

PRACTICE



GUIDELINES

Blood transfusion: summary of NICE guidance

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Although blood transfusion is common in clinical practice, it is associated with some risk. Alternatives to blood transfusion are also underused.¹ Audits in the United Kingdom show that the inappropriate use of blood components is 20% or more.² This puts patients at unnecessary risk of receiving the wrong blood and of complications such as circulatory overload and transfusion related acute lung injury, as well as wasting a scarce and costly resource. Measures for managing patients without blood transfusion are underused.¹

This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) on blood transfusion.³

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in *italic* in square brackets.

Alternatives to blood transfusion for patients having surgery

Erythropoietin

- Offer erythropoietin only if:
 - The patient has anaemia and meets the criteria for blood transfusion but declines it because of religious or other reasons, or
 - The appropriate blood type is not available because of the patient's red cell antibodies.
- Do not offer erythropoietin otherwise to reduce the need for blood transfusion in patients having surgery.

[Based on very low to low quality evidence from randomised controlled trials (RCTs) and cost effectiveness evidence.]

Intravenous and oral iron

- Offer oral iron before and after surgery to patients with iron deficiency anaemia. *[Based on very low to low quality evidence from RCTs, cost effectiveness evidence, and the experience and opinion of the Guideline Development Group (GDG).]*
- Consider intravenous iron before or after surgery for patients who:
 - Have iron deficiency anaemia and cannot tolerate or absorb oral iron or are unable to adhere to oral iron treatment⁴
 - Are diagnosed as having functional iron deficiency, or
 - Are diagnosed as having iron deficiency anaemia and the interval between the diagnosis of anaemia and surgery is predicted to be too short for oral iron to be effective.

[Based on very low to low quality evidence from RCTs, cost effectiveness evidence, and the experience and opinion of the GDG.]

- For patients with anaemia and chronic kidney disease, consult the NICE guideline on management of anaemia in chronic kidney disease.⁵

Cell salvage and tranexamic acid

- Offer tranexamic acid to adults undergoing surgery who are expected to have at least moderate blood loss (>500 mL). *[Based on low to moderate quality evidence from RCTs and original cost effectiveness analysis.]*
- Consider tranexamic acid for children undergoing surgery who are expected to have at least moderate blood loss (>10% blood volume). *[Based on low to moderate quality evidence from RCTs.]*

What you need to know

- Consider alternatives to blood transfusion in surgical patients
- Offer tranexamic acid to adults undergoing surgery who are expected to have at least moderate blood loss (>500 mL). Do not use cell salvage alone without tranexamic acid
- For patients who need red blood cell transfusions and do not have major haemorrhage or acute coronary syndrome, use a restrictive haemoglobin concentration threshold of 70 g/L and a haemoglobin concentration target of 70-90 g/L after transfusion
- Consider single unit red blood cell transfusions for patients who do not have active bleeding and reassess patients after each transfusion

What's new in this guidance

- Electronic patient identification systems can improve the safety and efficiency of routine transfusion
- Patients who may have or who have had a transfusion, and their family members or carers, require verbal and written information about transfusion and its alternatives

- Do not routinely use cell salvage without tranexamic acid. *[Based on very low to low quality evidence from RCTs and original cost effectiveness analysis.]*
- Consider intraoperative cell salvage with tranexamic acid for patients who are expected to lose a very high volume of blood (for example, in cardiac and complex vascular surgery, major obstetric procedures, pelvic reconstruction, and scoliosis surgery). *[Based on very low quality evidence from RCTs, original cost effectiveness analysis, and the experience and opinion of the GDG.]*

Red blood cells

- For patients who need red blood cell transfusions and who do not have major haemorrhage or acute coronary syndrome, and those who require regular blood transfusions for chronic anaemia, use restrictive red blood cell transfusion thresholds (see below). *[Based on very low to low quality evidence from RCTs and cost effectiveness evidence.]*
- Consider a threshold of 70 g/L and a haemoglobin concentration target of 70-90 g/L after transfusion. *[Based on very low to low quality evidence from RCTs.]*
- For patients with acute coronary syndrome, consider a red blood cell transfusion threshold of 80 g/L and a haemoglobin concentration target of 80-100 g/L after transfusion. *[Based on very low to low quality evidence from RCTs.]*
- For each patient with chronic anaemia requiring regular blood transfusions, consider setting individual thresholds and haemoglobin concentration targets. *[Based on the experience and opinion of the GDG.]*
- For people who are not actively bleeding, consider single unit red blood cell transfusions for adults, or equivalent volumes calculated from body weight for children or adults with low body weight. *[Based on the experience and opinion of the GDG.]*
- After each single unit red blood cell transfusion (or equivalent volumes, calculated from body weight, for children or adults with low body weight), clinically reassess and check haemoglobin levels and give further transfusions if needed. *[Based on the experience and opinion of the GDG.]*

