Identification and Management of Preoperative Anaemia in Adults: A British Society for Haematology Guideline Update

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Methodology

This guideline was compiled according to the BSH process at [https://bsh.org.uk/media/16732/bsh-guidance-development-process-dec-5-18.pdf]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) nomenclature was used to evaluate levels of evidence and to assess the strength of recommendations.

The GRADE criteria can be found at http://www.gradeworkinggroup.org and is summarised in appendix 3 of the guidance document linked above.

Literature review details

The literature review was performed initially in March 2022 with a further search in March 2023. For full details please refer to Appendix 2. Literature was searched from 01/09/2014 (date of literature search for previous guideline) - present. Resulting references were screened and those evaluating a strategy for treating anaemia before surgery and reporting transfusion and/or other outcomes were included. Additional primary literature was suggested by writing group members.

Review of the manuscript

Review of the manuscript was performed by the British Society for Haematology (BSH) Guidelines Committee Transfusion Task Force, the BSH Guidelines Committee and the Transfusion sounding board of BSH. It was also on the members section of the BSH website for comment. It has also been reviewed by NAME of other bodies (including patient groups where available); these organisations do not necessarily approve or endorse the contents.

Commented [KH1]: Intend to ask for review by:
RCOA
Association of anaesthetists
RCGP
RCS
RCP
BS Gynae Endoscopy
RCOG
RCPath TM SAC
Introduction

The previous version of this guideline was published in 2015 (1) and provided a comprehensive review of the available literature. Since then, a number of key clinical trials have reported findings relevant to the investigation and management of preoperative anaemia including those considering optimal dosing of oral iron (2, 3) and the use of intravenous iron for patients undergoing major surgery (4, 5).

The SARS-CoV2 pandemic has placed extra importance on the appropriate management of preoperative patients, with a now huge number of patients (6) awaiting elective surgical procedures postponed by the pandemic. All UK nations have published recovery plans which outline actions that will be undertaken to address the care backlog, including those affecting elective surgery (7-10). A BSH Good Practice Paper published in 2021 (11) made recommendations for best patient blood management while working within the limitations imposed by the need to minimise hospital attendances to reduce risk of SARS-CoV2 infection. Many of the recommendations made at that time remain relevant and where appropriate have been incorporated into the current guideline.

The blood supply is particularly challenging at present with NHS Blood and Transplant declaring an amber alert in October 2022 (12). This unprecedented event led to a rapid push to implement patient blood management wherever possible to reduce demand for blood. Managing the demand for blood in elective surgical patients by appropriately identifying and managing anaemia in the preoperative setting is therefore important not just at an individual patient level, but at a system wide level to ensure blood is available for all who need it.
This updated guideline is cognisant of the role of Primary Care in the management of these patients, and this is reflected in the writing group membership as well as the recommendations made. The guideline writing group is pleased to have representation from all four UK nations to ensure this guidance is widely applicable. It sits alongside the newly published Centre for Perioperative Care (CPOC) guideline for the management of anaemia in the perioperative pathway (13).

The association of preoperative anaemia on patient outcome after surgery

Anaemia is associated with an increased likelihood of requiring transfusion, as well as mortality and morbidity after major surgery. Preoperative anaemia is also, in principle, modifiable with appropriate treatment though it is unclear under what circumstances such modification translates to patient benefit. Definitions of patient blood management (PBM) have evolved over the years since its inception, with the recent publication of a global definition as follows: ‘Patient blood management is a patient-centred, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient’s own blood, while promoting patient safety and empowerment’. (14). Preoperative anaemia diagnosis and management therefore falls under the PBM umbrella. Patients requiring surgical intervention who present with anaemia are more likely to receive a transfusion of packed red cells. Preoperative anaemia and blood transfusion have been associated with increased morbidity and mortality as shown by several systematic reviews and observational studies (15-17). Studies reviewing prevalence of anaemia in the preoperative population vary, but demonstrate up to 35-50% of preoperative patients to be anaemic (18-20) and are influenced by the presenting disease i.e. cancer population, the burden of comorbidities, age, gender, and surgical procedure.

