\\_events](http://www.transfusion.com.au/adverse_events)

## 22. TRANSFUSION RISKS TABLES AND CALMAN CHART FOR EXPLAINING TRANSFUSION RELATED RISKS TO PATIENTS

**Classification of transfusion-related adverse reactions and estimated incidence**

	Immunological	Incidence*	Non-immunologica	Incidence*
Acute (<24 hours)	Haemolytic transfusion reactions	1:40,000 <sup>c</sup>	Massive transfusion complications	Variable <sup>c,d</sup>
		1:76,000 <sup>c</sup>	<u>Non-immune mediated haemolysis</u> (physical or chemical destruction of blood)	Rare <sup>c</sup>
Delayed (>24hours)	Fatal	1:1.8 million <sup>c</sup>	<u>Transfusion associated sepsis</u> (for clinically apparent reactions)	At least 1:75,000 <sup>a</sup>
	<u>Febrile non-haemolytic transfusion reactions</u>	0.1%–1% of transfusions with universal leucocyte depletion <sup>c</sup>	Red cells	At least 1:500,000 <sup>b</sup>
	Allergic reactions	1%–3% of transfusions <sup>c</sup>	<u>Transfusion-associated circulatory overload (TACO)</u>	Less than 1% of patients <sup>c</sup>
	<u>Mild (urticarial)</u>			
	<u>Severe (anaphylaxis)</u>	1:20,000–1:50,000 <sup>b,c</sup>		
	<u>Transfusion-related Acute Lung Injury (TRALI)</u>	1:1,200–1:190,000 <sup>c</sup>		
	<u>Delayed haemolytic transfusion reaction</u>	1:2,500–1:11,000 <sup>c,d</sup>	<u>Iron overload</u>	May occur after 10–20 RBC units <sup>e</sup>
	<u>Post-transfusion purpura</u>	Rare <sup>c</sup>	Iron overload requiring chelation therapy	May occur after 50–100 RBC units <sup>c</sup>
	<u>Transfusion-associated graft versus host disease (TA-GVHD)</u>	Rare <sup>c</sup>	Transfusion-transmissible infections	For incidence rates refer to risk estimates for transfusion-transmissible infection
	<u>Alloimmunisation</u>	1:100 <sup>c</sup>		
<u>Transfusion-related immune modulation (TRIM)</u>	1:10 <sup>c</sup>			
		Not known <sup>c</sup>		

Note: \*Includes overseas data. Risks per unit transfused unless specified.

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## Risks of transfusion-transmissible infection calculated on Blood Service data

Agent and testing standard	Window period	Estimate of residual risk 'per unit' (a)
HIV (antibody + NAT)	5.9 days	Less than 1 in 1 million(1)
HCV (antibody + NAT)	2.6 days	Less than 1 in 1 million(1)
HBV (HBsAg + NAT)	15.1 days	Approximately 1 in 468,000(1,4)
HTLV 1 & 2 (antibody)	51 days	Less than 1 in 1 million(1)
vCJD [No testing]		Possible, not yet reported in Australia
Malaria (antibody)	7–14 days	Less than 1 in 1 million(2)

Notes: vCJD=variant Creutzfeldt-Jakob Disease; (a) The risk estimates for HIV, HCV and HBV are based on Blood Service data from 1 January 2011 to 31 December 2013. The HTLV estimates are based on data for the period 1 January 2010 to 31 December 2013. OBI risk function (ref 4) estimated on data from 1 January 2013 to 23 March 2014.

