Centre for Perioperative Care

Guideline for the Management of Anaemia in the Perioperative Pathway

September 2022

Anaemia Guideline Working Group

Please see below a full list of contributors to this guidance and their organisational affiliations. We would like to thank the following members of the CPOC Anaemia Guideline Working Group for their valuable contribution to the drafting of this guideline.

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With special thanks to

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Please note

Please note the importance of this guidance in light of the current blood transfusion situation.

November 2022

Guideline review

This is version 1.0 of this guidance document, published in 2022. Any updates made to this guidance will be reflected in the table below and included in subsequent versions.

Version	Change	Date
1.0	First publication	7 September 2022
2.0	Second publication	4 November 2022

Date of review: September 2023

Scope of guideline

This guidance includes elective (planned) surgery and emergency (urgent) surgery. It applies to people of all ages, but specifically to two main groups of patients:

- people planned to have major surgery, with expected blood loss of over 500ml or 10% of their blood volume, who are anaemic or at risk of becoming anaemic
- people having less major surgery, who have been identified as having anaemia.

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FOREWORD

The Centre for Perioperative Care (CPOC), a cross organisational body, was established in 2019 to facilitate and promote delivery of high-quality, whole pathway, perioperative care. CPOC is therefore in a unique position to collate, develop, implement and evaluate new guidelines across the whole perioperative pathway.

Anaemia is common, present in over a third of patients having major surgery. It is associated with adverse outcomes of surgery. Interventions can be effective. A Patient Blood Management (PBM) approach improves postoperative outcomes.[1] What is needed is standardised protocols for assessment and generalised advice, but with care individualised to the patient.

Best practice guidance exists. Implementation is, however, patchy despite the evidence of benefit. CPOC believes this is because available guidance is written for specific specialties rather than being patient and pathway centred. CPOC have published perioperative guidelines on diabetes and frailty that are being successfully translated into routine clinical care. This perioperative anaemia guideline has been developed using a similar whole pathway approach. It contains recommendations for patients of all ages undergoing surgery and for healthcare professionals in both emergency and elective surgical settings and across specialties. It builds on and incorporates existing work including:

- NICE NG45 Blood tests[2]
- NICE NG24 Blood transfusion[3]
- NATA (Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis)[4]
- British Society of Gastroenterology[5]
- NICE B12 and folate deficiency.[6]

Management of anaemia for patients undergoing surgery gives an opportunity to reduce complications in the short term and improve longer term health.

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SUMMARY

Why is this new guideline important?

Anaemia means having a low blood level of haemoglobin (Hb), which carries oxygen around the body. Anaemia is common in people having many types of surgery. One in three people are anaemic at the time of the operation and more become anaemic after surgery due to blood loss. We know that people who have anaemia at the time of the operation don't recover as well as those without anaemia. They are especially more likely to have poor wound healing, slow recovery and more than double the rates of complications.

There are many causes for anaemia but often it is related to iron deficiency. We know from previous research that we can reduce complications after surgery by treating anaemia before, during and after the operation. Interventions that work include preventing and treating anaemia early, reducing blood loss during the operation, and making sure the patient's body is in the best state to tolerate anaemia.

While this has been known for some time, putting it into practice remains a very real obstacle and too often patients are brought through surgery despite preventable anaemia not having been corrected.

The aim of this guideline is to ensure that the patient is at the centre of the whole process, and that everyone involved in their care carries out their individual responsibilities to minimise the risk from anaemia.

To make the best of this approach we need to make sure patients and all healthcare professionals including GPs and multidisciplinary hospital teams work together to:

1. Identify anaemia early in the pathway.

2. Make the patient aware of this and all actions going forward.

3. Find the cause of the anaemia.

4. Use tried and tested treatments for anaemia before surgery. This could include advice on changes in diet, oral treatments such as iron supplements and the use of intravenous iron when necessary.

5. Make sure the patient has a personalised treatment programme including providing appropriate information about the pros and cons of the different approaches suggested to the patient and how long these should be continued.

6. Communicate clearly between different members of the team so that operations are not cancelled unnecessarily and improve the interface between primary care and hospitals.

7. Talk openly to the patient about the benefits and risks of managing anaemia and the surgery.

Things that can improve results for patients having surgery who have anaemia

- Nutrition – this is a key factor
- Early diagnosis:
  - of the type of anaemia (eg Iron deficiency (IDA), functional iron deficiency or B12 deficiency). Please see types of anaemia and causes
  - of the *cause* of anaemia (eg heavy periods or gastrointestinal loss)
- Early treatment if there is a clear cause (eg a bowel cancer causing IDA, or medications that should be stopped)
- Providing information about oral iron and how to take it, so it is more palatable
- Reducing blood loss before (if relevant), during and after the operation
- Using blood transfusion carefully (because it can alter immunity and cause other problems)
- Improving patient fitness to cope with anaemia and providing realistic practical advice on how to do this.
- Having good communication between primary care and hospitals.
- Shared Decision Making (SDM) so that the patient and senior clinician discuss the patient's values, expectations and the possible procedure. Talking through 'BRAN' – the Benefits, Risks, Alternatives and what happens if Nothing is done (see Appendix 21).
- Creating local systems that work to pick up anaemia early and are not hampered by a GP vs hospital hurdle.
- Ensuring there is an area equipped to give intravenous iron when needed in a stress-free environment.
- Educating staff about putting the patient at the centre of the process, communicating appropriately and reducing unnecessary delays including prompt requesting of investigations and acting on results.
- Having a culture where senior clinicians are involved early in complex cases where there is no straightforward intervention.
- Showing good leadership so that lines of responsibility are clear.
- Having a culture of data collection and audit against best practice so that each centre is always striving to improve how well they manage anaemia around the time of operations.

Why does management of perioperative anaemia matter?

The evidence is now clear. More than a third of people having major surgery are anaemic before their operation. The blood loss of surgery or trauma can cause or worsen anaemia. People who have anaemia have a worse result from their operation including poorer wound healing, slower mobilisation and an increased risk of death. Risk ratios in the published literature suggest people with anaemia have two or three times the rate of complications.[7–15] Anaemia is often associated with other conditions, but as an independent risk factor, anaemia is responsible for around 20% more complications[12,16–20] Interventional studies adopting a Patient Blood Management (PBM) approach, including addressing anaemia, lead to reduced blood transfusion, length of stay, complications[8,9,20–26] and hospital costs.[7] Blood transfusion itself carries risks, particularly affecting immunity, exposure to multiple donors and transfusion reactions.[20,23,27–30]

Anaemia is frequently diagnosed late in the work up of patients for surgery. It is increasingly apparent that a pathway approach to care works best. Pathways should be set up that allow a Patient Blood management (PBM) approach: anaemia should be diagnosed early and its cause investigated. Treatment should be given, intraoperative blood loss minimised and the patient's physiological response optimised. The pathway should anticipate potential problems. Many guidelines suggest a delay of four weeks to correct anaemia for benign disease.[4,26,31,32] Oral iron takes four weeks to have an impact on haemoglobin levels. It can take three to six months to replenish iron stores.[33,34] The randomised clinical trial, PREVENTT, comparing intravenous iron to placebo in patients with anaemia undergoing major abdominal or pelvic surgery did not show a reduction in the primary outcome of blood transfusion rate, but did show significantly higher postoperative haemoglobin and significantly fewer readmissions.[35,36]

'Anaemia should be viewed as a serious and treatable medical condition, rather than simply an abnormal laboratory value.'[4]

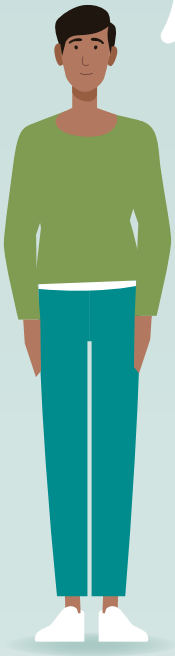
The biology of anaemia is complex. Whilst many patients may have iron deficiency anaemia (IDA), the causes are often multifactorial. Iron is poorly absorbed from the gut in the presence of inflammation (functional anaemia from chronic disease). Algorithms and explanations in this new guideline allow all staff to understand the types of anaemia, the rationale for testing and how to advise on simple optimisation including diet, oral replacement regimes and indications for intravenous iron. Although all patients should follow a generalised pathway, care should then be individualised, especially when results are made available. Senior clinical staff can then have clear shared decision making discussions with patients balancing risks of delaying surgery and the different options for treating anaemia. For example, IDA may be caused by underlying malignancy. SDM includes considering 'BRAN' Benefits, Risks, Alternatives and what happens if Nothing is done. Patients have different risks depending on their cause of anaemia, their other conditions and their type of operation.

Patient vignettes

'I got loss of sight in one eye as a result of severe sudden anaemia – not many people know about this'.

Staff need to know to take iron. You shouldn't take it with food or tea.

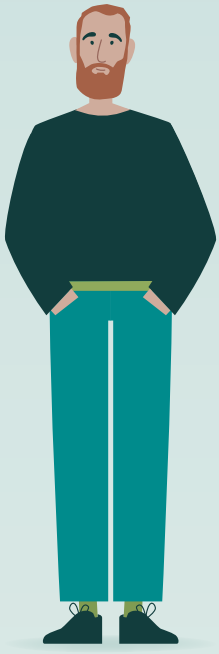
Multiple transfusions mean more antibodies and difficult future transfusions.
'I've had 15 units over the years – each time I get antibodies, so it takes a while to find blood for me. It would be good to get iron earlier and avoid the need for transfusion.'



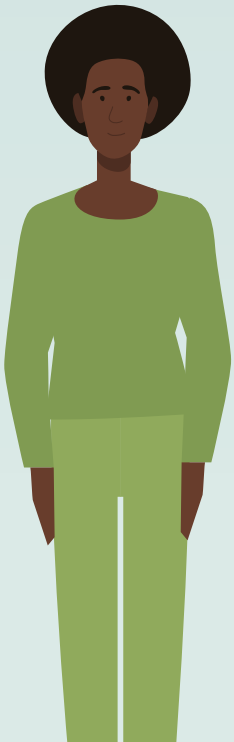
Patients need to be empowered. For example, if a patient knows they have a Hb of 90, they can start taking iron:
'I got mine up to 120 and it went down to 68 after op'.

'If they know I'm going [for surgery], they get to give it earlier. Below 70 is a long way to climb back up from.'

'Surgeons are presented with issues late, so there is a binary decision to cancel or not.'



'It feels as if everything happens a bit late – the surgeon gets told the Hb by preassessment and has to come up with a plan before the operation date.'



STANDARDS OF CARE

1 All hospitals should work to develop pathways of perioperative care for surgical patients with anaemia that comply with the recommendations in these guidelines.

2 All hospitals should establish data capture systems to allow auditing against the metrics and recommendations provided.

3 All patients referred for surgery who fulfil the NICE preoperative testing criteria should have a full blood count (FBC) at referral to surgery or at first surgical consultation.

4 All children and young people should be screened for anaemia before procedures associated with a 10% risk of transfusion as early as possible in the pathway.

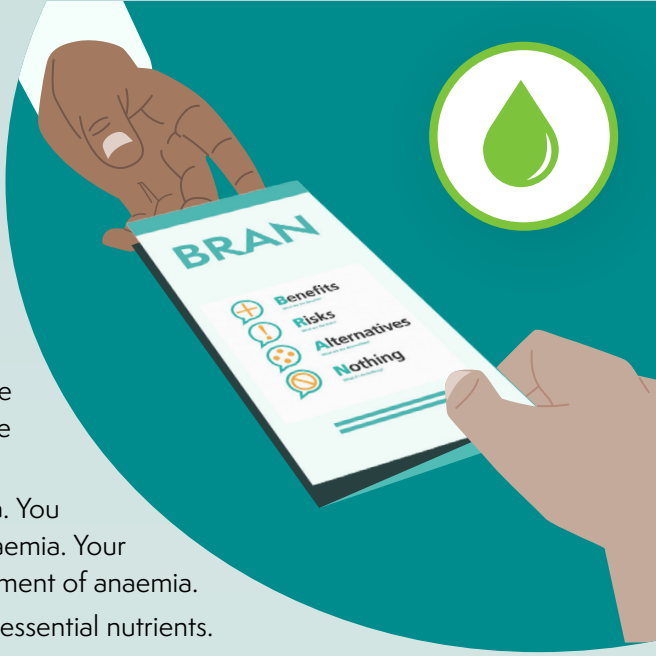
5 All patients undergoing surgery with a clinical finding of anaemia should have documentation of the type and likely cause of anaemia.