The severity of anaemia has also been linked to outcome (16). Patients with Hb > 100 g/L classified as mildly anaemic had a 30% increased relative risk to complications and death.
The identification of links between preoperative anaemia and adverse outcomes have led to further investigation by perioperative care teams into the causes of anaemia in the surgical patient. Hung et al demonstrated by bone marrow sampling of anaemic patients presenting for cardiac surgery that most (80%) were iron deficient (21). This figure was corroborated in patients undergoing major, abdominal surgery in the PREVENT study where 82% had iron deficiency (22). Recent perioperative guidelines suggest identifying and managing the underlying cause of anaemia is essential in its management (13).

Transfusing a patient for haematocrit deficiencies without a significant symptom burden to justify it, exposes patients to unnecessary risks associated with transfusion such as transfusion reactions, fluid overload, incorrect component transfusions, and more rarely infection (23). Transfusion for haematocrit deficiency in the absence of symptoms is therefore reportable to SHOT as an avoidable transfusion (24). Transfusing without replacing the haematocrit deficiency also leaves the patient at risk of the adverse effects of the deficiency itself and a relapse of the anaemia as the transfused red cells senesce.

Detection of anaemia as part of the preoperative risk assessment is predictive of higher transfusion requirements and poorer outcomes including death. It is however unclear whether preoperative anaemia increases risk or reflects ongoing burden of comorbidities in the patient. Treatment of preoperative anaemia has become a plausible and attractive therapeutic target and the preoperative period is an opportunity for screening, investigation, and initial management.

- Assessment for anaemia in patients undergoing elective surgery should be performed early in the preoperative pathway (1C)
• Patients undergoing major surgery should be screened for anaemia by full blood count (including red cell indices) in the first instance (2B)

• Patients should be provided with information regarding the results of preoperative screening tests as well as potential treatment options to allow shared decision making regarding further management (2B)

Diagnosis of Anaemia

Definition of anaemia

The World Health Organization (WHO) (25) defines anaemia as Hb <130g/l for men and <120g/l for women, with recent work suggesting further evidence is required to change global disease defining thresholds (26). A 2017 Europe wide consensus statement (27) proposed a pragmatic a threshold of 130g/l for all, based on the observation that the transfusion rate for non-pregnant women with an Hb of 120g/l is twice that of men with an Hb of 130g/l. In addition, iron depletion without anaemia is common in non-pregnant women(28). In the preoperative setting, the focus should be on identification of those who may benefit from preoperative optimisation of Hb, and those that may have a serious underlying pathology.

• In the preoperative context, Hb <130g/l should be considered as anaemia in both men and women (1B)

Iron Deficiency Anaemia and iron metabolism:

The most common cause of preoperative anaemia is iron deficiency anaemia (IDA) and may be suspected when the Mean Cell Haemoglobin concentration (MCH) and Mean Cell Volume (MCV) are low. Iron deficiency may be due to blood loss related to the presenting surgical problem (for example gastrointestinal cancer), or unrelated (for example heavy menstrual bleeding).
Iron depletion results in iron restricted erythropoiesis progressing IDA (29). Iron restricted erythropoiesis occurs in non-pregnant women as the ferritin falls to <25μg/l (30).

**Diagnosing iron deficiency**

The single most useful test to diagnose iron deficiency is the serum ferritin, with a ferritin of <15μg/l (with or without evidence of inflammation) indicative of absolute iron deficiency (AID) (31). In the preoperative setting, a ferritin <30μg/l has been suggested as a sensitive and specific marker of absolute iron depletion or deficiency (27), regardless of gender or whether there is anaemia or not. This is the same threshold advised for the diagnosis of iron deficiency in pregnancy (32). Ferritin behaves as an acute phase protein. In the presence of inflammation, anaemia with moderately reduced ferritin levels remains strongly suggestive of iron deficiency. The WHO suggest a ferritin threshold of 70μg/l be used to diagnose iron deficiency in patients with concomitant inflammation (as evidenced by elevated levels of C-reactive protein (CRP) for example) (33).

Other markers of iron status may be used in combination with serum ferritin levels to help diagnose iron deficiency. These may be particularly pertinent when iron deficiency is suspected but ferritin levels are falsely elevated due to an acute phase response. As iron deficiency develops, the serum iron falls, and the transferrin saturation (TSAT) also falls. A TSAT threshold of <20% has been widely used in the diagnosis of iron deficiency though this is based more on consensus opinion rather than clinical trial data (31).