Source: [www.transfusion.com.au](http://www.transfusion.com.au)

## The Calman chart for explaining risk (UK risk per 1 year)

Classification	Risk range	Example
Negligible	$\leq 1,000,000$	Death from a lightning strike
Minimal	1:100,000–1:1,000,000	Death from a train accident
Very low	1:10,000–1:100,000	Death from an accident at work
Low	1:1,000–1:10,000	Death from a road accident
Moderate	1:100–1:1,000	Death from smoking 10 cigarettes per day
High	$\geq 1:100$	Transmission of chickenpox to susceptible household contacts

The chance of dying in a road accident, for example, is about 1 in 10,000 per year which is considered a 'low' risk. Comparatively, all the viral risk estimates are well below this level, being considered as either 'minimal' (HBV) or 'negligible' (HIV and HCV)

Source: Calman K. Cancer: science and society and the communication of risk. BMJ 1996;313:801.



# 23. SINGLE UNIT TRANSFUSION

Single unit red blood cell (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.

## Key messages

- The Patient Blood Management Guidelines support restrictive transfusion and a single unit transfusion guideline in patients who are not critically bleeding.<sup>1-3</sup>
- RBC transfusion is associated with increased morbidity, mortality, ICU and hospital length of stay.<sup>1</sup>
- Transfused blood carries risks in a dose-dependent manner.<sup>4,5</sup>
- Limited studies to date have shown that a single unit strategy reduces RBC usage without adverse effects.

## Clinical implications

- Traditionally, single-unit red blood cell transfusions were believed to be insufficient to treat anaemia, but recent data suggest that they may lead to a safe reduction of transfusion requirements.<sup>6</sup>
- Each RBC transfusion should be an independent clinical decision based on the risk, benefits and alternatives.
- Transfuse to alleviate patient signs and symptoms of anaemia.
- 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 haemoglobin level.<sup>1-3</sup>
- Each unit of RBCs contains enough haemoglobin to raise the haemoglobin concentration in an average sized adult by approximately 10 g/L.<sup>7</sup>

## Background

Transfusion is a live tissue transplant. Risks associated with transfusion are dose dependent.<sup>4,5</sup> A study of almost 12,000 coronary artery bypass graft patients showed 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.<sup>4</sup> 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.<sup>5</sup> Transfusion Associated Circulatory Overload (TACO) is among the highest risks associated with RBC transfusion, estimated at up to 1 in 100 per unit transfused.<sup>2,8-9</sup> This is of particular concern in patients with chronic heart failure.<sup>2</sup>

Several recent studies have shown that single-unit RBC transfusions remain rare, despite lack of evidence for prescribing multiple units in response to a haemoglobin trigger.<sup>10</sup> Berger and colleagues 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.<sup>6</sup>

Joseph and colleagues found that in a large UK tertiary referral centre and teaching hospital, 74% of RBCs were transfused to patients with medical diagnoses, rather than surgical patients. For medical and surgical patients, respectively, 31 and 10% of all RBC units were transfused for anaemia without evidence of bleeding, and 38 and 12% were transfused for non-life-threatening bleeding. Eight-five percent of all patients who received transfusions had stable vital signs before transfusion.<sup>10</sup> Their model suggested that 11% of RBCs would be conserved by cancellation of major surgery, whereas 23% to 47% of all RBCs could be conserved by controlling transfusions to medical patients. Their data strongly support focusing on target haemoglobin values and using single-unit transfusions as an effective method of reducing and conserving RBC use.

Ma and colleagues 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.<sup>11</sup>

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## Additional Resources

- Refer to the [National Blood Authority Single Unit Transfusion Guide](#) for further information and resources to assist with implementation.

# 24. RESTRICTIVE TRANSFUSION STRATEGY

Restrictive transfusion thresholds (triggers) are an effective method of reducing and conserving red blood cell (RBC) use. RBC transfusion should not be dictated by a haemoglobin 'trigger' alone.<sup>1-4</sup>

## Key messages

- The Patient Blood Management Guidelines support restrictive transfusion in patients who are not critically bleeding.<sup>1-3</sup>
- Restrictive transfusion strategies reduce the risk of receiving a RBC transfusion and reduce the volume of RBCs transfused.<sup>5</sup>
- There is extensive evidence supporting restrictive transfusion strategies without impacting on patient morbidity or mortality, with some studies showing improved outcomes.<sup>6-9</sup>

