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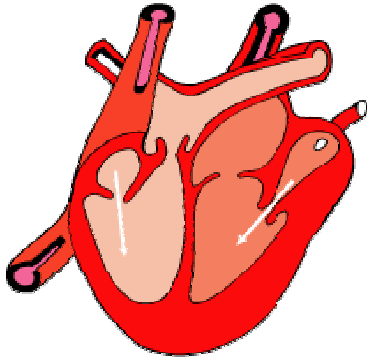
When is Transfusion Indicated?



Janet Birchall NHS Blood &Transplant and
North Bristol NHS Trust

RTC Preparation for surgery & perioperative blood use

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Aims of talk

- Concept of Patient Blood Management
- What do red cells, FFP and platelets do
- Evidence that blood transfusion is beneficial
- Recommended indications for use
  - National guidelines
  - Protocols for specific situations

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Patient Blood Management

- Aim to achieve better patient outcome by relying on patients own blood rather than donor blood
- Goes beyond appropriate use as pre-empts and ↓ need for donor blood by addressing modifiable risk factors
  - Maximise patients red cell mass
  - Minimise bleeding
  - Optimise patients physiological reserve

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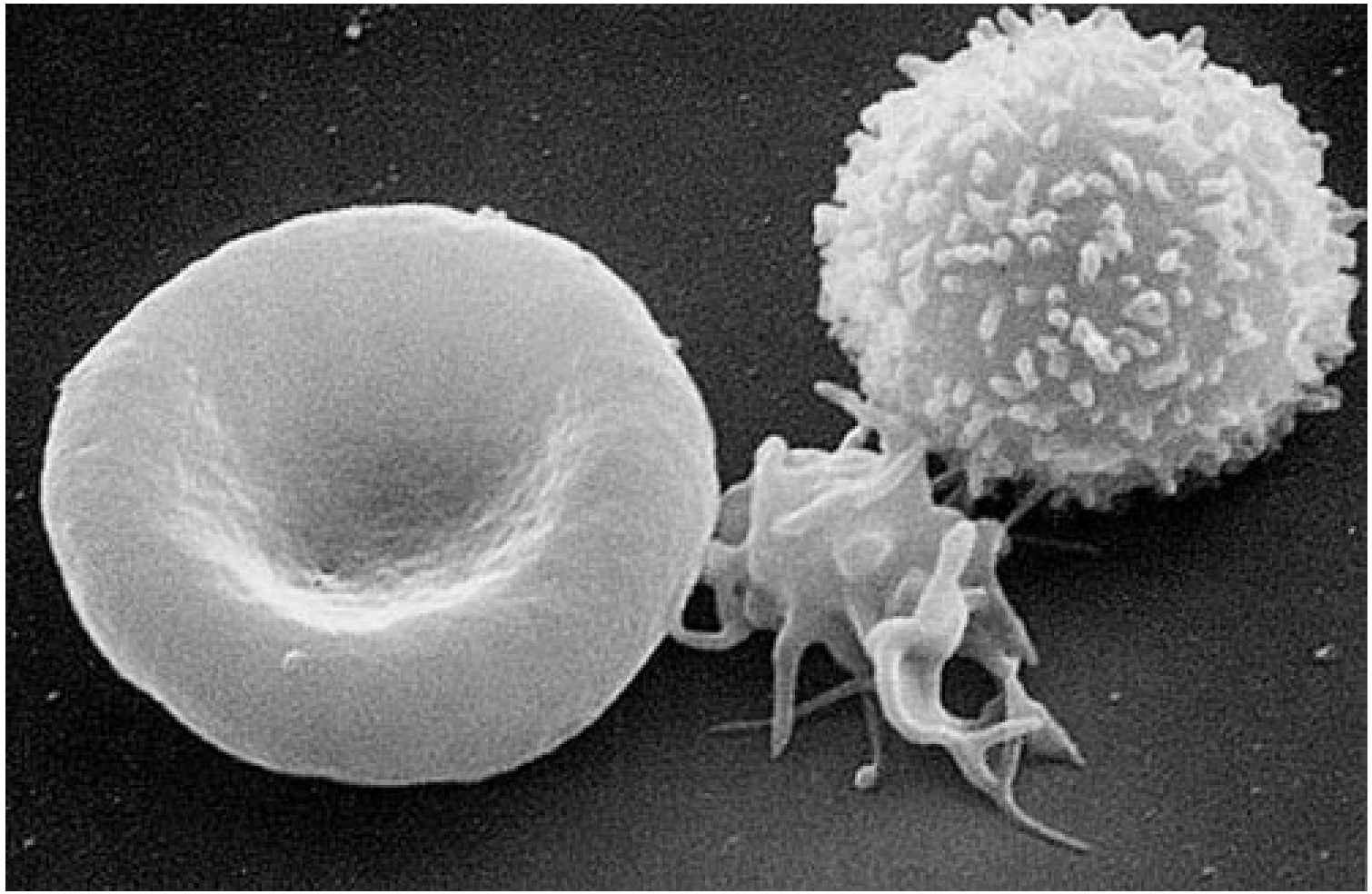

Electron Microscopy Facility at The National Cancer Institute at Frederick (NCI-Frederick)

RTC Preparation for surgery and perioperative blood use

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What do blood components do?

