Haemoglobin thresholds for blood transfusion

Two meta-analyses report that restricting transfusion of red blood cells to people with a haemoglobin level of either less than 7.0 g/dl or 6.4 g/dl to 9.7 g/dl reduces mortality and serious infection, but does not significantly affect the overall risk of infection.

Overview: Blood transfusions are widely used in clinical care to replace blood lost during major surgery, childbirth or a severe accident; to treat anaemia that has failed to respond to other treatments; and to treat inherited blood disorders, such as thalassaemia or sickle cell anaemia (NHS Choices 2013). In the UK, 2.9 million blood components were issued for transfusion in 2012 (Bolton-Maggs and Cohen 2013).

Blood transfusion is associated with clinical risks, such as acute transfusion reaction (allergic reaction or anaphylaxis) and fluid overload. In 2012, the risk of transfusion-related death in the UK was 3.1 per million blood components issued (Bolton-Maggs and Cohen 2013). The risk of major morbidity was 46.7 per million blood components issued.

These risks, as well as the cost and scarcity of blood components, are driving measures to reduce the inappropriate use of blood transfusion, in particular in people with potentially reversible anaemia or whose haemoglobin levels are low but sufficient.

Current advice: Guidelines from the British Society for Haematology on the clinical use of red cell transfusions state that there is no universal threshold for red blood cell transfusions: that is, there is no haemoglobin concentration at which transfusion of red blood cells is appropriate for all patients. Clinical judgement plays a vital role in the decision to transfuse red cells or not.

However, the guideline adds that red blood cell transfusion is not indicated when estimates of actual and anticipated haemoglobin concentrations are greater than 10 g/dl. Transfusion of red blood cells is indicated at a haemoglobin concentration of less than 7 g/dl. The correct strategy for transfusion of patients with haemoglobin concentrations between 7 and 10 g/dl is less clear.

NICE is currently preparing guidance on blood transfusion.

New evidence: Two meta-analyses have assessed the effect of restricting blood transfusion to patients with a haemoglobin level of either less than 7.0 g/dl or 6 g/dl to 10 g/dl compared with more liberal thresholds.

Salpeter et al. (2014) assessed 3 randomised controlled trials (n=2364) that compared red blood cell transfusion in patients with a haemoglobin level of less than 7 g/dl (restrictive strategy) versus more liberal thresholds. These studies assessed patients aged on average 45.7 years (SD±16 years) in adult or paediatric critical care, or with acute upper gastrointestinal bleeding.

Compared with more liberal thresholds, the restrictive strategy was associated with lower in-hospital mortality (risk ratio [RR]=0.74, 95% confidence interval [CI] 0.60 to 0.92), 30-day mortality (RR=0.77, 95% CI 0.61 to 0.96) and total mortality (RR=0.80, 95% CI 0.65 to 0.98). The number needed to treat
with the restrictive threshold to prevent 1 death was 33. The restrictive threshold was also found to reduce re-bleeding (RR=0.64, 95% CI 0.45 to 0.90), acute coronary syndrome (RR=0.44, 95% CI 0.22 to 0.89) and pulmonary oedema (RR=0.48, 95% CI 0.33 to 0.72). The restrictive threshold did not appear to significantly reduce the risk of bacterial infections (RR=0.86, 95% CI 0.73 to 1.00).

When studies with a haemoglobin threshold of 7.5 g/dl to 10 g/dl were analysed (16 studies, n=4572), this restrictive strategy had no significant effect on in-hospital mortality (RR=0.65, 95% CI 0.37 to 1.15), total mortality (RR=1.03, 95% CI 0.81 to 1.31) or other outcomes compared with a more liberal strategy.

A meta-analysis by Rohde et al. (2014) concentrated on how restrictive transfusion approaches affect the risk of infection compared with more liberal strategies. The study analysed 17 randomised controlled trials (n=7456) that compared restrictive haemoglobin thresholds of 6.4 g/dl to 9.7 g/dl with a more liberal threshold. The patient populations were adult and paediatric patients receiving transfusions for cardiac, gastrointestinal or orthopaedic indications, or who were critically ill, had sepsis or were of low birth weight.

Compared with a more liberal approach, a restrictive threshold for blood transfusion was not associated with a significantly lower risk of infection (RR=0.92, 95% CI 0.82 to 1.04). When the analysis was restricted to the 3 trials (n=2364) that used a haemoglobin threshold of less than 7.0 g/dl for the restrictive strategy, the risk of infection was likewise not significantly reduced (RR=0.86, 95% CI 0.72 to 1.02).

However, the restrictive threshold was associated with a lower risk of serious infection than a more liberal approach (RR=0.84, 95% CI, 0.73 to 0.96, p=0.012). The absolute risk of any serious infection with the restrictive strategy was 10.6% (95% CI 5.6% to 15.9%). For patients on the liberal transfusion threshold, this risk was 12.7% (95% CI 7.0% to 18.7%).

Commentary: “Challenges interpreting the literature on red cell transfusion include heterogeneity between trial participant groups, disparities in what comprised restrictive versus liberal practice, and potential effect modifiers such as red cell leucodepletion. Baseline variation in risk, indications for transfusion, and red cell exposure are also relevant. The risk–benefit profile for red cell transfusion to treat bleeding patients with liver disease may be very different from that for blood replacement during elective surgery.

“Despite this, these 2 meta-analyses add knowledge to the field. The Salpeter et al. (2014) study suggests that benefit from very restrictive red cell transfusion thresholds persists, and the benefit was stronger compared with moderately restrictive transfusion triggers. The Rohde et al. (2014) study reported no overall effect of restrictive thresholds on infections, but restrictive practice was statistically significant for more important outcomes (severe infection) and in higher risk groups (patients with sepsis). In patients with septic shock, Holst and colleagues (2014) recently found that a haemoglobin trigger of 7 g/dl resulted in improved survival and similar ischaemic complications compared with a liberal approach; infections were not measured in this trial.

“Evidence supports limiting red cell transfusions to people with a haemoglobin level of 7 g/dl for most patients and clinical situations. Uncertainty still remains for subgroups who are under-represented in these trials, including patients with acute and chronic cardiovascular disease, and acute brain injuries. Virtually no trials have measured quality of life or healthcare costs associated with restrictive red cell transfusion thresholds, which makes the assessment of cost effectiveness challenging.” – Professor Tim Walsh, Professor of Critical Care, Edinburgh University

Study sponsorship: Salpeter et al. (2014) did not receive any funding, and Rodhe et al. (2014) was funded by the US National Heart, Lung, and Blood Institute.
About this article: This article appeared in the January 2015 issue of the Eyes on Evidence e-bulletin. This free monthly e-bulletin from NICE Evidence outlines interesting new evidence and what it means for current practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

To receive the Eyes on Evidence e-bulletin, please complete the online registration form.