## Clinical implications

- In critically ill patients, a restrictive transfusion strategy should be employed (CC-R1).<sup>3</sup>
- RBC transfusion should not be dictated by a haemoglobin 'trigger' alone, but should be based on assessment of the patient's clinical status (PO-PP2, MED-PP1, CC-PP1).<sup>1-4</sup>
- Where indicated, transfusion of 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 Hb level (PO-PP3, MED-PP2, MED-PP3, CC-PP2).<sup>1-3</sup>
- The Patient Blood Management Guidelines provide guidance on Hb 'triggers' where appropriate (but always in the context of the patient's clinical status).<sup>1-3</sup>
- Evidence in patients with acute upper gastrointestinal bleeding show that a restrictive transfusion strategy significantly improves patient outcomes.<sup>6</sup>

## Background

The threshold for RBC transfusion in both medical settings and in the postoperative surgical period has evolved over the years. There is now extensive evidence from the literature supporting restrictive transfusion strategies. For example:

[TRICC](#), a large multicentre randomized, controlled trial comparing a restrictive (Hb < 70 g/L) to a liberal (Hb < 100 g/L) RBC transfusion strategy in ICU patients found no difference in 30-day mortality regardless of the Hb threshold employed. They did find lower rates with the restrictive strategy in patients who were acutely ill and among those < 55 years of age. The mortality rate during hospitalisation was significantly lower in the restrictive group.<sup>7</sup>

[TRACS](#), a large single unit, prospective, non-inferiority, randomized, controlled trial comparing a restrictive (HCT ≥ 24%) to a liberal (HCT ≥ 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.<sup>8</sup>

[FOCUS](#), a large, randomized, controlled trial comparing a restrictive (Hb < 80 g/L) to a liberal (Hb < 100 g/L) RBC transfusion strategy in patients who had undergone surgery for hip fracture and who had a history or risk factors for cardiovascular disease, found that a liberal transfusion strategy, as compared with a restrictive 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.<sup>9</sup>

[Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion](#), a 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).<sup>5</sup>

[Transfusion strategies for acute upper gastrointestinal bleeding](#), a large randomised 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 (eg. cirrhosis, peptic ulcer); lower rates of further bleeding, lower rates of rescue therapy, lower overall complication rates, and shorter length of hospital stay. Fifty-one percent 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.<sup>6</sup>

## Recommendations and practice points with Hb 'triggers' from the Patient Blood Management Guidelines

### Perioperative

In the absence of acute myocardial or cerebrovascular ischaemia, postoperative transfusion may be inappropriate for patients with a haemoglobin level of >80 g/L.<sup>1</sup>

Patients should not receive a transfusion when the haemoglobin level is  $\geq 100$  g/L.

In postoperative patients with acute myocardial or cerebrovascular ischaemia and a haemoglobin level of 70–100 g/L, transfusion of a single unit of RBC, followed by reassessment of clinical efficacy, is appropriate (PO-PP3).<sup>1</sup>

### Medical

Direct evidence is not available in general medical patients. Evidence from other patient groups and Clinical Reference Group (CRG) consensus suggests that, with a:

- **Hb concentration <70g/L**, RBC transfusion may be associated with reduced mortality and is likely to be appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.
- **Hb concentration of 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 anaemia, and the patient's response to previous transfusions. No evidence was found to warrant a different approach for patients who are elderly or who have respiratory or cerebrovascular disease.
- **Hb concentration > 100g/L**, RBC transfusion is likely to be unnecessary and is usually inappropriate. Transfusion has been associated with increased mortality in patients with acute coronary syndrome (ACS) (MED-PP3).<sup>2</sup>

In ACS patients with a:

- **Hb concentration <80 g/L**, RBC transfusion may be associated with reduced mortality and is likely to be appropriate (MED-PP5, CC-PP4).<sup>2,3</sup>