Red cells

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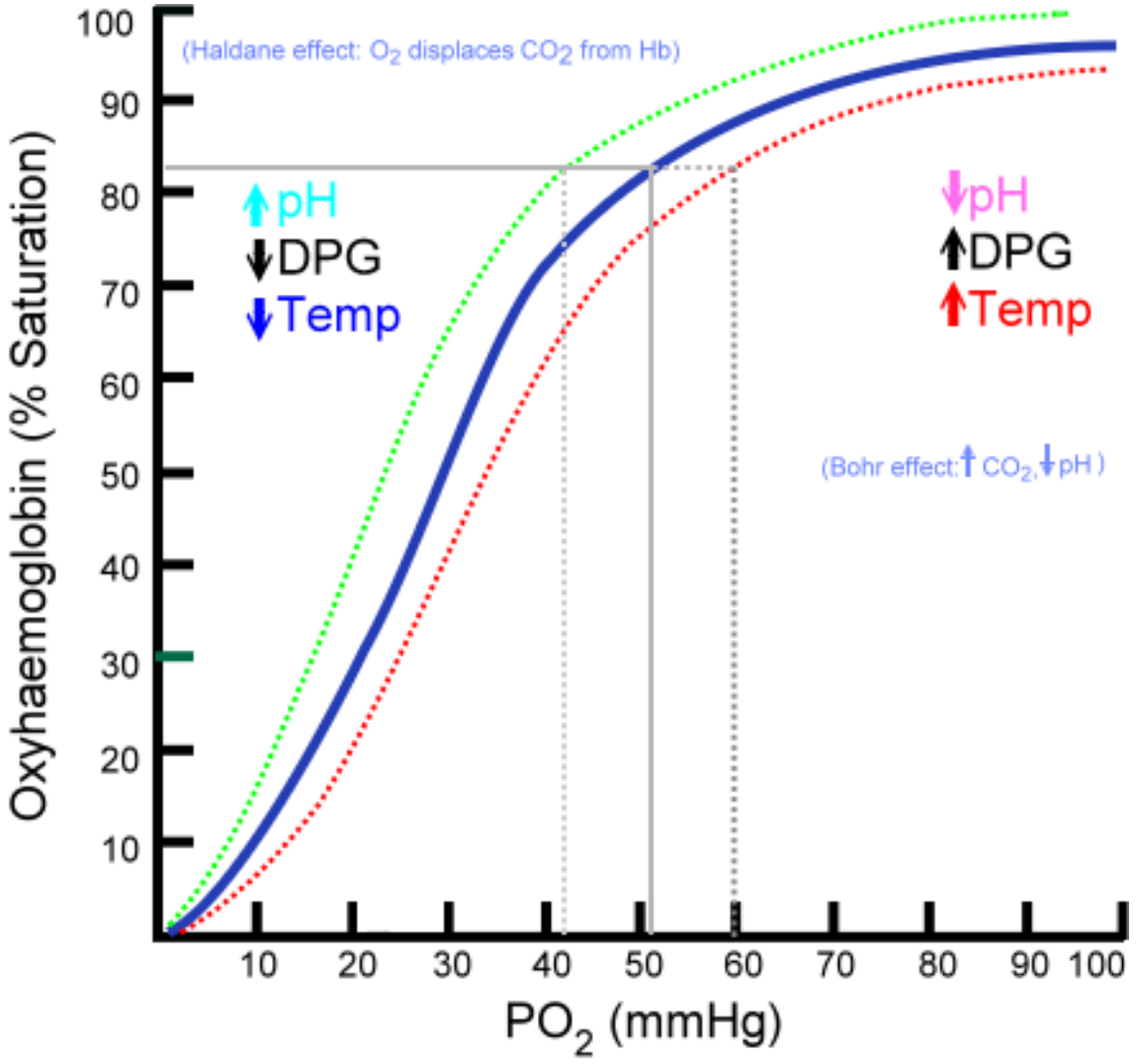
Role of RBC

- O_2 delivery lungs to tissues, return CO_2

- **Dependant on -**
  - transfer lungs -> blood
  - storage on Hb & transport in circulation
  - release from blood to tissues
- **Physiological response -**
  - Increased cardiac output
  - Reduced blood viscosity
  - Peripheral vasodilatation
  - Chronic anaemia - increased 2,3 DPG

Oxygen dissociation curve

Original uploader was Ratznium at en.wikipedia



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When is RBC transfusion necessary?

- no reliable measure of O2 delivery to critical organs
  - lactic acidosis indicates inadequate O2 delivery
  - low central venous O2 saturation
  - Haemoglobin
- Identify benefit expected against risk
  - Cause acute - likely further blood loss?
  - State of patient
    - symptoms - SOB, lethargy, palpitations, headaches, cardiac failure, angina & confusion in elderly
    - observations - pulse, BP, RR, ECG
    - Co-morbidity ↓ ability to compensate - age, CVD, infection
- No consensus on indications for red cell transfusion
  - poor evidence base

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Mortality and morbidity in patients with very low postoperative Hb levels

Hb level (g/dl)	% mortality	% mortality/morbidity
1.1 - 2.0	100%	100%
2.1 - 3.0	54.2%	91.7%
3.1 - 4.0	25%	52.6%
4.1 - 5.0	34.4%	57.7%
5.1 - 6.0	9.3%	28.6%
6.1 - 7.0	8.9%	22%
7.1 - 8.0	0%	9.4%

Odds of death in patients with post-op Hb <8 g/dl increased 2.5 fold for each gram decrease in Hb. (Transfusion 2002, 42, 812-818)

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Transfusion triggers in critically ill patients

Hebert PC, Wells G, Blajchman MA, et al. N Eng J Med. 1999;340:409-417

- Randomised to either
  - restrictive transfusion arm - maintain Hb 7-9 g/dl
  - liberal transfusion arm - maintain Hb 10-12g/dl
- Results
  - trend towards decreased 30-day mortality in restrictive arm
  - significant decrease in mortality in patients who were less acutely ill in restrictive arm
- Conclusion - restrictive arm at least equivalent and possibly superior to liberal policy

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Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery Carson JL, NEJM 2011;365:2453-62

- Randomised prospective, 2016 patients > 50 with CVD or risk factors. Liberal Tx (< 10g/dl) v Restrictive Tx (< 8g/dl). No difference in 1°outcome of death or inability to walk 10 feet unaided at 60 days

