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SOUTH AFRICAN SOCIETY
OF ANAESTHESIOLOGISTS (SASA)

South African Society of Anaesthesiologists Perioperative Patient Blood Management Guidelines 2020

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Abbreviations and acronyms

AAGBI	Association of Anaesthetists of Great Britain and Ireland
ACT	activated clotting time
ACS	acute coronary syndrome
AKI	acute kidney injury
ALI	acute lung injury
APACHE	acute physiology and chronic health evaluation
aPPT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
ASA	aspirin (acetylsalicylic acid)
AT	antithrombin
ATG	antithymocyte globulin
CABG	coronary artery bypass graft
CaO_2	arterial oxygen content
CI	confidence interval
CNS	central nervous system
COI	conflict of interest
CPB	cardiopulmonary bypass
CRASH	Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage
DAPT	dual antiplatelet therapy
DDAVP	desmopressin
DIC	disseminated intravascular coagulation
DO_2	oxygen delivery
EACA	epsilon amino-caproic acid
EACTA	European Association of Cardiothoracic Anaesthesiology
EACTS	European Association for Cardio-Thoracic Surgery
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EMA	European Medicines Agency
EPO	erythropoietin
ESA	erythropoiesis-stimulating agent
FDP	freeze-dried plasma

FFP	fresh frozen plasma
GCS	Glasgow coma scale
GI	gastrointestinal
GP IIb/IIIa	glycoprotein IIb/IIIa
Hb	haemoglobin
HIT	heparin-induced thrombocytopenia
HLA	human leukocyte antigen
HT	high-titre
ICU	intensive care unit
INR	international normalised ratio
IV	intravenous
LMWH	low molecular weight heparin
MI	myocardial infarction
MiECC	minimal invasive extracorporeal circulation
NHMRC	National Health and Medical Research Council
OACs	oral anticoagulants
PBM	patient blood management
PCC	prothrombin complex concentrate
POC	point-of-care
PRBC	packed red blood cells
PT	prothrombin time
RBC	red blood cell
RCC	red cell concentrate
RCT	randomised controlled trial
rFVIIa	recombinant human factor VIIa
RR	relative risk
SAH	sub-arachnoid haemorrhage
SANBS	South African National Blood Service
SASA	South African Society of Anaesthesiologists
TA-GVHD	transfusion-associated graft-versus-host disease
TBI	traumatic brain injury
TRICC	transfusion requirements in critical care
TTP	thrombotic thrombocytopaenic purpura
TXA	tranexamic acid
UFH	unfractionated heparin
VKAs	vitamin K antagonists
VTE	venous thromboembolism
WCBS	Western Cape Blood Service

Disclaimer

While every effort has been made to ensure scientific accuracy, the SASA shall not be responsible or in any way liable for errors, omissions or inaccuracies in this publication, whether arising from negligence or otherwise or for any consequences arising therefrom. These guidelines are designed to provide a guide to the minimum standards considered best clinical care. However, every clinician retains responsibility for the care of the patient and must exercise independent clinical judgement.

Introduction

Anaesthesiologists regularly request and administer blood components to their patients, a potentially life-saving intervention. All anaesthesiologists must be familiar with the indications and appropriate use of blood and blood components and their alternatives, but close liaison with haematologists and their local haematology blood sciences laboratory is encouraged. In the last decade, there have been considerable changes in approaches to optimal use of blood components, together with the use of alternative products, with a need to update previous guidelines and adapt them for anaesthesiologists working throughout the hospital system.

The SASA Patient Blood Management (PBM) Guidelines have been developed to improve perioperative PBM in South Africa. These recommendations have been compiled through a thorough and meticulous process by a group of experts working in the field in South Africa. The process started in 2018 and comprised a Delphi technique, collation and review of the latest and relevant medical literature, and a consensus meeting that took place at the SASA National Congress (Port Elizabeth, March 2019).

The guidelines focus on the broader principles of PBM, incorporating transfusion medicine (transfusion guidelines), management of anaemia, optimisation of coagulopathy, and administrative and ethical considerations.

There is a mix of low-middle income and high-income healthcare structures within South Africa. However, blood products are provided by the same not-for-profit non-governmental organisations to both private and public sectors. This environment faces several challenges related to PBM, most notably a high prevalence of anaemia (as much as 50% in preoperative patients in South African government hospitals) and iron deficiency, a frequent shortage of blood products, a small donor population, and a healthcare system under financial strain.[1,2] The rational and equitable use of blood products is essential to help ensure optimal care for as many perioperative patients as possible.

The summary of the recommendations provides key practice points for the day-to-day management of perioperative patients. A more detailed description of the evidence used to make these recommendations follows in the full clinical guidelines section.

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Summary of recommendations

Grading of recommendation

Each recommendation has been given a grade, using the following definitions, set by the Australian National Health and Medical Research Council (NHMRC):

GRADE A	Body of evidence can be trusted to guide practice.
GRADE B	Body of evidence can be trusted to guide practice in most situations.
GRADE C	Body of evidence provides some support for recommendation(s), but care should be taken in its application.
GRADE D	Body of evidence is weak and recommendations must be applied with caution.

Recommendations

	General PBM statements and measures
1.1	All patients should have their haemoglobin concentration (Hb) measured before listing for major elective surgery.
1.2	Patients who are anaemic (Hb < 13 g/dL) should be investigated before elective surgery and treated appropriately, and elective non-urgent surgery other than Caesarean section should be delayed when possible.
1.3	Where blood transfusion is anticipated, this and alternatives to transfusion, should be discussed with the patient and documented.
1.4	Red cell concentrate (RCC, previously called RBCs) should be transfused one unit at a time, and the patient's Hb should be checked before each unit transfused, unless there is ongoing bleeding or a large deficit that needs correcting.
1.5	The use of intraoperative cell salvage and tranexamic acid (TXA) administration should be considered in all trauma, major obstetric and non-obstetric patients where blood loss > 500 ml is expected.
1.6	Blood components should be prescribed for paediatric patients by volume rather than number of units.
1.7	Every institution should have a massive transfusion protocol which is regularly audited and reviewed every 2 years.
1.8	Group O RCC should be readily available in the clinical area, in case of life-threatening haemorrhage.
1.9	During major haemorrhage due to trauma and obstetrics, consideration should be given to transfusing red cells and fresh frozen plasma/ freeze-dried plasma (FFP/FDP) in preference to other intravenous(IV) fluid.
1.10	Patients who continue to actively bleed should be monitored by point-of-care (POC) and/ or regular laboratory tests for coagulation, fibrinogen and platelet counts or function.

PBM measures for patients expected to bleed significantly during surgery

		Consensus	Grade
	Preoperative		
2.1	Preoperative Hb should be measured, recorded and optimised as required.	Yes	A
2.2	Elective surgery should be postponed in patients with untreated anaemia.	Yes	A
2.3	Review and consider stopping antiplatelet and anticoagulant medication the recommended number of days before surgery.	Yes	B
2.4	Consider minimally invasive or laparoscopic surgical technique.	Yes	B
2.5	POC testing should be available with appropriate training.	Yes	C
	Intraoperative		
2.6	Position patient carefully to optimise venous drainage.	Yes	B
2.7	Use patient warming to maintain temperature > 36 °C.	Yes	A
2.8	Consider cell salvage if blood loss > 500 ml anticipated.	Yes	B
2.9	Consider giving TXA if blood loss > 500 ml anticipated.	Yes	C
2.10	The dose of TXA should be 15 mg/kg.	Yes	C
2.11	Apply restrictive transfusion threshold (Hb 7–8 g/dL) depending on patient characteristics and haemodynamics).	Yes	B
2.12	Consider use of topical haemostatic agents.	Yes	C
	Postoperative		
2.13	Maintain oxygen delivery, targeting oxygen saturation levels > 92%.	Yes	A
2.14	Single unit blood transfusion policy, with subsequent re-assessment of Hb concentration and clinical need between RCC units.	Yes	A
2.15	Consider postoperative drains for cell salvage.	Yes	A

General perioperative measures and management

	Anaemia		
3.1	Patients who are anaemic (Hb < 13 g/dL) should be investigated and the cause treated appropriately.	Yes	A
3.2	Patient pathways and pre-assessment clinics should be established to allow timely and appropriate management, and elective surgery should be delayed if required.	Yes	B

Cell salvage			
4.1	The use of cell salvage should be considered for high- or medium-risk surgery in non-obstetric adult patients where blood loss > 500 ml is likely.	Yes	B
4.2	The use of cell salvage should be considered for major obstetric haemorrhage.	Yes	B
4.3	In patients with malignancy or obstetric haemorrhage, a leucocyte filter must be used.	Yes	C
4.4	Bacterial contamination of the surgical field remains a relative contra-indication. Use of a leucocyte filter is advised.	Yes	C
4.5	Cell salvage may also be continued in the postoperative period.	Yes	B

Special situations

Major haemorrhage – initial resuscitation			
5.1	FDP can be substituted for FFP in the South African context.	Yes	B
5.2	15–20 ml/kg is the correct initial dose of FDP.	Yes	B
5.3	15–20 ml/kg is the correct initial dose of FFP.	Yes	B
5.4	Group O RCC should be readily available and transfused if haemorrhage is life-threatening.	Yes	B
5.5	POC or laboratory testing should be used to guide management.	Yes	C
5.6	During resuscitation, the following should be prevented/treated: hypothermia; acidosis; hypocalcaemia (aim for ionised calcium > 1.0 mmol/L); and hyperkalaemia.	Yes	A
Major haemorrhage – protocol			
5.7	Policies should be defined in an institutional major haemorrhage protocol.	Yes	A
5.8	To avoid unnecessary delay, blood products should be released without approval from a haematologist/senior.	Yes	A
5.9	Activation of the protocol should mobilise other equipment (blood warmers, pressure infusers, cell salvage etc).	Yes	A
Critical care			
6.1	Evidence does not support increasing oxygen delivery with RCC transfusion when the Hb is > 7 g/dL, unless the patient has acute cardiac ischaemia.	Yes	A
6.2	In patients with haematological malignancies, the same broad principles of restrictive use of RCC commonly apply (7–8 g/dL for RCC transfusion).	No	C
Obstetrics			
7.1	Early recognition of abnormal bleeding improves outcome.	Yes	A

7.2	As soon as abnormal bleeding is recognised, > 500 ml after a vaginal delivery and > 1 000 ml after a Caesarean section, the obstetrician, anaesthesiologist and senior midwife should attend to the mother.	Yes	A
7.3	Following abnormal bleeding as described in 7.2, blood should be taken for full blood count, clotting studies, group and screen, and a venous blood gas for rapid Hb measurement and lactate.	Yes	B
7.4	Cell salvage is recommended if abnormal bleeding occurs during Caesarean section.	Yes	B
7.5	A leucocyte filter should be used for autotransfusion of processed blood.	Yes	B
7.6	POC testing is recommended in this setting.	Yes	B
7.7	Fibrinogen replacement with cryoprecipitate or fibrinogen concentrate should be considered in these circumstances, if there is bleeding.	Yes	B
7.8	Fibrinogen should be replaced in obstetric haemorrhage if less than 2 g/L.	Yes	A
7.9	TXA reduces total blood loss and should be given if postpartum haemorrhage is diagnosed.	Yes	B
7.10	An initial dose of 1 g is suitable for TXA.	Yes	A
7.11	Early use of FFP/FDP before RCC may be required.	No	C
7.12	If coagulation tests are not known, then FFP/FDP should be withheld until four units of RCC have been given.	No	C
7.13	If no coagulation results are available and bleeding is ongoing, then, after four units of RCC, four units of FFP/FDP should be infused and 1:1 ratio of RCC–FFP/FDP transfusion maintained until the results of haemostatic tests are known and can guide further decisions.	No	D
	Paediatrics		
8.1	There is little direct evidence to guide the use of blood products in children, and generally the guidance intended for adults can be safely applied to children with some modifications.	Yes	C
8.2	'Restrictive' approaches to transfusion are appropriate for almost all children older than 3 months of age.	Yes	B
8.3	A transfusion of 10 ml/kg of RCC should increase Hb by approximately 2 g/dL.	Yes	A
8.4	Cryoprecipitate should be given in a dose of 5–10 ml/kg.	Yes	B
8.5	Platelets should be given in a dose of 10–20 ml/kg.	Yes	B
8.6	FFP/FDP may be given in doses of 10–15 ml/kg.	Yes	B
8.7	TXA can be used in children: a loading dose of 15 mg/kg followed by infusion 2 mg/kg/h should be used in trauma.	Yes	B

8.8	The guidance suggested for major haemorrhage in adults can be generally applied, though requires an awareness of the size of the child and the clinical context of the bleeding.	Yes	B
8.9	Higher transfusion thresholds are often applied to neonates and children with congenital heart disease.	No	C
8.10	Cell salvage can be useful in children, even if the absolute volume of blood loss is less than 500 ml.	No	C
	Trauma		
9.1	Ensure clinical treatment is constantly directed towards haemorrhage control (damage-control protocols).	Yes	A
9.2	Do not try to normalise blood pressure during active haemorrhage.	Yes	A
9.3	Maintain a minimum acceptable preload and blood pressure with volume resuscitation alone; this may need to be modified in the presence of trauma in head and spinal injuries.	Yes	A
9.4	During uncontrolled haemorrhage, avoid clear fluids for volume resuscitation unless there is profound hypotension and no imminent availability of blood products.	Yes	B
9.5	In cases of trauma-induced coagulopathy, deliver blood products empirically at first.	Yes	A
9.6	Use laboratory or RCC tests of coagulation to guide therapy as soon as available.	Yes	B
9.7	Give TXA 1 g immediately, but avoid if more than 3 hours after injury, unless there is evidence of ongoing hyperfibrinolysis.	Yes	A
9.8	Whilst haemorrhage is being controlled, administration of RCC and FFP/FDP in a ratio of 1:1.	Yes	B
9.9	The use of vasopressors should be avoided during active haemorrhage.	No	D
	Cardiac surgery		
10.1	There is no difference in outcome and thus no need to use liberal transfusion triggers (9.5 g/dL intraoperatively or ICU, or 8.5 g/dL in non-ICU ward) versus a restrictive transfusion trigger (7.5 g/dL in cardiac surgical patients).	Yes	A
10.2	The effect of cardiopulmonary bypass on platelet function may make the use of a higher platelet count (> 75) necessary after bypass.	Yes	A
10.3	There is no clear evidence of the benefit of platelet function analysis except in those patients who have taken P2Y12 receptor inhibitors such as clopidogrel within 5 days of surgery.	No	C