6 All patients with anaemia having a major operation (with expected blood loss of >500ml or 10% blood volume) should have a documented plan for preoperative, intraoperative and postoperative management of anaemia, in line with Patient Blood Management (PBM).

7 All patients undergoing surgery with anaemia or at risk of anaemia should be proactively provided with information (paper and/or digital) regarding causes and treatment of anaemia including options for blood transfusion.

8 All staff working in perioperative settings should have training in anaemia, PBM and blood transfusion. This includes those working with patients receiving emergency surgical care.

RECOMMENDATIONS FOR PEOPLE WITH ANAEMIA AND THEIR CARERS



- Be aware that anaemia is common, treatments are possible and that addressing anaemia may reduce postoperative complications.
- Be aware that there are many causes for anaemia. You are likely to have tests to discover the type of anaemia. Your surgery may be delayed for investigation or treatment of anaemia.
- Many people have anaemia due to low intake of essential nutrients. Please try to improve this:
  - Iron is found in: red meat, beans and nuts
  - B12 is found in: meat, fish, cheese or eggs
  - Folate is found in: green leafy vegetables, broccoli, brussel sprouts, asparagus, peas, chickpeas, brown rice and liver.
- Be aware that some patients are treated with blood products and your medical team may discuss this with you.
- Prepare for surgery or other treatment in good time. This may include:
  - increasing your physical activity/exercise, stopping smoking, preparing psychologically and practically. These interventions are proven to improve outcomes from surgery. There is more information on cpoc.org.uk/patients. Exercise should include: fitness, strength and balance – try sit-to-stand exercises.

- There are often different ways of investigating or treating anaemia. Patients are encouraged to ask questions, eg BRAN: 'what are the Benefits, Risks, Alternatives and what if Nothing is done'. Work out what matters to you. This is Shared Decision Making.

- If you are given oral iron:
  - note that the dose for treating anaemia is several times higher than for health supplements
  - it is best to take iron tablets on an empty stomach (ie one hour before or two hours after eating). Absorption can reduce by up 75% if taken with food
  - taking iron tablets with vitamin C does not seem to increase absorption[5]
  - taking iron tablets on alternate days will improve iron absorption and may minimise side effects
  - avoid taking iron with tea or with phytates (found in beans, seeds, nuts or grains) as this limits absorption
  - if you get diarrhoea or constipation, try taking iron on alternate days
  - if side effects are bad, ask the perioperative team if there is another treatment option.

Iron in your diet (NHS BT)

Anaemia Patient Information (NHS BT)

BRAN leaflet (CWUK)

Detailed explanations about reducing the reliance on blood transfusion

Iron deficiency in pregnancy – a matter of public health

For patients: High Spec Blood

RECOMMENDATIONS FOR ORGANISATIONS WHERE SURGICAL SERVICES ARE PROVIDED FOR PEOPLE WHO MAY HAVE ANAEMIA

Commissioning bodies should:

- Work collaboratively with providers to develop a system wide approach to support patients undergoing surgery who have anaemia. This will require cross boundary working with community, primary and secondary care services to develop the necessary pathways of care
- Work with providers to ensure mechanisms are in place for screening, assessing and optimising anaemia in patients undergoing surgery as early in the surgical pathway as possible
- Work with providers to develop a standardised referral form, so that requests for a surgical consultation include an FBC if the patient or possible procedure would require an FBC in accordance with NICE preoperative testing guidelines[2]

Developing clinical services; hospitals should:

- Appoint a clinical lead for perioperative patients with anaemia (this may be the same lead as for diabetes or frailty in the perioperative setting, see previous CPOC guidance)
- Support the clinical lead in developing, implementing and auditing policies and processes of care to ensure quality perioperative care for people with anaemia
- Support the clinical lead to:
  - Work with data or information from national initiatives such as HQIP (Healthcare Quality Improvement Partnership) audits and GIRFT (Getting It Right First Time) teams and ensure linkage
  - Support service development by working across primary and secondary care (surgery, anaesthetic, haematology, gastroenterology and general/geriatric medicine services)
  - Signpost local teams to relevant education and training resources (anaemia and blood transfusion)
  - Establish and lead multidisciplinary and multispecialty governance, audit, and morbidity and mortality meetings. Use SHOT (UK serious harm of transfusion) reports as a powerful educational tool
  - Standardise primary care referrals and if appropriate include latest Hb (if available), perform a frailty score if aged over 65 years using a recognised tool such as the Clinical Frailty Score (CFS) or the Electronic Frailty Index (eFI) and HbA1c if diabetes present
  - Ensure preoperative assessment occurs as soon after the decision to operate as possible to maximise the time available for optimisation
  - Work with pathology departments that receive blood tests from patients due to undergo surgery and develop pathways to:
    - formalise the additional tests they will undertake automatically preoperatively (eg including renal/eGFR, CRP, ferritin, Transferrin saturation, B12 and folate, with CHr and reticulocytes) if anaemia is identified
    - accept add-on requests for other tests if clinically appropriate
  - Develop a clear policy whereby abnormal test results are highlighted to a named senior clinician. They are responsible for further Shared Decision Making with the patient, considering all options, including whether to delay or talk through alternatives to operation, and for recommending or prescribing a treatment plan if needed
  - Ensure the transfusion committee at each Trust/Heath Board includes anaemia and PBM in their remit

Supporting infrastructure; hospitals should:

- Promote use of Enhanced Recovery programmes incorporating this guidance for all surgical patients with anaemia
- Allow necessary variation in the perioperative pathway, when clinically appropriate, eg pauses to the cancer pathways to optimise anaemia. This will facilitate patient assessment, optimisation and shared decision making prior to surgery
- Invest in technologies to support identification of people with anaemia on patient administration electronic systems that can be accessed across primary and secondary care.

RECOMMENDATIONS FOR STAFF WORKING IN SURGICAL OUTPATIENTS AND PREOPERATIVE ASSESSMENT SERVICES

Surgical and preoperative assessment teams should:

- Ensure Hb is checked as early as possible for patients being considered for surgery according to NICE preoperative testing guidelines
- Consider developing pathways to ensure early Hb check:
  - for example, if a patient requires a diagnostic CT scan with renal blood test before contrast, Hb should also be measured
  - for example, point of care testing, such as haemoglobin concentration screen (Hemocue®) or blood gas analysis (venous or arterial)
- Be aware of the Hb required for a diagnosis of anaemia (see Figure 1)
- Assess for causes of newly identified anaemia if patient undergoing surgical procedures with anticipated moderate-to-high (>500ml) blood loss.[26] This usually requires:
  - Thorough history and appropriate clinical examination
  - Accurate medication history including use of anticoagulant or antiplatelet medications or Non-Steroidal Anti-Inflammatory drugs (NSAIDs)
  - Assessment of frailty and cognition for all patients aged over 65 years
  - Identification of any previous delays in obtaining blood products for the patient due to antibodies
  - Blood tests:
    - Serum ferritin (SF)
    - Transferrin saturations (T-Sat)
    - C Reactive Protein (CRP)
    - Renal function (Renal profile, Creatinine, eGFR)
    - Folate and Vitamin B12
    - Reticulocyte haemoglobin content (CHr) where available
  - If relevant, also consider:
    - Liver function tests
    - Tests for coeliac disease if malabsorption likely
- Clearly document the decision to continue, withhold or discontinue any medications in the medical notes
- Give advice to patients about whether to stop anticoagulants (and other medications that may increase the risk of bleeding) before elective surgery, and if so how and when (see UKCPA for the latest recommendations)
- Proceed with surgery if the patient is undergoing minor surgery, or surgery with blood loss expected ≤500ml whilst anaemia investigation and treatment continues[26]
- Use a shared decision making process to inform postponement of major surgery to facilitate diagnosis and management of anaemia[26]

- Document whether the patient is being referred back to primary care for further assessment and inform the patient accordingly. This information should include detail on when results might be available and the Hb threshold for surgery to proceed
- Ensure documentation of who will review results of investigations for cause of anaemia and plan further treatment
- Investigate for malignancy in case of new true iron deficiency anaemia, and simultaneously start replacement of iron[26]
- Discuss treatment options for the type of anaemia identified with the patient (see Figure 7). For iron deficiency anaemia and functional iron deficiency:
  - PBM should start at the time surgery is booked and continue through to full recovery
  - f the interval before surgery is at least four weeks and there are no contraindications, provide dietary advice and start oral iron (any commercially available iron preparation – one tablet per day or one/two tablets alternate days (may be as effective but better tolerated).[5] (More detail is included in the section on iron dosing)
  - If surgery is within four weeks, then consider postponing surgery or initiating IV. iron therapy
  - If oral iron is contraindicated or poorly tolerated, then IV. iron should be administered
  - Routine preoperative use of erythropoietin is not recommended; however, it may be beneficial in functional iron deficiency where there is insufficient response to iron replacement[37]
  - Non-anaemic iron deficiency requires specific strategies for detection and treatment. If there is significant expected intraoperative blood loss and/or risk of developing postoperative anaemia, consider oral iron administration
  - Document patient preference on use of blood products
  - Provide advice to patients on optimisation of physiological reserve, eg physical activity and exercise[38]
- Ensure coexisting medical comorbidities are assessed and optimised to improve physiological reserve (eg optimisation of chronic obstructive airways disease or cardiac disease[39])
- Consider specific preoperative interventions to minimise intraoperative blood loss, eg embolisation of tumours.[40]

RECOMMENDATIONS FOR STAFF ADMITTING EMERGENCY PATIENTS FOR SURGERY

In addition to the recommendations above, staff working with patients admitted through emergency departments or surgical admission units should:

- Ensure robust admission processes are in place to identify those patients with a history of blood loss (acute or chronic), symptoms or clinical features suggestive of anaemia and/or hypovolaemia
- Document cardiovascular status including assessment for hypovolaemia or shock as this may mean measured Hb is falsely high
- Complete urgent serum blood tests to include: Hb, Ferritin, T-Sats, CRP, eGFR or Creatinine, B12 and folate, and LFTs, Lactate and Group & Save if relevant (see Figure 6)
- Consider point of care testing, such as haemoglobin concentration screen (Hemocue®) or blood gas analysis (venous or arterial) on admission to identify anaemia
- Activate Major Haemorrhage Protocol early if major blood loss or signs of shock
- Consider bleeding risk and how to mitigate this. Clearly document the decision to continue, withhold or discontinue any medications
- Differentiate resuscitation from assessment and optimisation of anaemia[41]
- Develop specialty specific protocols for preoperative optimisation then intraoperative and postoperative management of patients with anaemia, particularly in those with frailty
- Ensure early senior decision making regarding timing and urgency of operative intervention
- Use a shared decision making process to consent for blood transfusion and conservation techniques
- Specific specialties:
  - Urology patients with haematuria are often on antiplatelet or anticoagulant medication. Some reversal agents may be indicated – see the UKCPA for further advice
  - Vascular – Critical Limb Ischaemia (CLI) patients may need higher blood transfusion thresholds
  - Hip fracture patients – 19% of patients are under-resuscitated and 50% are anaemic preoperatively.[42] Many benefit from early resuscitation, including consideration of early blood transfusion[43]
  - Emergency general surgery – patients are very varied and have a higher incidence of perioperative blood transfusion
  - The National Emergency Laparotomy Audit (NELA) reports-only 24% of patients over 70 had geriatrician input.[44] Standard protocols are helpful especially out-of-hours.