- **Hb concentration of 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 (MED-PP6, CC-PP4).<sup>2,3</sup>
- **Hb concentration >100 g/L**, RBC transfusion is not advisable because of an association with increased mortality (MED-R1, CC-PP4).<sup>2,3</sup>

In patients with thalassaemia, the evidence does not support any change to the current practice of maintaining a pretransfusion Hb concentration of 90 – 100 g/L, with transfusions at about monthly intervals (MED-PP23).<sup>2</sup>

In patients with myelodysplasia who are regularly and chronically transfused, there is no evidence to guide particular Hb thresholds. Decisions around appropriate triggers and frequency of transfusion need to be individualised, taking into account anaemia-related symptoms, functional or performance status, and the patient’s response to previous transfusions (MED-PP24).<sup>2</sup>

## Critically ill

In critically ill patients, a restrictive transfusion strategy should be employed (CC-R1).<sup>3</sup>

In critically ill patients, expert clinical consensus suggests that, with a:

- **Hb concentration <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 concentration of 70–90 g/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 anaemia.
- **Hb concentration >90 g/L**, RBC transfusion is generally unnecessary.

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# 25. CLINICAL INDICATIONS FOR PLATELETS

Platelet transfusion is indicated for the treatment and prevention of bleeding in patients with severe thrombocytopaenia and/or impaired platelet production and/or function.<sup>1</sup>

## Key messages

- Platelet transfusion is indicated for all patients with clinically significant bleeding in whom thrombocytopenia is thought to be a major contributory factor.
- Platelet transfusion may be indicated for the prevention and treatment of haemorrhage in patients with thrombocytopenia or platelet function defects.<sup>2</sup>
- Prophylactic platelet transfusion may be indicated in certain clinical scenarios.
- Each platelet transfusion should be an independent clinical decision and take into account the relative risks and benefits to the patient.<sup>3</sup>
- Platelet transfusions are not indicated in all causes of thrombocytopenia, and may be contraindicated in certain conditions.<sup>2</sup>

## Clinical implications

- The cause of the thrombocytopenia should always be established.<sup>2</sup>
- In patients with chronic failure of platelet production a specific threshold for transfusion may not be appropriate.<sup>2</sup>
- Long-term prophylactic platelet transfusions may lead to complications.<sup>2</sup>
- In patients undergoing invasive procedures, there is insufficient evidence to define a threshold platelet count that is associated with increasing risk of bleeding, however consensus guidance has been developed for certain conditions.

## Background

The Patient Blood Management Guidelines have recommendations and practice points regarding platelet transfusion. These have subsequently been expanded upon in a consensus process to develop:

- Indications for platelet transfusion for patients with clinically significant bleeding;
- Indications for prophylactic platelet transfusion for prevention of bleeding; and
- Clinical contraindications for platelet transfusions.<sup>4</sup>

## Clinical Indications for platelet transfusion for patients with clinically significant bleeding include:

1. Platelet transfusion is indicated for patients with clinically significant bleeding in whom thrombocytopenia is thought to be a major contributory factor, even if the platelet count is  $>10 \times 10^9/L$ .
2. In patients with critical bleeding requiring massive blood transfusion. In these patients, the use of a Massive Transfusion Protocol (MTP) which includes platelet transfusions may reduce the risk of mortality.
3. Platelet transfusion is indicated for patients with congenital or acquired functional platelet defects including complex cardiac surgery or patients on antiplatelet therapy (other than aspirin alone) requiring surgical intervention who are actively bleeding. Platelet counts are not a reliable indicator in this case.
4. Whilst there is no consensus on a target platelet threshold for the management of bleeding patients with thrombocytopenia secondary to Disseminated Intravascular Coagulopathy (DIC), aiming to maintain platelet counts  $>50 \times 10^9/L$  would seem to be reasonable, as well as correction of the underlying aetiology and replacement of coagulation factors. Platelet transfusion is not indicated for patients with chronic DIC or for whom there is no bleeding.
5. In general, platelet transfusion is not indicated in immune thrombocytopenia unless there is clinically significant bleeding.