Predicting perioperative bleeding

		Consensus	Grade
10.4.1	Preoperative fibrinogen levels may be considered to identify patients at high risk of bleeding.	EACTS/ EACTA	C
10.4.2	Routine use of viscoelastic and platelet function testing is not recommended to predict bleeding in patients without antithrombotic treatment.	EACTS/ EACTA	C
10.4.3	Platelet function testing may be considered to guide the decision on the timing of cardiac surgery in patients who have recently received P2Y12 inhibitors or who have ongoing dual antiplatelet therapy (DAPT).	EACTS/ EACTA	B

Management of preoperative anticoagulant and antiplatelet drugs

		Consensus	Grade
10.5.1	In patients undergoing coronary artery bypass grafting (CABG), aspirin (ASA) should be continued throughout the preoperative period.	EACTS/ EACTA	C
10.5.2	In patients at high risk of bleeding or refusing blood transfusions and undergoing non-coronary cardiac surgery, stopping ASA should be considered at least 5 days preoperatively.	EACTS/ EACTA	C
10.5.3	It is recommended that ASA be restarted as soon as there is no concern over bleeding (within 24 hours) after isolated CABG.	EACTS/ EACTA	B
10.5.4	In patients taking DAPT who need to have non-emergent cardiac surgery, postponing surgery for at least 3 days after discontinuation of ticagrelor, 5 days after clopidogrel and 7 days after prasugrel should be considered.	EACTS/ EACTA	B
10.5.5	It is recommended that GP IIb/IIIa inhibitors be discontinued at least 4 hours before surgery.	EACTS/ EACTA	C
10.5.6	To reduce the risk of bleeding, preoperative bridging of oral anticoagulation with unfractionated heparin/ low molecular weight heparin (UFH/LMWH) is only indicated in patients at high risk of thrombotic events.	EACTS/ EACTA	B
10.5.7	It is recommended that prophylactic LMWH be discontinued at least 12 hours before surgery and fondaparinux 24 hours before surgery. A longer interval may be necessary for patients with impaired renal function and/or therapeutic doses.	EACTS/ EACTA	B
10.5.8	It is recommended that oral anticoagulants (OACs) be bridged with UFH.	EACTS/ EACTA	B
10.5.9	Bridging OACs with subcutaneous LMWH should be considered an alternative to bridging with UFH.	EACTS/ EACTA	B

10.5.10	Elective cardiac surgery should be performed if the international normalised ratio (INR) is < 1.5 in patients taking vitamin K antagonists (VKAs). When surgery cannot be postponed, coagulation factors should be used to reverse the effect.	EACTS/ EACTA	C
10.5.11	In patients having elective cardiac surgery, direct oral anticoagulants (DOACs) should be stopped at least 48 hours before surgery. A longer interval may be necessary for patients with impaired renal function.	EACTS/ EACTA	C

Preoperative surgical planning

		Consensus	Grade
10.6.1	Oral or IV iron alone prior to cardiac surgery may be considered in mildly anaemic patients (Hb 10–13 g/dL) or in severely anaemic patients (Hb ≤ 10 g/dL) to improve erythropoiesis.	EACTS/ EACTA (adjusted)	C
10.6.2	Erythropoietin with iron supplementation should be considered to reduce postoperative transfusions in patients with non-iron deficiency (e.g. EPO, vitamin D or folate acid deficiency) undergoing elective surgery.	EACTS/ EACTA	B
10.6.3	Preoperative erythrocyte transfusion is not routinely recommended in preoperative anaemic patients to prevent postoperative acute kidney injury (AKI).	EACTS/ EACTA	C

Intraoperative management

		Consensus	Grade
10.7.1	It is recommended that the members of the multidisciplinary team discuss the optimal surgical strategy based on clinical status, comorbidities, bleeding risk and team expertise.	EACTS/ EACTA	C
10.7.2	Off-pump CABG surgery may be considered in selected patients to reduce perioperative transfusions.	EACTS/ EACTA	B
10.7.3	Minimal invasive extracorporeal circulation (MiECC) systems should be considered over standard conventional cardiopulmonary bypass (CPB) systems to reduce perioperative transfusions.	EACTS/ EACTA	B
10.7.4	Minimally invasive heart valve surgery may be considered to reduce blood loss and the need for transfusions.	EACTS/ EACTA	B
10.7.5	Routine use of topical sealants in cardiac surgery is not recommended.	EACTS/ EACTA	B
10.7.6	Topical sealants may be considered in clinical situations where conventional approaches to surgical and medical improvement of haemostasis are insufficient, and where bleeding problems are more local than generalised.	EACTS/ EACTA	C

Management of cardiopulmonary bypass

		Consensus	Grade
10.8.1	Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	EACTS/ EACTA	C
10.8.2	The use of a closed extracorporeal circuit may be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.8.3	The use of a biocompatible coating to reduce perioperative bleeding and transfusions may be considered.	EACTS/ EACTA	B
10.8.4	The routine use of cell salvage should be considered to prevent transfusions.	EACTS/ EACTA	B
10.8.5	(Modified) ultrafiltration may be considered as part of a blood conservation strategy to minimise haemodilution.	EACTS/ EACTA	B
10.8.6	Retrograde and antegrade autologous priming should be considered as part of a blood conservation strategy to reduce transfusions.	EACTS/ EACTA	A
10.8.7	Normothermia during CPB (temperature > 36 °C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	EACTS/ EACTA	B

Management of intraoperative anticoagulation

		Consensus	Grade
10.9.1	Heparin level-guided heparin management should be considered over ACT-guided heparin management to reduce bleeding.	EACTS/ EACTA	B
10.9.2	Heparin level-guided protamine dosing may be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.9.3	Protamine should be administered in a protamine-to-heparin dosing ratio < 1mg:100IU to reduce bleeding.	EACTS/ EACTA	B
10.9.4	Antithrombin (AT) supplementation is ideally indicated in patients with AT deficiency to improve heparin sensitivity. Since AT supplementation is currently not available in South Africa, FFP or FDP should be used.	EACTS/ EACTA (adjusted)	B
10.9.5	AT supplementation is not recommended to reduce bleeding following CPB.	EACTS/ EACTA	C
10.9.6	In patients with heparin-induced thrombocytopenia (HIT) antibodies for whom surgery cannot be postponed, anticoagulation with fondaparinux should be considered when the bleeding risk is acceptable. The use of heparin in the pre- and postoperative periods should be avoided.	EACTS/ EACTA (adjusted)	C

Management of intravascular volume

		Consensus	Grade
10.10.1	The use of goal-directed haemodynamic therapy to reduce transfusions is not recommended.	EACTS/ EACTA	C
10.10.2	The use of modern low-molecular weight starches in priming and non-priming solutions to reduce bleeding and transfusions is not recommended.	EACTS/ EACTA	C
10.10.3	Limitation of haemodilution is recommended as part of a blood conservation strategy to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.10.4	Preoperative autologous blood donation in patients with high Hb levels (> 11 g/dL) may be considered to reduce postoperative transfusions.	EACTS/ EACTA	B
10.10.5	Acute normovolaemic haemodilution may be considered to reduce postoperative transfusions.	EACTS/ EACTA	B

Management of procoagulant interventions

		Consensus	Grade
10.11.1	Antifibrinolytic therapy (TXA, aprotinin and EACA) is recommended to reduce bleeding and transfusions of blood products and to reduce re-operations for bleeding (TXA and aprotinin).	EACTS/ EACTA	A
10.11.2	The prophylactic use of FFP/FDP to reduce bleeding is not recommended.	EACTS/ EACTA (adjusted)	B
10.11.3	The use of prothrombin complex concentrate (PCC) or FFP/FDP may be considered to reverse the action of VKAs.	EACTS/ EACTA (adjusted)	B
10.11.4	In patients with factor XIII activity < 70% after CPB, the administration of FFP/FDP and/or cryoprecipitate may be considered to reduce bleeding.	EACTS/ EACTA	B
10.11.5	Prophylactic fibrinogen or cryoprecipitate administration is not recommended.	EACTS/ EACTA (adjusted)	B
10.11.6	In the bleeding patient with a low fibrinogen level (< 1.5 g/L), fibrinogen substitution (cryoprecipitate) may be considered to reduce postoperative bleeding and transfusions.	EACTS/ EACTA (adjusted)	B
10.11.7	In patients where bleeding is related to coagulation factor deficiency, PCC or FFP/FDP administration should be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.11.8	The prophylactic use of desmopressin (DDAVP) to reduce bleeding is not recommended.	EACTS/ EACTA	B
10.11.9	In bleeding patients with platelet dysfunction on the basis of an inherited or acquired bleeding disorder, the use of DDAVP should be considered to reduce bleeding and the requirement for transfusions.	EACTS/ EACTA	C

10.11.10	The prophylactic use of recombinant human factor VIIa (rFVIIa) to prevent bleeding is not recommended.	EACTS/ EACTA	B
10.11.11	In patients with refractory, non-surgical bleeding, off-label use of rFVIIa may be considered to reduce bleeding.	EACTS/ EACTA	B

Management of transfusion strategies

		Consensus	Grade
10.12.1	Implementation of a PBM protocol for the bleeding patient is recommended.	EACTS/ EACTA	C
10.12.2	The use of RCCs of all ages is recommended, because the storage time of the RCC does not affect the outcomes.	EACTS/ EACTA	A
10.12.3	The use of leucocyte-depleted RCCs is recommended to reduce infectious complications.	EACTS/ EACTA	B
10.12.4	Perioperative treatment algorithms for the bleeding patient based on viscoelastic POC tests should be considered to reduce the number of transfusions.	EACTS/ EACTA	B
10.12.5	It is recommended that one transfuse RCCs on the basis of the clinical condition of the patient rather than on a fixed Hb threshold.	EACTS/ EACTA	B
10.12.6	A haematocrit of 21–24% may be considered during CPB when an adequate DO_2 (4 273 ml O_2/min/m^2) level is maintained.	EACTS/ EACTA	B
10.12.7	Platelet concentrate should be transfused in bleeding patients with a platelet count below 50 (x10^9/L) or patients on antiplatelet therapy with bleeding complications.	EACTS/ EACTA	C

Anticoagulation management during extracorporeal life support

		Consensus	Grade
10.13	Argatroban (not available in South Africa) may be considered as alternatives for heparin anticoagulation for prolonged extracorporeal life support/ extracorporeal membrane oxygenation (ECLS/ECMO) therapy to prevent HIT type 2. In South Africa, Fondaparinux is an available alternative, (long half-time is a concern).	EACTS/ EACTA (adjusted)	C

Neuroanaesthesia

		Consensus	Grade
11.1	Anaemia is associated with poor outcomes in traumatic and elective neurosurgery and should be corrected preoperatively using a standardised approach for identifying and treating reversible causes, thus avoiding unnecessary blood product transfusions.	Yes	B
11.2	In traumatic brain injury (TBI), and provided there is no other indication for transfusion, a restrictive (> 7–8 g/dL) transfusion threshold should be used as it decreases the risk of severe progressive haemorrhagic injury and thromboembolism.	Yes	C

11.3	Until better evidence is available, a transfusion target of 9 g/dL should be used for aneurysmal subarachnoid haemorrhage (SAH).	Yes	C
11.4	TXA should be used in paediatric cranial vault surgery and early (immediate administration on presentation within 3 hours of injury) in mild to moderate TBI.	Yes	B
11.5	Perioperative blood conservation strategies are favoured and include the pharmacological correction of anaemia, the use of TXA, and cell salvage.	Yes	B
11.6	Preoperative autologous donation and acute normovolaemic haemodilution are not recommended as blood conservation techniques.	Yes	C
11.7	Intraoperative nonsteroidal anti-inflammatory agents are not recommended for intracranial procedures.	Yes	C

Coagulation, laboratory and monitoring

		Consensus	Grade
	Laboratory tests		
12.1	Activated partial thromboplastin time (aPPT), prothrombin time (PT) and INR have little relevance in acute ongoing haemorrhage.	Yes	N/A
	RCC testing		
13.1	The use of validated POC tests is a more relevant reflection of coagulation status and are preferred.	Yes	B
13.2	Patients at high risk (> 10% risk of thrombotic events per year) of thrombosis should be considered for bridging anticoagulation, or in the following circumstances:[3-5] • Embolic stroke or systemic embolic event within the previous three months. • Mechanical mitral valve. • Mechanical aortic valve and additional stroke risk factors. • Atrial fibrillation and very high risk of stroke (e.g. CHADS2 score of 5 or 6, stroke or systemic embolism within the previous 12 weeks, concomitant rheumatic valvular heart disease with mitral stenosis). • Venous thromboembolism (VTE) within the previous three months (preoperative and postoperative bridging). • Recent coronary stenting (e.g. within the previous 12 weeks). • Previous thromboembolism during interruption of chronic anticoagulation.	Yes	B
13.3	Bridging anticoagulation usually consists of LMWH.	Yes	C

Blood component therapy

	Packed red blood cells		
14.1	A general Hb threshold of 7 g/dL should apply as a guide for red cell transfusion.	Yes	B

14.2	Uncertainty remains for patients with ischaemic heart disease, including acute coronary syndrome (ACS) and after cardiac surgery, and higher thresholds (8 g/dL) may be more appropriate in such circumstances.	Yes	A
	FFP/FDP		
15.1	The recommended initial therapeutic dose is 15–20 ml/kg.	Yes	A
15.2	Indications for FFP/FDP use include the following:		
15.2.1	Maintenance of coagulation factors during major haemorrhage, particularly trauma and obstetrics.	Yes	A
15.2.2	Acute disseminated intravascular coagulation (DIC) with bleeding.	Yes	C
15.2.3	In patients who are actively bleeding and whose INR is > 1.5 (or POC equivalent).	Yes	B
15.2.4	Immediate reversal of warfarin-induced haemorrhage when PCC is not available (PCC is the first choice).	Yes	B
15.2.5	Thrombotic thrombocytopenic purpura (preferably using pathogen-inactivated FFP or FDP), with plasmapheresis if no response.	Yes	A
15.2.6	Replacement of coagulation factors when specific factors are not available in the presence of active bleeding or to prevent bleeding during an invasive procedure (uncommon).	Yes	B
15.3	FFP/FDP is not recommended for routine use in patients with cirrhosis/liver disease unless significant coagulopathy and haemorrhage are identified.	Yes	B
	Cryoprecipitate		
16.1	Indications for cryoprecipitate include the following:		
16.1.1	Hypofibrinogenaemia due to major haemorrhage and massive transfusion.	Yes	A
16.1.2	During major haemorrhage, fibrinogen should be maintained > 1.5 g/L, except in active obstetric haemorrhage where fibrinogen should be maintained > 2 g/L.	Yes	A
16.1.3	Bleeding associated with thrombolytic therapy.	Yes	C
16.1.4	DIC with fibrinogen < 1.0 g/L.	Yes	B
16.1.5	Advanced liver disease, to maintain fibrinogen level > 1.0 g/L.	Yes	B
16.1.6	Combined liver and renal failure with bleeding.	No	C
16.2	The initial dose of cryoprecipitate should be 1 unit/10kg (typically 15–20 ml/10kg).	Yes	A
	Platelets		
17.1	Indications for platelets include the following:		
17.1.1	Prevention and treatment of bleeding due to thrombocytopenia or platelet function defects.	Yes	B