RECOMMENDATIONS FOR ALL STAFF IN THEATRE AND RECOVERY

Staff working in theatre and recovery or PACU (Post Anaesthetic Care Unit) should:

- Adhere to the three pillars of patient blood management:
  - timely and appropriate management of anaemia
  - prevention of blood loss
  - optimising the patient's physiological tolerance including restrictive transfusion where appropriate[45,46]
- Use the five steps for safer surgery (briefing, sign-in, timeout, sign-out and debriefing) in the WHO Surgical Safety Checklist[47] to discuss and plan ahead for the blood management of each patient on the operating list
- Control blood pressure carefully in the intra and postoperative setting
- Use point of care haemoglobin and coagulation monitoring when required
- Use intravenous fluids judiciously and avoid haemodilution
- Make appropriate use of anti-fibrinolytics (ie Tranexamic acid). See NICE guidelines on this topic[48]
- Consider techniques to minimise blood loss including tourniquets, meticulous haemostasis and laparoscopic surgery
- If considering the benefit versus cost of using cell salvage, or if the team are unable to predict blood loss during the proposed surgery, consider initially setting up equipment for 'collection only'
- Consider blood transfusion when haemoglobin levels <70g/.[49] The theatre and recovery team should be aware of the transfusion threshold individualised to the patient[50]
- Undertake risk assessment prior to every unit of blood transfused, which considers the perception of risk of both perioperative anaemia and blood transfusion[51]
- Re-check haemoglobin levels between each unit of blood, unless actively haemorrhaging, and utilise point of care testing to inform decision making[45,46,50,52]
- All perioperative personnel should be aware of the major haemorrhage protocols of their organisation and understand their role in relation to major transfusion procedures.[53]

RECOMMENDATIONS FOR PERSONNEL IN SCRUB AND CIRCULATING ROLES

Nurses, operating department practitioners (ODPs) and theatre support workers should work collaboratively to:

- Maintain awareness of the potential for blood loss, including the surgical procedures and patients most at risk[50]
- Monitor blood loss throughout the procedure, including blood loss in suction canisters, in surgical swabs, clots and the surgical drapes[54]
- Ensure the volume of suction, irrigation volume and fluid output is visible or recorded, such as ensuring the urometer is visible
- Communicate accurate and timely blood loss estimates with the team to enable effective decision making, and ensure blood loss estimates are clearly visible to the anaesthetist throughout the procedure[55,56]
- Ensure staff are trained and maintain competence in the use of cell salvage systems,[57] including indications for use[58]
- Swab washing may be considered to allow blood that would normally be lost in swabs, to be salvaged during intraoperative cell salvage. This can significantly increase the volume of RBCs for reinfusion. Follow guidance from Joint Professional Advisory Committee (JPAC) for the correct procedure[58]
- Intraoperative Cell Salvage can be useful for: spinal surgery, penetrating trauma, gynaecological surgery including ectopic, urology and cardiac surgery.

RECOMMENDATIONS FOR THE INTRAOPERATIVE TEAM

- Perform meticulous surgical technique to minimise blood loss[45,50,57,59]
- Consider prophylactic antifibrinolytics to reduce blood loss prior to the removal of a tourniquet[60]
- Consider topical haemostatic agents to assist with localised bleeding[59,61]
- Consider the use of cell salvage where appropriate.[50,61,62] Positive outcomes are reported in major surgery, including revision hip arthroplasty[52,63]
- Consider invasive haemodynamic monitoring in all high risk procedures[45]
- Maintain physiological measurements within optimal parameters for haemostasis, including normothermia, to maintain core temperature ≥36°C and pH >7.2[45,59,61]
- Consider utilising a hypotensive anaesthesia approach for specific surgical procedures in order to reduce intraoperative blood loss. The benefits and risks need to be outlined beforehand[50,64]
- Make informed decisions about transfusion of blood products using information concerning the ongoing bleeding rate, intravascular volume status, signs of organ ischaemia, point of care testing and cardio-pulmonary reserve for compensation[52]
- Consider antifibrinolytic (ie tranexamic acid) if expected blood loss >500ml[40,50]
- Optimise cardiovascular and pulmonary tolerance of intraoperative anaemia[45]
- Consider perioperative haemodynamic goal directed therapy (GDT) in high-risk surgical patients.

RECOMMENDATIONS FOR ANAEMIA IN PREGNANCY WITH POTENTIAL SURGERY

- Healthcare workers should be aware that iron deficiency is the most common cause of anaemia in pregnancy and the risk of iron deficiency should be considered in all pregnant women[65]
- Haemoglobin concentration should be routinely measured at booking and at around 28 weeks' gestation or 20 weeks in multiple pregnancy[66]
- Systems must be in place for timely review of blood test results, including monitoring the response to therapy[67]
- Other than pregnancy if no other cause of anaemia is found a diagnostic trial of oral iron should be given without delay, with a repeat FBC in two to three weeks[65]
- Serum ferritin should be measured in women with a known haemoglobinopathy to identify concomitant iron deficiency and exclude iron loading states
- Non-anaemic women at risk of iron deficiency should be identified and either started on prophylactic iron empirically or have serum ferritin checked first[65]
- A serum ferritin level of<30µg/l in pregnancy is indicative of iron deficiency. Levels higher than this do not rule out iron deficiency or depletion[65]
- All pregnant women should receive dietary advice[65]
- Ferrous iron salts are the current preparation of choice for oral iron supplementation[65]
- Consider alternate day dosing[65]
- A trial of oral iron should be considered as the first line diagnostic test for normocytic or microcytic anaemia in pregnant women with no haemoglobinopathy. Absorption of iron can be promoted by morning dosage, one hour pre-food.-Tolerance and efficacy of oral iron can be improved by reducing dosage or frequency, laxatives for constipation, and antacids (rather than proton pump inhibitors) for heartburn
- In women with unknown haemoglobinopathy status, a trial of iron should be offered. However, haemoglobinopathy screening should be undertaken without delay in accordance with the NHS sickle cell and thalassaemia screening programme guideline, but with awareness that iron deficiency can lower the haemoglobin A2 percentage[66]
- IV. iron should be considered from the second trimester onwards for women with confirmed iron deficiency anaemia who are intolerant of, or do not to respond to, oral iron[65]
- IV. iron should be considered in women who present after 34 weeks' gestation with confirmed iron deficiency anaemia and a Hb of<100g/L[65]. A Cochrane review[69] suggested that it was associated with a greater improvement in haematological indices, that its effects lasted up to three months and that it avoided side effects such as heartburn and constipation. It does however carry the risk of anaphylaxis
- Women with iron deficiency anaemia with a Hb of <100g/L should deliver in an obstetrician-led unit[65]
- Consider the use of cell salvage where appropriate intraoperatively
- Women with iron deficiency anaemia should have active management of the third stage of labour[65]
- All women with over 500ml blood loss should have Hb check within 48 hours[65]
- Units need to promote a care pathway (with pharmacy and haematology) that facilitates administration of IV. iron postpartum to women who are previously intolerant of, or do not respond to, oral iron and/or where the severity of symptoms of anaemia requires prompt management[65]
- Obstetric units should have guidelines for the criteria to be used for postnatal red cell transfusion in anaemic women who are not actively bleeding.[65]

RECOMMENDATIONS FOR STAFF INVOLVED WITH CHILDREN WITH ANAEMIA UNDERGOING SURGERY

Guidelines specific to the perioperative management of paediatric patients undergoing surgery at risk of bleeding and transfusion are available, as are specific paediatric blood management strategies.[3,67,68,70]

Specific perioperative recommendations:

- Preoperative Hb should be optimised by treating iron deficiency anaemia (see Figure 13)
- Tranexamic acid should be considered in all children undergoing surgery where there is risk of significant bleeding (see detailed paediatric section for dosing)
- Red cell salvage should be considered in all children at risk of significant bleeding undergoing surgery, children undergoing cardiac surgery with cardiopulmonary bypass (CPB) and where transfusion may be required
- A postoperative Hb transfusion threshold of 70g/L should be used in stable patients without major comorbidity or bleeding
- For surgery in neonates, use the same transfusion triggers used for non-surgical neonates, but adjust according to level of respiratory support and post-natal age (see Figure 12)
- Transfusion volumes for non-bleeding infants and children should be calculated to take the post-transfusion Hb to no more than 20g/L above the transfusion threshold. The following calculation may be used:

$$\textit{Volume to transfuse}\ (\text{ml}) = \frac{\text{Desired Hb (g/l)} - \text{Actual Hb (g/l)} \times \text{Weight (kg)} \times \text{Factor}}{10}$$

  It is reasonable to use a factor of 4 to avoid over-transfusion, but this should be assessed on an individual patient basis. 4ml/kg approximates to a one unit transfusion for a 70–80kg adult, typically giving an Hb increment of 10g/L[69]
- When using a restrictive red blood cell transfusion threshold, consider a threshold of 70g/L and a haemoglobin concentration target of 70–90g/L after transfusion
- There is insufficient evidence to make a recommendation regarding an appropriate transfusion threshold during cardiopulmonary bypass (CPB) for non-cyanotic or cyanotic patients
- For stable children with non-cyanotic heart disease, a restrictive transfusion threshold of 70g/L following CPB is recommended. There is insufficient evidence to make a recommendation for children with cyanotic heart disease
- In neonates (both cyanotic and non-cyanotic) or actively bleeding or unstable children following CPB, a higher Hb threshold may be appropriate, and signs of inadequate oxygen delivery can provide additional information to support transfusion
- Patients should be reassessed clinically and Hb checked after each unit of red blood cell they receive unless they are bleeding
- Where Hb monitoring is feasible and available, via point of care sampling or non-invasively, this should be used to ensure the smallest necessary volume is transfused over three to four hours, although more rapid rates should be used in hypovolaemia
- It is recommended that recipients under one year of age be transfused with components with neonatal/infant specification, eg Paedipacks
- Hospitals should develop policies to minimize exposure of infants to multiple donors.

RECOMMENDATIONS FOR STAFF DELIVERING POSTOPERATIVE WARD CARE

- Ensure regular review to assess degree of postoperative bleeding and prompt surgical review to consider need for early return to theatre
- Check Hb postoperatively based on local policies or patient symptoms. Be aware that Hb will be falsely elevated in hypovolaemic patients
- Use haemoglobin and coagulation status point of care tests where indicated
- Staff should be aware that postoperative anaemia is common (affecting up to 90% of patients) following major surgery. The main causes include:
  - Preoperative anaemia
  - Perioperative blood loss
  - Blood sampling
- Mobilise early and not according to Hb levels
- Discharge from hospital should not be solely determined by Hb level
- Do not prescribe oral iron in the immediate postoperative period (postoperative inflammatory response releases hepcidin reducing gut absorption of iron)[26]
- Note that current evidence for use of postoperative intravenous iron following lower limb arthroplasty, gastrectomy and postpartum haemorrhage is weak[4,26]
- Note that intravenous iron should be avoided or used with caution in active infection due to concerns it could worsen infection.[71]

RECOMMENDATIONS FOR SAFE AND EFFECTIVE COMMUNICATION, DISCHARGE AND FOLLOW UP

Consider using template letters to facilitate timely communication with primary care:

- Preoperatively
  - To describe anaemia, investigations, likely or definitive cause, follow up plans
  - To describe treatment initiated for anaemia (eg oral iron/IV. iron)
  - To clarify whether anaemia affects the patient pathway or not
- Postoperatively:
  - Provision of timely (day of discharge) written discharge documentation to the patient and primary care team to include, if a new anaemia has been found:
    - Cause of anaemia
    - Hb at discharge from hospital
    - Outstanding investigations (and who will need to follow up)
    - Treatment during admission and ongoing management plan
    - Information provided to patient (eg dietary advice)
    - Whether the patient has received any blood products

RECOMMENDATIONS FOR EDUCATION AND TRAINING

- Providers of undergraduate training for all healthcare professionals should consider the practicalities of how to include anaemia and PBM in relevant programmes. This may involve discussions on PBM rather than a focus on the practicalities of blood transfusion
- Healthcare providers should review the content of both induction and mandatory training updates about blood transfusion to ensure that anaemia and the principles of PBM are included
- Providers of postgraduate training programmes for all healthcare professionals should ensure that PBM principles are included in curriculum reviews and assessment
- Equipping the workforce:
  - all staff (including registered and other staff) who are involved in the surgical patient pathway should understand principles of PBM and complete eLfH (e-Learning for Heatlhcare) basic Skills for Healthcare on anaemia and blood management or equivalent
  - all registered staff members should complete eLfH intermediate Skills for Healthcare on anaemia and blood management or equivalent
  - perioperative leads should complete advanced Skills for Healthcare on anaemia and blood management or equivalent
  - all senior decision makers should have access to advanced training Skills for Healthcare on anaemia and blood management
- Clinical staff working in perioperative care settings should be aware of:
  - what information needs to be discussed with patients
  - what written or digital information is available for patients
- Administrative, managerial and clerical staff should be supported to undertake education about anaemia and should understand how to access information resources for patients
- Additional useful resources include:
  - NHS Blood and Transplant information on Patient Blood Management resources and education
  - Patient Blood Management information is available on the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) website
  - NHS Blood and Transplant The Preoperative anaemia Toolkit
  - NHS Blood and Transplant The Patient Blood Management Toolkit
  - Specific anaemia eLearning modules are available on e-LfH, for which all healthcare professionals can register for access. Modules include:
    - Anaemia – the only introduction you need
    - Anaemia in primary care patients
    - Anaemia in hospital patients
- Blooducation podcast on Patient Blood Management and Iron deficiency
- Questions and answers on iron deficiency treatment selection and the use of intravenous iron in routine clinical practice.