Increased Mortality, Morbidity & Cost after Transfusion of Red Cells in Cardiac Surgery Patients G.J. Murphy, Circulation.2007;116:2544-2552

- Retrospective, 8,500 patients, Infection - OR 3.38, ischaemia - OR 3.35 for Txed and Mortality – Adjusted hazard ratio 30 days 6.69

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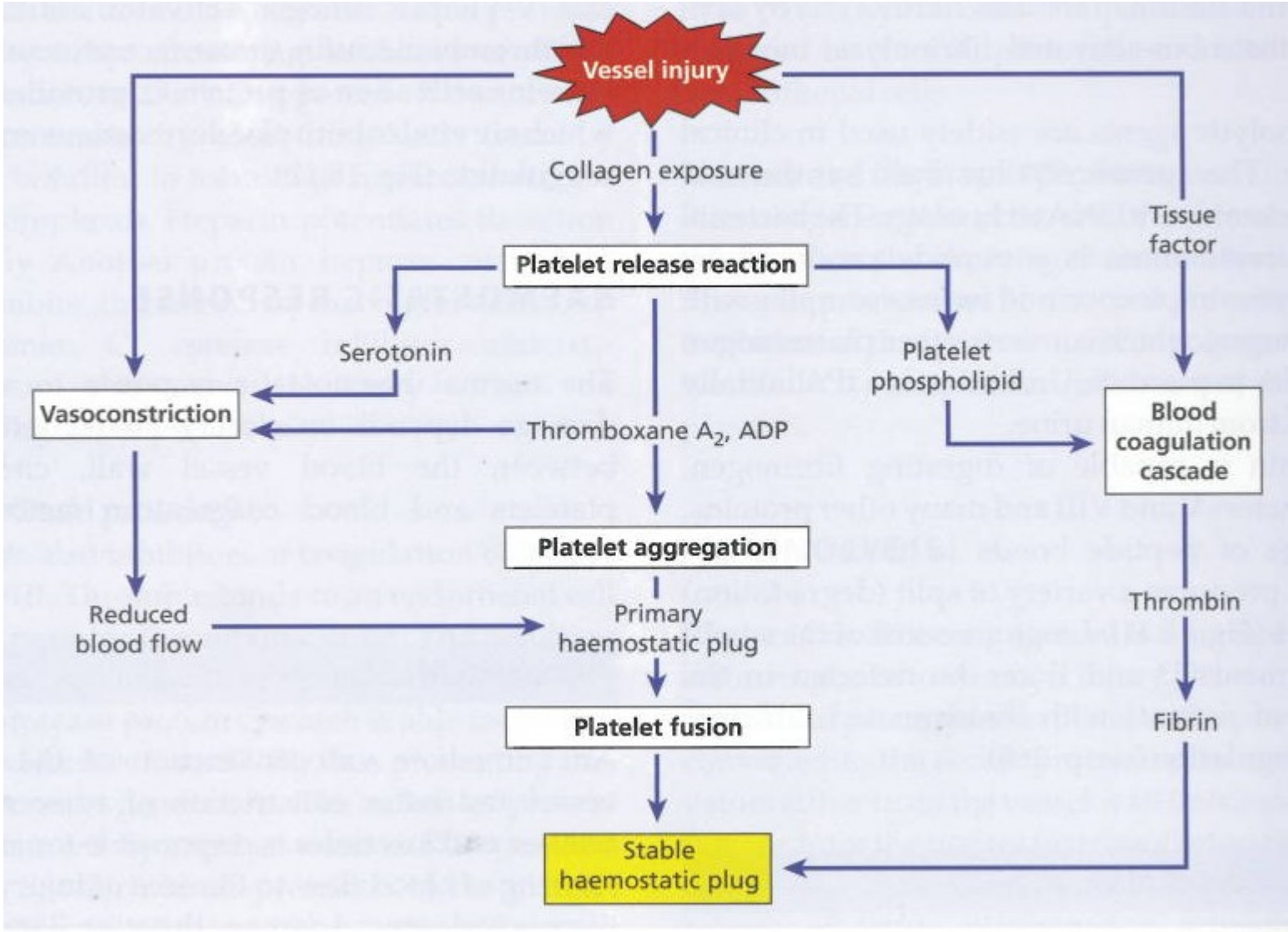
What do blood components do?

Platelets

Plasma

Overview of bleeding control

Essential Haematology AV Hoffbrand, JE Petit and PAH Moss, Fourth Edition



Platelet transfusion: principles, risks, alternatives and best practice

Indication	Transfusion Indicated/not indicated
Routine prophylactic use - Reversible bone marrow failure	 10
- Chronic bone marrow failure, peripheral destruction/consumption, abnormal platelet function	Not indicated
***Prophylactic use in the presence of risk factors for bleeding (e.g. sepsis, antibiotic treatment, abnormalities of haemostasis)** - Reversible/chronic bone marrow failure	 20
- Peripheral destruction/consumption, abnormal platelet function	Not indicated
Prophylactic use preprocedure except eyes or brain - Reversible/chronic bone marrow failure and platelet destruction/consumption if urgent/other therapy failed - Bone marrow aspirate or trephine - Epidural anaesthesia - ^All other procedures	 Not indicated 80 50
- Abnormal platelet function - Bone marrow aspirate and trephine - all other procedures in selected patients if alternative therapy failed/contraindicated	 Not indicated Not possible to state threshold
Prophylactic use preprocedure involving eyes or brain - Reversible/chronic bone marrow failure and platelet destruction/consumption if urgent/other therapy failed	 100
- Abnormal platelet function in selected patients if alternative therapy failed/contraindicated	Not possible to state threshold
Therapeutic use $Massive transfusion - all categories except abnormal platelet function where not possible to state threshold For patients with multiple trauma or CNS injury	 75 100