17.1.2	If patient is actively bleeding, transfuse to a platelet count > 50 x 10^9/L (> 75 x 10^9/L for neurosurgical and ophthalmic bleeding).	Yes	B
17.2	If not bleeding, the following triggers should be applied:		
17.2.1	Routine prophylactic use: 10 x 10^9/L.	Yes	B
17.2.2	Prophylactic use with additional risk factors (e.g. sepsis): 10 – 20 x 10^9/L.	Yes	C
17.2.3	Other major surgery or invasive procedures: 50 x 10^9/L.	Yes	C
17.2.4	Neuraxial blockade: 50 x 10^9/L.	Yes	B
17.2.5	Prophylactic use in closed compartment surgery (eye, brain): 100 x 10^9/L.	Yes	B

Drugs and novel therapies

18.1	TXA should be administered empirically in critically ill patients with severe trauma within 3 hours of the injury.	Yes	A
18.2	The dose of TXA in severe trauma is 1 g stat and then 1 g over 8 hours.	Yes	A
18.3	TXA should be administered empirically in bleeding obstetric patients.	Yes	B
18.4	The dose of TXA in bleeding obstetric patients is 1g stat, and 1 g after 30 min if bleeding persists or recurs within 24 hours.	Yes	B
18.5	Empiric use of TXA is not recommended in patients with upper gastrointestinal bleeding.	Yes	B
18.6	TXA is recommended for patients with TBI and Glasgow coma scale (GCS) 8–13 presenting within 3 hours of injury.	Yes	B
18.7	Where available POC viscoelastic testing should be used to guide therapy with TXA.	Yes	C
18.8	With the use of warfarin: INR to be kept between 2.0 and 2.5 according to indication. Perioperative use: stop 3–5 days before surgery; INR reduction to < 1.5 if you are using bridging therapy. Bridging necessary only in patients with a very high thrombotic risk.	Yes	B
18.9	Direct acting anticoagulants – stop 48 hours before surgery. If renal impairment then stop earlier: If creatinine clearance > 80 ml/min/1.73m^2 > 48 hr. If creatinine clearance 50–79 ml/min/1.73m^2 > 72 hr. If creatinine clearance < 50 ml/min/1.73m^2 > 96 hr.	Yes	B
18.10	Antiplatelet therapy: Aspirin – don't stop unless operating on a non-compressible site. Ticagrelor – stop 3 days before surgery. Clopidogrel – stop 5 days before surgery. Prasugrel – stop 7 days before surgery. If need to continue due to high risk of thrombosis, consider options such as GP IIb/IIIa.	Yes	B

18.11	GP IIb/IIIa antagonists – stop at least 4 hours before surgery. (Stop Abciximab earlier as a longer time is required for recovery of platelet function 24–48 hours).	Yes	B
18.12	LMWH – stop at least 12 hours before surgery if used prophylactically, and 24 hours before surgery if used in therapeutic doses. The anticoagulation effect can partially be reversed by protamine sulphate, but not completely. Consider bridging with LMWH/UFH only in patients with a high risk for thrombosis who are on oral anticoagulants. Enoxaparin – stop at least 12 hours before surgery. Fondaparinux – stop 24 hours before surgery. Stop for longer duration in patients with impaired renal function.	Yes	B

Administration

19.1	The use of blood and blood products must be directed by established protocols.	Yes	B
19.2	The use of blood and blood products must be subjected to gatekeeping controls.	Yes	C

Ethics

			Grade
20.1	Both blood donors and recipients must be protected through safe blood management practices.		N/A
20.2	Blood transfusion services must comply with the provisions of the standards of practice for blood transfusions in South Africa.		N/A
20.3	All blood and blood products require informed consent prior to transfusion.		N/A
20.4	If consent cannot be provided by the patient, consent may be provided by a person mandated in writing by the patient, a person authorised by any law or court order or any surrogate decision maker.		N/A
20.5	Advanced directives (or 'living wills'), while having no legal force, should be ethically honoured.		N/A
20.6	An adult may refuse blood and blood products solely on religious grounds if the patient is of sound mind and understands the risks and consequences of such refusal.		N/A
20.7	No parent or guardian may refuse blood or blood products of a minor solely on religious grounds if the blood or blood product would be life-preserving.		N/A
20.8	If a clinician is uncertain of any reason a patient would refuse blood and there is a clear indication for the use of blood or a blood product to preserve life, the best interests of the patient must prevail.		N/A

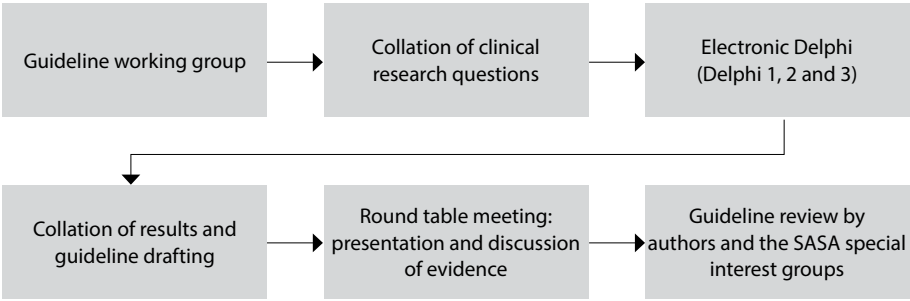
20.9	Blood and blood products should be triaged in a resource-limited environment.		N/A
20.10	Health authorities should ensure that blood services are progressively developed to ensure the needs of the patients are met.		N/A

Guideline development

The development of the document involved a multi-step process. Experts in the field of anaesthesia and those with an interest in PBM were invited to participate after a call for interested parties through SASA communication. An effort was made to ensure representation from all major centres across South Africa.

Clinical research questions

The clinical research questions were derived from the AAGBI Use of Blood Components and Their Alternatives (2016), and the Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA).[6,7] The questions were selected and reviewed for relevance to the Southern African context. Additional questions were added based on local clinical experience. All questions were compiled in a survey format that was tested amongst the group for ambiguity and clarity.



Delphi process

A Delphi process was run using the questions developed above. Consensus was achieved at 80%. Results were collated and where consensus was not reached the questions were selected for further review and research.

Review and research

Questions where consensus was not reached in the electronic Delphi process were divided amongst the working group, as were different topics within the guidelines. Each question was allocated to members of the working group who were tasked with researching the question further, collating the summary of the available data on the topic and incorporating these into the guidelines.

Round table congress meeting (and final Delphi) – Port Elizabeth, March 2019

The data on the questions where consensus was not reached was presented at a round table meeting held in Port Elizabeth on 7 March 2019. The questions where consensus was still not reached were discussed further and a final Delphi process was completed. Where consensus was still not reached but there was consensus within a narrow range, this was noted. If no consensus was possible this was also noted. The guidelines were then distributed to special interest groups within the SASA for comments and approval.

Formulation of recommendations

The results of the Delphi rounds and data synthesis from the members of the working group were collated to form the backbone of the current guidelines. Each recommendation is derived from the responses to the clinical research questions from the expert working group.

Introduction

Transfusion medicine is changing rapidly in response to new developments. Considerable changes in approaches to transfusion, together with the use of alternative agents, have become apparent over the past decade. Blood transfusion can be lifesaving, but this is a scarce and costly resource. There is increased focus on appropriate transfusion practice to ensure quality of service provision, and transfusion has been proposed as a quality indicator in surgical care. Blood transfusion usage remains high, particularly in trauma, obstetrics, critical care and cardiovascular surgery.

Anaesthesiologists are frequently involved in transfusion decisions, the administration of blood and blood components and as part of the team managing any major haemorrhage. However, the use of allogeneic blood components has serious implications and warrants careful consideration.[8] As a consequence, there has recently been an expansion of interest in safeguarding and checklists, blood conservation, preservation techniques, coagulation profiling and the use of haemostatic agents. Appropriate use of blood components in patient care is of utmost importance.

Several recent publications related to transfusion practice examined aspects of patient safety, outcomes and individualised care, including: use of restrictive transfusion protocols; adjuvant therapies; substitution of blood components with pooled factor concentrates; and use of POC testing to target specific component use.

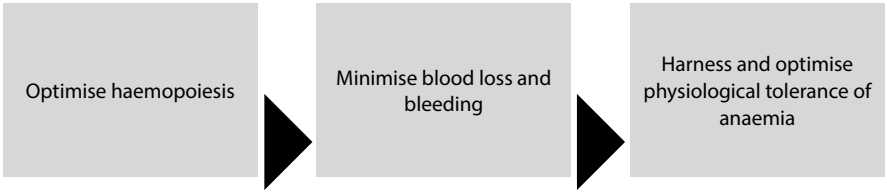
It is essential that our practice of blood transfusion is safe and based on current, scientific, evidence-based knowledge. A multidisciplinary approach that aims to benefit patients by the reduction in inappropriate transfusions is paramount. This working party aimed to formalise guidance on the clinical indications and risks of transfusion, blood conservation and the transfusion process.

Clinical guidelines

1. General PBM statements and measures

1.1	All patients should have their Hb concentration measured before listing for major elective surgery.
1.2	Patients who are anaemic (Hb < 13 g/dL) should be investigated before elective surgery and treated appropriately, and elective non-urgent surgery other than Caesarean section should be delayed when possible.
1.3	Where blood transfusion is anticipated, this and alternatives to transfusion, should be discussed with the patient and documented.
1.4	Red cell concentrate (RCC, previously called RBCs) should be transfused one unit at a time, and the patient's Hb should be checked before each unit transfused, unless there is ongoing bleeding or a large deficit that needs correcting.
1.5	The use of intraoperative cell salvage and TXA administration should be considered in all trauma, major obstetric and non-obstetric patients where blood loss > 500 ml is expected.
1.6	Blood components should be prescribed for small children by volume rather than number of units.
1.7	Every institution should have a massive transfusion protocol that is regularly audited and reviewed every 2 years.
1.8	Group O RCC should be readily available in the clinical area, in case of life-threatening haemorrhage.
1.9	During major haemorrhage due to trauma and obstetrics, consideration should be given to transfusing red cells and FFP/FDP in preference to other IV fluid.
1.10	Patients who continue to actively bleed should be monitored by POC and/or regular laboratory tests for coagulation, fibrinogen and platelet counts or function.

The three pillars of PBM should be observed throughout a patient's journey of care.[9]



In resource-limited environments where blood products are scarce, attention should be given to alternative techniques for blood collection, in particular cell salvage. We also recommend the establishment of active Patient Blood Management Committees within every hospital. These committees should meet monthly and ensure the appropriate use of blood products and PBM principles within their institutions.

Clinicians and PBM committees should be cognisant of the difficulties some areas face in accessing blood products, and these should be considered when ordering and using blood products.

2. PBM measures for patients expected to bleed significantly during surgery

		Consensus	Grade
	Preoperative		
2.1	Preoperative Hb should be measured, recorded and optimised as required.	Yes	A
2.2	Elective surgery should be postponed in patients with untreated anaemia.	Yes	A
2.3	Review and consider stopping antiplatelet and anticoagulant medication the recommended number of days before surgery.	Yes	B
2.4	Consider minimally invasive or laparoscopic surgical technique.	Yes	B
2.5	POC testing should be available with appropriate training.	Yes	C
	Intraoperative		
2.6	Position patient carefully to optimise venous drainage.	Yes	B
2.7	Use patient warming to maintain temperature > 36 °C.	Yes	A
2.8	Consider cell salvage if blood loss > 500 ml anticipated.	Yes	B
2.9	Consider giving TXA if blood loss > 500 ml anticipated.	Yes	C
2.10	The dose of TXA should be 15 mg/kg.	Yes	C
2.11	Apply restrictive transfusion threshold (Hb 7–8 g/dL) depending on patient characteristics and haemodynamics.	Yes	B
2.12	Consider use of topical haemostatic agents.	Yes	C
	Postoperative		
2.13	Maintain oxygen delivery, targeting oxygen saturation levels > 92%.	Yes	A
2.14	Single unit blood transfusion policy, with subsequent re-assessment of Hb concentration and clinical need between RCC units.	Yes	A
2.15	Consider postoperative drains for cell salvage.	Yes	A

Patient blood management is a patient-based approach aimed at reducing the unnecessary utilisation of blood products and improving patients' clinical outcomes and safety, and focuses on the optimisation of three perioperative factors: patient, surgical and anaesthetic.[10] It has been recommended as a standard of care in South Africa.[9] PBM focuses on three 'pillars' of care in surgical patients: detection and treatment of perioperative anaemia; reduction of perioperative blood loss; and harnessing and optimising the patient-specific physiological reserve of anaemia.[11] In recent years, transfusion medicine has been a focus of research,

however, as much emphasis should be placed on the other pillars of PBM, in particular the early management of anaemia.

We recommend a national drive for early screening and management for anaemia for all patients who are to undergo surgery. Where possible, anaemia should be treated preoperatively with appropriate investigations and management with pharmacological agents, to avoid operating on anaemic patients and unnecessary administration of blood products.

General perioperative measures and management

3. Anaemia

		Consensus	Grade
	Anaemia		
3.1	Patients who are anaemic (Hb < 13 g/dL) should be investigated and the cause treated appropriately.	Yes	A
3.2	Patient pathways and pre-assessment clinics should be established to allow timely and appropriate management, and elective surgery should be delayed if required.	Yes	B

Preoperative anaemia is common and is associated with worse outcomes. It occurs in up to a third of patients before surgery (and in as many as 50% of patients at government hospitals in South Africa). All patients should have their Hb checked before listing for surgery. Patients who are anaemic (Hb < 13 g/dL) should be investigated and the cause treated appropriately.[9,12,13] Patient pathways and pre-assessment clinics should be established to allow timely and appropriate management, and elective surgery should be delayed if more time is required for the Hb to increase.[14] If anaemia clinics are not possible, then all patients should be screened preoperatively at their respective outpatient departments or clinics, with subsequent appropriate therapy for the anaemia. Whenever possible, the objective should be to operate on patients who are not anaemic (in particular, elective procedures).