Platelets**Patients with thrombocytopenia who are bleeding**

- Offer platelet transfusions to patients with thrombocytopenia who have clinically significant bleeding (World Health Organization bleeding grade 2—for example, prolonged epistaxis, extensive skin bleeding, haematemesis, or melaena) and a platelet count below $30 \times 10^9/L$. *[Based on the experience and opinion of the GDG.]*
- Use higher platelet thresholds (maximum of $100 \times 10^9/L$) for patients with thrombocytopenia and either of the following:
 - Severe bleeding (WHO grades 3 and 4—for example, bleeding that requires a red cell transfusion)
 - Bleeding at critical sites, such as the central nervous system (including eyes).

[Based on the experience and opinion of the GDG.]

Patients with thrombocytopenia who are having invasive procedures or surgery

- Consider prophylactic platelet transfusions to raise the platelet count above $50 \times 10^9/L$ in patients who are having invasive procedures or surgery. *[Based on very low to low quality evidence from RCTs and the experience and opinion of the GDG.]*
- Consider a higher threshold (such as $50-75 \times 10^9/L$) for patients with a high risk of bleeding who are having invasive procedures or surgery, after taking into account:
 - The specific procedure the patient is having
 - The cause of the thrombocytopenia
 - Whether the patient's platelet count is falling, and
 - Any coexisting causes of abnormal haemostasis.

[Based on very low to low quality evidence from RCTs and the experience and opinion of the GDG.]

- Consider prophylactic platelet transfusions to raise the platelet count above $100 \times 10^9/L$ in patients having surgery in critical sites, such as the central nervous system (including the posterior segment of the eyes). *[Based on very low to low quality evidence from RCTs and the experience and opinion of the GDG.]*

Patients with thrombocytopenia who are not bleeding or having invasive procedures or surgery

- Offer prophylactic platelet transfusions to patients with a platelet count below $10 \times 10^9/L$ who are not bleeding or having invasive procedures or surgery, unless there is an alternative treatment for the condition or they have a contraindication to platelet transfusion, for example:
 - Chronic bone marrow failure
 - Autoimmune thrombocytopenia
 - Heparin induced thrombocytopenia, or
 - Thrombotic thrombocytopenic purpura.

[Based on very low to low quality evidence from RCTs and the experience and opinion of the GDG.]

When prophylactic platelet transfusions are not indicated

- Do not routinely offer prophylactic platelet transfusions to patients with any of the following:
 - Chronic bone marrow failure
 - Autoimmune thrombocytopenia
 - Heparin induced thrombocytopenia, or
 - Thrombotic thrombocytopenic purpura.

[Based on the experience and opinion of the GDG.]

- Do not offer prophylactic platelet transfusions to patients having procedures with a low risk of bleeding, such as adults having central venous cannulation or any patients having bone marrow aspiration and trephine biopsy. [Based on the experience and opinion of the GDG.]

Doses

- Do not routinely transfuse more than a single dose of platelets.
- Consider giving more than a single dose of platelets only in patients with severe thrombocytopenia who are bleeding in a critical site, such as the central nervous system (including eyes).
- Reassess the patient's clinical condition and check the platelet count after each platelet transfusion; give further doses if needed.

[All points based on the experience and opinion of the GDG.]

Fresh frozen plasma

- Consider fresh frozen plasma transfusion for patients with clinically significant bleeding but without major haemorrhage only if they have abnormal coagulation test results (for example, prothrombin time ratio or activated partial thromboplastin time ratio above 1.5). [Based on very low quality evidence from RCTs and observational studies and the experience and opinion of the GDG.]
- Do not offer fresh frozen plasma transfusions to correct abnormal coagulation in patients who:
 - Are not bleeding (unless they are having invasive procedures or surgery with a risk of clinically significant bleeding), or
 - Require reversal of a vitamin K antagonist.

[Based on the experience and opinion of the GDG.]

- Consider prophylactic fresh frozen plasma transfusions for patients with abnormal coagulation who are having invasive

procedures or surgery with a risk of clinically significant bleeding. [Based on very low quality evidence from RCTs and the experience and opinion of the GDG.]