RECOMMENDATIONS FOR QUALITY IMPROVEMENT

The clinical lead for perioperative anaemia should support implementation of this guideline, through local quality improvement programmes. This will require:

- patient and public involvement in co-design/co-production
- identification of local key performance indicators based on the metrics below
- collaboration with local data analysts/informatics to support robust data collection (ideally through linkage with existing datasets, for example Getting it Right First Time, Perioperative Quality Improvement Programme, Healthcare Quality Improvement Partnership)
- local measurement using a time series approach (eg statistical process control charts)
- local collaborative, interdisciplinary audit/morbidity/mortality meetings to review the data and inform quality improvement programmes

To support measurement for improvement the following metrics may be used:

Metrics to support the development of the clinical pathway

- Number/proportion of patients presenting for major surgery identified to have anaemia
- Number/proportion of patients with anaemia who required an intervention (eg iron infusion, blood transfusion) preoperatively
- Number/proportion of patients with anaemia who required an intervention (eg blood transfusion) intraoperatively
- Number/proportion of patients with anaemia who have required an intervention (eg iron infusion, blood transfusion) postoperatively
- Number/proportion of patients with anaemia who have had surgery postponed/cancelled
- Number/proportion of patients with anaemia who are referred postoperatively for further follow-up or management of anaemia at discharge
- Number/proportion of patients living with anaemia who have documentation of treatment escalation plans and advance care plans (eg Jehovah's Witness)

Metrics to measure process

- Availability of hospital guideline for detection and management of anaemia applicable to the perioperative setting
- Length of hospital stay of patients undergoing major surgery who have anaemia
- Length of hospital stay of patients undergoing major surgery who have needed an intervention (eg blood transfusion) to treat their anaemia
- 30-day readmission in patients with anaemia undergoing surgery

Metrics to measure patient reported outcomes

- Decisional regret
- Satisfaction with shared decision making (eg using SDMQ9)
- Quality of life measures such as EQ-5D-5L

Metrics to support workforce development

- Number/proportion of staff working in perioperative care settings who have completed training up to (and including) eLFH level 3 training or equivalent
- Availability of a team to support/deliver perioperative management of anaemia.

RECOMMENDATIONS FOR RESEARCH

- What are the barriers and enablers in implementing perioperative anaemia services on a national scale (examining feasibility, acceptability, uptake, fidelity)?
- What is the clinical and cost effectiveness of perioperative anaemia services in the elective and/or emergency surgical setting?
- What is the interface between perioperative services for anaemia and other perioperative services (eg frailty, diabetes, hypertension etc)
- What is the experience for patients living with anaemia of:
  - undergoing preoperative treatment for anaemia?
  - delays or cancellation of surgery related to diagnosis of anaemia?
  - the impact of surgery on longer term functional and psychological recovery?
- How can we improve quality of perioperative consultations for patients living with anaemia?
- Can we develop decision aid tools for patients living with anaemia undergoing surgery?
- What is the skillset required for teams providing perioperative care for the detection and treatment of people with anaemia? (In particular, for services running at nights, weekends or 168 hours per week, what is the minimum skillset required when specialised staff are not available)
- What is the role of postoperative oral iron administration?
- What is the optimal paediatric oral iron dosing?

GUIDELINE FOR THE MANAGEMENT OF ANAEMIA IN THE PERIOPERATIVE PATHWAY

Background

Anaemia is a condition in which there is a reduced number of red blood cells (RBCs) resulting in a lower oxygen carrying capacity. It is a common finding in the preoperative period, with a reported prevalence of around 35% in the surgical population, varying between 5% and 75% across specialties.[72] Symptoms include fatigue (tiredness), breathlessness and feeling faint;[1] however, there may be no symptoms. It is measured in the blood by the level of haemoglobin (Hb). Preoperative anaemia is associated with adverse perioperative outcomes and is an independent predictive risk factor for increased postoperative morbidity and mortality.[15] The presence of anaemia also substantially increases healthcare costs in surgical patients,[7] with additional costs incurred in the community.[34] Blood transfusions in the perioperative period are associated with poor outcomes and their use should be restricted to those with clinical instability,[15] acute symptoms requiring immediate correction or poor physiological reserve. Effective strategies used to treat perioperative anaemia without giving blood transfusions include oral or intravenous (IV.) iron therapy, correcting nutritional deficiencies (iron, vitamin B12 or folate) and giving erythropoietin stimulating therapy. Iron supplementation for elective procedures may require the postponement of surgery to facilitate optimisation and for urgent procedures there is support for the use of IV. iron to minimise any further delay in treatment.[26] Anaemia is a marker of physiological sub-optimal status and should be included in a shared decision making discussion with the patient around optimisation and whether the surgery should proceed.

Definition of Anaemia

The World Health Organization (WHO) and the National Institute for Health and Care Excellence (NICE) define anaemia as a haemoglobin (Hb) concentration below 130g/L in men over 15 years of age,[1,73] below 120g/L in non-pregnant women over 15 years of age and below 110g/L in pregnant women in the second and third trimester. This threshold adopted by WHO since 1968 is based on healthy and predominantly white populations. WHO is currently reviewing these definitions which are likely to change.[74]

There is growing opinion,[75] with an international consensus statement[26] suggesting that a Hb concentration ≤120g/L in women is suboptimal and that a preoperative Hb target of ≥130g/L in both sexes should be used.[76,77] Different thresholds reduce the option to improve health and may perpetuate other inequalities.[78] Women who menstruate are more likely to be anaemic due to iron deficiency, have a smaller circulating blood volume compared with men and may lose a proportionally higher blood volume when undergoing the same surgical procedure therefore the transfusion trigger may be reached sooner. Worse outcomes are observed in women than men with anaemia following cardiac surgery.[79] A number of institutions already use a definition of anaemia as Hb ≤130g/L for both sexes. Whilst adopting this may lead to many women being labelled 'anaemic' this provides an opportunity

for early identification and treatment of iron deficiency anaemia for long term health benefits. The algorithms have been developed to provide a structured approach whilst allowing individualised care. The definition of anaemia is based on age (Figure 1).

Figure 1 Definition of anaemia (based on: WHO definition of anaemia)[1,80]

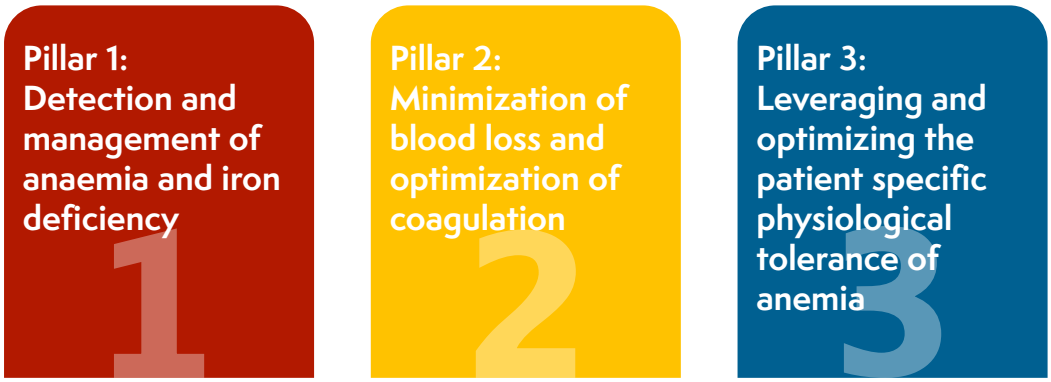
Age (years)	Haemoglobin (g/L)
<5	110
5–11	115
12–15	120
Non-pregnant girls over 15	120
Boys over 15 years and men	130
Non-pregnant women	120 (WHO definition) 130 (International consensus definition)
Pregnant women	110

A Patient Blood Management (PBM) approach

Patient Blood Management (PBM) is a multidisciplinary, evidence-based approach to optimising the care of patients who might need a blood transfusion. It brings together a number of national and international initiatives over the past 20 years to put the patient at the heart of decisions. PBM is a clinical concept which aims to avoid unnecessary blood transfusions and improve patient safety and outcomes. It centres on three 'pillars' of care (Figure 2):[1]

1. Detection and management of anaemia
2. Minimisation of blood loss
3. Optimising the patient's physiological tolerance of anaemia

Figure 2 The three pillars of Patient Blood Management (PBM)[1]



Strategies employed for minimisation of blood loss and correction of anaemia are relevant for all three phases of the perioperative pathway, preoperative, intraoperative and postoperative, and should be specified in individualised PBM plans. Allogenic blood transfusions are commonly and frequently

inappropriately given to treat anaemia in the perioperative setting and may be associated with adverse outcome: transfusion reactions, adverse cardiovascular events, recurrence of cancer, financial cost and increased mortality.[81,82] Blood transfusions for any person who may become pregnant in the future are a particular cause of concern, because creation of antibodies can cause Haemolytic disease of the newborn or recurrent miscarriages; whilst Rhesus antibodies are well known, others are implicated. Furthermore, blood is a finite resource.

There are effective strategies used to treat pre and postoperative anaemia without giving blood transfusions which include intravenous iron infusions, correcting nutritional deficiencies and giving erythropoietin stimulating therapy, where indicated.[83]

There remain scenarios where preoperative blood transfusions are the correct approach, such as inherited anaemias, some myelodysplastic syndromes or where there is insufficient time to optimise the anaemia and transfusion remains an effective intervention.

An example of PBM – restrictive or liberal transfusion triggers

NICE and NHS Blood and Transplant (NHSBT) recommend having a restrictive blood transfusion trigger of Hb ≤70g/L (with a target of 70–90g/L after transfusion) in patients who do not have major haemorrhage, acute coronary syndrome (ACS) or chronic anaemia requiring regular blood transfusions.[3]

A transfusion threshold of Hb ≤80g/L should be considered in patients with ACS (with a post-transfusion target of 80–100g/L).

Individual transfusion thresholds should be considered for patients with chronic anaemia who require regular blood transfusions.

It is deemed best practice to administer single-unit blood transfusions (or equivalent based upon body weight for children) if there is no active bleeding. Clinical assessment and checking of Hb is recommended prior to further transfusions.[84]

An example of PBM – intraoperative strategies to reduce bleeding

The Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 2 (CRASH-2) trial showed that early administration of tranexamic acid to bleeding trauma patients reduced the risk of death. Tranexamic acid (an antifibrinolytic) is inexpensive, safe and reduces mortality in traumatic haemorrhage and bleeding and transfusion in many surgical procedures.[84]

Intraoperative techniques to reduce bleeding during surgery are highly effective. Tourniquets and good haemostasis are important. Measurement of blood loss and involvement of the whole team help this.

One meta-analysis of PBM interventions showed the two most effective interventions for reducing bleeding and transfusions in major surgery were use of tranexamic acid and having a restrictive transfusion trigger;[25] thus addressing preoperative anaemia should occur alongside other approaches.[1]

Types of anaemia and causes

There are several types of anaemia, each with different causes and management (see Figure 3).

Iron deficiency anaemia and difficulties with testing

The commonest cause of anaemia is iron deficiency (ID) which is estimated to affect two billion people globally. ID, with or without anaemia, may be a feature of underlying disease such as gastrointestinal malignancy, chronic renal disease, heart failure, inflammatory arthritis and inflammatory bowel disease. These underlying disease states may worsen perioperative outcomes and should be taken into consideration during preoperative optimisation. Perioperative anaemia is an independent risk factor for increased length of hospital and intensive care stay, postoperative medical and surgical complications, and increased mortality.[15]

The causes of iron deficiency anaemia are:

1 Increased losses (eg inflammatory bowel disease, heavy periods, haematuria, gastrointestinal bleeding)
2 Limited supply (eg poor dietary intake, malabsorption – coeliac disease, post-bariatric surgery)
3 Increased demand (eg infancy and growth during adolescence)

Assessment of iron deficiency anaemia requires a careful history, clinical examination and interpretation of a set of laboratory tests in the absence of a single diagnostic assay. For example, 5% of people with Iron Deficiency Anaemia are found to have coeliac disease, so testing for this should be considered.[85]

Total body iron content is typically 50mg/kg body weight (3–4g iron in males and 2–3g iron in females). The majority of iron (approximately 70%) is distributed in haemoglobin, 10% as myoglobin in muscle, 15–20% is stored in the liver and reticuloendothelial system and approximately 100mg can be found as haem and in tissues and cytochromes.[86] Approximately 25mg per day is required for the bone marrow to produce red blood cells (RBCs) however only 1–2mg per day is absorbed from the gut. The remaining iron is provided by recycling senescent RBCs. Iron is not only used to make red blood cells (erythropoiesis) but is also essential for oxygen transport, cellular respiration, formation of adenosine triphosphate (ATP) and is an integral component of the immune system.