- Ferritin <30μg/l, suggests absolute iron depletion/deficiency likely to benefit from iron supplementation (1B)
- Ferritin 30-100μg/l with a low transferrin saturation (<20%) indicates possible iron depletion/deficiency in the context of inflammation that may benefit from iron supplementation (2B)
Investigation of individuals with iron deficiency

The prevalence of cancer in unexplained IDA approaches 15% and accordingly, British and American Gastroenterology guidelines recommend referral for endoscopic investigations, except in pre-menopausal women (34, 35). Hypoferritinaemia in the absence of anaemia (<15μg/l) is associated with a cancer prevalence of 0·9% in men and postmenopausal women and referral is also indicated in this context (34). Serological testing for coeliac disease should also be performed.

- Patients with unexplained absolute iron deficiency should be referred for investigation according to local criteria or those set out by British Society for Gastroenterology (1B)

Non-iron deficiency related anaemia

While iron deficiency is a common cause of anaemia in the preoperative population, preoperative blood tests may also identify anaemia of other causes. Other contributory causes should also be considered if iron therapy fails to achieve the expected response. In cases where no cause is readily identified by tests discussed below, or if anaemia is associated with other cytopenias, advice from a haematologist may be required.

Vitamin B12 and Folate deficiency

Serum Folate and B12 are easily tested for and the presence of macrocytic anaemia with a low serum B12 or folate is suggestive of the presence of deficiency. The interpretation of results is not however always straightforward and specialist advice is often necessary (36).

Chronic Kidney Disease

In the presence of an estimated Glomerular Filtration Rate (eGFR) of <30 ml/min/1.73 m², anaemia is likely to be due to chronic kidney disease, particularly if other causes are excluded (37, 38).
Haemoglobinopathies

These inherited conditions may occur in all ethnic groups, though they are more frequently identified in individuals of non-northern European origin. Thalassaemia presents with a microcytic anaemia and can be confused with iron deficiency. Patients with haemoglobinopathies may have other causes of anaemia including iron deficiency and should be investigated in the usual way. This is especially important if the Hb for an individual falls below their historical norm, which generally remains constant throughout adult life.

Sickle cell disease generally presents with a normochromic normocytic anaemia and presents specific challenges for surgery requiring specialist collaboration (39).

- In unexplained anaemia without iron deficiency, referral to haematology should be considered according to the severity of anaemia (e.g., men with Hb <120g/l, women with Hb <100g/l, or according to locally agreed criteria). The likelihood of a serious cause or haemoglobinopathy is proportional to anaemia severity (1B)

Algorithms for anaemia investigation

A 2017 international consensus statement on the perioperative management of anaemia and iron deficiency (27) has suggested perioperative anaemia and iron deficiency be managed in accordance with a perioperative care pathway. Anaemia identification and treatment is integral to this. In the UK, General Practitioners are the gatekeepers to this pathway, and it is important that they be involved from the outset. Such pathways may benefit from the reflex testing of preoperative patients found to be anaemic, or the use of a standardised battery of tests, rather than sequential testing thus minimising patient visits and associated resource costs.
Anaemia pathways and testing algorithms should be locally designed in order that they can be implemented without disrupting surgical pathways. Example frameworks are given in Appendix 1, that can be adapted for use locally with input from both primary and secondary care providers.

- Commissioners and provider organisations should formalise integrated pathways for the referral of patients found to be anaemic during surgical workup (2B)
- The use of reflex testing aiming to identify the cause of anaemia may reduce delays in anaemia diagnosis and minimise patient visits (2B)

Treatment of Preoperative Anaemia

Treatment of iron deficiency

Treatment options for iron deficiency anaemia predominantly include oral or intravenous iron (40, 41). However, in randomised trials of preoperative IV iron, the treatment effect to increase haemoglobin levels (42) has not translated into reduced allogeneic transfusion or improved endpoints of patient benefit such a complications or length of hospital stay (43, 44).