4. Cell salvage

		Consensus	Grade
4.1	The use of cell salvage should be considered for high- or medium-risk surgery in non-obstetric adult patients where blood loss > 500 ml is likely.	Yes	B
4.2	The use of cell salvage should be considered for obstetric major haemorrhage.	Yes	B
4.3	In patients with malignancy or obstetric haemorrhage, a leucocyte filter must be used.	Yes	C
4.4	Bacterial contamination of the surgical field remains a relative contraindication. Use of a leucocyte filter is advised.	Yes	C

4.5	Cell salvage may also be continued in the postoperative period.	Yes	B

Cell salvage represents a key strategy in reducing exposure to allogeneic blood transfusion and preserving donor blood. International guidelines are applicable to the South African context,[15] and recommend that cell salvage should be used when it will reduce the likelihood of blood transfusion or severe postoperative anaemia. It should ideally be available after-hours, necessitating appropriate staff training and availability of equipment. The use of cell salvage should be considered for high- or medium-risk surgery in non-obstetric adult patients where blood loss > 500 ml is likely, and in major obstetric haemorrhage. Blood should be collected from the start of surgery, but the decision to process blood can be based on the volume collected, to minimise the risk of opening expensive processing sets that are not used. In patients with malignancy or obstetric haemorrhage, a leucocyte filter must be used. Bacterial contamination of the surgical field remains a relative contraindication, and should also be given through a leucocyte filter if transfused. Cell salvage may also be continued in the postoperative period.[16]

Special situations

5. Major haemorrhage

		Consensus	Grade
	Major haemorrhage – initial resuscitation		
5.1	FDP can be substituted for FFP in the South African context.	Yes	B
5.2	15–20 ml/kg is the correct initial dose of FDP.	Yes	B
5.3	15–20 ml/kg is the correct initial dose of FFP.	Yes	B
5.4	Group O RCC should be readily available and transfused if haemorrhage is life-threatening.	Yes	B
5.5	POC or laboratory testing should be used to guide management.	Yes	C
5.6	During resuscitation, the following should be prevented/treated: hypothermia; acidosis; hypocalcaemia (aim for ionised calcium > 1.0 mmol/L); and hyperkalaemia.	Yes	A
	Major haemorrhage – protocol		
5.7	Policies should be defined in an institutional major haemorrhage protocol.	Yes	A
5.8	To avoid unnecessary delay, blood products should be released without approval from a haematologist/senior.	Yes	A
5.9	Activation of the protocol should mobilise other equipment (blood warmers, pressure infusers, cell salvage etc).	Yes	A

Policies should be defined in an institutional major haemorrhage protocol. Activation of the protocol should result in the immediate release and administration of blood components for initial resuscitation, without prior approval from a haematologist. Such protocols perform best when specific to clinical areas such as the emergency department or the labour ward, and are designed to include robust and clearly understood activation and communication from bedside to laboratory. Their activation should also mobilise other resources, such as additional senior staff, porters, blood warmers, pressure infusers and cell salvage devices.[17]

A clear mechanism for the escalation of a team response and for identifying individuals with sufficient seniority and experience to undertake the key roles of team leader (e.g. senior anaesthesiologist) and coordinator is essential to the process, as is enabling a single point of contact with the laboratory and other support services.

Initial resuscitation

Most major haemorrhage packs will contain four units of RCCs and four units of FFP/FDP (equivalent to 15–20 ml/kg in a standard adult); platelet concentrate may also be provided. Administration should be via wide-bore IV access, or intra-osseous access until the former can be obtained.

Group O RCC should be readily available and transfused if haemorrhage is life-threatening and cross-matched red cells are not obtainable. It is preferable to give group O Rh-negative red cells to children and women of childbearing potential, but group O Rh-positive red cells may be used in adult men.

Group-specific RCC should be rapidly made available (within 15–20 min) by the laboratory after receiving a correctly labelled blood group sample and being informed of the emergency requirement for blood. Emergency Group O RCC should continue to be provided where timely and safe issue of group-specific RCC is not possible.

Haemostatic resuscitation

This describes the process of restoring and sustaining acceptable tissue perfusion with the emphasis on preservation of effective clotting. Coagulopathy is associated with haemorrhage (loss of platelets and clotting factors) and transfusion of blood products and synthetic fluids (dilution), as well as the mechanism of injury in trauma; this may exacerbate the haemorrhage and resultant morbidity. POC or laboratory testing should be used to guide management.

During resuscitation, the following should be prevented/treated: hypothermia; acidosis; hypocalcaemia (aim for ionised calcium > 1.0 mmol/L); and hyperkalaemia.

6. Critical care

		Consensus	Grade
6.1	Evidence does not support increasing oxygen delivery with RCC transfusion when the Hb is > 7 g/dL, unless the patient has acute cardiac ischaemia.	Yes	A
6.2	In patients with haematological malignancies, the same broad principles of restrictive use of RCC commonly apply (7–8 g/dL for RCC transfusion).	No	C

Anaemia is common during critical illness. In addition to blood loss and sampling, haemodilution and impaired erythropoiesis may be important contributors.[18]

Although biochemical markers of tissue hypoxia, notably blood lactate concentration, are frequently elevated, evidence does not support increasing oxygen delivery with RCC transfusion when the Hb is 7 g/dL, except possibly the patient with acute cardiac ischaemia.[19]

Patients with haematological malignancies form an important group of patients admitted to ICU. Overall, patients with cancer form one of the larger groups of recipients of blood components. However, unlike other patient groups, anaemia in patients with haematological malignancies reflect an underlying bone marrow failure, and therefore, it is unclear to what extent findings from the majority of randomised trials conducted in surgery or general critical care can be extrapolated to cancer, although the same broad principles of restrictive use of red cells commonly apply.

7. Obstetrics

		Consensus	Grade
7.1	Early recognition of abnormal bleeding improves outcome.	Yes	A
7.2	As soon as abnormal bleeding is recognised, > 500 ml after a vaginal delivery and > 1 000 ml after a Caesarean section, the obstetrician, anaesthesiologist and senior midwife should attend to the mother.	Yes	A
7.3	Following abnormal bleeding as described in 7.2, blood should be taken for full blood count, clotting studies, group and screen, and a venous blood gas for rapid Hb measurement and lactate.	Yes	B
7.4	Cell salvage is recommended if abnormal bleeding occurs during Caesarean section.	Yes	B
7.5	A leucocyte filter should be used for autotransfusion of processed blood.	Yes	B
7.6	POC testing is recommended in this setting.	Yes	B
7.7	Fibrinogen replacement with cryoprecipitate or fibrinogen concentrate should be considered in these circumstances, if there is bleeding.	Yes	B

7.8	Fibrinogen should be replaced in obstetric haemorrhage if less than 2g/L.	Yes	A
7.9	TXA reduces total blood loss and should be given if postpartum haemorrhage is diagnosed.	Yes	B
7.10	An initial dose of 1 g is suitable for TXA.	Yes	A
7.11	Early use of FFP/FDP before RCC may be required.	No	C
7.12	If coagulation tests are not known, then FFP/FDP should be withheld until four units of RCC have been given.	No	C
7.13	If no coagulation results are available and bleeding is ongoing, then, after four units of RCC, four units of FFP/FDP should be infused and 1:1 ratio of RCC–FFP/FDP transfusion maintained until the results of haemostatic tests are known and can guide further decisions.	No	D

Estimating blood loss at delivery is notoriously difficult, and every effort should be made to directly measure abnormal bleeding across all settings in the delivery suite.[20] Early recognition of bleeding by changing bed linen and pads immediately after delivery and systematically weighing new blood-soaked pads correlates with the fall in Hb concentration and improves outcome.

As soon as abnormal bleeding is recognised (> 500 ml after a vaginal delivery and > 1 000 ml after a Caesarean section) the obstetrician, anaesthesiologist and senior midwife should attend to the mother. Blood should be taken for full blood count (Hb), clotting studies, group and screen, and a venous blood gas for rapid Hb measurement and lactate (> 2 mmol/L is an indicator of shock). Cell salvage is recommended if abnormal bleeding occurs during Caesarean section, and a leucocyte filter should be used for autotransfusion of processed blood.

In resource-constrained areas where access to blood products takes more than 2 hours, it is advised to order crossmatched RCC on a returnable basis (cooler box) when the preoperative Hb is less than 9 g/dL (or the postoperative Hb is expected to drop below 7 g/dL). Any unused RCC should be kept in the sealed cooler box and returned to the nearest blood bank within 12 hours.

Severe early consumptive coagulopathy is associated with abruption, amniotic fluid embolus and severe bleeding with preeclampsia. Early use of FFP/FDP before RCC may be required.

Postpartum haemorrhage associated with uterine atony or trauma is unlikely to be associated with haemostatic impairment unless the diagnosis is delayed. Protocol-led use of blood products will lead to over-transfusion of FFP/FDP in the majority of cases.[21] If coagulation tests are not known, then FFP/FDP should be withheld until four units of RCC have been given. If no coagulation results are available and bleeding is ongoing, then, after four units of RCC, four units of FFP/FDP should be infused and a 1:1 ratio of RCC to FFP/FDP transfusion maintained until the results of haemostatic tests are known. POC testing is recommended in this setting.[22]

Hypofibrinogenaemia, below normal levels for pregnancy, predicts the risks of ongoing postpartum haemorrhage. The normal plasma fibrinogen concentration in pregnancy is 4–6 g/L, and a laboratory fibrinogen of < 3 and especially < 2 g/L, with ongoing bleeding, is associated with progression to major obstetric bleeding.[23] Fibrinogen replacement with cryoprecipitate or fibrinogen concentrate should be considered in these circumstances, if there is ongoing bleeding.

Monitoring of haemostatic function in obstetric haemorrhage is particularly important; laboratory testing is often too slow during obstetric haemorrhage, and therefore, POC testing is preferred. Tests should include plasma fibrinogen concentration or POC equivalent.[22] With ongoing bleeding, any abnormalities should be treated, as this indicates significant haemostatic impairment in the obstetric patient. Platelet transfusions are rarely required and should only be given once the platelet count is known.

TXA reduces total blood loss and should be given once postpartum haemorrhage is diagnosed (> 500 ml after a vaginal delivery and > 1 000 ml after a Caesarean section), at an initial dose of 1 g.

8. Paediatrics

		Consensus	Grade
8.1	There is little direct evidence to guide the use of blood products in children, and generally the guidance intended for adults can be safely applied to children with some modifications.	Yes	C
8.2	'Restrictive' approaches to transfusion are appropriate for almost all children older than 3 months of age.	Yes	B
8.3	A transfusion of 10 ml/kg of RCC should increase Hb by approximately 2 g/dL.	Yes	A
8.4	Cryoprecipitate should be given in a dose of 5–10 ml/kg.	Yes	B
8.5	Platelets should be given in a dose of 10–20 ml/kg.	Yes	B
8.6	FFP/FDP may be given in doses of 10–15 ml/kg.	Yes	B
8.7	TXA can be used in children: a loading dose of 15 mg/kg followed by infusion 2 mg/kg/h should be used in trauma.	Yes	B
8.8	The guidance suggested for major haemorrhage in adults can be generally applied, though requires an awareness of the size of the child and the clinical context of the bleeding.	Yes	B
8.9	Higher transfusion thresholds are often applied to neonates and children with congenital heart disease.	No	C
8.10	Cell salvage can be useful in children, even if the absolute volume of blood loss is less than 500 ml.	No	C

There is little direct evidence to guide the use of blood products in children, and generally the guidance intended for adults can be safely applied to children with some modifications (specifically in transfusion volumes). 'Restrictive' approaches to transfusion are appropriate for almost all children older than 3 months of age. Higher transfusion thresholds are often applied to neonates and children with congenital heart disease. Although thresholds are not clearly defined, there is evidence that quantities of transfusion can be reduced in these patients by applying moderately restrictive thresholds for transfusion without adverse effect on outcome.[24,25] Neonates should receive components specified for neonatal use, O or ABO compatible with maternal and neonatal plasma, Rh-D negative, crossmatch compatible with maternal and neonatal plasma, < 5 days old, irradiated (must be transfused within 24 hours of irradiation) and leucocyte-depleted.

The volume of blood to be administered requires modification depending on the size of the patient. It is recommended that blood in children should be prescribed in volume rather than number of units. In practice, sensible rounding to the nearest unit will be more efficient.

- A transfusion of 10 ml/kg of RCC should increase Hb by approximately 2 g/dL.
- Cryoprecipitate should be given in a dose of 5–10 ml/kg.
- Platelets should be given in a dose of 10–20 ml/kg.
- FFP may be given in doses of 10–15 ml/kg.

TXA can be used in children: a loading dose of 15 mg/kg followed by infusion 2 mg/kg/h should be used in trauma.[26]

With technical refinements, cell salvage can be useful in children, even if the absolute volume of blood loss is less than 500 ml.[27]

Major haemorrhage is rare in children outside of highly specialised areas of practice. The guidance suggested for adults can be generally applied, though requires an awareness of the size of the child and the clinical context of the bleeding. Blood volume of a child is estimated at 70 ml/kg but may be as high as 100 ml/kg in newborns. Devices for vascular access and rapid administration of blood should be appropriate for the size of the child and rate of blood loss. Children are at particular risk of electrolyte imbalance and hypothermia during rapid administration of blood products.

9. Trauma

		Consensus	Grade
9.1	Ensure clinical treatment is constantly directed towards haemorrhage control (damage-control protocols).	Yes	A
9.2	Do not try to normalise blood pressure during active haemorrhage.	Yes	A

9.3	Maintain a minimum acceptable preload and blood pressure with volume resuscitation alone; this may need to be modified in the presence of trauma in head and spinal injuries.	Yes	A
9.4	During uncontrolled haemorrhage, avoid clear fluids for volume resuscitation unless there is profound hypotension and no imminent availability of blood products.	Yes	B
9.5	In cases of trauma-induced coagulopathy, deliver blood products empirically at first.	Yes	A
9.6	Use laboratory or RCC tests of coagulation to guide therapy as soon as available.	Yes	B
9.7	Give TXA 1 g immediately, but avoid if more than 3 hours after injury, unless there is evidence of ongoing hyperfibrinolysis.	Yes	A
9.8	Whilst haemorrhage is being controlled, administration of RCC and FFP/FDP in a ratio of 1:1.	Yes	B
9.9	The use of vasopressors should be avoided during active haemorrhage.	No	D

Only around 5–7% of trauma cases qualify for damage-control resuscitation. Inappropriate use of blood products in less serious trauma should be avoided.

During active bleeding, follow the principles of damage control resuscitation:

Early haemorrhage control

Ensure clinical treatment is constantly directed towards haemorrhage control. Use temporary haemostatic devices (pressure, tourniquets, etc.) followed as soon as practically possible by surgery or interventional radiological control of haemorrhage.