Ferritin is an intracellular protein that stores iron. It is a large protein which provides a reservoir for iron storage but also allows non-toxic iron to be sequestered in times of metabolic need. **Serum ferritin** can be measured and when low (<30mcg/L) is indicative of ID anaemia; a level below 15mcg/L is diagnostic of absolute iron deficiency.[87]

Serum ferritin is an acute phase protein and levels are elevated in chronic inflammatory states such as inflammatory bowel disease and autoimmune arthropathy. As a consequence, ID can be present with normal serum ferritin levels. Inflammatory markers and other tests will aid diagnostics. Serum ferritin levels are also raised in chronic liver disease and hence a normal ferritin level does not exclude iron deficiency. A serum ferritin level of less than 50mcg/L, or less than 100mcg/L in the context of chronic kidney disease (CKD) is strongly suggestive of iron deficiency even in the presence of concurrent inflammation. Serum C reactive protein (**CRP**) is included in the recommended 'battery of tests' as an aid to interpretation of serum ferritin levels. Liver function tests **(LFTs)** can be requested if relevant.

Recently absorbed (or sequestered) iron is bound to transferrin, a transfer protein, for distribution around the body. Transferrin can bind 1–2 atoms of iron and these usually occupy 30% of available binding sites. Serum transferrin saturation (**T-Sat**) is a marker of iron transfer to the bone marrow and is a useful additional test even in the context of coexisting inflammatory states: a level of <20% is suggestive of absolute iron deficiency, even if serum ferritin is not reduced. However, T-Sat fluctuates due to diurnal variations of serum iron, and serum iron levels also decrease in infection, inflammation, and malignancy and increase in liver disease. Serum iron is not sufficiently sensitive or specific for determining iron status and should not be used in isolation.[88]

CHr (reticulocytes haemoglobin content) reflects the amount of iron available for haemoglobin production in the bone marrow. CHr, requested alongside **reticulocyte count** as additional parameters with FBC requests, is becoming commonly available with the use of modern fully automated blood differential counters and should be checked where available. CHr is a useful marker of iron status and a value less than 30pg serves as a sensitive marker of iron deficiency.[89] There are limitations of CHr as it is also low in the presence of other causes of hypochromic microcytic red cell indices, such as patients with thalassaemia and carrier states.[90] However, it is a very useful adjunctive tool in overall assessment of iron status. CHr and reticulocyte counts also serve as useful indicators of response to iron replacement therapy.

In established chronic iron deficiency, a **FBC** typically has a low MCV (Mean Corpuscular Volume) meaning size of red cells, with a 'microcytic picture'; and a low MCH (Mean Corpuscular Haemoglobin) with low colour or 'hypochromic'.

Low MCV and MCH values are also seen in various types of thalassaemia and carrier states. Furthermore, normal values do not exclude iron deficiency. Indeed, as many as 40% of iron deficiency anaemias have normal MCV.[91] MCV and MCH should not be relied upon to diagnose or exclude iron deficiency.

Hepcidin is a protein hormone. High levels occur with inflammation and reduce iron absorption in the gut. Hepcidin also increases after surgery and may make intake of oral iron less effective.

Functional iron deficiency

Functional Iron deficiency is also known as 'anaemia of chronic disease' and is the second most common cause of anaemia worldwide. It is essentially a multifactorial anaemia and is associated with a variety of chronic and inflammatory diseases such as infection, autoimmune diseases, chronic kidney disease or malignancy. The underlying pathophysiology is complex and includes reduced absorption of iron from the gastrointestinal (GI) tract and sequestration of iron in macrophages both due to an increase in hepcidin levels, resulting in reduced availability for erythropoiesis (functional iron deficiency). Additionally, suboptimal production and effectiveness of erythropoietin and probably reduced red cell life span due to increased macrophage activity resulting in haemophagocytosis also contribute.[92] Oral iron supplementation is unlikely to be of benefit in this scenario due to hepcidin's function in blocking absorption of iron from the GI tract, and intravenous iron supplementation may be necessary.[93]

An estimated glomerular filtration rate (eGFR) can be calculated from a serum blood test as a measure of kidney function. CKD is a potential cause for anaemia in anyone with eGFR of less than 60mL/min/1.73m^2, even with normal T-Sat and Ferritin.[94]

The diagnosis of functional iron deficiency is essentially a process of exclusion of absolute iron deficiency and other causes of nutritional deficiency anaemia such as vitamin B12 and folate deficiencies. Additionally, if anaemia coexists with other abnormalities of blood counts such as significant leucopenia, leucocytosis and or thrombocytopenia, additional haematological investigations may be necessary to exclude rarer haematological causes of anaemia.

No single laboratory parameter is diagnostic. Serum iron levels are typically very low or low normal in functional iron deficiency, and ferritin is typically normal or moderately high. CHr may be normal or low. Serum Hepcidin levels are typically elevated, but this assay is still not available routinely due to lack of standardisation between methods and laboratories. Generally, functional iron deficiency is determined by a normal or high ferritin in the context of a T-Sat <20% and frequently an elevated CRP, even just mildly. It is a good rule of thumb that true iron deficiency is very unlikely if ferritin is >100mcg/L and T-Sat>20%.

B12 deficiency and folate deficiency

Serum vitamin **B12** and **Folate** levels should be routinely checked as part of recommended 'battery of tests' and deficiencies corrected. B12 deficiency and folate deficiency typically cause macrocytic anaemia (meaning large red blood cells and high MCV). With co-existing iron deficiency, MCV may appear in the normal range. B12 deficiency is very common, affecting 20% of the UK population over the age of 65.[95]

Vitamin B12 deficiency causes many symptoms, including balance problems and joint pain, that may present as, or mimic, surgical conditions.[96] Once recognised, the deficiency is easy to treat.[97]

The prevalence of B12 deficiency is increasing as it is very difficult to obtain B12 requirements from a plant-based diet and vegan diets are increasingly popular. Medications including proton pump inhibitors, H2-receptor antagonists, metformin and colchicine are also linked to B12 deficiency.[98] Vitamin B12 is poorly absorbed orally, especially after total or partial gastrectomy, ileal resection or Crohn's disease or with congenital intrinsic factor deficiency. Many supplements are insufficient. B12 is difficult to measure and tests can be falsely reassuring.[99]

Treatment of B12 deficiency includes initial treatment with hydroxocobalamin 1mg intramuscularly (IM) three times a week for two weeks.[6] This is followed by either oral maintenance treatment (cyanocobalamin) or IM maintenance treatment (hydroxocobalamin) depending on likely cause – see NICE for more details.[6]

Folate deficiency is often caused by insufficient dietary intake either alone or in combination with increased folate usage, or malabsorption. Causes include medications (including alcohol, anticonvulsants, nitrofurantoin, sulfasalazine, methotrexate and trimethoprim), excessive requirements in pregnancy, malignancy, blood disorders, malabsorption or excessive urinary excretion. Folate is found in green leafy vegetables, broccoli, brussel sprouts, asparagus, peas, chickpeas, brown rice and liver.

Other causes of anaemia and specialist referral for additional investigations

There are several, relatively rare haematological causes of anaemia which warrant referral to a haematology department. Specific criteria for referral and further blood tests should be agreed locally and incorporated into the local algorithm. The finding of a haematological cause for anaemia, such as a new diagnosis of myelodysplastic syndrome, should not be an automatic reason for cancelling the operation until the patient has had full investigations including a bone marrow biopsy. In many cases this can happen after the operation.

Gastroenterology referral must be considered for all cases of unexplained and significant iron deficiency anaemia in adult men and postmenopausal women.[5]

A new diagnosis of significant renal impairment, discovered during the course of these investigations, should prompt a discussion with a Nephrologist. Referral criteria should be locally agreed with nephrology team.

Figure 3 Types of anaemia and causes

Type of anaemia	Causes
Iron deficiency anaemia	■ Excessive bleeding ● Menstrual bleeding ● Gastrointestinal blood loss ○ Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) ○ Gastrointestinal pathologies, including cancer ■ Reduced intake ● Diet deficient in iron ● Poor absorption of iron ○ Crohn's Disease ○ Coeliac Disease ○ Previous stomach/intestine surgery including bariatric surgery
Anaemia related to inflammation ALSO KNOWN AS: Functional iron deficiency/ anaemia of chronic disease/ anaemia of chronic inflammation	■ Chronic kidney disease ■ Congestive heart failure ■ Rheumatoid arthritis ■ Inflammatory bowel disease
Megaloblastic anaemia (B12 or folate deficiency)	■ Diet low in B12 (plant-based diets) ■ Poor absorption ● Pernicious anaemia ● Medications, eg long-term metformin, proton pump inhibitors, H2-receptor antagonists, colchicine
Inherited blood disorders	■ Sickle cell anaemia* ■ Thalassaemia ■ Rare inherited anaemias (eg Diamon-Blackfan anaemia) *Many patients with sickle cell anaemia will need an exchange transfusion. Management should be individualised and guided by haematology
Others	■ Copper deficiency can cause intractable anaemia.[100] It is required to produce haemoglobin and gut uptake is blocked by excess iron or zinc intake

Preoperative diagnosis of anaemia – testing strategy

Timing of investigations

All patients being considered for elective major surgery should be screened for anaemia at the earliest opportunity in their surgical referral pathway, where surgery is considered a likely outcome. Ideally this should take place in primary care setting as part of 'fit for referral' assessments. Where this opportunity has been missed in primary care, patients should be screened for anaemia at their first consultation. Early screening facilitates the optimisation of anaemia prior to surgery, ensuring that appropriate investigations and treatment can be instituted without delay and avoiding cancellation of operations further down the line.

Local algorithms and patient pathways for screening, diagnosis and preoperative treatment of anaemia should be designed in collaboration with primary care, surgical and anaesthetic teams, patient blood management team (Hospital Transfusion Team), haematology, nephrology, gastroenterology and pharmacy.

Preoperative assessments tend to occur late in surgical pathways and should not be routinely employed as the first opportunity to screen or diagnose anaemia in elective surgery. Relatively urgent surgical procedures entailing a risk of significant blood loss should incorporate within their pathways a process for diagnosis and treatment of anaemia at the earliest opportunity.

Failure of screening for anaemia in primary care or at initial surgical consultation should be regarded as a failure in the pathway and addressed as a quality improvement initiative.

Investigations

A FBC should be checked as the initial screening test. Alternatively, appropriately validated and well managed point of care Hb tests may be used as a screening tool to identify patients with low Haemoglobin at the earliest opportunity in their surgical pathway. Where a point of care test is used as a screen for anaemia, the diagnosis should be confirmed with a laboratory FBC.

All surgical clinics should have a clear pathway specifying actions and responsibilities to ensure the screening results are promptly reviewed. Patients identified as being anaemic should undergo a further set of blood tests or referrals, as recommended in flow chart (see Figure 6).

Many NHS Trusts or Health Boards have developed preoperative anaemia pathways which are broadly similar and take local organisational issues into consideration. The QISTAnaemia team found that allowing flexibility in the specifics of pathway development at each Trust was very important in getting these implemented and working, with wide involvement from staff.[101]

To minimise a delay to time of surgery, additional investigations should be undertaken simultaneously rather than sequential testing. Some units have a routine battery of tests including haematinics. Others are able to automatically request further blood tests if anaemia is identified in the initial FBC without then requiring further sampling from the patient. There is huge variation in IT infrastructure, which can help or hinder this process and allow comparison to what is normal for the patient in the past. Many people will know they are anaemic already and a clinical discussion may help plan care.

Whilst ordering multiple tests for each patient is costly and may not change that patient's care, the resources and disruption involved in dealing with cancellations, complications, longer stays, unwarranted surgery or sub-optimal surgical outcomes justify a thorough approach from the point of referring the patient for an operation. As with other aspects of perioperative care, what works best is an expected local pathway (such as common blood tests) and individualisation for patients where this is required.

The critical point is that anaemia is often diagnosed late. It should ideally be identified before or at the time of referral, or from the surgical clinic – using point of care testing if needed. When a patient is going for a CT scan, they routinely need a renal blood test before contrast, and a FBC should be done at that point. Hb should be done as a routine at entry point to the pathway, ideally before referral.

Testing for causes of anaemia and treatment can occur at the same time.