The definition of iron deficiency anaemia in the surgical patient has been heterogenous in clinical trials (45). Reanalysis of the PREVENTT trial suggested a greater preoperative haemoglobin response appears in those with absolute iron deficiency (AID) (ferritin <30ug/L) and less so in those with functional iron deficiency (FID)(Ferritin < 100ug/L +/- TSATS<20%)(22). Similar results were seen in the cardiac surgery population, with improved peak oxygen uptake following IV iron only seen in patients with ferritin <30ug/L in a reanalysis of the IronIC trial (46, 47). The FiT study randomised 202 patients with colorectal cancer to receive oral or IV iron preoperatively: haemoglobin at the time of...
surgery did not differ between the study groups but was significantly improved at later
timepoints in IV iron recipients (5). Iron therapy in patients with AID is indicated regardless
of whether the patient is on a surgical pathway and therapy should be initiated in a timely
manner wherever it is diagnosed. Additional preoperative visits specifically for iron
treatment and/or opting for IV therapy outside of established indications are likely to
represent low-value care.

Oral iron is a safe, cheap and effective as the first line treatment for correcting iron
deficiency anaemia and is recommended as first line treatment by NICE (23). Iron is better
absorbed on an empty stomach and compliance is improved with once daily dosing (48).
This is supported by early phase studies that suggest gastrointestinal absorption of iron is
similar in patients on twice daily or alternate day dosing schedules (2, 3). No oral iron
preparation has proven superiority in the preoperative setting and any of the commonly
commercially available preparations could be chosen (Table 1) To minimise side effects, a
total daily dose of 45-65mg and no more than 100mg of elemental iron is recommended.

Oral iron should be started as soon as iron deficiency is identified. A Hb rise of 10g/dL
within 4 weeks of starting treatment with an increase in serum Ferritin to above 30ug/L by
3 months is indicative of response to treatment. Oral iron should be continued for a further
3 months to allow full replenishment of iron stores (34).

Table 1 Oral iron preparations

<table>
<thead>
<tr>
<th>Iron salts</th>
<th>strength</th>
<th>Elemental iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous fumarate</td>
<td>210mg</td>
<td>68mg</td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>305mg</td>
<td>100mg</td>
</tr>
<tr>
<td>Ferrous fumarate liquid</td>
<td>140mg/5ml</td>
<td>45mg / 5mL</td>
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</tbody>
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For patients unable to tolerate oral iron or where there is no response, then intravenous (IV) iron is indicated. Modern IV iron preparations are safe and effective treatments to treat IDA with side effect profiles comparable to other intravenous therapies (27, 34). Dosage should be obtained from the dosage tables in the product literature or by using the Ganzoni equation (49, 50). They have the advantage of being able to be given in either one or two doses to achieve full correction of iron deficiency. Serious infusion related reactions are now rare, flushing reactions and minor hypersensitivity reactions (complement mediated) may occur and are self-limiting. Staff and patient education are vital.

**Timing of iron therapy**

No trial has demonstrated an optimum time to give an IV iron intervention and given this paucity of evidence the writing group do not make a recommendation regarding timing of iron therapy. There is therefore an ongoing need to enrol patients with preoperative anaemia for management in clinical trials where available. Until clear evidence is available the timing should be individualised based on the resources that the centre has available. If there a robust system for IV treatment already in place pre-surgery that is patient focused and convenient, its use in patients with absolute iron deficiency is encouraged. If no such system exists, centre leads should be aware that the current evidence to definitively recommend IV treatment specifically prior to surgery are lacking. Therefore, if IV treatment is required and has not been administered preoperatively, consideration should be given to administration at the time surgery or in the post-surgical period. Data are encouraging in terms of improvement in Hb and reduction in transfusion rates with post operative IV iron therapy (51-53). Set-up of preoperative anaemia treatment programmes at scale (across
multiple hospitals) is possible with targeted support but is resource intensive and has not led to improved patient outcomes.

- Patients diagnosed with absolute iron deficiency anaemia should be treated with iron replacement. Oral iron therapy should be offered as first line treatment (1B)
- Intravenous iron may be considered in patients with confirmed iron deficiency who are intolerant of oral iron, or for patients where there is a suboptimal response to oral iron (2B)
- Intravenous iron should not be offered indiscriminately to all patients with anaemia preoperatively (1A)
- Evaluation and audit of practice is encouraged to contribute to the evidence base for timing of iron therapy (1C)

Treatment of B12 or folate deficiency

Where B12 deficiency is detected as part of investigation of preoperative anaemia, treatment should be initiated. Options include oral cyanocobalamin and intramuscular hydroxocobalamin with a review by Cochrane noting that the low-quality evidence available does not favour one over the other in terms of efficacy where B12 deficiency is dietary in origin (54). For patients confirmed to have pernicious anaemia and in the preoperative setting where time to response is important it is reasonable to consider intramuscular replacement as first line. This is in line with current British Society for Haematology (BSH) guidance for the diagnosis and treatment of cobalamin and folate disorders (36). Folate deficiency should be treated with oral folic acid 5mg (55).