Permissive hypotension

Do not try to normalise blood pressure during active haemorrhage. Maintain a minimum acceptable preload and blood pressure (systolic blood pressure > 70 mmHg, mean arterial pressure > 50 mmHg) with volume resuscitation alone; this may need to be modified in the presence of trauma in head and spinal injuries.[28] The use of vasopressors should be avoided during active haemorrhage. This period should be as short as possible and seen as a bridging strategy to definitive haemorrhage control.

Avoid crystalloid and colloid administration

During uncontrolled haemorrhage, avoid clear fluids for volume resuscitation unless there is profound hypotension and no imminent availability of blood products.

Target trauma-induced coagulopathy

Deliver blood products empirically at first, and use laboratory or POC tests of coagulation to guide therapy as soon as available.[29] Give TXA 1 g immediately, but avoid if more than 3 h after injury, unless there is ongoing evidence of hyperfibrinolysis (as suggested by POC testing).

Whilst haemorrhage is being controlled, administration of RCC and FFP/FDP in a ratio of 1:1 should be used to replace fluid volume.[30] Consider the administration of cryoprecipitate (1 unit/10 kg) and platelets (one adult therapeutic dose) until test results are available and bleeding is controlled. Once control is achieved, blood components should be administered as guided by testing at the earliest opportunity (see Monitoring section, blood components).

Once haemorrhage is controlled and Hb and coagulation targets have been met, judicious use of crystalloids and colloids for further volume resuscitation is acceptable, but crystalloid overload should be avoided.

10. Cardiac surgery

		Consensus	Grade
10.1	There is no difference in outcome and thus no need to use liberal transfusion triggers (9.5 g/dL intraoperatively or ICU, or 8.5 g/dL in non-ICU ward) versus a restrictive transfusion trigger (7.5 g/dL in cardiac surgical patients.	Yes	A
10.2	The effect of cardiopulmonary bypass on platelet function may make the use of a higher platelet count (> 75) necessary after bypass.	Yes	A
10.3	There is no clear evidence of the benefit of platelet function analysis except in those patients who have taken P2Y12 receptor inhibitors such as clopidogrel within 5 days of surgery.	No	C

PBM in cardiac surgery is a multidisciplinary effort with different leadership structures in private and government settings in South Africa. Depending on the environment and locale, different members of the team may or may not have independent jurisdiction or decision-making powers on the decision to transfuse or to not transfuse blood or blood products.

Critically important role-players in this process include the anaesthesiologists, surgeons, perfusionists, and critical care specialists (if involved in the intensive care unit). Differences in practices should be aligned to provide the best practice based on the available evidence and expert recommendations. These guidelines provide a framework for decision-making.

The SASA supports a multidisciplinary approach that is based on published evidence and best practice recognised internationally, which may need to be adjusted due to the availability of blood, blood products, and drugs available in South Africa.

Anaemic patients have an increased risk of mortality and complications following cardiac surgery.[31] Elective cardiac surgery should not be undertaken in anaemic patients without prior investigation and treatment as necessary (mostly based on observational studies). There is an increased risk of requiring transfusions in anaemic patients presenting for cardiac surgery.

Viscoelastic testing is recommended to guide transfusion.[32] The use of local transfusion protocols guided by RCC testing may lead to appropriate transfusion with reduced costs. The evidence base for the efficacy of routine use of FFP/FDP in the context of cardiac surgery haemorrhage is minimal and of poor quality.[33] The effect of cardiopulmonary bypass on platelet function may make the use of a higher platelet count (> 75 x $10^9.L^{-1}$) necessary after bypass.

There is no clear evidence of the benefit of platelet function analysis except in those patients who have taken P2Y12 receptor inhibitors such as clopidogrel within 5 days of surgery.[34]

The following recommendations regarding preoperative and intraoperative strategies to improve PBM in cardiac surgery are derived from EACTA and EACTS recommendations published by Boer et al.[7]

Predicting perioperative bleeding			
		Consensus	**Grade**
10.4.1	Preoperative fibrinogen levels may be considered to identify patients at high risk of bleeding.	EACTS/ EACTA	C
10.4.2	Routine use of viscoelastic and platelet function testing is not recommended to predict bleeding in patients without antithrombotic treatment.	EACTS/ EACTA	C
10.4.3	Platelet function testing may be considered to guide the decision on the timing of cardiac surgery in patients who have recently received P2Y12 inhibitors or who have ongoing DAPT.	EACTS/ EACTA	B
Management of preoperative anticoagulant and antiplatelet drugs			
		Consensus	**Grade**
10.5.1	In patients undergoing CABG, ASA should be continued throughout the preoperative period.	EACTS/ EACTA	C
10.5.2	In patients at high risk of bleeding or refusing blood transfusions and undergoing non-coronary cardiac surgery, stopping ASA should be considered at least 5 days preoperatively.	EACTS/ EACTA	C
10.5.3	It is recommended that ASA be restarted as soon as there is no concern over bleeding (within 24 hours) after isolated CABG.	EACTS/ EACTA	B

10.5.4	In patients taking DAPT who need to have non-emergent cardiac surgery, postponing surgery for at least 3 days after discontinuation of ticagrelor, 5 days after clopidogrel and 7 days after prasugrel should be considered.	EACTS/ EACTA	B
10.5.5	It is recommended that GP IIb/IIIa inhibitors be discontinued at least 4 hours before surgery.	EACTS/ EACTA	C
10.5.6	To reduce the risk of bleeding, preoperative bridging of oral anticoagulation with UFH/LMWH is only indicated in patients at high risk of thrombotic events.	EACTS/ EACTA	B
10.5.7	It is recommended that prophylactic LMWH be discontinued at least 12 hours before surgery and fondaparinux 24 hours before surgery. A longer interval may be necessary for patients with impaired renal function and/or therapeutic doses.	EACTS/ EACTA	B
10.5.8	It is recommended that OACs be bridged with UFH.	EACTS/ EACTA	B
10.5.9	Bridging OACs with subcutaneous LMWH should be considered an alternative to bridging with UFH.	EACTS/ EACTA	B

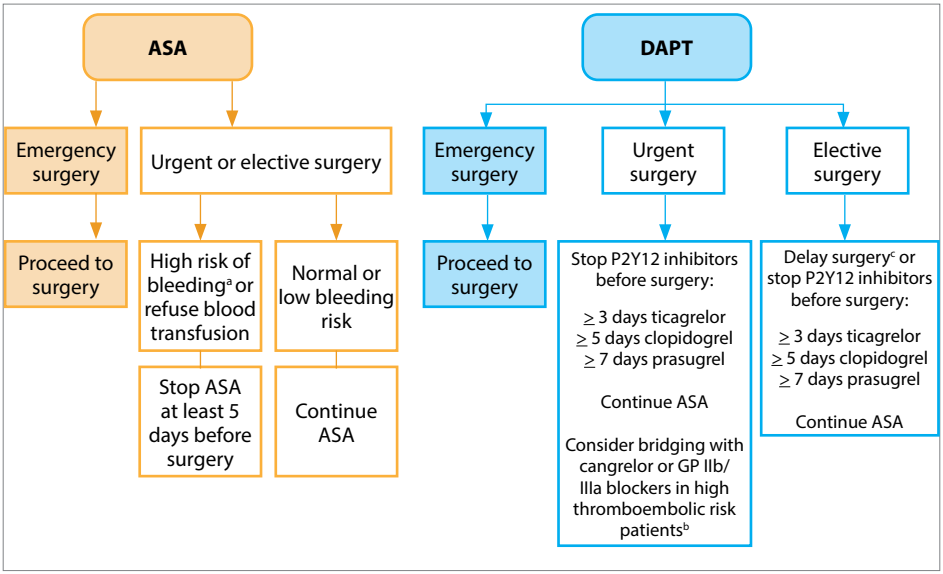


Figure 1: Management of antiplatelet therapy in patients having coronary artery bypass grafting surgery.[7]

[a] Complex and redo-operations, severe renal insufficiency, haematological diseases and hereditary deficiencies in platelet function.
[b] Recent stent implantation, recent thromboembolic event and alarming angiographic results.
[c] Until the recommended DAPT period is completed.
ASA – acetylsalicylic acid, DAPT – dual antiplatelet therapy, GP IIb/IIIa – glycoprotein IIb/IIIa

10.5.10	Elective cardiac surgery should be performed if the INR is < 1.5 in patients taking VKAs. When surgery cannot be postponed, coagulation factors should be used to reverse the effect.	EACTS/ EACTA	C
10.5.11	In patients having elective cardiac surgery, DOACs should be stopped at least 48 hours before surgery. A longer interval may be necessary for patients with impaired renal function.	EACTS/ EACTA	C

Preoperative surgical planning			
		Consensus	**Grade**
10.6.1	Oral or IV iron alone prior to cardiac surgery may be considered in mildly anaemic patients (Hb 10–13 g/dL) or in severely anaemic patients (Hb ≤ 10 g/dL) to improve erythropoiesis.	EACTS/ EACTA (adjusted)	C
10.6.2	Erythropoietin with iron supplementation should be considered to reduce postoperative transfusions in patients with non-iron deficiency (e.g. EPO, vitamin D or folate acid deficiency) undergoing elective surgery.	EACTS/ EACTA	B
10.6.3	Preoperative erythrocyte transfusion is not routinely recommended in preoperative anaemic patients to prevent postoperative AKI.	EACTS/ EACTA	C
Intraoperative considerations			
		Consensus	**Grade**
10.7.1	It is recommended that the members of the multidisciplinary team discuss the optimal surgical strategy based on clinical status, comorbidities, bleeding risk and team expertise.	EACTS/ EACTA	C
10.7.2	Off-pump CABG surgery may be considered in selected patients to reduce perioperative transfusions.	EACTS/ EACTA	B
10.7.3	MiECC systems should be considered over standard conventional CPB systems to reduce perioperative transfusions.	EACTS/ EACTA	B
10.7.4	Minimally invasive heart valve surgery may be considered to reduce blood loss and the need for transfusions.	EACTS/ EACTA	B
10.7.5	Routine use of topical sealants in cardiac surgery is not recommended.	EACTS/ EACTA	B
10.7.6	Topical sealants may be considered in clinical situations where conventional approaches to surgical and medical improvement of haemostasis are insufficient and where bleeding problems are more local than generalised.	EACTS/ EACTA	C

Management of cardiopulmonary bypass			
		Consensus	**Grade**
10.8.1	Implementation of institutional measures to reduce haemodilution by fluid infusion and CPB, during cardiac surgery to reduce the risk of bleeding and the need for transfusions is recommended.	EACTS/ EACTA	C
10.8.2	The use of a closed extracorporeal circuit may be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.8.3	The use of a biocompatible coating to reduce perioperative bleeding and transfusions may be considered.	EACTS/ EACTA	B
10.8.4	The routine use of cell salvage should be considered to prevent transfusions.	EACTS/ EACTA	B
10.8.5	(Modified) ultrafiltration may be considered as part of a blood conservation strategy to minimise haemodilution.	EACTS/ EACTA	
10.8.6	Retrograde and antegrade autologous priming should be considered as part of a blood conservation strategy to reduce transfusions.	EACTS/ EACTA	A
10.8.7	Normothermia during CPB (temperature > 36 °C) and maintenance of a normal pH (7.35–7.45) may contribute to a reduced risk of postoperative bleeding.	EACTS/ EACTA	B
Management of intraoperative anticoagulation			
		Consensus	**Grade**
10.9.1	Heparin level-guided heparin management should be considered over ACT-guided heparin management to reduce bleeding.	EACTS/ EACTA	B
10.9.2	Heparin level-guided protamine dosing may be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.9.3	Protamine should be administered in a protamine-to-heparin dosing ratio < 1mg:100IU to reduce bleeding.	EACTS/ EACTA	B
10.9.4	AT supplementation is ideally indicated in patients with AT deficiency to improve heparin sensitivity. Since AT supplementation is currently not available in South Africa, FFP or FDP should be used.	EACTS/ EACTA (adjusted)	B
10.9.5	AT supplementation is not recommended to reduce bleeding following CPB.	EACTS/ EACTA	C
10.9.6	In patients with HIT antibodies for whom surgery cannot be postponed, anticoagulation with fondaparinux should be considered when the bleeding risk is acceptable. The use of heparin in the pre- and postoperative periods should be avoided.	EACTS/ EACTA (adjusted)	C

Management of intravascular volume			
		Consensus	**Grade**
10.10.1	The use of goal-directed haemodynamic therapy to reduce transfusions is not recommended.	EACTS/ EACTA	C
10.10.2	The use of modern low-molecular weight starches in priming and non-priming solutions to reduce bleeding and transfusions is not recommended.	EACTS/ EACTA	C
10.10.3	Limitation of haemodilution is recommended as part of a blood conservation strategy to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.10.4	Preoperative autologous blood donation in patients with high Hb levels (> 11 g/dL) may be considered to reduce postoperative transfusions.	EACTS/ EACTA	B
10.10.5	Acute normovolaemic haemodilution may be considered to reduce postoperative transfusions.	EACTS/ EACTA	B
Management of procoagulant interventions			
		Consensus	**Grade**
10.11.1	Antifibrinolytic therapy (TXA, aprotinin and EACA) is recommended to reduce bleeding and transfusions of blood products and reduce re-operations for bleeding (TXA and aprotinin).	EACTS/ EACTA	A
10.11.2	The prophylactic use of FFP/FDP to reduce bleeding is not recommended.	EACTS/ EACTA (adjusted)	B
10.11.3	The use of PCC or FFP/FDP may be considered to reverse the action of VKAs.	EACTS/ EACTA (adjusted)	B
10.11.4	In patients with factor XIII activity < 70% after CPB, the administration of FFP/FDP and/or cryoprecipitate may be considered to reduce bleeding.	EACTS/ EACTA	B
10.11.5	Prophylactic fibrinogen or cryoprecipitate administration is not recommended.	EACTS/ EACTA (adjusted)	B
10.11.6	In the bleeding patient with a low fibrinogen level (< 1.5 g/L), fibrinogen substitution (cryoprecipitate) may be considered to reduce postoperative bleeding and transfusions.	EACTS/ EACTA (adjusted)	B
10.11.7	In patients where bleeding is related to coagulation factor deficiency, PCC or FFP/FDP administration should be considered to reduce bleeding and transfusions.	EACTS/ EACTA	B
10.11.8	The prophylactic use of DDAVP to reduce bleeding is not recommended.	EACTS/ EACTA	B
10.11.9	In bleeding patients with platelet dysfunction on the basis of an inherited or acquired bleeding disorder, the use of DDAVP should be considered to reduce bleeding and the requirement for transfusions.	EACTS/ EACTA	C