## Clinical Indications for prophylactic platelet transfusion for prevention of bleeding include:

1. Patients with severe thrombocytopenia undergoing chemotherapy and haematopoietic stem cell transplantation should be considered for prophylactic platelet transfusion at a platelet count of  $<10 \times 10^9/L$  in the absence of risk factors and at  $<20 \times 10^9/L$  in the presence of risk factors (e.g. fever).
2. In critically ill patients, in the absence of acute bleeding, the administration of platelet transfusion may be considered appropriate at a platelet count of  $<20 \times 10^9/L$  (CC-PP11).<sup>3</sup> The administration of platelet transfusion may be considered appropriate at a higher platelet count for neonates, such as  $<25 \times 10^9/L$  for term neonates and  $<30-50 \times 10^9/L$  for preterm neonates or any neonate with Neonatal Alloimmune Thrombocytopenia (NAIT). Although in NAIT it is preferable to give platelets without the relevant HPA antigen, random donor platelets may be effective.
3. For patients with other causes of bone marrow failure with chronic failure of platelet production (e.g. myelodysplasia and aplastic anaemia), there is insufficient evidence to recommend a specific threshold for transfusion and such patients should be managed on an individual basis. Long term prophylactic platelet transfusion carries risks of complications such as alloimmunisation which may contribute to platelet transfusion refractoriness.
4. In patients undergoing invasive procedures, there is insufficient evidence to define a threshold platelet count that is associated with increasing risk of bleeding, however:
  - In general, for patients undergoing procedures such as insertion of central venous catheters, endoscopy and biopsy, lumbar puncture and laparotomy, a platelet count  $\geq 50 \times 10^9/L$  is considered safe.
  - A lower platelet count may be tolerated for minor procedures such as simple dental extractions, skin biopsy and insertion of peripherally inserted central catheters (PICC) where adequate surface pressure can be applied.
  - For patients undergoing intracranial, intraocular and neuraxial surgery, it is generally suggested that the platelet count should be  $\geq 100 \times 10^9/L$ .
5. In patients with head injury, it is suggested to keep the platelet count  $>100 \times 10^9/L$ .

6. Functional platelet disorders include inherited or acquired platelet function disorders. In these patients, prophylactic platelets may be considered before invasive procedures.

### Clinical contraindications for platelet transfusions include:

1. Platelet transfusion is not indicated in patients where bleeding is unrelated to proven or anticipated decreased platelet count or to functional platelet defects.
2. For patients with Heparin Induced Thrombocytopenia (HIT) and Thrombotic Thrombocytopenic Purpura (TTP), platelet transfusion is contraindicated unless there is life-threatening haemorrhage as it can exacerbate the underlying conditions. There are limited case reports regarding the successful use of platelets in patients with Haemolytic Uraemic Syndrome (HUS) and TTP to cover invasive procedures that cannot be postponed until the underlying disease has been resolved (e.g. central line placement for plasma exchange therapy).
3. The routine prophylactic use of platelets after cardiac surgery is not supported.

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5. National Blood Authority [Patient blood management guidelines: Module 2 – Perioperative](#). Australia, 2012.

### Additional resources

- National Blood [Authority Patient blood management guidelines: Module 1 – Critical Bleeding Massive Transfusion](#). Australia, 2012.
- Stanworth SJ et al. [The Effect of a No-Prophylactic Versus Prophylactic Platelet Transfusion Strategy On Bleeding in Patients with Hematological Malignancies and Severe Thrombocytopenia \(TOPPS trial\). A Randomized Controlled, Non-Inferiority Trial](#). 54th ASH Annual Meeting Plenary Scientific Session 2012.
- [BCSH Transfusion guidelines for neonates and older children](#). British Journal of Haematology 2004; 124: 433- 453.
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- Australian Red Cross Blood Service. [Blood Component Information Circular of Information – An extension of blood component labels](#). Australia 2012.