The British Society of Gastroenterology have produced recommendations[5], including:

- Further testing in iron deficiency anaemia should include urinalysis or urine microscopy to identify bleeding from the renal tract
- A third of men and post-menopausal women with iron deficiency anaemia will have a have an underlying pathological abnormality, most commonly in the gastrointestinal tract; we recommend that if they have newly diagnosed iron deficiency anaemia, they should generally be referred to gastroenterology for consideration of gastroscopy and colonoscopy
- In the elderly, the risks and benefits of invasive investigations should be weighed up against the likelihood of treatment and benefit.[5]

Considerations with emergency presentations

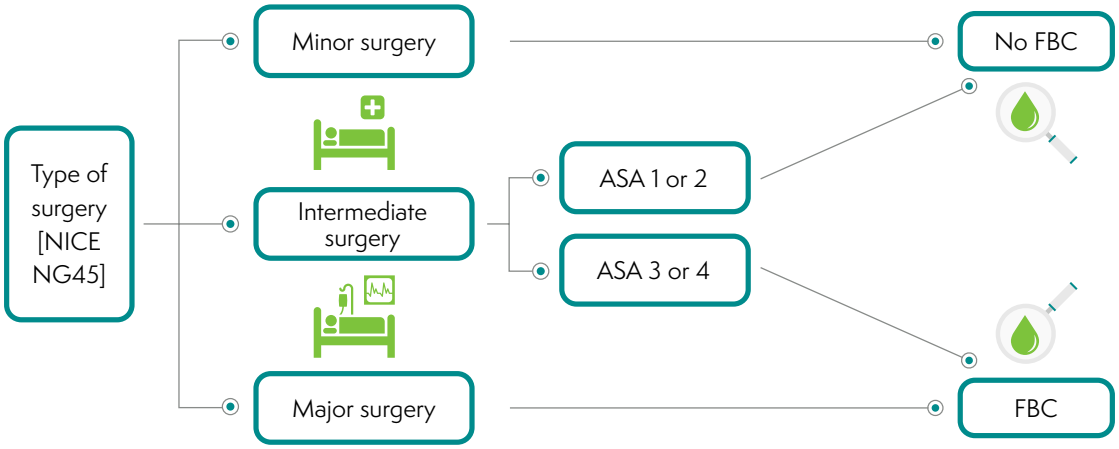
Many emergency presentations can be protocolised, to ensure early identification of information on which to plan interventions.

The incidence of anaemia is not well reported in emergency surgical patients but the general benefits of assessment and optimisation of anaemia, particularly in older surgical patients,[41,81] are well recognised. Large studies have identified that patients with anaemia are more likely to be higher risk of worse outcomes. Studies of emergency surgical patients found that more than 50% of those requiring emergency laparotomy were anaemic at presentation.[102] Preoperative anaemia was associated with increased length of stay, return to theatre, postoperative mortality and morbidity.[102] Intraoperative blood transfusion also carries risk and the effects of both are modified by the underlying pathology and treatment required.[103,104] In addition, in frail patients, preoperative anaemia is also associated with chronic or occult hypovolaemia and appropriate volume resuscitation is needed, rather than reliance on transfusion thresholds.[15,42,105]

Anaemia pathway

NICE guidance [NG45] on routine preoperative tests for elective surgery (Figure 4) recommends that a FBC is only needed for patients having major or complex surgery or those having intermediate surgery who are also ASA 3 (with severe systemic disease) or ASA 4 (with severe systemic disease that is a constant threat to life).[2]

Figure 4 NICE guidance on types of surgery requiring preoperative FBC blood test



For each patient, a series of steps should be considered (Figure 5). A senior clinician should make the decision on whether surgery should be delayed for treatment of anaemia, balancing the benefits against the risks of delay. Although most evidence shows preoperative anaemia is associated with adverse outcomes, the PREVENTT trial did not show a difference in perioperative outcomes between patients who received IV. iron preoperatively compared with those that did not.[35] This makes the actual shop floor decision making tricky. Hopefully, increasing awareness of the importance of recognising anaemia and treating it early in the pathway will reduce the incidence of these tricky decisions on the day of surgery, which sometimes lead to cancellations and wastage of valuable theatre slots.

Figure 5 Steps to consider for each patient

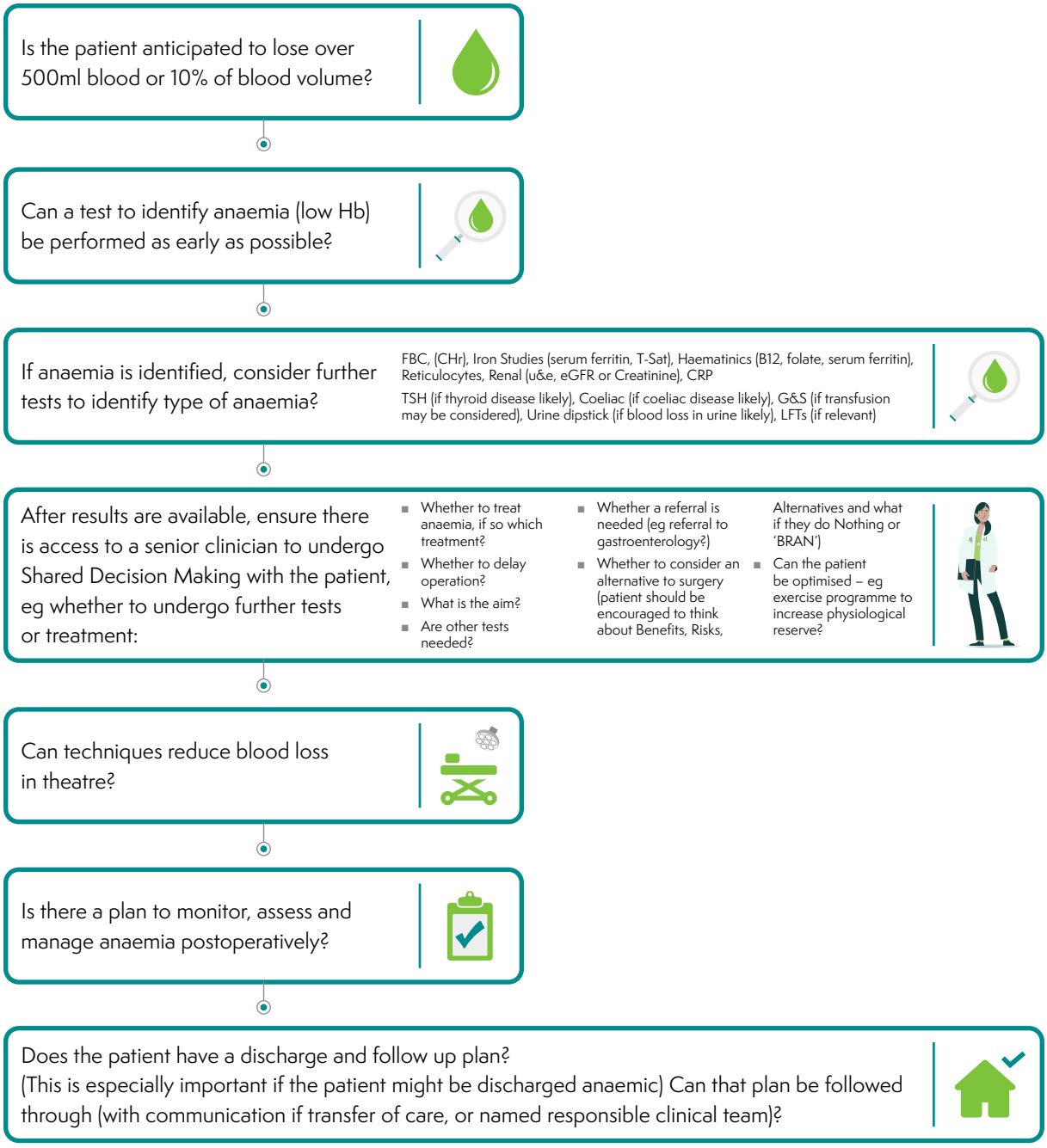
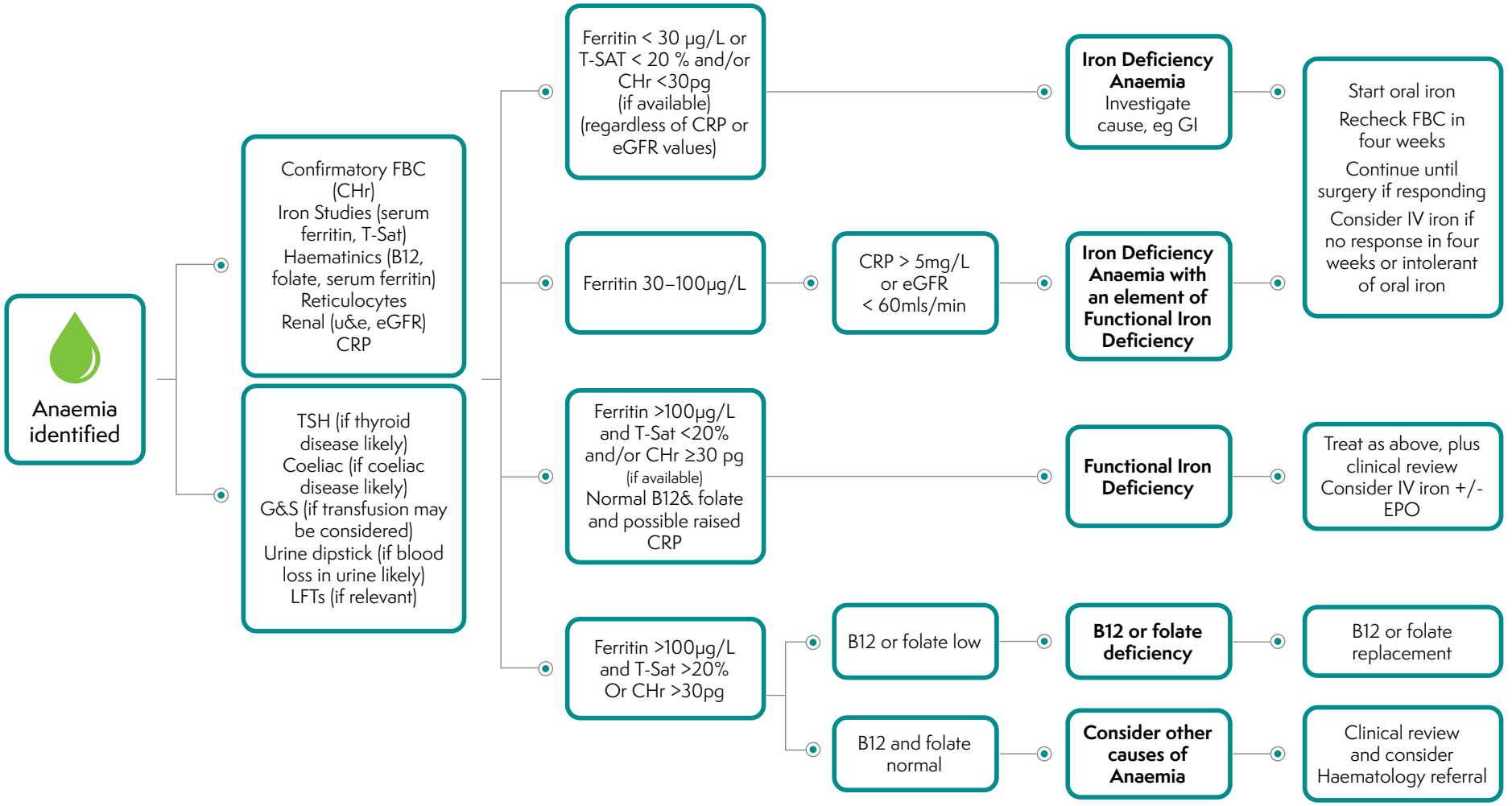


Figure 6 Suggested flow chart for establishing type of anaemia and management



Underpinning principles

- All decisions should be individualised to the patient with shared decision making
- Different services may have different sectors responsible for further investigations. This needs good communication
- Re-check Hb after intervention (eg at four weeks)
- If patient is known to have a specific type of long-standing anaemia, they may not need intensive testing, but their haematologist should be involved in planning their perioperative care
- If less than four weeks to surgery, IV. iron may be more appropriate than oral, or blood transfusion may be required
- If in doubt, seek senior review
- If new kidney disease, referral criteria should be determined locally in collaboration with nephrology

Patient blood management intervention options

Interventions should be tailored to the patient (see Figure 7). For example, if surgery is urgent and the patient is symptomatic with shortness of breath, treatment should start rapidly.