Summary of Quality Criteria For RTC's investigating use of FFP

Clinical area	No. of RCTs identified	No. of trials with method of randomization described	No. of trials with method of allocation concealment described	No. of trials with blinding described	Mean size per arm (no. of patients)*
FFP vs. No FFP					
Liver	1	1	0	0	10
Cardiovascular	5	1	0	2	18
DIC (neonates)	1	1	0	0	11
HUS	2	2	2	0	28
Neonatal medicine	7	5	0	0	35
Other clinical conditions	2	0	0	0	8
FFP vs. alternative colloid					
Cardiovascular	5	3	1	2	31
Neonatal medicine	5	2	1	1	78
Other clinical conditions	5	4	1	0	45
FFP vs. alternative/blood/plasma product					
Liver	4	3	0	2	19
Cardiovascular	3	1	0	0	28
Warfarin-treated	2	1	0	1	22
DIC/massive transfusion	2	1	0	1	20
TTP	5	3	0	0	23
Burns	3	2	0	0	69
Other groups	5	2	1	1	29

RCTs, randomized controlled trials; DIC, disseminated intravascular coagulation; HUS, haemolytic uraemic syndrome; TTP, thrombotic thrombocytopenic purpura.

*Numbers for cross-over studies counted as applying in both arms.

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Controversy in Trauma Resuscitation: Do Ratios of Plasma to RBCs Matter?

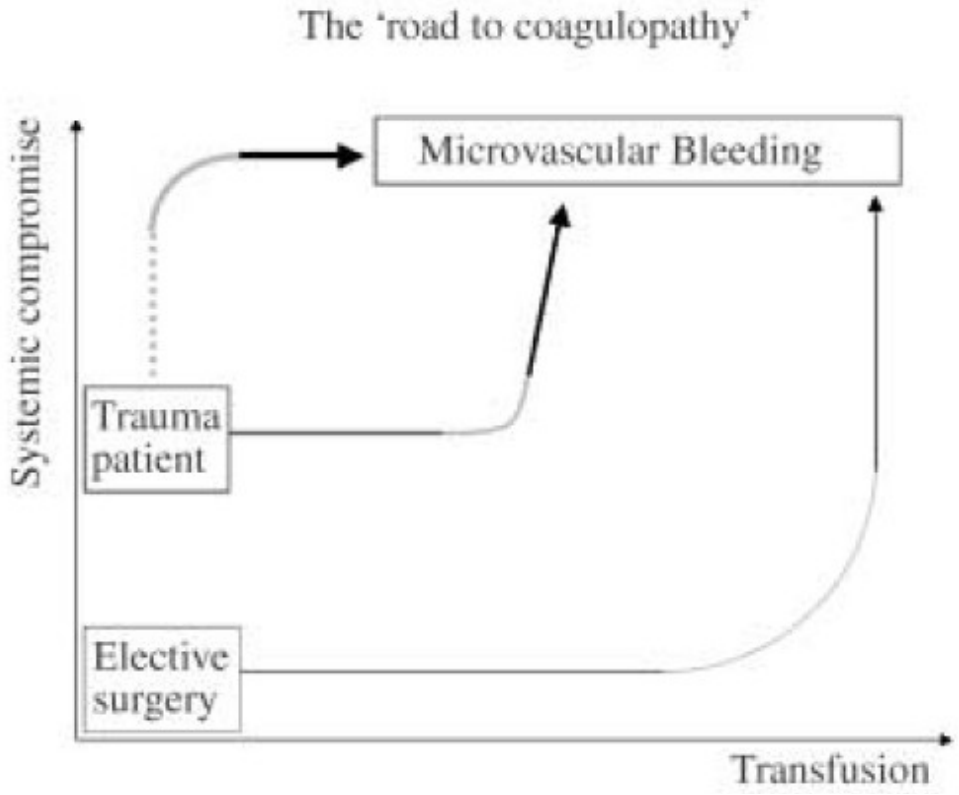
Stansbury LG et al. Transfusion Medicine reviews. 2009;23:255-265

One to One replacement saves lives

- Observational, voluntary, retrospective data
- Use of historic controls
- Majority healthy young males
- Survival bias - Snyder 2009 – trauma with 10 units rbc's in 24 hrs→ ↓ mortality with ↑ plasma:rbc ratio. Reanalysed data at set time points no difference in mortality. "takes time to be massively transfused and massively injured bleed to death quickly"

Coagulopathy of Massive Transfusion

JF Hardy, P de Moerloose & CM Samama. Vox Sanguinus. 2005;89:123-129



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National Blood Transfusion Committee Indication Codes for Transfusion 2011

"Indications for transfusion taken from UK national guidelines for use of blood components

Although clinical judgment plays essential part in decision to transfuse or not, purpose of drawing available guidelines together into one short document is to help clinicians decide when blood transfusion is appropriate and to facilitate documentation of the indication for transfusion."

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The Chief Medical Officer's
National Blood Transfusion Committee

Issued 11/11

Indication Codes for Transfusion – an Audit Tool

The indications for transfusion provided below are taken from UK national guidelines for the use of blood components (see references). Although it is accepted that clinical judgement plays an essential part in the decision to transfuse or not, the purpose of listing the liklihi transfusion guidelines together into one short document is to help clinicians decide when blood transfusion is appropriate and to facilitate documentation of the indication for transfusion. Each indication has been assigned a number which may be used by clinicians when requesting blood or for documentation purposes. Specific details regarding the patient's diagnosis and any relevant procedures to be undertaken should also be provided. These are current guidelines and may change depending on new evidence.

Red cell concentrates

R1. Acute blood loss [1,2,3,4]

In patients with haemorrhage, the haemoglobin concentration (Hb) is a poor indicator of acute blood loss and estimation of blood loss may be difficult. Empirical decisions about the immediate use of red cell transfusion are required by clinicians experienced in resuscitation. The following is a guide to the likelihood of the need for blood transfusion:

- <20% loss of blood volume (< 1000ml in an adult) transfusion rarely indicated. Red cell transfusion is unlikely to be necessary.
- 20–30% loss of blood volume (1000-2000ml in an adult) rapid volume replacement is required with crystalloid/colloid. Red cell transfusion will probably be required to maintain recommended Hb levels.
- >40% loss of blood volume (>2000ml in an adult) rapid volume replacement including red cell transfusion is required.

