By J Pigou

Patient Blood Management Guidelines Module 3: Medical

1. In medical patients, is anaemia an independent risk factor for adverse outcomes?

Anaemia as defined by WHO Hb level of ≤130 g/L in males and ≤120 g/L in females.

	Independent risk factor for mortality	Independent risk factor for reduced quality of life	Other factors it is an independent risk factor for
ACS	Hb<150-160g/L risk factor. Hb<100g/L significantly increased risk.	-	Increase risk of MI and recurrent ischaemia.
Heart failure	Yes	Yes	
Elderly community dwelling population	Yes (not necessarily due to cardiac events)	Yes	
Cancer	Yes	Uncertain	
Chronic Kidney Disease	Yes – with all cause and with CVS mortality.	Yes (including dialysis patients.	Stroke

Community dwelling elderly - those aged >65 years who were community dwelling and had no significant morbidity

2. In medical patients, what is the effect of RBC transfusion on patient outcomes?

Medical population

In medical patients, the effect of a restrictive versus liberal RBC transfusion strategy on mortality is uncertain

Direct evidence is not available in general medical patients. However:

Hb g/L	Transfuse	Rational
<70	Yes	Transfusion may be associated with reduced mortality and is likely to be appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.
70-100	Maybe	BC transfusion is not associated with reduced mortality. The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions. No evidence was found to warrant a different approach for patients who are elderly or who have respiratory or cerebrovascular disease.
>100	No	Transfusion is likely to be unnecessary and is usually inappropriate.

In patients with iron deficiency anaemia, iron therapy is required to replenish iron stores regardless of whether a transfusion is indicated.

Acute coronary syndrome

Hb g/L	Transfuse	Rational
<80	Yes	Transfusion may associated with a lower risk of mortality and is likely to be appropriate.
80-100	Likely no	Effect of transfusion on mortality is uncertain and may be associated with an increased risk of recurrence of MI.
>100	No	Transfusion associated with a higher risk of mortality, proportional to Hb concentration

RBC transfusion may be associated with an increased risk of recurrence (up to 6 months) of MI.

Heart failure
In patients with heart failure, the effect of RBC transfusion on the risk of mortality is uncertain. In all patients with heart failure, there is an increased risk of transfusion-associated circulatory overload. This needs to be considered in all transfusion decisions.

Cancer
In patients with cancer, the aetiology of anaemia is often multifactorial; where appropriate, reversible causes should be identified and treated.
There is a lack of specific evidence relating to the effects of RBC transfusion in patients with cancer. Any decision to transfuse should be based on the need to relieve clinical signs and symptoms of anaemia.

3. In medical patients, what is the effect of non-transfusion interventions to increase Hb concentration on morbidity, mortality and need for RBC blood transfusion?

Erythropoietin is secreted by the kidneys in response to hypoxia and stimulates erythropoiesis in the marrow. A reduction in renal mass may contribute to reduced erythropoietin levels, and therefore anaemia
Iron deficiency results when iron losses or requirements exceed absorption; it is often multifactorial, and may be absolute or relative.

Relative iron deficiency is commonly referred to as functional iron deficiency (FID). A patient with FID has adequate stores of iron, but the iron cannot be mobilized for erythropoiesis, which is mediated by elevated hepcidin
The serum ferritin level is the most readily available and useful index of iron deficiency.
Ferritin level <15 mcg/L = iron deficiency,
Ferritin level 15 – 30 mcg/L = highly suggestive iron deficiency
Ferritin is also an acute-phase protein and is elevated in inflammation, infection, liver disease and malignancy.

	Cancer	Heart failure	CRF	Elderly	IBD	Myelodysplasia
ESA + Mortality	Increases	Unknown	Unknown – to a Hb 100-110	Unknown		Unknown
ESA + functional status	Improves	Improve	Maybe improves	Unknown		Unknown
ESA+transfusion need	Decreases	Unknown	Decreases			Decreases
ESA+ thrombotic events	Increases	Unknown	Increases if targeting Hb>130	Unknown		Unknown
ESA + Iron	Unknown effect on mortality					
Iron +mortality	Unknown	Unknown	Unknown		Unknown	
Iron + functional status	Unknown	Improves	Improve		Unknown	
Iron+transfusion Need			Improved if on dialysis Unknown if not on dialysis			

ESA use is less effective in patients with chronic renal failure who have absolute or functional iron deficiency.