- Reassess the patient's clinical condition and repeat the coagulation tests after fresh frozen plasma transfusion to ensure that they are getting an adequate dose, and give further doses if needed. [Based on the experience and opinion of the GDG.]

Cryoprecipitate

- Consider cryoprecipitate transfusions for patients without major haemorrhage who have clinically significant bleeding and fibrinogen concentration below 1.5 g/L.

[Based on very low quality evidence from one observational study and the experience and opinion of the GDG.]

- Do not offer cryoprecipitate transfusions to correct the fibrinogen concentration in patients who are not bleeding, and are not having invasive procedures or surgery with a risk of clinically significant bleeding.

[Based on the experience and opinion of the GDG.]

- Consider prophylactic cryoprecipitate transfusions for patients with a fibrinogen concentration below 1.0 g/L who are having invasive procedures or surgery with a risk of clinically significant bleeding. [Based on the experience and opinion of the GDG.]
- Use an adult dose of two pools when giving cryoprecipitate transfusions (for children, use 5-10 mL/kg up to a maximum of two pools). [Based on the experience and opinion of the GDG.]
- Reassess the patient's clinical condition, repeat the fibrinogen measurement, and give further doses if needed. [Based on the experience and opinion of the GDG.]

Prothrombin complex concentrate

- Offer immediate prothrombin complex concentrate transfusions for the emergency reversal of warfarin anticoagulation in patients with either:
 - Severe bleeding, or
 - Head injury with suspected intracerebral haemorrhage.

[Based on the experience and opinion of the GDG.]

For guidance on reversing anticoagulation treatment in people who have a stroke and a primary intracerebral haemorrhage, see NICE guideline on the initial diagnosis and management of stroke.⁶

- Consider immediate prothrombin complex concentrate transfusions to reverse warfarin anticoagulation in patients having emergency surgery, depending on the level of anticoagulation and the bleeding risk. [Based on the experience and opinion of the GDG.]
- Monitor the international normalised ratio (INR) to confirm that warfarin anticoagulation has been adequately reversed and consider further prothrombin complex concentrate. [Based on the experience and opinion of the GDG.]

Blood transfusions for patients with acute upper gastrointestinal bleeding

For guidance on blood transfusions for people with acute upper gastrointestinal bleeding, see NICE guideline on acute upper gastrointestinal bleeding.⁷

Patient safety*Monitoring for acute blood transfusion reactions*

- Monitor the patient's condition and vital signs before, during, and after blood transfusion to detect acute transfusion reactions that may need immediate investigation and treatment. [Based on the experience and opinion of the Guideline Development Group (GDG).]
- Observe patients who are having or have had a blood transfusion in a suitable environment with staff who can monitor and manage acute reactions. [Based on the experience and opinion of the GDG.]

Electronic patient identification systems

- Consider using a system that electronically identifies patients to improve the safety and efficiency of the blood transfusion process. [Based on very low quality evidence from observational studies, cost analysis, and the experience and opinion of the GDG.]

Patient information

- Provide verbal and written information to patients who may have or who have had a transfusion and their family members or carers (as appropriate), explaining:
 - The reason for the transfusion
 - The risks and benefits
 - The transfusion process
 - Any transfusion needs specific to them
 - Any alternatives that are available and how these might reduce the need for a transfusion
 - That they are no longer eligible to donate blood
 - That they are encouraged to ask questions.

[Based on low quality evidence from qualitative studies and the experience and opinion of the Guideline Development Group (GDG).]

- Document discussions in the patient's notes. [Based on low quality evidence from qualitative studies and the experience and opinion of the GDG.]
- Provide patients and their general practitioners with copies of the discharge summary or other written communication that explains:
 - The details of any transfusions they had
 - The reasons for the transfusion
 - Any adverse events
 - That they are no longer eligible to donate blood.

[Based on low quality evidence from qualitative studies and the experience and opinion of the GDG.]

For guidance on communication and patient centred care for adults, see the NICE guideline on patient experience in adult NHS Services.⁸

Overcoming barriers

Three recommendations that could have a big impact on practice are the use of tranexamic acid in surgery in patients expected to have at least moderate blood loss; the implementation of electronic patient identification systems to improve the safety and efficiency of routine transfusion practice; and the provision of patient information to ensure that patients are adequately informed about transfusion and its alternatives.⁹ Implementation of electronic patient identification systems will cost money, but there are substantial savings, such as in nursing and laboratory staff time and reduced red blood cell unit wastage. Implementing many of the other recommendations is likely to reduce the use of blood components and therefore blood costs in hospitals. Organisations should identify local barriers to implementation and develop action plans for overcoming them.