# 26. CLINICAL INDICATIONS FOR FRESH FROZEN PLASMA

Fresh Frozen Plasma (FFP) is indicated in patients with a coagulopathy who are bleeding or at risk of bleeding where a specific therapy such as vitamin K or factor concentrate is not appropriate or available.<sup>1</sup>

## Key messages

- FFP contains all coagulation factors including Factors VIII and V.<sup>1</sup>
- Each FFP transfusion should be an independent clinical decision and take into account the relative risks and benefits to the patient.<sup>2</sup>
- Assessment of bleeding risk is complex and requires careful consideration of patients' clinical status and laboratory parameters. Specialist haematology advice may also be required.<sup>3</sup>

## Clinical implications

- In patients with critical bleeding requiring massive transfusion, suggested doses of blood components is FFP: 15 mL/kg or as per the local Massive Transfusion Protocol.<sup>4</sup>
- The prophylactic use of FFP in cardiac surgery is not recommended.<sup>5</sup>
- The routine use of FFP in medical patients with coagulopathy (including those with liver impairment) is not supported.<sup>2</sup>
- The routine use of FFP in critically ill patients with coagulopathy is not advised. The underlying causes of coagulopathy should be identified.<sup>3</sup>
- For guidance on the use of FFP in warfarin reversal or in specific patient groups, refer to<sup>5</sup>:
  - ♦ An update of consensus guidelines for warfarin reversal, on behalf of the Australasian Society of Thrombosis and Haemostasis (2013).<sup>6</sup>
  - ♦ Australian Haemophilia Centre Directors' Organisation (AHCDO) guidelines for patients with specific factor deficiencies ([www.ahcdo.org.au](http://www.ahcdo.org.au))
  - ♦ Thrombotic Thrombocytopenic Purpura: Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant (2004).<sup>7</sup>

## Background

The National Blood Authority [Patient Blood Management Guidelines](#) provides some guidance on the use of FFP:

In patients with critical bleeding requiring massive transfusion, suggested doses of blood components is FFP: 15 mL/kg (CBMT-PP10) or as per the local Massive Transfusion Protocol.<sup>4</sup>

The prophylactic use of FFP in cardiac surgery is not recommended (PO –R21).<sup>5</sup>

The routine use of FFP in medical patients with coagulopathy (including those with liver impairment) is not supported. Tests for coagulation correlate poorly with bleeding risk in liver impairment. The underlying causes of coagulopathy should be assessed. Where FFP transfusion is considered necessary the risks and benefits should be considered for each patient, and expert guidance sought (MED- PP16).<sup>2</sup>

The administration of FFP may be independently associated with adverse events, including adult respiratory distress syndrome (ARDS) and acute lung injury (ALI). The decision to transfuse these products to an individual patient should take into account the relative risks and benefits (CC-PP6).<sup>3</sup>

Assessment of bleeding risk is complex and requires careful consideration of patients' clinical status and laboratory parameters. Specialist haematology advice may also be required. However, patients with an INR  $\leq 2$  may not benefit from the administration of FFP and can generally undergo invasive procedures within the ICU without any serious bleeding; higher INRs may be tolerated in certain clinical situations (CC-PP7).<sup>3</sup>

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# 27. CLINICAL INDICATIONS FOR CRYOPRECIPITATE AND FIBRINOGEN CONCENTRATE

Cryoprecipitate is indicated in the treatment of fibrinogen deficiency or dysfibrinogenaemia.<sup>1</sup>

Fibrinogen concentrate is licenced for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenaemia and hypofibrinogenaemia,<sup>2</sup> and is currently funded under the National Blood Agreement.