Erythropoiesis stimulating agent (ESA) therapy
The role of erythropoiesis stimulating agents (ESA), for example recombinant erythropoietin, in the management of anaemia of chronic kidney disease is well established, leading to reduced transfusion requirements and improvement in quality of life (56). Trial data in this setting has raised concerns regarding cardiovascular risk associated with using these agents to correct Hb to normal or near normal levels (57). Patients must be iron replete when considering the use of ESA to ensure efficacy, with correction of absolute iron deficiency prior to commencing ESA therapy and concomitant iron therapy in cases of functional deficiency. Current UK guidance in this population suggests iron and ESA are used to achieve a target Hb between 100 and 120g/L for adult patients (38).

How these data should be used when formulating treatment plans for patients who are identified to be anaemic preoperatively is less clear, and the previous version of this guideline noted the need for further research in this area, recommending ESA use only where transfusion avoidance (for example highly alloimmunised patients of patients who decline transfusion) was desirable (1). This approach was also endorsed by the NICE transfusion guideline published in 2015 (23).

The primary focus of trials investigating the use of ESA preoperatively has been the impact on transfusion rates (58, 59). In elective orthopaedic surgery, the use of preoperative erythropoietin reduces transfusion rates but there is little evidence that it improves other operative outcomes. The licensed preoperative dose for non-iron deficient preoperative orthopaedic patients is 600units/kg once weekly for three weeks. Several recent, small studies have examined alternative ESA dosing regimens, including the use of a smaller number of larger doses immediately preoperatively which appeared to be safe and resulted in reduced transfusion rates (60). A further study found no additional benefit of an increased number of doses of preoperative ESA when compared with the standard of care of 4 doses (61). Spahn investigated the impact of a combination of intravenous iron, ESA, B12 and folate given the day before surgery to anaemic patients undergoing cardiac...
surgery and demonstrated a reduction in transfusions and higher haemoglobin the
treatment group (62). This immediately preoperative therapy may be attractive if anaemia
has not been detected and managed in a preoperative clinic, however again there were no
differences seen between treatment and placebo groups when considering secondary
outcomes such as length of hospital stay, and higher costs were incurred in the treatment
group. The recommendations regarding perioperative ESA use therefore remain unchanged.

- **Erythropoiesis-stimulating agent (ESA) therapy may be indicated to treat pre-
  operative anaemia in patients who refuse transfusion therapy or in patients
  who have complex red cell antibodies (2B).**

- **When ESA therapy is indicated pre-operatively, it should be given with iron
  supplementation to maximise its efficacy (1A)**

**Role of preoperative transfusion**

Red cell transfusion plays a limited role in anaemia management for patients who are to
undergo elective surgery. Ideally, such patients will have attended a preoperative
assessment clinic in plenty of time to allow anaemia to be fully diagnosed and treated
allowing them to proceed to surgery with an adequate haemoglobin. The potential for
avoidable transfusion related adverse events is well documented where transfusion is
used in place of appropriate haematinic replacement. Of 56 cases (including 6 obstetric
and 1 paediatric) of avoidable transfusions for patients with haematinic deficiency reported
to SHOT 2016-2020, 10/56 (17.9%) developed transfusion-associated circulatory overload
(TACO), highlighting the very real need to manage such patients appropriately (63).

In some circumstances, preoperative assessment may not have occurred, or there may
have been a suboptimal response to anaemia treatment, in which case ‘top up’ transfusion
may be considered. Correction of anaemia using transfusion has not been demonstrated
to improve surgical outcomes for anaemic patients. A recent, retrospective review (64) of
the impact of preoperative transfusion on outcomes in patients with cancer undergoing
abdominal surgery demonstrated higher rates of intra and postoperative transfusion in
patients who underwent preoperative transfusion, as well as longer hospital stays and
higher rates of surgical site infections. Historically, there have been concerns that
preoperative transfusion may worsen oncological outcomes in patients with colorectal
cancer. (65) However, a recent study in this patient group (66) identified preoperative
anaemia itself as an independent prognostic factor for overall survival which was not
impacted by preoperative transfusion.