10.11.10	The prophylactic use of rFVIIa to prevent bleeding is not recommended.	EACTS/ EACTA	B
10.11.11	In patients with refractory, non-surgical bleeding, off-label use of rFVIIa may be considered to reduce bleeding.	EACTS/ EACTA	B
	Management of transfusion strategies		
		Consensus	**Grade**
10.12.1	Implementation of a PBM protocol for the bleeding patient is recommended.	EACTS/ EACTA	C
10.12.2	The use of RCCs of all ages is recommended, because the storage time of the RCCs does not affect the outcomes.	EACTS/ EACTA	A
10.12.3	The use of leucocyte-depleted RCCs is recommended to reduce infectious complications.	EACTS/ EACTA	B
10.12.4	Perioperative treatment algorithms for the bleeding patient based on viscoelastic POC tests should be considered to reduce the number of transfusions.	EACTS/ EACTA	B
10.12.5	It is recommended that one transfuse RCCs on the basis of the clinical condition of the patient rather than on a fixed Hb threshold.	EACTS/ EACTA	B
10.12.6	A haematocrit of 21–24% may be considered during CPB when an adequate DO_2 (4 273 ml O_2/min/m^2) level is maintained.	EACTS/ EACTA	B
10.12.7	Platelet concentrate should be transfused in bleeding patients with a platelet count below 50 (x10^9/L) or patients on antiplatelet therapy with bleeding complications.	EACTS/ EACTA	C
	Anticoagulation management during extracorporeal life support		
		Consensus	**Grade**
10.13	Argatroban (not available in South Africa) may be considered as alternatives for heparin anticoagulation for prolonged ECLS/ECMO therapy to prevent HIT type 2. In South Africa, fondaparinux is an available alternative, (long half-time is a concern).	EACTS/ EACTA (adjusted)	C

11. Neuroanaesthesia

	Neuroanaesthesia		
		Consensus	**Grade**
11.1	Anaemia is associated with poor outcomes in traumatic and elective neurosurgery and should be corrected preoperatively using a standardised approach for identifying and treating reversible causes, thus avoiding unnecessary blood product transfusions.	Yes	B

11.2	In TBI, and provided there is no other indication for transfusion, a restrictive (> 7–8 g/dL) transfusion threshold should be used as it decreases the risk of severe progressive haemorrhagic injury and thromboembolism.	Yes	C
11.3	Until better evidence is available, a transfusion target of 9 g/dL should be used for aneurysmal SAH.	Yes	C
11.4	TXA should be used in paediatric cranial vault surgery and early (immediate administration on presentation within 3 hours of injury) in mild to moderate TBI.	Yes	B
11.5	Perioperative blood conservation strategies are favoured and include the pharmacological correction of anaemia, the use of TXA, and cell salvage.	Yes	B
11.6	Preoperative autologous donation and acute normovolaemic haemodilution are not recommended as blood conservation techniques.	Yes	C
11.7	Intraoperative nonsteroidal anti-inflammatory agents are not recommended for intracranial procedures.	Yes	C

Maintaining the balance

The brain has high metabolic requirements and receives 20–25% of cardiac output. During normovolaemic anaemia, the reduced blood viscosity results in increased cardiac output and allows for improved flow characteristics. These compensatory mechanisms are limited and anaemia may worsen cerebral oxygen delivery (i.e. reduced CaO_2) and a 'second-hit' hypoxic insult may result. However, cerebral function is relatively well maintained in patients without TBI down to a Hb level of about 7 g/dL.[35]

In neurosurgical patients, the benefits of anaemia include decreased blood viscosity and improved cerebral blood flow. This needs to be balanced against the risk of cerebral vasospasm, cerebral hypoxia with potential for ischaemic injury, potentially poorer neurological outcomes and subsequent mortality.[36,37] Anaemia is common in neurosurgical populations with up to half of critically ill patients with TBI and SAH.[38] The causes may be multifactorial such as bleeding, aggressive fluid resuscitation, systemic inflammatory- mediated suppression of erythropoiesis and regular phlebotomy in hospital. Anaemic patients presenting for elective intracranial neurosurgery have an increased 30 day mortality (4.1% vs 1.3%; OR = 2.77; 95% CI: 1.65–4.66) and length of stay.[39,40] In turn, transfusion, which aims to increase cerebral oxygen delivery and prevent secondary brain injury, is associated with thromboembolic events, progression of a haemorrhagic injury and an increase in mortality.[41-43] Therefore, preoperative anaemia should be corrected by pharmacological measures for elective surgery, and perioperative transfusion limited to avoid the deleterious effects of unnecessary blood products.

Transfusion in neurosurgery and traumatic brain injury

Neurosurgery covers a broad range of elective and emergency pathologies, and this makes research and guidelines in the field difficult. Depending on the type of surgery, the rate of transfusion ranges from 10% in complex skull base procedures, to 36% in TBI and > 45% in paediatric craniosynostosis surgery. However, transfusion itself confers risks of immune modulation, infections, allergic reactions and other complications.[42]

The optimal Hb threshold for transfusion in TBI is still unclear.[44] In a randomised control trial of 200 TBI patients, a higher Hb transfusion threshold of 10 g/dL v 7 g/dL was associated with an increased risk of severe progressive haemorrhagic injury.[45] There was also an increased risk of thromboembolic events with no significant improvement in neurological outcomes. A liberal (Hb > 10 g/dL) transfusion strategy has not been shown to improve outcomes in isolated TBI.[46] Lelubre et al. showed there is probably benefit in transfusing TBI patients with Hb < 7 g/dL.[44] These beneficial effects appear to diminish around 8 g/dL, but a Hb > 9 g/dL was associated with an increase in-hospital mortality, and further harmful effects. Another study comparing a liberal versus a restrictive blood transfusion strategy (10 g/dL vs 7 g/dL) showed a slightly better brain tissue oxygenation in the liberal group, but a higher intracranial pressure, with no difference in long term (6 month) neurological outcomes.[47]

A restrictive blood transfusion strategy (Hb 7–8 g/dL) for TBI patients should be used if no other clinical indication for transfusion exists, particularly in patients that are awake and conscious. If patients deteriorate neurologically or have a severe grade injury (GCS < 9), transfusion may be optimised using mixed venous saturations > 70% target, serum lactate and cerebral oxygenation monitors, optimised to the patient's comorbidities.[44] However, there is no data on how exactly these measures may be used to guide transfusion of RCC in these patients.

Transfusion in subarachnoid haemorrhage

In aneurysmal SAH, about 50% of patients suffer subsequent cerebral vasospasm. Triple-H therapy of hypertension, hypervolaemia and haemodilution is still used during an episode of symptomatic vasospasm, however, the risks associated with this strategy and lack of evidence to support a significant benefit has meant that it is no longer supported practice.[48]

In a study of 441 patients with SAH, intraoperative transfusion was associated with worse outcome and postoperative transfusion with vasospasm.[43] RBC transfusion is also related to an increase in complications, length of stay, wound infection, pneumonia, cardiovascular accident and acute renal failure.[49] There is debate in the current literature regarding a Hb target for patients with intracranial pathology, with recent reviews suggesting a range of Hb 9–10 g/dL as optimum,[36] but there are few randomised control trials to support this.[50]

Minimising anaemia and transfusion

Perioperative blood conservation strategies in neurosurgery include the correction of pre-operative coagulopathy, correction of iron deficiency anaemia, the use of cell salvage and anti-fibrinolytic agents, and the avoidance of nonsteroidal anti-inflammatory agents.[36] Oral or IV iron may be used within established protocols, depending on time constraints.[51] There is limited evidence for preoperative autologous donation and acute normovolaemic haemodilution in neurosurgery.[36] Nonsteroidal anti-inflammatory drugs have various effects on platelet function and should be avoided in intracranial surgery.

Antifibrinolytic therapy

TXA is recommended to prevent blood loss and the risk of transfusion in paediatric craniosynostosis surgery and complex base of skull surgery.[52] TXA may be used when blood loss of more than 500 ml is expected, in resections for meningioma and cerebellopontine angle tumours as well as vascular intracranial pathologies and spine surgeries.[53] However, TXA is not recommended in patients with hypersensitivity or allergy to the drug, history of venous or arterial thrombosis, or thrombophilia, cardiovascular disease, acute renal failure or subarachnoid haemorrhage, or in patients with a history of seizures or epilepsy.[54]

A Cochrane review of TXA in aneurysmal subarachnoid haemorrhage did not show a reduction in poor outcome but did reduce the risk of re-bleeding (with a high heterogeneity of studies).[54] In mild to moderate TBI, early treatment (within three hours of injury) with TXA is recommended to reduce mortality.[55]

Cell salvage

Intraoperative cell salvage has shown to be safe and cost-effective in spinal fusion and cranial vault surgery. However, there is concern over the use of cell salvage in tumour surgery, and the effect of leukocyte depletion filters on tumour cell recirculation has not been extensively investigated. There is no universally accepted decision as to the safety of cell salvage in central nervous system (CNS) oncological surgery. The use of cell salvage should be a joint decision between surgeon and anaesthetist, on the basis of risk versus benefit.[56]

Coagulation, laboratory and monitoring

12. Laboratory tests

		Consensus	Grade
12.1	aPPT, PT and INR have little relevance in acute ongoing haemorrhage.	Yes	N/A

Traditional tests such as aPPT, PT and INR have been standardised for the monitoring of anticoagulants and are designed to diagnose and manage factor deficiencies such as haemophilia. Standardisation within laboratories has made the results very reliable.

The PT and aPTT were not designed to monitor coagulation deficiencies during haemorrhage and suggested INR and aPTT ratios or triggers, which are widely quoted to guide coagulation product replacement, are based on small historic studies that have little relevance today. Slow turnaround time also means that the results do not reflect the dynamic clinical situation during ongoing haemorrhage.[57]

13. RCC testing

		Consensus	Grade
13.1	The use of validated POC tests is a more relevant reflection of coagulation status and is preferred.	Yes	B
13.2	Patients at high risk (> 10% risk of thrombotic events per year) of thrombosis should be considered for bridging anticoagulation, or in the following circumstances:[3-5] • Embolic stroke or systemic embolic event within the previous three months. • Mechanical mitral valve. • Mechanical aortic valve and additional stroke risk factors. • Atrial fibrillation and very high risk of stroke (e.g. CHADS2 score of 5 or 6, stroke or systemic embolism within the previous 12 weeks, concomitant rheumatic valvular heart disease with mitral stenosis). • VTE within the previous three months (preoperative and postoperative bridging) • Recent coronary stenting (e.g. within the previous 12 weeks). • Previous thromboembolism during interruption of chronic anticoagulation.	Yes	B
13.3	Bridging anticoagulation usually consists of LMWH.	Yes	C

POC testing has a shorter turnaround time and represents a more global and relevant reflection of coagulation status.[58] POC testing is increasingly popular in general and cardiac surgery, trauma units, intensive care and obstetrics. POC testing for Hb concentration is commonly used, such as blood gas analysis or the HemoCue® (Angelholm, Sweden), where both correlate well with laboratory measurements.[59] The activated clotting time (ACT) is also well validated and should be used routinely whenever heparin is administered, particularly in cardiac and vascular surgery.

Targeted blood component therapy based on POC testing has been shown to be safe and effective, and decreases blood product usage. However, there are currently no studies that show improved patient outcome compared with standard treatment.[34]

At the current time, there are two commercially available semi-automated viscoelastic machines that use similar technology: thromboelastometry (ROTEM, TEM International, Munich, Germany) and thromboelastography (TEG, Haemonetics Corp, Braintree, MA, USA). One manufacturer cannot be recommended above the other.

There are no universal algorithms across the specialities, and local protocols are required based on institutional procedures. There is limited interchangeability between TEG and ROTEM, and development and validation of separate treatment algorithms for the two devices are required.[60]

There are concerns about standardisation of both assays with poor quality control and assurance and a wide variation in results between centres.[61] It is good practice to pair coagulation samples and send a second sample for laboratory-based analysis.

Blood component therapy

Before administration of any blood component, the patient's details should be checked against those on the bag (see red blood cell transfusion section). Blood components have specific storage and expiry times. Every effort must be made to avoid wastage.

In haematological malignancy, the clinical team must be consulted before administering blood components because of the need for specific requirements. The transfusion threshold may be different to non-haematological patients. A small subset of patients requires transfusion with irradiated blood components to prevent them developing transfusion-associated graft-versus-host disease (TA-GVHD), which is rare, but usually fatal. Patients with the following conditions require irradiated blood: congenital immunodeficiency states, for example Di-George's syndrome; allogeneic bone marrow transplant recipients and donors; autologous bone marrow-transplanted patients; Hodgkin's lymphoma; purine analogue therapy (e.g. fludarabine, cladribine) as well as newer agents clofarabine and bendamustine; and patients who receive antithymocyte globulin (ATG), or certain monoclonal antibody therapies (e.g. anti-CD52 monoclonal antibody therapy (alemtuzumab).[62]

14. Packed red blood cells

		Consensus	Grade
14.1	A general Hb threshold of 7 g/dL should apply as a guide for red cell transfusion.	Yes	B
14.2	Uncertainty remains for patients with ischaemic heart disease, including ACS and after cardiac surgery, and higher thresholds (8 g/dL) may be more appropriate in such circumstances.	Yes	A

RBC transfusion is potentially life-saving for the treatment of blood loss and is the recommended therapy for restoring the diminished oxygen-carrying capacity in most circumstances.

The goals of RBC therapy are twofold;

1. to increase oxygen-carrying capacity of blood to meet tissue demand, and
2. to replace the oxygen-carrying elements of the intravascular volume lost during acute blood loss.

In patients who do not have active bleeding and in normovolaemic patients, the Hb should be measured before and after every unit of RCC transfused. Near-patient measurement of Hb may be particularly useful, but laboratory measurement remains the gold standard. Haemoglobin concentration is dependent on both red cell mass and plasma volume and it may fall due to haemodilution due to IV fluid administration. In the bleeding patient, inadequate fluid resuscitation may result in a falsely elevated Hb concentration despite significant blood loss. In the absence of blood products, or immediate need for blood products, the initial intravascular volume replacement strategies should mainly be synthetic crystalloid and colloid fluids. The controversy on choice of synthetic colloid solutions is beyond the scope of this guideline.