When normovolaemia has been achieved/maintained, frequent measurement of Hb (for example, by point of testing) can be used to guide the use of red cell transfusion. Maintain circulating blood volume and Hb >7 g/dl in otherwise fit patients, and >8g/dl in elderly patients and those with known cardiovascular disease.

Peri-operative transfusion [4,5]

Many patients undergoing elective surgical operations will not require transfusion support if their Hb is normal before surgery. Assuming normovolaemia has been maintained, the Hb can be used to guide the use of red cell transfusion.

R2. Hb <7g/dl.

R3. Hb <8g/dl in a patient with known cardiovascular disease, or those with significant risk factors for cardiovascular disease (e.g. elderly patients, and those with hypertension, diabetes mellitus, peripheral vascular disease).

Critical Care [6]

R4. Transfuse to maintain the Hb >7g/dl, and <8g/dl in elderly patients and those with known cardiovascular disease.

Post-chemotherapy

R5. There is no evidence base to guide practice. Most hospitals use a transfusion threshold of a Hb of 8 or 9g/dl.

Radiotherapy

R6. Limited evidence for maintaining Hb above 10-11g/dl in patients receiving radiotherapy for cervical and possibly other tumours.

Chronic anaemia [4]

R7. Transfuse to maintain the haemoglobin concentration to prevent symptoms of anaemia. Many patients with chronic anaemia may be asymptomatic with a Hb <8g/dl.

Fresh frozen plasma [4,6]

(Dose - 12 - 15ml/kg body weight equivalent to 4 units for an adult)

F1. Replacement of single coagulation factor deficiencies, where a specific or combined factor concentrate is unavailable e.g. factor V.

F2. Immediate reversal of warfarin effect, in the presence of life-threatening bleeding. Treatment in complex circumstances is the responsibility of a clinician. PCC only has a partial effect and is not the optimal treatment.

F3. Acute disseminated intravascular coagulation (DIC) in the presence of bleeding and abnormal coagulation results.

F4. Thrombotic thrombocytopenic purpura (TTP), usually in conjunction with plasma exchange.

F5. Massive transfusion. If emergency uncontrolled bleeding and massive haemorrhage is anticipated, early initiation of FFP (15ml/kg) is recommended to treat coagulopathy. Local protocols should be followed, and the later use of FFP should be guided by timely tests of coagulation including near patient testing. Where there is anticipated large volume blood loss associated with massive surgery, guidelines suggest the FFT and APTT ratio should be maintained at < 1.5. This is likely to occur after replacement of 1-1.5 x the patient's blood volume.

F6. Liver disease, there is no evidence of benefit from FFP in patients with a PT ratio of less than or equal to 1.5.

Cryoprecipitate [4,6]

(Dose - 2 pooled units, equivalent to 10 individual donor units, for an adult (contains approximately 2g of fibrinogen)
Cryoprecipitate should be used in combination with FFP unless there is an isolated deficiency of fibrinogen.

C1. Acute disseminated intravascular coagulation (DIC) where there is bleeding and a fibrinogen level <1g/l.

C2. Abdominal liver disease, to correct bleeding or to prophylaxis before surgery when the fibrinogen level is 1g/l.

C3. Bleeding associated with thrombolysis therapy causing hypofibrinogenaemia.

C4. Hypofibrinogenaemia secondary to massive transfusion.
Maintain fibrinogen above 1g/l. A level of 1.5g/l may be required.

C5. Renal failure or liver failure associated with abnormal bleeding where DDAVP is contraindicated or ineffective.

C6. Inherited hypofibrinogenaemia, where fibrinogen concentrate is not readily available.

Platelet concentrates [1,4,6,7]

(Dose - 15 ml/kg body weight for children <20kg; 1 adult therapeutic dose for adults and older children)

Bone marrow failure

P1. Treatment/prevention of bleeding in patients with reversible bone marrow failure where the platelet count is 10×10^9/l. Prophylactic platelet transfusions are not indicated in chronic stable thrombocytopenia.

P2. Treatment/prevention of bleeding where the platelet count is 20×10^9/l in the presence of additional risk factors for bleeding such as sepsis or haemostatic abnormalities.

P3. Treatment/prevention of bleeding associated with invasive procedures. The platelet count should be raised to $>80 \times 10^9$/l before lumbar puncture, insertion of jugular/subclavian line, transbronchial and liver biopsy, and laparotomy, to $>80 \times 10^9$/l before epidural anaesthesia and to $>100 \times 10^9$/l before surgery in critical sites such as the brain or the eyes.

Critical care/surgery

P4. Massive blood transfusion. Empirical use of platelets, according to a specific blood component ratio, is required for the patient with severe trauma. Aim to maintain platelet count $>75 \times 10^9$/l and $>100 \times 10^9$/l if multiple eye or CNS trauma.

P5. Acquired platelet dysfunction e.g. post-cardiopulmonary bypass, use of potent anti-platelet agents such as clopidogrel, with non-surgically correctable bleeding.

P6. Acute disseminated intravascular coagulation (DIC) in the presence of bleeding and severe thrombocytopenia.

P7. Inherited platelet dysfunction disorders e.g. Glanzmann's thrombasthenia with bleeding or as prophylaxis before surgery.

Immune thrombocytopenia

P8. Primary immune thrombocytopenia, as emergency treatment in advance of surgery or in the presence of major haemorrhage. Platelet count of >80 is recommended for major surgery and a count of > 70×10^9/l for obstetrics regional (mid) anaesthesia.