4. In medical patients, what is the effect of FFP, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

Fresh frozen plasma
The routine use of FFP in medical patients with coagulopathy (including those with liver impairment) is not supported.
Tests for coagulation correlate poorly with bleeding risk in liver impairment
Fibrinogen and cryoprecipitate
The routine use of cryoprecipitate or fibrinogen concentrate in medical patients with coagulopathy is not advised
Platelet transfusion
Platelet transfusion may be indicated for the prevention and treatment of haemorrhage in patients with thrombocytopenia or platelet function defects.
Platelet transfusionsare not indicated in all causes of thrombocytopenia, and may be contraindicated in certain conditions (e.g. TTP and HIT). Thus, the cause of the thrombocytopenia should be established and expert opinion sought.
In patients with chronic failure of platelet production (e.g. myelodysplasia or aplastic anaemia), a specific threshold for transfusion may not be appropriate. These patients are best managed on an individual basis, in consultation with a relevant expert.
Long-term prophylactic platelet transfusions may be best avoided because of the risk of complications (e.g. alloimmunisation and platelet refractoriness).
Therapeutic platelet transfusions could be considered for treatment of bleeding

5. In medical patients, at what INR (PT/APTT) for FFP, fibrinogen level for cryoprecipitate and platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

Chemotherapy and haematopoietic stem cell transplantation,
Prophylactic use of platelets: is transfusion at a platelet count of
<10 × 109/L transfusion of platelets in the absence of risk factors
<20 × 109/L transfusion of platelets in presence of risk factors (e.g. fever, minor bleeding).
In patients undergoing chemotherapy and haematopoietic stem cell transplantation, there is no evidence to support:
• a lower trigger for prophylactic platelet transfusion for patients with risk factors (e.g. fever, minor bleeding)
• a strategy of therapeutic-only platelet transfusions (i.e. for treatment of clinically significant bleeding).

6.In specific regularly and chronically transfused patients, at what Hb threshold should patients be transfused to avoid adverse outcomes?

Thalassaemia:
Maintain a pretransfusion Hb concentration of 90 – 100 g/L, with transfusions at about monthly intervals. Myelodysplasia:
Who are regularly and chronically transfused, there is no evidence to guide particular Hb thresholds.

Transfusion risks

TRANSFUSION RISK	ESTIMATED RATE[a] (HIGHEST TO LOWEST RISK)	CALMAN RATING[b]
Transfusion-associated circulatory overload (iatrogenic)	Up to 1 in 100 transfusions	High
Transfusion-related acute lung injury	1 in 1200 – 190,000	Low to minimal
Haemolytic reactions	Delayed: 1 in 2500 – 11,000 Acute: 1 in 76,000 Fatal: Less than 1 in 1 million	Low to very low Very low Negligible
Anaphylactoid reactions or anaphylaxis (usually due to IgA deficiency)	1 in 20,000 – 50,000	Very low
Bacterial sepsis: platelets	1 in 75,000	Very low
Bacterial sepsis: red blood cells	1 in 500,000	Minimal
Hepatitis B	Less than 1 in 1 million	Negligible
Hepatitis C	Less than 1 in 1 million	Negligible
Human immunodeficiency virus	Less than 1 in 1 million	Negligible
Human T-lymphotropic virus (types 1 and 2)	Less than 1 in 1 million	Negligible
Malaria	Less than 1 in 1 million	Negligible
Variant Creutzfeldt-Jakob disease (not tested)	Never reported in Australia	Negligible
Transfusion-associated graft-versus-host disease	Rare	Negligible
Transfusion-related immunomodulation	Not quantified	Unknown

Calman Chart[a] (United Kingdom risk per one year)

RATING	RATE	EXAMPLE
Negligible	<1 in 1,000,000	Death from lightning strike
Minimal	1 in 100,000 – 1,000,000	Death from train accident
Very low	1 in 10,000 – 100,000	Death from an accident at work
Low	1 in 1,000 – 10,000	Death from a road accident
High	>1 in 1,000	Transmission of chicken pox to susceptible household contacts