Optimum Hb transfusion trigger

Recent publications comparing more liberal transfusion strategies (typical transfusion trigger Hb 9–10 g/dL) with more restrictive strategies (typical transfusion trigger Hb 7–8 g/dL) did not show any difference in patient outcomes.[63, 64] Therefore, a general Hb threshold of 7 g/dL should apply as a guide for red cell transfusion. Uncertainty remains for patients with ischaemic heart disease, including ACS and after cardiac surgery,[65] and higher thresholds (8 g/dL) may be more appropriate in such circumstances (including patients going for major surgery and diminished oxygen reserve estimates). A recent context-specific meta-analysis showed restrictive transfusion strategies were associated with an increased risk of complications in situations combining high risk patients with major surgery.[66] Those with cardiovascular disease undergoing cardiac or vascular procedures seemed to have more events reflecting inadequate oxygen supply, higher mortality rates, or both. It remains difficult to identify such patients in every clinical situation, and new transfusion algorithms should aim to integrate additional clinical parameters, such as patient comorbidities, and particular clinical settings.

15. FFP/FDP

		Consensus	Grade
15.1	The recommended initial therapeutic dose is 15–20 ml/kg.	Yes	A
15.2	Indications for FFP/FDP use include the following:		
15.2.1	• Maintenance of coagulation factors during major haemorrhage, particularly trauma and obstetrics.	Yes	A
15.2.2	• Acute DIC with bleeding.	Yes	C

15.2.3	• In patients who are actively bleeding and whose INR is > 1.5 (or POC equivalent).	Yes	B
15.2.4	• Immediate reversal of warfarin-induced haemorrhage when PCC is not available (PCC is the first choice).	Yes	B
15.2.5	• Thrombotic thrombocytopenic purpura (preferably using pathogen-inactivated FFP or FDP) usually with plasmapheresis if no response.	Yes	A
15.2.6	• Replacement of coagulation factors when specific factors are not available in the presence of active bleeding or to prevent bleeding during an invasive procedure (uncommon).	Yes	C
15.3	FFP/FDP is not recommended for routine use in patients with cirrhosis/liver disease unless significant coagulopathy and haemorrhage are identified.	Yes	B

FFP is leucodepleted plasma rapidly frozen to below -25 °C to maintain the integrity of labile coagulation factors. The use of FFP has increased significantly in the past few years.[67] Coagulation tests (PT or INR and aPTT) should preferably be obtained prior to the administration of FFP in a bleeding patient. Transfusion of FFP is not indicated if PT, INR, and aPTT are normal (unless a patient has a condition such as thrombotic thrombocytopaenic purpura (TTP) or something like Factor XIII deficiency where both PT and aPTT may be normal).[68]

FFP needs to be thawed before use. Once out of the fridge, it must be used within 30 min, and once thawed, it should never be refrozen. The approximate volume per bag is 300 ml.

FFP contains all the factors of the soluble coagulation system, including the labile factors V and VIII to a varying degree. The fibrinogen content of four units of FFP is approximately 2 g, compared with approximately 4 g fibrinogen in two pools of cryoprecipitate. FFP should be the same group as the patient. If the blood group is unknown, group AB FFP is preferred, as it does not contain any anti-A or anti-B. If group O FFP is given to non-group O children, it should be high-titre (HT) negative. The recommended therapeutic dose is 15 ml/kg.

FDP has a haemostatic function similar to that of FFP. It is stored as dry powder at room temperature (below 25 °C) with a shelf life greater than that of FFP. Electrolyte and protein levels are comparable with those of FFP. Coagulant activities of factors I, II, V, VII, VIII, IX and X may be 10–30% lower than those of FFP and stable during storage for up to one year. The ability to store at ambient temperature eliminates errors that occur with cold chain storage and would allow availability in remote, rural and underdeveloped locations. The median time of reconstitution is 1.5 minutes with consequent reduced time to transfusion and early intervention. It is available either as a 50 ml or 200 ml pack size and infused through a standard blood administration set.

Indications for FFP/FDP use include the following:[69-71]

- replacement of coagulation factors during major haemorrhage, particularly trauma and obstetrics;
- DIC with bleeding;
- in patients who are actively bleeding and whose INR is > 1.5 (or POC equivalent);
- immediate reversal of warfarin-induced haemorrhage when PCC is not available (PCC is the first choice);
- thrombocytopenic purpura usually with plasmapheresis preferably using pathogen-inactivated FFP; and
- replacement of coagulation factors when specific factors are not available in the presence of active bleeding or in order to prevent bleeding, in the case of surgery or invasive procedures (uncommon).[72-74]

There is a very limited role for FFP in the management of (mild–moderate) coagulation abnormalities frequently seen in many non-bleeding critically ill patients before invasive procedures. FFP is not recommended for routine use in patients with cirrhosis/liver disease unless significant coagulopathy or haemorrhage is identified, as again current understanding indicates that isolated abnormalities of the PT or aPPT do not reflect a 'balanced haemostasis'. FFP should not be used simply as routine circulatory volume replacement.

16. Cryoprecipitate

		Consensus	Grade
16.1	Indications for cryoprecipitate include the following:		
16.1.1	• Hypofibrinogenaemia due to major haemorrhage and massive transfusion.	Yes	A
16.1.2	• During major haemorrhage, fibrinogen should be maintained > 1.5 g/L, except in active obstetric haemorrhage where fibrinogen should be maintained > 2 g/L.	Yes	A
16.1.3	• Bleeding associated with thrombolytic therapy.	Yes	C
16.1.4	• Disseminated intravascular coagulation with fibrinogen < 1.0 g/L.	Yes	B
16.1.5	• Advanced liver disease, to maintain fibrinogen level > 1.0 g/L.	Yes	B
16.1.6	• Combined liver and renal failure with bleeding.	No	C
16.2	The initial dose of cryoprecipitate should be 1 unit/10 kg (typically 15–20 ml/kg).	Yes	A

Cryoprecipitate is also a leucodepleted plasma product containing concentrated factor VIII, von Willebrand factor, fibrinogen, factor XIII and fibronectin, produced by further processing of FFP. Note that it is not appropriate for warfarin reversal, as it does not contain the vitamin K-dependent factors. It is stored at -25 °C; once thawed for administration, it can be kept at ambient temperature for 4 h, and should not be kept in the fridge again.[62]

In South Africa, cryoprecipitate is mainly in individual units of 15–20 ml, but may also be prepared as a pool of 10 units. Each single unit has approximately 400–450 mg of fibrinogen.

The adult dose is 1 unit/10 kg (100 IU/10 kg); transfuse using a standard blood-giving set with a 170- to 200-micron filter (standard blood administration set).

Indications for cryoprecipitate include the following:

- hypofibrinogenaemia due to major haemorrhage and massive transfusion. There is increased use of cryoprecipitate in major trauma, obstetric haemorrhage and cardiac surgical bleeding. During major haemorrhage, fibrinogen should be maintained > 1.5 g/L, except in active obstetric haemorrhage where fibrinogen should be maintained > 2 g/L;
- bleeding associated with thrombolytic therapy;
- disseminated intravascular coagulation with fibrinogen < 1.0 g/L;
- advanced liver disease, to maintain fibrinogen level >1.0 g/L; and
- combined liver and renal failure with bleeding (no consensus amongst the SASA guideline working group).

17. Platelets

		Consensus	Grade
17.1	Indications for platelets include the following:		
17.1.1	• Prevention and treatment of bleeding due to thrombocytopenia or platelet function defects.	Yes	B
17.1.2	• If patient is actively bleeding, transfuse to a platelet count > 50 x 10^9/L (> 75 x 10^9/L for neurosurgical and ophthalmic bleeding).	Yes	B
17.2	If not bleeding, the following triggers should be applied:		
17.2.1	• Routine prophylactic use: 10 x 10^9/L.	Yes	B
17.2.2	• Prophylactic use with additional risk factors (e.g. sepsis): 10–20 x 10^9/L.	Yes	C
17.2.3	• Other major surgery or invasive procedures: 50 x 10^9/L.	Yes	C
17.2.4	• Neuraxial blockade: 50 x 10^9/L.	Yes	B
17.2.5	• Prophylactic use in closed compartment surgery (eye, brain): 100 x 10^9/L.	Yes	B

Platelets are either made from pooled buffy coat-derived platelets from 4–6 whole blood donations, suspended in platelet additive solution and the plasma of one of the four donors (who is male), or as an adult therapeutic dose obtained from a single donor by apheresis donation. Both can be used interchangeably, except for haematology, transplant or chronically transfused patients, where limited exposure to human leukocyte antigen (HLA) antigens is required to avoid problems during transplant or to prevent HLA sensitisation and platelet-refractoriness.

There is increased use of platelets in the last few years. The greatest demand is for haemoncology patients; platelets should not be administered to patients with chemotherapy-induced thrombocytopenia in the absence of bleeding, unless their platelet count is < 10 x 10^9/L.

The risk of transmission of bacterial infection (1 in 12 000) is higher than other blood components because platelets are stored at 22 °C. This risk is reduced by bacterial screening before release.

Platelets do not have to be the same group as the patient, but where group O platelets are given to a non-group O child they should be selected to be HT negative. D-negative children and women of childbearing potential should receive D-negative platelets because of the small risk of developing immune anti-D.

Platelet concentrate should be stored at 22 °C with constant gentle agitation in an approved incubator. Platelets must not be placed in a refrigerator. Transfusion should ideally be commenced within 30 min of removal from the platelet storage incubator. Each pack contains 250–350 ml; platelet count in the pack is > 2.4 x 10^{10}/L per adult dose, and transfusion should lead to an increase in the patient's platelet count by approximately 30 x 10^9/L. The patient's platelet count should be repeated after transfusion.

A standard adult therapeutic dose should be infused over a period of 30 min through a standard blood administration set or platelet administration set incorporating a 170- to 200-micron filter (standard blood administration set). Do not give through a set that has already been used for red cells. No drugs should be added directly to the unit of platelets.

Indications for platelets include the following:

- prevention and treatment of bleeding due to thrombocytopenia or platelet function defects; and/or
- if patient is actively bleeding, transfuse to a platelet count > 50 x 10^9/L or until bleeding stops (higher targets (e.g. 75–100 x 10^9/L) may be required in patients with neurosurgical or eye bleeds).

If not bleeding, the following triggers should be applied:

- routine prophylactic use: 10 x 10^9/L;
- prophylactic use with additional risk factors (e.g. sepsis): 10–20 x 10^9/L;
- other major surgery or invasive procedures: 50 x 10^9/L;
- neuraxial blockade: 50 x 10^9/L, and
- prophylactic use in closed compartment surgery (eye, brain): 100 x 10^9/L.

In South Africa, the availability of platelets is centralised at blood banks, and thus access will depend on the demand and distance from nearest blood bank. Clinicians need to be aware of local laboratory arrangements and normal time interval for obtaining platelets from central storage.

Drugs and novel therapies

		Consensus	Grade
18.1	TXA should be administered empirically in critically ill patients with severe trauma within 3 hours of the injury.	Yes	A
18.2	The dose of TXA in severe trauma is 1 g stat and then 1 g over 8 hours.	Yes	A
18.3	TXA should be administered empirically in bleeding obstetric patients.	Yes	B
18.4	The dose of TXA in bleeding obstetric patients is 1 g stat, and 1 g after 30 min if bleeding persists or recurs within 24 hours.	Yes	B
18.5	Empiric use of TXA is not recommended in patients with upper gastrointestinal bleeding.	Yes	B
18.6	TXA is recommended for patients with TBI and GCS 8–13 presenting within 3 hours of injury.	Yes	B
18.7	Where available POC viscoelastic testing should be used to guide therapy with TXA.	Yes	C
18.8	With the use of warfarin: INR to be kept between 2.0 and 2.5 according to indication. Perioperative use: stop 3–5 days before surgery; INR reduction to < 1.5, if bridging therapy. Bridging necessary only in patients with a very high thrombotic risk.	Yes	B
18.9	Direct acting anticoagulants – stop 48 hours before surgery. If renal impairment then stop earlier: If creatinine clearance > 80 ml/min/1.73m^2 > 48 hr. If creatinine clearance 50–79 ml/min/1.73m^2 > 72 hr. If creatinine clearance < 50 ml/min/1,73m^2 > 96 hr.	Yes	B
18.10	Antiplatelet therapy: Aspirin – don't stop, unless operating on a non-compressible site. Ticagrelor – stop 3 days before surgery. Clopidogrel – stop 5 days before surgery. Prasugrel – stop 7 days before surgery. If need to continue due to high risk of thrombosis, consider options such as GP IIb/IIIa.	Yes	B
18.11	GP IIb/IIIa antagonists – stop at least 4 hours before surgery. (Stop Abciximab earlier as a longer time is required for recovery of platelet function 24–48 hours).	Yes	B
18.12	LMWH – stop at least12 hours before surgery if used prophylactically, and 24 hours before surgery if used in therapeutic doses. The anticoagulation effect can partially be reversed by protamine sulphate, but not completely. Consider bridging with LMWH/UFH only in patients with a high risk for thrombosis who are on oral anticoagulants. Enoxaparin – stop at least 12 hours before surgery. Fondaparinux – stop 24 hours before surgery. Stop for longer duration in patients with impaired renal function.	Yes	B

An increasing number of patients take either anticoagulants or antiplatelet agents. All patients require careful preoperative medication optimisation before surgery. The management of drugs related to antithrombotic therapy in the perioperative setting is a common problem, balancing bleeding risk with thrombosis.

Patients at high risk (> 10% risk of thrombotic events per year) of thrombosis should be considered for bridging anticoagulation, or in the following circumstances:

- venous thromboembolic event within the last 3 months, or
- prosthetic (mechanical) heart valve.

Bridging anticoagulation usually consists of LMWH. The dose and type of the LMWH depends on the patient's weight, timing of surgery, type of procedure and thrombotic risks.

Warfarin (Vitamin K antagonist)

The INR is used to monitor the effectiveness of warfarin. In most situations, INR is maintained between 2.0 and 3.0. The perioperative management of warfarin is summarised in Figure 2.[7] In patients with atrial fibrillation on warfarin, routine use of bridging anticoagulation with LMWH before surgery is not recommended.

For emergency reversal of warfarin, prothrombin complex concentrate (PCC) 50 IU/kg is recommended. IV vitamin K (10 mg) may also be given, but this may preclude re-warfarinisation for a number of days. FFP (or FDP) is an alternative if PCC is not available,[61] but should not be used as elective prophylaxis in patients taking warfarin.

Novel oral anticoagulants

Novel OACs have more predictable pharmacodynamics and a faster onset of action with a shorter half-life than warfarin. There are currently three drugs on the market (a fourth drug, Edoxaban, is not available in South Africa); these are increasingly used for management of patients with atrial fibrillation; after stroke and transient ischaemic attacks; and prophylaxis/management of venous thromboembolism.[67]

Their half-life varies, especially in the presence of renal impairment. Currently, there are no specific routine coagulation tests to determine their effectiveness.