P9. Post-infection purpura, in the presence of major haemorrhage.

P10. Neonatal alloimmune thrombocytopenia, to treat bleeding or as prophylaxis to maintain the platelet count > 30×10^9/l.

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South West Regional Transfusion Committee Bookmark

- Based on NBTC indication codes

- Addition of some clinical indications taken from - A Manual for Blood Conservation (Dafydd Thomas, John Thompson, Biddy Ridler)

SW Regional Transfusion Committee

Guidance for the use of Blood Components

This guidance is based on the NBTC Indication Codes for Transfusion (2011).

Red Cell Concentrates

- **R1 Acute blood loss** Emergency uncontrolled. Hb unreliable, resuscitation by experienced clinician. When normovolaemic keep Hb >7g/dl.
- **R2 Peri-operative transfusion** in a controlled situation, with adequate volume replacement – transfuse if blood loss > 30%. This equates to a Hb of <7g/dl.
- **R3 Known cardiovascular disease (CVD)** or significant risk factors, suggest Hb <8g/dl instead of <7g/dl for indication above.
- **R4 Critical care –** maintain Hb >7g/dl (>8g/dl if CVD or risk factors).
- **R5 Post-chemotherapy** – suggest Hb threshold of 8 or 9g/dl.
- **R6 Radiotherapy** – suggest maintain Hb >10g/dl
- **R7 Chronic anaemia** – maintain Hb to prevent symptoms of anaemia. Hb >8g/dl appropriate for many patients.
- **Symptoms / signs of anaemia** for which red cells may be required include; increased angina, new ischaemia on ECG, syncope/postural hypotension or breathless and/or tachycardia for no other reason (Thomas et al. 2005).

Transfusion to above a Hb of 10g/dl is rarely required.

FFP (12-15ml/kg)

- **F1 Coagulation factor deficiency** where factor concentrate unavailable.
- **F2 Reversal of warfarin** if critical bleeding Prothrombin complex conc. treatment of choice.
- **F3 Disseminated intravascular coagulation (DIC)** if bleeding and abnormal coagulation.
- **F4 Thrombotic thrombocytopenic purpura.**
- **F5 Massive transfusion** if bleeding emergency uncontrolled, early infusion of FFP recommended otherwise to maintain PT/APTT ratio < 1.5.
- **F6 Liver disease** patients with a PT ratio < 1.5 are unlikely to benefit.

References:

National Blood Transfusion Committee National Indication Codes – An Audit Tool
http://www.transfusionguidelines.org/docs/pdfs/nbtc_bbt_indication_codes_2011_10.pdf

Thomas D et al, A Manual for Blood Conservation (2005), tfm publishing Ltd.

PTO

Platelet concentrate (1 unit = 1 adult therapeutic dose or ATD)

Bone marrow failure (BMF)

- **P1 If reversible BMF** and count <10 x10^9/l. Not indicated in chronic stable BMF.
- **P2 BMF with additional risk factors** for bleeding e.g. sepsis if count <20 x10^9/l.
- **P3 Invasive procedure** keep count >50 x10^9/l, >80 x10^9/l if epidural, >100 x10^9/l if CNS or eye surgery.

Critical care

- **P4 Massive transfusion** aim for count of >75 x10^9/l, >100 x10^9/l if multiple, CNS or eye trauma.
- **P5 Acquired platelet dysfunction** if non-surgically correctable bleeding.
- **P6 Acute DIC & bleeding** keep count >50 x10^9/l.
- **P7 Inherited platelet dysfunction** with bleeding or presurgery.

Immune thrombocytopenia

- **P8 1° immune thrombocytopenia** as emergency presurgery or with haemorrhage (aim for count >80 x10^9/l pre major surgery & >70 x10^9/l for obstetric regional axial anaesthesia).
- **P9 Post-transfusion purpura** if major haemorrhage.
- **P10 Neonatal alloimmune thrombocytopenia** maintain count >30 x10^9/l.

Cryoprecipitate (use with FFP unless isolated fibrinogen deficiency)

- **C1 DIC & bleeding** when fibrinogen <1g/l
- **C2 Liver disease** with bleeding or presurgery when fibrinogen <1g/l.
- **C3 Bleeding with thrombolytic therapy** causing hypofibrinogenaemia.
- **C4 2° to massive transfusion** maintain fibrinogen >1g/l, may require fibrinogen >1.5g/l
- **C5 Renal or liver failure** with abnormal bleeding when DDAVP not appropriate.
- **C6 Inherited hypofibrinogenaemia** when concentrate not available.

Further information on blood transfusion will be available on hospital intranet sites or from the blood transfusion laboratory.

February 2012 (For review February 2013)

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Protocol

Post operative assessment of anaemia

Is the patient bleeding?

↙ Stable and normovolaemic

↘ Unstable with haemorrhage

↓

Known/likely cardiovascular d?
Symptoms / signs of anaemia - SOB, angina/ST depression, tachycardia, postural hypotension