Figure 7 Intervention options for Patient Blood Management (PBM)

Intervention	Difficulties	Advice
Dietary improvements	■ B12 is poorly absorbed orally and is very difficult to get from a plant-based diet. The best source is shellfish and liver; legumes contain some ■ Iron is also poorly absorbed from the diet	■ Iron absorption can be increased if patients are advised to avoid drinking tea or eating phytates at the same time as iron. Iron tablets should be on an empty stomach. There is no evidence that Vitamin C aids absorption
Oral iron	■ Can take four weeks to be effective ■ If Hb has not incremented with oral iron four weeks before surgery then intravenous (IV.) iron therapy should be considered ■ Can cause constipation – an osmotic laxative, eg lactulose, may help which can be bought from a chemist ■ Can reduce absorption of other medications, eg may need to take iron four hours away from levothyroxine or two hours away from tetracycline or quinolone antibiotics – see BNF for advice. Can interact with Parkinson's medication (levodopa and entacapone) see BNF for advice.	■ Ferrous sulphate, fumarate or gluconate may be used; a daily dose of one tablet is practical (see section on dosing below and Figure 8) ■ Alternate day (with one or two tablets) may be better tolerated[26] and reduces the impact of hepcidin being stimulated which reduces absorption; side effects are also fewer ■ Oral iron should be taken on an empty stomach. Taking iron with meals can reduce bioavailability by up to 75%[5] ■ A good response to iron therapy (Hb rise ≥10g/L within two weeks in anaemic patients is highly suggestive of absolute iron deficiency[5]

IV. Iron	■ Needs careful monitoring as hypersensitivity-type and infusion reactions occur in 0.5% Anaphylaxis is a risk[106] ■ Can cause permanent skin discolouration if extravasation occurs ■ Need a protocol	■ Parenteral iron should be considered when oral iron is contraindicated, ineffective or not tolerated ■ If operation within four weeks, IV. iron should be considered ■ In emergency setting, IV. iron may help postoperatively ■ There are five commercially available preparations, with different dosing regimes (see section on iron dosing)
B12 and folate	■ Initial treatment for B12 deficiency involves an intramuscular (i.m.) injection	Treatment of B12 deficiency in people with no neurologic involvement should include:[6] ■ Initial treatment with hydroxocobalamin 1mg I.M. three times a week for two weeks followed by an oral or I.M. maintenance dose. See Vitamin B12 deficiency information[97]
Blood transfusion	■ Risks: incompatibility, infection, immunomodulation and difficulty cross-matching for future transfusions ■ Blood transfusions should be avoided in individuals who may become pregnant in the future because antibodies that are created can cause recurrent miscarriages or Haemolytic Disease of the Newborn ■ Errors also occasionally occur with catastrophic effects (see SHOT [Serious Harm of Transfusion] reports). Exposure to multiple donors, immune-modulation and risk to future care ■ One unit of packed red cells contains about 200mg of elemental iron, so will not replenish the iron store deficit in severe IDA. Restrictive transfusion should be followed by adequate iron replacement[5] ■ Avoid Transfusion Associated Circulatory Overload (TACO)	

Erythropoietin		■ May be considered in patients with Chronic Kidney Disease after or in parallel with iron therapy[107] ■ May be helpful, eg if blood transfusion not possible, eg Jehovah's Witness patients, or in patients who have not responded to IV. iron
Tranexamic acid	■ Contraindicated if recent stroke or Myocardial Infarction (as risk of Venous ThromboEmbolism VTE)	■ Reduces bleeding in patients with major traumatic hemorrhage or at risk of significant bleeding after trauma ■ Adult patients having major in-patient surgery should receive 1 gram of tranexamic acid prior to skin incision to reduce major surgical bleeding and reduce the need for blood transfusion,[108] whether they have anaemia or are at risk [109,110] ■ Inexpensive, safe[84]
Re-Transfusion drains	■ Concerns over infection risk ■ Concerns over local anaesthetic infiltration – this may be over-emphasised	■ May be useful in revision surgery, not standard surgery – often the collected drained blood is not used

Specific dietary issues

Absorption of iron is more reliable from animal foods than from plant foods, and the phytate found in whole grains, nuts, seeds, and legumes is a major inhibitor of iron absorption. The phytate content can be reduced if these foods are processed by fermentation, sprouting or soaking, with the water thrown away after soaking.[111] Polyphenols, found generally in plants, and especially rich in fruits and vegetables, are also inhibitors of iron absorption. Thus, a dietary pattern low in animal foods and rich in plant foods is an additional risk factor for iron deficiency, especially when iron-containing supplements and iron-fortified foods such as enriched flour are not used.[110] Vegan diets do not contain vitamin B12 without supplementation.

Dosing of iron

For oral iron, the traditional dose to treat anaemia is 100–200mg of elemental iron per day (for example, ferrous sulfate 200mg three times per day), yet such high doses have no rationale and are strongly discouraged. Side effects are common, principally diarrhoea and constipation. Hepcidin is stimulated by high doses of oral iron and this reduces future absorption of iron. A low dose on alternate days is probably the optimum regimen to increase iron and be tolerable.[26] The international consensus statement recommends 40–60mg of elemental iron per day or 80–100mg on alternate days in addition to dietary advice.[26] The content of elemental iron within preparations varies (see Figure 8). A practical suggestion is to use any of the common iron tablets combined with dietary advice at a dose of one tablet per day or two tablets on alternate days. This applies when needed preoperatively or postoperatively.

Figure 8 Elemental iron content of common commercially available preparations[112]

Commercially available preparation	Elemental iron content
ferrous fumarate 210mg	68mg
ferrous fumarate 305mg	100mg
ferrous fumarate 140mg/5mL liquid	45mg per 5mL
ferrous gluconate 300mg	35mg
ferrous sulfate 300mg	60mg
ferrous sulfate, dried 200mg	65mg
sodium feredate 190mg/5mL liquid	27.5mg per 5mL
'Iron health food supplement' Typically	14mg

Intravenous iron dosing

The Royal College of Nursing has published excellent guidelines about IV. iron. The dosing schedule is dependent on the product used with two preparations best suited for preoperative optimisation as an outpatient (see Figure 9). Product literature should be consulted and choice of IV. iron guided by Trust/ Health Board formularies.

Figure 9 IV. iron preparations

1	Ferric carboxymaltose	Ferinject®	■ Total dose of 20mg/kg but a maximum of 1g per dose so often requires two doses depending on weight and Hb, ■ Cheaper than Iron isomaltoside ■ Typically, second dose one week later ■ Administered over 30 minutes
2	Ferric derisomaltose 10mg/ml *(Previously known as iron isomaltoside 1000, 10%)*	Monofer®	■ 20mg/kg with no additional dose cap, often given as single total dose infusion over >15mins for doses ≤1,000mg or ≥30mins for >1,000mg ■ A one off dose providing the total dose doesn't exceed 20mg/kg
3	Low molecular weight iron (111) dextran	CosmoFer®	■ 20mg/kg with no additional dose cap, often given as single total dose infusion over four to six hour infusion
4	Iron sucrose	Venofer®	■ Requires repeated infusions
5	Ferric derisomaltose 50mg/ml *(Previously known as Iron isomaltoside 1000, 5%)*	Diafer®	■ Only licensed for use in haemodialysis patients

Patients should be informed that long lasting skin discolouration can result if paravenous leakage occurs during administration of IV. iron preparations. All IV. iron preparations have the potential to cause anaphylaxis, so careful monitoring is required. Clinicians should be aware of reports of hypophosphatasia. IV. iron is contraindicated in the first trimester of pregnancy.

Practical options that services should consider

Many services have established their perioperative pathways. Improvements can be considered at every stage, with examples in Figure 10.

Figure 10 Practical options services should consider

Expectation	Options to consider
Hb should be obtained early	■ Hb on referral ■ Hb as Point of Care testing in outpatient clinic ■ Hb on non-invasive monitor (eg for paediatric clinics) ■ Surgical clinic could request Hb and renal test when putting on the waiting list ■ Emergency patients – blood test in emergency department if complex surgery is anticipated
Other blood tests and history should be obtained early	■ Clear protocols about other types of blood test that may be needed ■ Possibility of reflexive testing so further blood tests are done automatically by the laboratory if Hb low
Results should be available to senior clinician to plan any treatment and shared decision making should occur with patient	■ All results should be followed up by an accountable team of clinicians, with a clear process to follow up abnormal results ■ Audit of results and late cancellations may help ■ Protocols should be written and followed when anaemia is detected for common conditions
Any treatment should be planned and available easily	■ Patients can be advised to buy oral iron from a pharmacy – this means patients do not need to return to the hospital to collect a prescription, or have it sent, when bloods are reviewed following day ■ Use of non-medical prescribers (eg nurses or pharmacists) or anaesthetists, surgeons or other doctors to prescribe oral or IV. iron ■ Patient Group Direction (PGD) for registered staff to administer/supply medication in specific situations ■ IV. Iron service staffed and planned ■ Preoperative Transfusion in emergency patients should be planned when required
Patient Blood Management should occur	■ Intraoperative planning should reduce blood loss

Postoperative treatment of anaemia should be based on patient symptoms	■ Usually, blood transfusion should not be based solely on a Hb result, except in the case of a very low Hb. For example, a restrictive blood transfusion trigger of Hb ≤70g/L is recommended by NICE3 ■ Therapists should aim to mobilise irrespective of Hb result, depending on the patient symptoms
Good communication should occur and postoperative plans followed	■ Plans for postoperative Hb measurement and follow-up of results should be in place

Likely blood loss in common operations

Operations have different expected magnitude of blood loss. Figure 11 from Thrombosis Canada gives simplified concepts. More detailed tables are available. Individual patient factors are also important.

Figure 11 Risk of significant blood loss by operation type adapted from Thrombosis Canada[113]

Low/Very low risk	Moderate risk	High risk of significant bleeding
■ Dental extractions (one or two teeth), endodontic (root canal) procedure, Subgingival scaling or other cleaning ■ Cataract surgery ■ Dermatological procedures (eg biopsy) ■ Gastroscopy or colonoscopy without biopsies ■ Coronary angiography ■ Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation not used) ■ Selected procedures (eg thoracentesis, paracentesis, arthoscopy)	■ Other intra-abdominal surgery (eg laparoscopic cholecystectomy, hernia repair, colon resection) ■ Other general surgery (eg breast) ■ Other intrathoracic surgery ■ Other orthopaedic surgery ■ Other vascular surgery ■ Non-cataract ophthalmologic surgery ■ Gastroscopy or colonoscopy with biopsies ■ Selected procedures (eg bone marrow biopsy, lymph node biopsy) ■ Complex dental procedure (eg multiple tooth extractions)	■ Neurosurgery (intracranial or spinal) ■ Cardiac surgery (eg CABG, heart valve replacement) ■ Major intra-abdominal surgery (eg intestinal anastomosis) ■ Major vascular surgery (eg aortic aneurysm repair, aortofemoral bypass) ■ Major orthopaedic surgery (eg hip or knee replacement) ■ Lung resection surgery ■ Urological surgery (eg prostatectomy, bladder tumour resection) ■ Extensive cancer surgery (eg pancreas, liver) ■ Reconstructive plastic surgery ■ Selected procedures (eg kidney biopsy, prostate biopsy, cervical cone biopsy, pericardicentesis, colonic polypectomy)

Anaemia in pregnancy

Effects of anaemia in pregnancy

In the UK, 31% of babies are delivered by Caesarean section, of which 56% are as an emergency.[114] 12% of births have an instrumental delivery.[114] A small percentage of pregnant people require non-obstetric surgery, 22% sustain a post-partum haemorrhage, of which 13% (3% of deliveries) involves 1,500ml blood loss and 30% are anaemic after birth.[114,115] In the UK, at least 1 in 4 pregnant people experience anaemia in pregnancy.[116] Over 90% of this is secondary to iron deficiency. Data from the World Health Organisation demonstrates no significant decrease over the last decade.[117]

Anaemia is associated with worse outcomes for the baby: a significantly higher risk of perinatal and neonatal mortality, low birth weight and pre-term birth; a higher rate of stillbirth and small for gestational age infants.[65] Iron deficiency has a negative effect on neonatal neural development. Anaemia in pregnancy propagates neonatal anaemia. Since human breast milk is low in iron, the anaemia of pregnancy may have persistent effects into infanthood and beyond.

Anaemia in pregnancy has worse outcomes for the mother,[65,118,119] with increased maternal post-partum haemorrhage (PPH). Bleeding may occur with placenta previa (across the uterine opening) and placenta accreta (implanted deep in uterine muscle). For many individuals the recovery from anaemia post birth is prolonged, with difficulties with breastfeeding and mobility.