## Key messages

- Fibrinogen is an essential component of the coagulation system, due to its role in initial platelet aggregation and formation of a stable fibrin clot.<sup>3</sup>
- The decision to transfuse cryoprecipitate or fibrinogen concentrate to an individual patient should take into account the relative risks and benefits.<sup>3</sup>
- The routine use of cryoprecipitate or fibrinogen concentrate is not advised in medical or critically ill patients.<sup>2,4</sup>
- Cryoprecipitate or fibrinogen concentrate may be indicated in critical bleeding if fibrinogen levels are not maintained using FFP. In the setting of major obstetric haemorrhage, early administration of cryoprecipitate or fibrinogen concentrate may be necessary.<sup>3</sup>

## Clinical implications

- The routine use of cryoprecipitate or fibrinogen concentrate in medical or critically ill patients with coagulopathy is not advised. The underlying causes of coagulopathy should be identified; where transfusion is considered necessary, the risks and benefits should be considered for each patient. Specialist opinion is advised for the management of disseminated intravascular coagulopathy (MED-PP18, CC-PP7).<sup>2,4</sup>
- Cryoprecipitate or fibrinogen concentrate may be indicated in critical bleeding if fibrinogen levels are not maintained using FFP. In patients with critical bleeding requiring massive transfusion, suggested doses of blood components is 3-4g (CBMT-PP10)<sup>3</sup> in adults or as per the local Massive Transfusion Protocol.
- Published critical bleeding guidelines recommend keeping the fibrinogen level above 1.0 g/L.<sup>2</sup>
- Paediatric dosing is not established however common practise is 5mL/kg or 1-2 units per 10kg.
- If required, fibrinogen dose can be calculated based on the patient's plasma volume, actual

fibrinogen level and desired increment (e.g. using the formula in the AABB Technical Manual).<sup>5</sup>

- Refer to:
  - ♦ Australian Haemophilia Centre Directors' Organisation (AHCCDO) guidelines for patients with specific factor deficiencies ([www.ahccdo.org.au](http://www.ahccdo.org.au))
  - ♦ Thrombotic Thrombocytopenic Purpura: Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant (2004).<sup>6</sup>

## Background

Cryoprecipitate and fibrinogen concentrate are prepared from human plasma. Cryoprecipitate contains factors VIII and XIII, von Willebrand factor and fibronectin and fibrinogen, whereas the concentrate contains a purified form of fibrinogen.

In Australia there are two different sized bags of cryoprecipitate. A bag of apheresis cryoprecipitate is approximately equal to 2 bags of whole blood cryoprecipitate.<sup>1</sup> The fibrinogen content for a bag of apheresis cryoprecipitate is 856 +/- 298 mg per bag (mean +/- 1SD) and for whole blood cryoprecipitate is 378 +/- 125 mg per bag (mean +/- 1SD).<sup>1</sup>

Typically 1 bag of whole blood cryoprecipitate given per 5–10 kg body weight would be expected to increase the patient's fibrinogen concentration by 0.5–1.0 g/L.<sup>1</sup>

Typically 1 bag of cryoprecipitate apheresis given per 10–20 kg body weight would be expected to increase the patient's fibrinogen concentration by 0.5–1.0 g/L.<sup>1</sup>

A standard adult dose of cryoprecipitate (3–4g of fibrinogen for a 70kg adult) is equivalent to:

- 10 bags of whole blood cryoprecipitate or
- 5 bags of apheresis cryoprecipitate

When necessary, a standard adult dose can be made up of both types of bags using this conversion factor, taking care to avoid errors.

Paediatric dosing is not established however common practise is 5mL/kg or 1–2 whole blood cryoprecipitate units per 10kg. If in doubt, or in the case of neonates, contact a neonatologist, haematologist or senior transfusion laboratory scientist.