↙ No

Tx trigger 7-8
Maintain Hb 7-9

↘ Yes

Tx trigger 8-9
Maintain Hb 9-10

↓

Resuscitate

Hb unreliable

Tx to above 10g/dl is very rarely indicated

Managing anaemia in critically ill adults

Walsh TS et al. BMJ 2010: 341;547-551

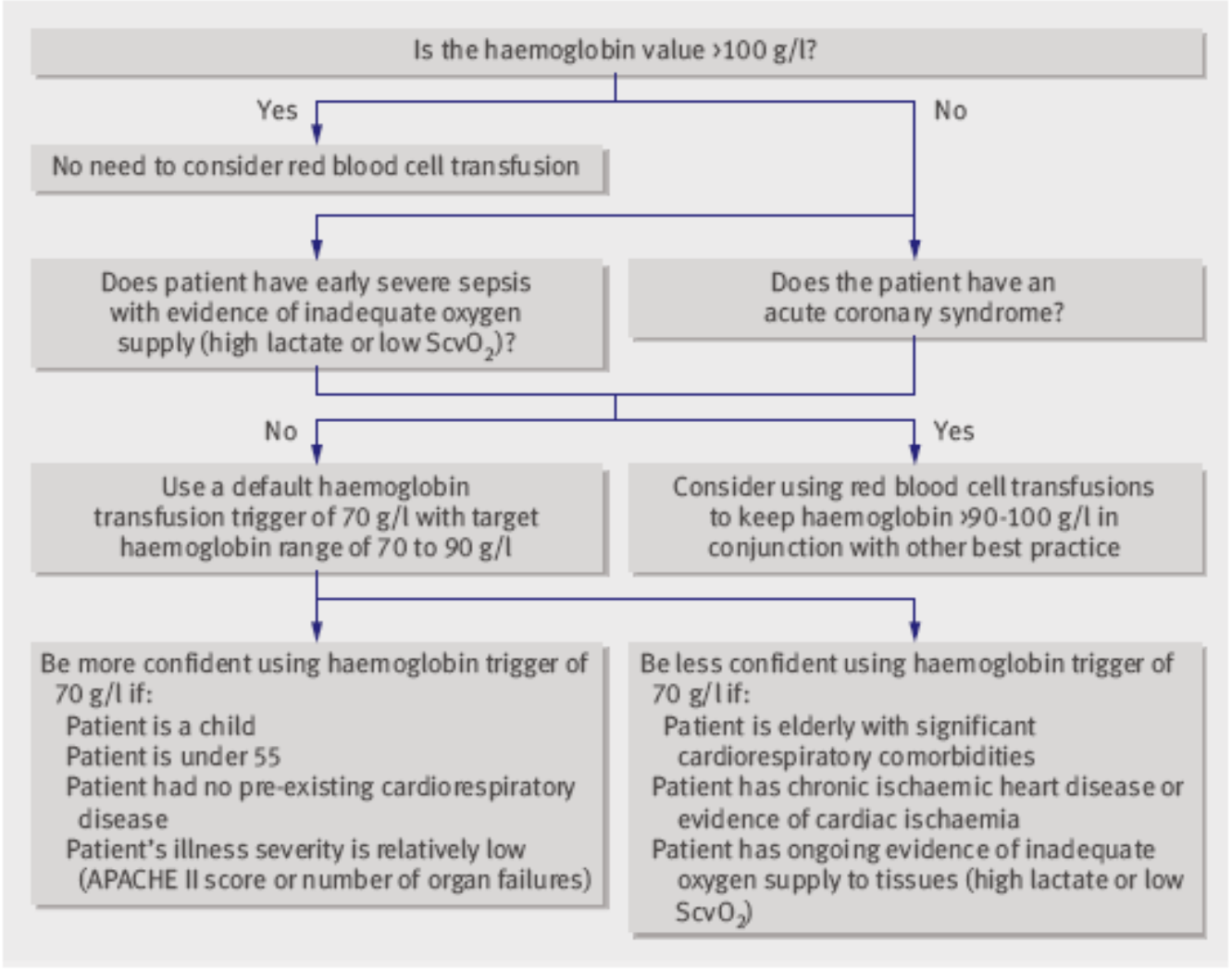
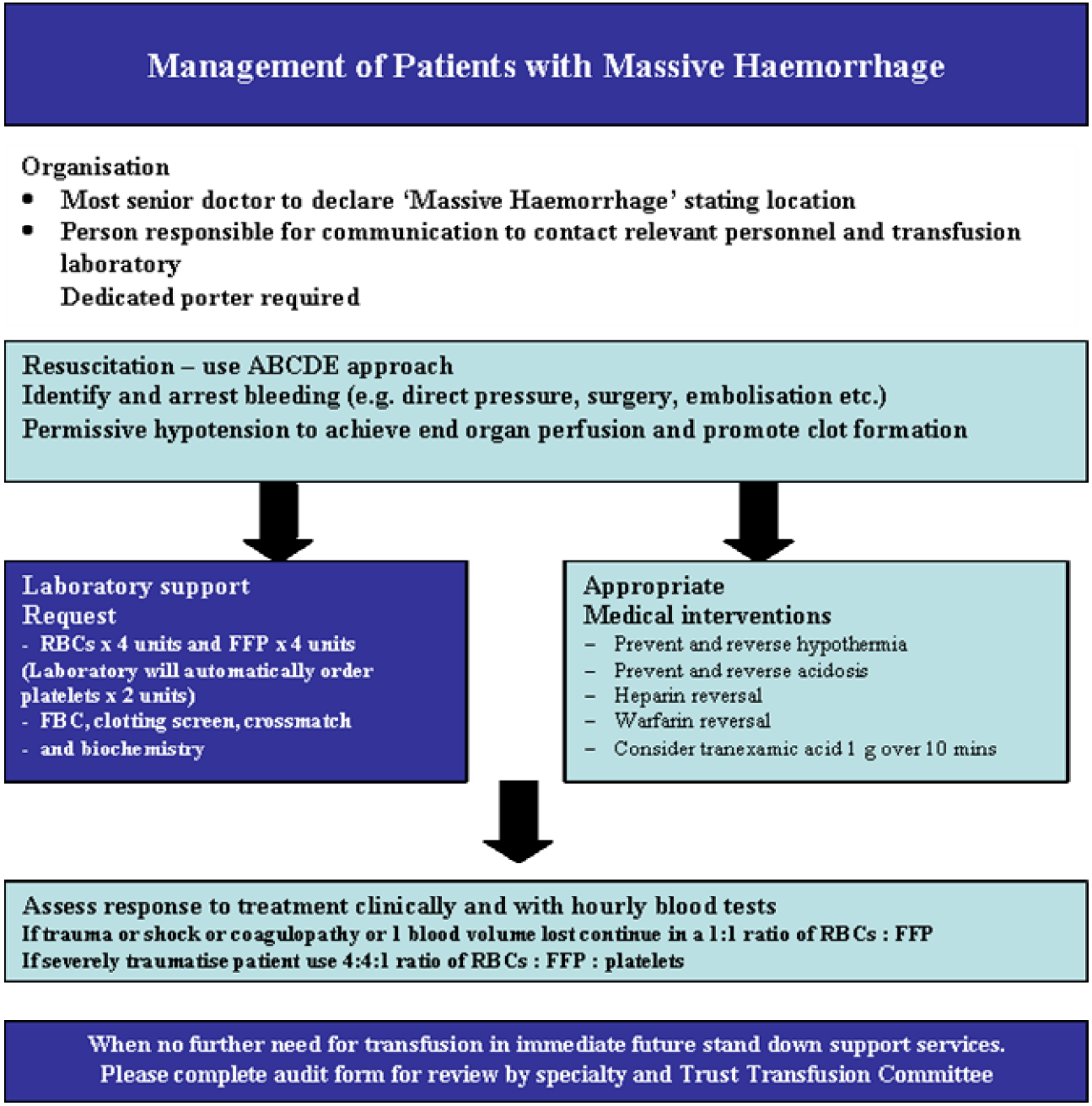
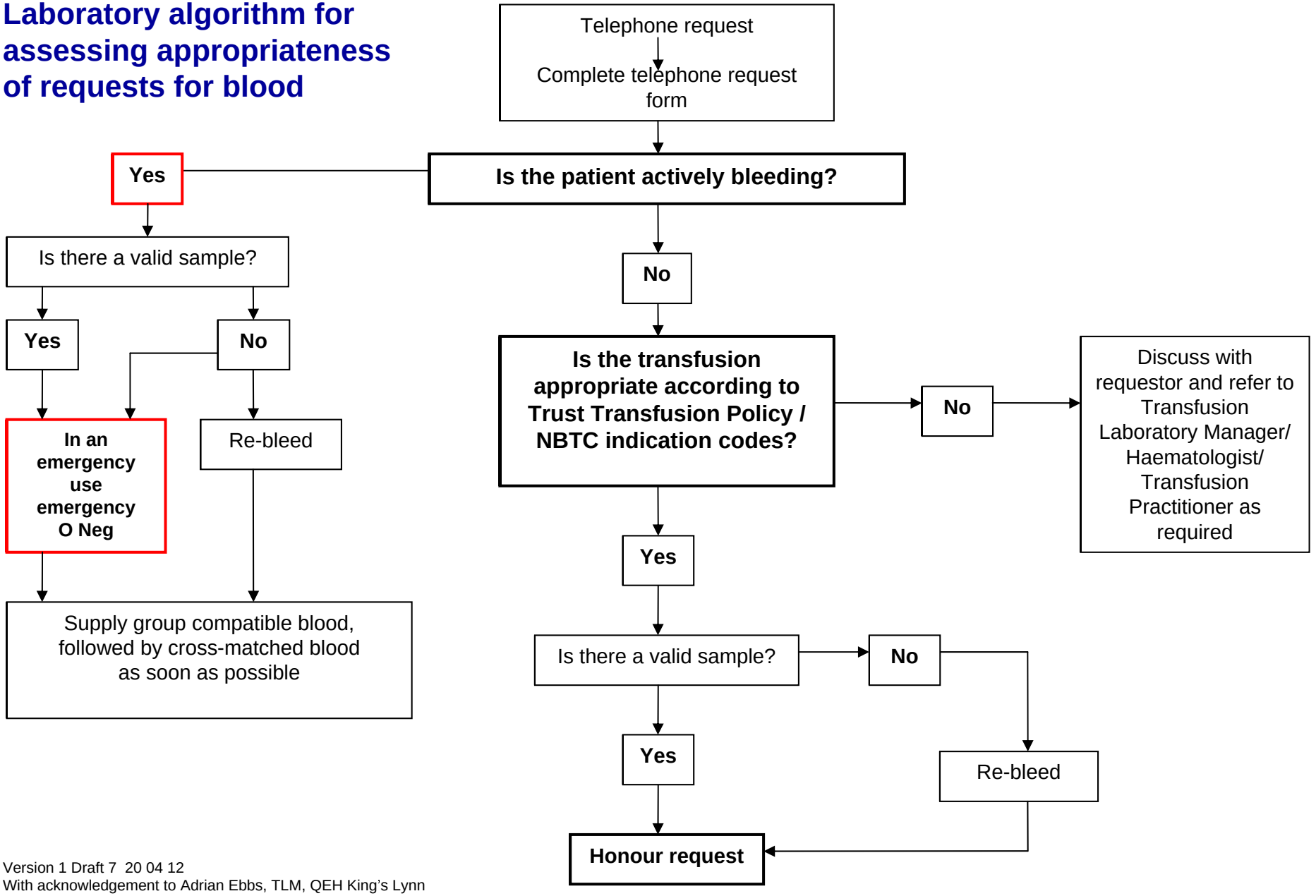


Fig 2 | Suggested approach to making transfusion decisions in critically ill patients with no evidence that haemorrhage is causing cardiovascular instability. $ScvO_2$=oxygen saturation of less than 70% in central venous blood

Massive Haemorrhage Guideline - example



Laboratory algorithm for assessing appropriateness of requests for blood



Version 1 Draft 7 20 04 12

With acknowledgement to Adrian Ebbs, TLM, QEH King's Lynn

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Summary

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- No reliable measure of O2 delivery to critical organs to determine need for red cells
- Poor evidence base for all blood components. Some studies indicate no benefit/harm.
- Guidelines aim to determine best practice
  - National Blood Tx Committee indication codes and bookmark provide summary
  - Guidelines available in clinical areas improve compliance