The overall rate of maternal death from haemorrhage is extremely low but this remains one of the most common causes of maternal mortality. Lessons have been drawn on the effects of antenatal anaemia from individuals who decline blood products and haemorrhage and from Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries (MBBRACE) case reviews of maternal mortality.[120]

Effect of treatment of iron deficiency in pregnancy

The World Health Organization has stated: '*Anaemia during pregnancy has been associated with poor maternal and birth outcomes, including premature birth, low birth weight and maternal, perinatal and neonatal mortality. Nevertheless, a 10g/L increase in haemoglobin has been estimated to decrease the risk of maternal mortality by 29%, and perinatal mortality by 28%. Anaemia in the first or second trimester significantly increases the risk of low birth weight and preterm birth. Prenatal iron supplementation increases birth weight and significantly reduces the risk of low birth weight, but not preterm birth. Finally, postpartum anaemia is associated with decreased quality of life, including increased tiredness, breathlessness, palpitations and infections. Women who have anaemia postpartum may also experience greater stress and depression, and be at greater risk of postpartum depression. Mothers with anaemia may also be less responsive, more controlling and more 'negative' towards their infants, which can have negative implications for infant development.*'[121]

Structure of antenatal care and opportunities for impact

NICE recommends two opportunities for identification of anaemia during pregnancy.[122] An FBC should be taken at first antenatal (booking) appointment and the NHS sickle cell and thalassaemia screening programme can be accessed.[66] At around 28 weeks (20 weeks in multiple pregnancies) a FBC, blood group and antibodies should be taken. Iron studies are rarely requested, but serum ferritin should be considered. Oral iron can be effective but often requires adjustment to its administration to improve tolerance and consistent advice to promote absorption. There is increasing use of IV. iron in pregnancy and post pregnancy, which has a good safety profile.[122] Blood transfusion will remain a life-saving intervention but optimisation of anaemia with IV. iron can reduce its use.[123]

These opportunities for intervention are frequently missed within timescales of efficacy before escalation to next intervention. There are organisational and cultural issues in promoting opportunities to treat and manage anaemia pre- and post-birth. These include a lack of structured operating practices and a lack of familiarity with options such as parenteral iron. For example, in the 28th week of pregnancy a full blood count should be taken as part of the care pathway for all individuals and a trial of oral iron commenced at 29 weeks if iron deficiency anaemia is present. By 34 weeks a repeat sample should have been taken and the response to iron can be assessed and options for parenteral iron discussed. This is important because most fetal iron is acquired during the third trimester in preparation for the high rate of growth and development in the first months of life.

Specific individual risk groups in pregnancy can be identified at pregnancy booking:

- Previous iron deficiency anaemia in pregnancy
- Pregnancy in individuals under 20 years
- Dietary intake that reduces opportunity for iron and iron absorption (vegetarian or vegan, coeliac disease or previous bariatric surgery)
- Previous pregnancy less than 12 months ago
- Multiple pregnancy
- Parity of three babies or more

Postpartum haemorrhage

Postpartum haemorrhage remains one of the most common complications of birth in the UK and the commonest global cause of maternal mortality. In the UK regional strategies are being employed to promote a more consistent approach. Many of the discussions promoting antenatal iron supplementation apply to this context and within postnatal care. Of note is the growing debate around the use of parenteral iron versus oral postnatally. There appears to be benefit from the use of parenteral iron in recovering haematological indices faster and data from observational studies to demonstrate benefit,[124] but further research is required. Hb should be checked postoperatively if there is any suspicion of anaemia.

Summary of anaemia in pregnancy

Awareness of anaemia in pregnancy should be improved and needs a holistic approach that recognises the benefits of treatment on mothers and babies. The need for iron accelerates in the third trimester of pregnancy and the structure of antenatal care facilitates intervention at this stage. This requires organisation structures that promote awareness and management, standardisation of pathways and promotion of treatments.

Anaemia in children undergoing surgery

While most surgery for children and young people does not involve transfusion, some children undergo elective surgery with over a 10% risk of transfusion. Examples include in orthopaedics: femoral/pelvic osteotomies and scoliosis surgery; in urology: nephrectomies, and bladder reconstructions; in general surgery: anorectal reconstruction and bowel resections: and in neurosurgery: craniotomies and craniosynostosis procedures.

The number of medically complex children booked for these types of surgery is also increasing; comorbidities such as prematurity, maternal iron deficiency, rapid growth periods, cerebral palsy, inflammatory bowel disease, renal conditions and childhood cancers increase the incidence of preoperative anaemia. In conjunction with a relatively small circulating blood volume this increases the risk of requiring transfusion.

Anaemia may also be found incidentally in children undergoing emergency surgery, for example appendectomy and trauma. The principles outlined in Recommendations for staff admitting emergency patients for surgery should be used for children and young people.

There is growing evidence of adverse perioperative outcomes in neonatal and paediatric patients undergoing surgical procedures with preoperative anaemia. Work shows high rates of anaemia (24–32%), higher odds of requiring a blood transfusion and increased mortality in anaemic children.[125,126]

Iron deficiency is the leading cause of anaemia in all paediatric age groups (except in very preterm infants in the first weeks of life).[67] The causes of neonatal anaemia are preterm delivery before establishment of normal red cell and iron stores in the last trimester, expansion of blood volume with growth, bone marrow depression, and increased red cell destruction, eg infection or haemolytic disease.

Blood transfusion carries additional risks, the highest being Transfusion Associated Circulation Overload (TACO) which is an iatrogenic complication occurring in up to 1 in 100 transfusions. Neonates and infants are at risk of hyperkalaemia following blood transfusion. To reduce this risk 'fresh blood' is recommended in this group, see Figure 12. The recommendations section includes consideration of tranexamic acid. A dosing regimen of 10 to 30 mg/kg (maximum 1g) loading dose of tranexamic acid followed by 2 to 10 mg/kg/hour maintenance infusion rate for paediatric trauma and surgery has been recommended.[127,128] Future research should focus on determining the ideal tranexamic acid plasma therapeutic concentration for maximum efficacy and minimal side-effects.[127] Figure 13 summarises preoperative options for children with anaemia. Iron dosing regimens are available in the children's BNF. Common preparations are Sodium feredetate (Sytron) or Ferrous Fumarate (Galfer syrup). The therapeutic oral dose of elemental iron to treat deficiency is 3–6mg/kg (max 200mg) daily. The current recommendation is that it is given in two to three divided doses, although Hepcidin may down-regulate absorption in children as it does in adults.

The Australian Blood Authority PBM guideline contains practical evidence-based advice and additional PBM strategies such as prevention of hypothermia and use of 'as-needed' rather than routine blood sampling.[129] There are studies suggesting that a high percentage of paediatric transfusion recipients receive only one transfusion during their admission, some of which may have been avoidable.[81,130]

As preventative medicine is becoming routine in preoperative care, it is worthwhile noting the potential association between iron deficiency in childhood and long-term adverse neurodevelopmental outcomes.[131]

Figure 12 Suggested transfusion thresholds for preterm neonates[68]

	Suggested transfusion threshold Hb (g/L)		
Postnatal age	**Ventilated**	**On oxygen or Non-invasive Positive Pressure Ventilation (NIPVV)**	**Off oxygen**
First 24 hours	<120	<120	<100
≤ week 1 (day 1–7)	<120	<100	<100
≤ week 2 (day 8–14)	<100	<95	<75 or <85*
> Week 3 (day 15 onwards)	<100	<85	<75 or <85*

Preterm is defined as <37 weeks gestational age at birth. This table also applies to very preterm neonates (<32 weeks).

*Depending on clinical situation.

Adapted from British Committee for Standards in Haematology (2016) Guidelines on transfusion for fetuses, neonates and older children[68]

Figure 13 Management of children with anaemia preoperatively[129]

Ferritin <20 mcg/L	Ferritin 20–50 mcg/L	Ferritin >50 mcg/L
Iron deficiency anaemia	**Possible iron deficiency anaemia**	**Unlikely iron deficiency anaemia**
Review clinical history and identify cause. Start treatment: ■ oral iron 3–6mg/kg/day of elemental iron **Address causes** of dietary iron deficiency: ■ increase dietary iron ■ if <1 year of age, cease cow's milk and use an infant formula ■ if 1 to 2 years of age, reduce cow's milk to <500mL daily Assess haematological response within two to four weeks. Continue treatment for three months after Hb recovery. If oral iron is ineffective or is not tolerated, **consider other causes of anaemia** and use of IV. iron.	Review and **address any causes** of iron deficiency: ■ increase dietary iron ■ if <1 year of age, cease cow's milk and use an infant formula ■ if 1 to 2 years of age, reduce cow's milk to <500mL daily Correlate with MCV/MCH and CRP. Consider therapeutic trial of iron: ■ oral iron 3mg/kg/day of elemental iron ■ Assess haematological response within two to four weeks. If anaemia persists, **consider other causes:** ■ Thalassaemia and other haemoglobinpathies ■ anaemia of chronic disease ■ haemolytic anaemia ■ B12 deficiency ■ folate deficiency ■ other	Correlate with MCH/MCV and CRP Ferritin may be elevated in the setting of inflammation. However, iron deficiency may still be present, particularly where TSAT <20%. **Consider other causes** of anaemia: ■ Thalassaemia and other haemoglobinpathies ■ anaemia of chronic disease ■ haemolytic anaemia ■ B12 deficiency ■ folate deficiency ■ other

This algorithm applies to all patients, including those undergoing procedures in which substantial blood loss is anticipated.

The reference ranges are based on criteria from the Royal College of Pathologists of Australasia, and they may require local adaptation.

Note Monofer® is unlicensed in <18yrs and Ferinject® <14 years.

Glossary and abbreviations

Abbreviation	Explanation
ASA	American Society of Anaesthesiologists
B12	Vitamin B12, Cobalamin
CHr	reticulocytes haemoglobin content
CKD	Chronic kidney disease
CRP	C reactive protein
EPO	Erythropoietin
FBC	Full Blood Count
FID	Functional iron deficiency
GIRFT	Getting It Right First Time
Hb	Haemoglobin
HQIP	Healthcare Quality Improvement Partnership
ID	Iron Deficiency
IDA	Iron deficiency anaemia
IV.	Intravenous
MCH	mean corpuscular haemoglobin
MCV	mean corpuscular volume
NICE	National Institute for Health and Care Excellence
NSAID	Non-Steroidal Anti-Inflammatory Drug
RBC	Red Blood Cell
Rcv	Red cell volume
SF	Serum Ferritin
T-Sat	Transferrin saturation

Paediatric patients (1 month to 18 years of age)

Neonatal patients	≤28 days of age
Infant	1–23 months of age
Child	2–12 years of age
Adolescent	13–18 years of age

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APPENDICES

Patient information for anaemia

General patient information

1 Preoperative intravenous iron therapy: patient information (Cardiff and Vale University Health Board)
2 Anaemia patient information (NHS Blood and Transplant)
3 Assessment of anaemia (BMJ Best Practice)
4 Anaemia, iron deficiency (BMJ Best Practice)
5 Patient Information Leaflet – Intravenous Iron (NHS County Durham and Darlington NHS Foundation Trust)
6 Iron therapy into a vein (Intravenous) patient information leaflet (Betsi Cadwaladr University Health Board)
7 Intravenous iron (University Hospitals Bristol and Weston NHS Foundation Trust)

Patient information on dietary issues

8 Iron in your diet patient information (NHS Blood and Transplant)
9 Iron: Food Factsheet (The Association of UK Dietitians)
10 Folic acid: Food Factsheet (The Association of UK Dietitians)

Patient information leaflets on treatment options

11 Iron Supplements: Patient information Factsheet (University Hospital Southampton NHS Foundation Trust)
12 Taking Iron Supplements: Information for patients (Oxford University Hospitals NHS Trust)

Example letters to the GP about the patient's care

13 Preoperative anaemia management letter: iron supplements (Betsi Cadwaladr University Health Board)
14 Preoperative anaemia management letter: intravenous iron therapy (Betsi Cadwaladr University Health Board)
15 Preoperative anaemia management letter: oral iron (The Leeds Teaching Hospitals NHS Trust)
16 Preoperative anaemia management letter: intravenous iron therapy (The Leeds Teaching Hospitals NHS Trust)

Example letter to patient

17 Patient letter: oral iron tablets (Betsi Cadwaladr University Health Board)
18 Patient letter: oral iron tablets (The Leeds Teaching Hospitals NHS Trust)
19 Patient letter: intravenous iron therapy (The Leeds Teaching Hospitals NHS Trust)

Example Patient Group Direction (PGD)

20 Supply of ferrous sulphate tablets for the treatment of anaemia (University Hospitals Bristol and Weston NHS Foundation Trust)

Shared Decision Making resources

21 BRAN: Making the Most of Your Appointment (Choosing Wisely UK)

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