Regarding **antidotes**, the United States Food and Drug Administration and the European Commission have recently approved the first of these, **idarucizumab (Praxbind**, Boehringer Ingelheim International, Ingelheim am Rhein, Germany), for the emergency reversal of dabigatran; other antidotes are currently undergoing clinical trials. **Andexanet** the antidote for reversal of Anti Xa inhibitors is not yet approved for use by the EMA (European Medicines Agency).

Dabigatran is a direct thrombin inhibitor. Half-life (14–17 hours) depends on extent of renal impairment (normally cessation duration 48–96 h). For major elective surgery, neuraxial blockade and in patients with renal dysfunction, the drug should be stopped 5 days before surgery. For others, it can be stopped 3 days before surgery.

Rivaroxaban and apixaban (Edoxaban) are direct factor Xa inhibitors. Half-life is 5–13 h and is less dependent on renal function. For major elective surgery, neuraxial blockade and in patients with renal dysfunction, the drug should be stopped 48 hours before surgery.

If surgery is urgent, consider PCC 50 IU/kg, correct other abnormal coagulation tests and check platelets. Bridging anticoagulation is not required except in patients with recent (< 3 months) history of pulmonary embolism or deep venous thrombosis. Bridging is required if there has been an acute thrombotic events < 4 weeks.[7]

Antiplatelet drugs

These drugs cause irreversible inhibition of platelets; replenishment of platelets occurs at a rate of 10–15% per day. The restoration of normal platelet function depends on the individual drug and dosage.

Aspirin inhibits the production of thromboxane. It should be continued for most procedures until the day before surgery. In patients at low risk of cardiovascular events having major surgery and those undergoing high-risk procedures such as intracranial surgery, aspirin should be discontinued 5 days before the procedure. Restart if discontinued, when bleeding risk subsided or within 48 hours.

Clopidogrel (1st generation) (stop ≥ 5 days before surgery) is an oral, thienopyridine-class antiplatelet agent, and the active metabolites circulate for up to 18 h after the last dose. Clopidogrel should be stopped 7 days before surgery unless formal platelet function testing is used to check platelet function.[7]

The drugs **prasugrel** (2nd generation) (stop 7 days before surgery) and **ticlopidine** (no indication, exceptional cases only) are also thienopyridine-class antiplatelet drugs similar to clopidogrel, and have the same recommendations as clopidogrel.

Ticagrelor is another drug in the same class (2nd generation) that should be stopped 3 days before surgery.

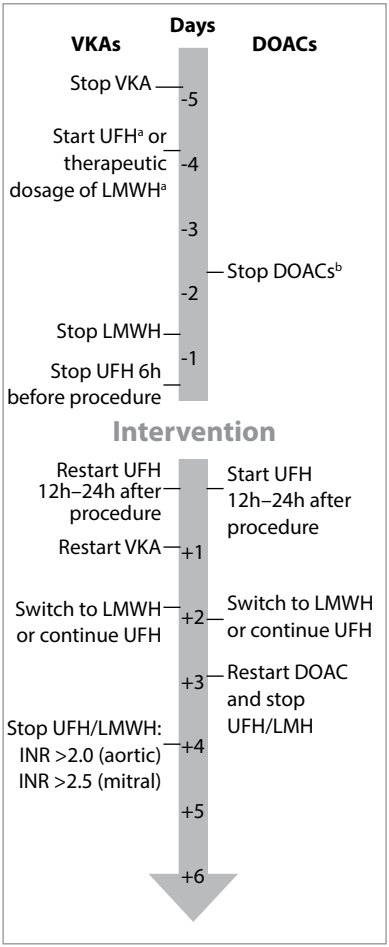


Figure 2: Management of oral anticoagulation in patients with an indication for pre- and/or postoperative bridging. a. Bridging with UFH/LMWH should start when INR values are below specific therapeutic ranges.
b. Discontinuation should be prolonged to > 72 h if creatinine clearance is 50–79 ml/min/1.73m^2 or ≥ 96 h if creatinine clearance is < 50 ml/min/1.73m^2.[7]

DOACs – direct oral anticoagulants,
INR – international normalised ratio,
LMWH – low-molecular-weight heparin,
UFH – unfractionated heparin,
VKAs – vitamin K antagonists

Antiplatelet drugs and non-cardiac surgery in patients with coronary stents, mostly DAPT

The management of these drugs in patients with coronary stents in situ depends on the type of stent, time after the coronary event and surgery type (major vs minor). Communication with the cardiology team is important. Elective surgery should be postponed for at least 4–6 weeks after bare metal stent implantation and 6 months after drug-eluting stent implantation. Aspirin may be continued during the perioperative period except in closed space surgery such as intracranial and spinal surgery.

For emergency surgery, management depends on the antiplatelet agent and when the last dose was taken. Platelet transfusion should be reserved as an additional measure for critical bleeding. If deemed appropriate, platelet function analysis can be used, but currently there is no evidence for its routine use.

Cangrelor is an IV, ultra-short half-life, P2Y12 inhibitor (currently not available in South Africa).

Drugs that decrease blood loss

TXA is a synthetic derivative of the amino acid lysine that inhibits plasminogen activation, thus preventing impairment of fibrinolysis. In the last few years, there is increased evidence that its use may reduce bleeding in trauma, cardiac surgery and other major surgery. Seizures have been reported when high doses are given, but there is little evidence of other side-effects.[75] The dose is variable, but a 1 g bolus is recommended in most instances for the majority of adults, with possibly an additional infusion of 500 mg.h^{-1} also considered.[76] A repeat dose has also been used clinically.

Aprotinin is a serine protease inhibitor antifibrinolytic that acts by inactivating free plasmin. The drug was withdrawn from the market in 2007 due to safety issues (BART researchers). Recently, regulators have licensed the drug only for myocardial revascularisation (coronary artery bypass surgery).[77]

Administration

		Consensus	Grade
19.1	The use of blood and blood products be directed by established protocols.	Yes	B
19.2	The use of blood and blood products be subjected to gatekeeping controls.	Yes	C

Administering the wrong blood type in error (with the risk of ABO incompatibility) is the most serious outcome of blood transfusion. Most of these incidents are due to the failure of the final identity checks carried out between the patient (at the patient's side) and the blood to be transfused. All members of staff involved in the administration of a blood component must be trained and competency-assessed as per local policy. Local policy will also stipulate if this is a one- or two-person bedside check, with each person performing the check independently.[78] RCC transfusions should start within 60 minutes of removal from a controlled temperature container. Thereafter, one can infuse RCCs at 1 to 2 ml/minute (60–120 ml/hour) for first 15 minutes and then as rapidly as tolerated thereafter. The total infusion time should not exceed four hours.

All prescriptions for transfusion must be documented in the patient record, either on the anaesthetic chart or on the drug/fluid prescription chart. Local policy for confirmation of the transfusion must be followed as it is a legal requirement that 100% of blood components must be traceable.[79] Where blood transfusion is anticipated, this should be discussed with the patient before surgery and valid consent to receive transfusion should be documented.[80] Patients should be informed that they have received blood or blood components before discharge from hospital, as they will otherwise be unaware; they should also be informed that this removes them from the donor pool for a period of six months. It is also important that the patient's general practitioner/clinical team is informed if possible.

The following guidance is for a manual checking process at the bedside (the preferred system is an electronic transfusion management system, but is not currently widely available in South Africa):

- The patient must be positively identified. All patients receiving blood components should ideally be wearing an identification wristband (or hospital identifier) containing four core identifiers: first name, last name, date of birth and patient identification number.

- Immediately before the transfusion, check the component next to the patient, against the prescription.
- Check the four core identifiers on the compatibility label attached to the blood component with the identification attached to the patient. If there are any discrepancies, do not proceed and call the transfusion laboratory.
- Check that the compatibility label attached to the blood component has the same blood group and numerical component donation number (or batch number for coagulation factors) as the sticker on the blood component.
- Visually check the blood component for any leakage, discolouration or presence of any clots or clumps.
- Check the expiry date and time.

Transfusing an unidentified patient

All hospitals should have a clear local policy for transfusion of patients whose identity is unknown. In emergency situations or where the patient cannot immediately be identified, the patient should still have identification attached stating unknown male or female and a unique identification number. The blood sample sent to the transfusion laboratory should contain these exact details. In the event that the patient's identity becomes known, new identification must be attached to the patient and a new transfusion sample collected and fully labelled with the known patient's details.

Monitoring for adverse events or reactions during transfusions

Clinical observations should include heart rate, blood pressure, temperature and respiratory rate, as per local guidelines (national guidelines define a minimum of pre-transfusion, and close observation for the first 30 minutes after transfusion). In cases of major blood loss, ideally pulse, blood pressure, respiratory rate and urinary output should be monitored every 15 minutes throughout the transfusion. In less severe cases the recipient's vital signs should be checked every half hour after the initial 30-minute observation. Patients at risk for circulatory overload should be observed for 12–24 hours after transfusion.[73] If there are any signs of a transfusion reaction, such as tachycardia, rash, breathlessness, hypotension or fever, stop the transfusion and contact the laboratory immediately.[81] Management may include the administration of antihistamine or steroid drugs, or intramuscular/IV adrenaline if life-threatening.[82] Diagnosis of a transfusion reaction during ongoing haemorrhage may be difficult, but if concern arises, the documentation should be double-checked for administration errors and further analyses performed as per local protocols.

Transferring blood with a patient

Blood components should be transferred with patients at high risk of requiring transfusion en route or immediately on arrival. There should be effective communication between the blood transfusion laboratories involved, according to regional policy. Blood components must be transported in a storage box suitable to maintain their integrity, along with accompanying paperwork, and careful handover is required. When the patient arrives at their destination, the receiving transfusion laboratory should be immediately informed that blood was transported. The patient should be issued with a new identity wristband (or hospital identifier), a new sample taken for cross-match and more blood issued; until this is available, blood transferred with the patient may be administered if required.

Ethics

		Grade
20.1	Both blood donors and recipients must be protected through safe blood management practices.	N/A
20.2	Blood transfusion services must comply with the provisions of the standards of practice for blood transfusions in South Africa.	N/A
20.3	All blood and blood products require informed consent prior to transfusion.	N/A
20.4	If consent cannot be provided by the patient, consent may be provided by a person mandated in writing by the patient, a person authorised by any law or court order or any surrogate decision maker.	N/A
20.5	Advanced directives (or 'living wills'), while having no legal force, should be ethically honoured.	N/A
20.6	An adult may refuse blood and blood products solely on religious grounds if the patient is of sound mind and understands the risks and consequences of such refusal.	N/A
20.7	No parent or guardian my refuse blood or blood products of a minor solely on religious grounds if the blood or blood product would be life-preserving.	N/A
20.8	If a clinician is uncertain of any reason a patient would refuse blood and there is a clear indication for the use of blood or a blood product to preserve life, the best interests of the patient must prevail.	N/A
20.9	Blood and blood products should be triaged in a resource-limited environment.	N/A
20.10	Health authorities should ensure that blood services are progressively developed to ensure the needs of the patients are met.	N/A

Blood bank practices

South African legislation regarding blood and blood products

The statutory provisions regarding all aspects of blood and blood product procurement, provision and use are set out in the National Health Act (Chapter 8, sections 56 to 68)[83] and the Regulations to the National Health Act (Regulations Relating to Blood and Blood Products).[84] While the National Health Act deals with the use of blood, blood products, tissue and gametes in humans, the regulation specifically deals with blood and blood products. The regulations provide for the following:

i. licensing of a national blood service provider,
ii. operational oversight,
iii. appointment and duties of health officers,
iv. aims of the blood transfusion service,
v. donor recruitment,
vi. mandatory donor blood testing,
vii. management of requests and administration of blood and blood products, and
viii. record keeping, including untoward reactions.

South African has two registered blood service providers: (i) South African National Blood Service (SANBS) and (ii) Western Cape Blood Service (WCBS).

Standards of practice

Ethical and professional standards relating to the collection, processing and testing, prescription and use of blood and blood products are set out in the Standards of Practice for Blood Transfusions in South Africa.[85] Apart from setting the requirements for establishing a blood management system, blood collection, processing and testing, the document sets donor selection criteria with the aim of protecting both donors and recipients. Notification of abnormal test results is an ethical standard requirement of blood donor management.

Patient-related practices

Consent

Informed consent is required prior to the transfusion of any blood or blood product. The patient must receive information relating to the range of therapeutic options available, the benefits, risks, costs and consequences of each option. The patient must also be of appropriate legal and mental capacity to make such decisions.[83]

Refusal of treatment

Patients may also be informed of their right to refuse blood and blood products.

They need to be informed of implications, risks and obligations of such refusal.

(a) Adult patients (> 18 years old) of sound mind and comprehending the implications of refusal of blood and blood products have the right to exercise their constitutional right to protect one's self and refusal of medical treatment. This refusal must be honoured even if this may result in fatality.[83]

(b) Children aged 12–18 years

Children between these ages have the right to independently make informed consent decisions as stipulated in the Children's Act. These children must be of sound mind and of sufficient maturity to understand the information presented to them.[86]

(c) Children < 12 years

Children who are aged < 12 years require a parent or guardian to consent to the provision of blood or blood products.[86]

Refusal of treatment based on religious grounds

No parent or guardian may refuse to provide consent to the transfusion of blood or blood products to a minor where the provision of such treatment would be considered life-preserving.[87] The legal burden rests with the parent or guardian to provide proof for an alternative treatment.

Advanced directives

Advanced directives in the form of a 'living will' or enduring power of attorney have no legal force in South Africa. If the authenticity of the advanced directive can be verified and it can be established that the instructions of the advanced directive are the current wishes of the patient, then the directive should be respected, failing which, the best interests of the patient should apply.

Limited resource/General ethical framework – utilitarian

Blood and blood products remain a scarce resource and should be managed accordingly. Fair and equitable distribution of these recourses must be justifiable. A utilitarian approach to blood and blood products prescriptions should be practiced.[88]

Implementation, monitoring and review of guidelines

Implementation of the guidelines may take place at:

- the level of the individual practitioner,
- hospital operating theatre complex/anaesthesiology department,
- institutional level, and/or
- regional level (district/provincial/national).

For maximum impact it is recommended that these guidelines be incorporated into comprehensive institutional or regional blood management guidelines and that they are implemented under the auspices of a dedicated institutional or regional blood management committee. The committee operationalises and reviews adherence to, and efficacy of, the guidelines.

It is recommended that frequent monitoring of adherence to the guidelines is conducted and that their effect on blood product utilisation is assessed. It is intended that these guidelines should be reviewed every 5 years. In the event of practice-changing research emerging prior to the 5-year review, a focused update should be provided.

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