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How patients were involved in the creation of this article

Guideline Development Group members involved in this guideline included lay members who contributed to the formulation of the recommendations summarised here. Patient organisations were among registered stakeholders consulted at scoping and development stages.

Further information on the guidance

The Guideline Development Group (GDG) considered evidence in challenging areas, such as the use of alternatives to blood transfusion in surgical patients and thresholds and targets for the use of blood components and products.

The GDG also considered the crucial aspect of patient safety, including electronic patient identification systems and electronic decision support systems.

It was necessary to limit the scope by excluding:

- Certain patient groups with special transfusion needs (for example, pregnant women and fetuses, neonates, and children under 1 year)
- Specialist areas already covered by other National Institute for Health and Care Excellence (NICE) guidelines (for example, anaemia in chronic kidney disease, upper gastrointestinal bleeding, and trauma and massive haemorrhage)
- The use and administration of blood products, such as intravenous immunoglobulin, anti-D immunoglobulin, and recombinant activated factor VII, and near patient testing for haemoglobin concentration and haemostasis
- Laboratory procedures relating to the safety and quality of blood, including pre-transfusion compatibility testing
- The diagnosis of anaemia, and
- The management of anaemia in medical patients.

Methods

This guidance was developed by the National Clinical Guideline Centre in accordance with NICE guideline development methods (www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview).

The GDG comprised three consultant haematologists (including the chair), two patient members, two critical care physicians, two transfusion practitioners, a paediatric haematologist, a transfusion practitioner nurse specialist, and a neurosurgeon.

The group developed clinical questions, collected and appraised clinical evidence, and evaluated the cost effectiveness of proposed interventions and management strategies through literature review and economic analysis. The draft guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the group took all comments into consideration when producing the final version of the guideline. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes rather than the quality of the clinical study. Where standard methods could not be applied, a customised quality assessment was done. These were either presented as a narrative summary of the evidence or in customised GRADE tables (for example, for observational studies and network meta-analysis). NICE has produced three different versions of the guideline: a full version; a summary version known as the "NICE guideline"; and a version for people who are receiving or have received blood transfusion, their family and carers, and the public (www.nice.org.uk/guidance/NG24). These, as well as a pathway, are available from the NICE website. Updates of the guideline will be produced as part of NICE's guideline development programme.

Network meta-analysis for alternatives to blood transfusion in surgical patients

Five network meta-analyses were conducted as part of the clinical review, enabling treatment effects to be calculated for all interventions simultaneously. This allows ranking based on efficacy, and uses all available direct and indirect evidence from randomised controlled trials, while preserving randomisation. On the basis of the network meta-analyses in the moderate risk group, tranexamic acid was found to be the most effective treatment for reducing the units of allogeneic blood transfused in patients undergoing surgery and expected to have at least moderate blood loss. Tranexamic acid was also the only intervention for which a significant decrease in mortality was seen.

Cost effectiveness analysis

An economic model was developed from an NHS and personal social services perspective to compare the cost effectiveness of different interventions as alternatives to blood transfusion in surgical patients. Tranexamic acid was the most cost effective treatment at a willingness to pay threshold of £20 000 (£27 860; \$30 660) per quality adjusted life year for both high risk and moderate risk patients. Sensitivity analyses indicated that the combination of intraoperative cell salvage and tranexamic acid could potentially become the most cost effective strategy in patients in whom the probability of being transfused and the volume transfused is expected to be very high.

Implementation tools

Organisations should evaluate their own practices to identify any barriers to guideline implementation. Benchmarking and feedback of data (including the use of dashboards) are examples of tools to drive change and monitor progress. These are greatly facilitated by the use of information technology, and the current introduction of electronic patient record systems into many hospitals in the NHS provides an excellent opportunity to facilitate the routine use of these tools.¹⁰

Future research

The GDG identified some priority areas for research:

- For patients with chronic cardiovascular disease, what are the clinical effectiveness and cost effectiveness of restrictive, compared with liberal, red blood cell thresholds and targets?
- What are the clinical effectiveness and cost effectiveness of an electronic decision support system compared with current practice in reducing inappropriate blood transfusions, overall rates of blood transfusion, and mortality?
- For patients having cardiac surgery with a high risk of postoperative blood loss, is postoperative cell salvage and reinfusion clinically and cost effective in reducing red blood cell use and improving clinical outcomes compared with existing practice?
- What dose of fresh frozen plasma is most clinically effective at preventing bleeding in patients with abnormal haemostasis who are having invasive procedures or surgery?