The table below indicates how many bags per cryoprecipitate type are suggested per patient weight range.<sup>7</sup>

	Dose of Cryo (number of bags) for patient weight <sup>7</sup>				
Patient weight (kg)	5–20	>20–35	>35–50	>50–65	>65
WHOLE BLOOD cryo	2	4	6	8	10
APHERESIS cryo	1	2	3	4	5

Some adult patients and children may be prescribed doses outside the above table based on their individual circumstances. Contact a haematologist or senior transfusion laboratory scientist for advice.

### References

1. Australian Red cross Blood Service. [Blood Component Information Circular of Information – An extension of blood component labels](#). Australia 2012.
2. National Blood Authority [Patient blood management guidelines: Module 3 – Medical](#). Australia, 2012.

3. National Blood Authority Patient blood management guidelines: [Module 1 – Critical Bleeding Massive Transfusion](#). Australia, 2012.
4. National Blood Authority [Patient blood management guidelines: Module 4 – Critical Care](#). Australia, 2012.
5. AABB Technical Manual, 17th Edition (2011)
6. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, et al. (2004). [Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant](#). British Journal of Haematology 126 (1): 11–28
7. South Australian Blood Management Committee.[unpublished meeting minutes] Paediatric Cryoprecipitate Dosing; meeting held 2013 December 3

#### Additional Resources

- National Blood Authority [Patient blood management guidelines: Module 2 – Perioperative](#). Australia, 2012.
- Tran HA, Chunilal SD, Harper PL, Tran H, Wood, EM et al. [An update of consensus guidelines for warfarin reversal](#). On behalf of the Australasian Society of Thrombosis and Haemostasis. Med J Aust 2013;198:198-199



## APPENDIX 1: PBM STRATEGIES AND TECHNIQUES – CONSIDERATIONS FOR ORGANISATIONS WANTING TO IMPROVE CLINICAL PRACTICE

In order to incorporate a PBM strategy or technique into routine practice, the use of clinical practice improvement methodology is recommended. Identifying a lead clinician or clinicians with an interest in PBM is an important starting point.

Clinical practice improvement (CPI) is the overarching name for a series of methodologies that can be taken to plan, implement and assess the impact of changes in the delivery of health services. Clinical practice improvement is not a one-off event but a continuing cycle of improvement activities. CPI methodology is described in detail in the [Easy Guide to Clinical Practice Improvement](#), and many organisations offer training courses that are based around the participant undertaking a project. Key steps of the CPI process are outlined below.

- Form a guidance team: Gain support from relevant hospital heads including relevant department head (eg. cardiothoracic surgery, orthopaedics, haematology and oncology etc, nursing and safety and quality).
- Collect baseline data: Undertake an audit of the frequency and current management of the strategy or technique.
- Establish a multidisciplinary project team consisting of the team leader and people with fundamental knowledge of the process: for example, surgeon or physician, clinical nurse consultant, nurse coordinator, registrar, resident medical officer, physiotherapist, anaesthetist, general practitioner (GP), GP liaison nurse, haematologist, transfusion nurse consultant and a consumer. Include a quality improvement facilitator.
- Develop an aim or mission statement that is SMART, ie Specific, Timely, Measurable, Appropriate, Result oriented and Time scheduled.
- Diagnostic phase: Map (flow-chart) current hospital processes for the strategy or technique, conduct a brainstorming session of the barriers and enablers to improvement with the project team, construct a cause and effect diagram and prioritise the causes in a Pareto chart.
- Intervention phase: Achieve consensus within the team on where to focus improvement energy. Use a plan-do-study-act (PDSA) framework for improvement cycles. A number of tools and resources may exist to support this process -customisation by local experts may be required to suit local needs.
- Impact and implementation phase: measure the impact of changes in order to be sure the intervention has resulted in an improvement, and to provide the evidence required to justify permanent implementation of these changes.
- Sustaining improvement phase: Mechanisms, such as standardisation of existing systems and process, documentation of associated policies, procedures, protocols and guidelines, training and education of staff, and ongoing measurement and review, need to be established to sustain the improvement.