National guidance (23) supports the use of so called ‘restrictive' transfusion thresholds in
almost all patient groups, the exception being those on regular transfusion programmes or
those suffering acute coronary syndrome or major haemorrhage. Taking together the
potential adverse effects of preoperative transfusion, and guidance supporting the use of
restrictive transfusion thresholds, preoperative transfusion should only be considered at a
haemoglobin threshold of 70g/L and only when there is an urgency for surgery which
cannot wait for correction of anaemia by other means.

- Preoperative ‘top up' transfusion should only be considered when urgency of
surgery precludes other options for management of anaemia, or when these
have been instituted but have not had the desired effect. Restrictive
transfusion thresholds should be employed wherever possible (2B)

Future work

Further good quality, randomised controlled trials are required to confirm:

1. When in the patient journey is iron supplementation most helpful

2. The relative contributions of treatment of preoperative anaemia with iron and other
patient blood management interventions to reduced blood transfusion rates
3. The mechanism of functional iron deficiency in surgical patients to further inform how best to manage it

4. Whether the positive post operative effects of iron supplementation suggested by the FIT and PREVENTT trials can be confirmed and how to maximise these

5. Build on work such as that performed as part of the IVICA trial (67) to assess the impact of management of preoperative anaemia on patient related outcomes such as measures of quality of life.

There are novel agents in development which may have a role in preoperative anaemia management, for example hypoxia-inducible factor prolyl hydroxylase inhibitors and it will be interesting to understand whether these have potential in this setting.

Acknowledgements

The authors wish to thank Niche Science and Technology for help in undertaking the initial literature review.

The BSH Transfusion task force members at the time of writing this guideline were Edwin Massey, Shruthi Narayan, Chloe George, Katie Hands, Richard Haggas, Paul Kerr, Wendy McSporran, Fiona Regan, Susan Robinson, Laura Green, Anne Lockhart and Catherine Booth. The authors would like to thank them, the BSH sounding board, and the BSH guidelines committee for their support in preparing this guideline.

Declaration of Interests

The BSH paid the expenses incurred during the writing of this guidance.

All authors have made a declaration of interests to the BSH and Task Force Chairs which may be viewed on request. JD has worked as a consultant for the WHO Departments of Nutrition and Food Safety and the Maternal Health Unit within the Department for Maternal, Newborn, Child and Adolescent Health and Ageing. This has included personal
fees for work on postpartum anaemia, multiple micronutrients and intravenous iron use in
women of childbearing age. CE has received educational grants and honoraria for
speaking roles for Pharmacosmos. The following members of the writing group: KH, SN,
CT have no conflicts of interest to declare.

Review Process
Members of the writing group will inform the writing group Chair if any new evidence
document becomes available that would alter the strength of the recommendations made in this
document or render it obsolete. The document will be reviewed regularly by the relevant
Task Force and the literature search will be re-run every three years to search
systematically for any new evidence that may have been missed. The document will be
archived and removed from the BSH current guidelines website if it becomes obsolete. If
new recommendations are made an addendum will be published on the BSH guidelines
website (www.b-s-h.org.uk/guidelines).

Disclaimer
While the advice and information in this guidance is believed to be true and accurate at the
time of going to press, neither the authors, the BSH nor the publishers accept any legal
responsibility for the content of this guidance.

Audit Tool
Blank Audit template can be found for writing group to complete here.
## Appendix 1 Framework for Preoperative anaemia pathway

<table>
<thead>
<tr>
<th>Identification</th>
<th>Accountability</th>
</tr>
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<tbody>
<tr>
<td><strong>GP’s referring physician should consider the possibility of anaemia prior to surgical referral and consider investigating and treating these as for</strong></td>
<td>General Practitioner/practice nurse/physician associate to act on blood results and escalate concerns</td>
</tr>
<tr>
<td><strong>Referral letter should include all relevant clinical information</strong></td>
<td>If assessment and triage carried out in primary care, GP/practice nurse/physician associate to action</td>
</tr>
<tr>
<td><strong>Pre-operative assessment should take place at a minimum of 4 weeks from the decision to operate and prior to listing for theatre</strong></td>
<td>If assessment in PAC - implement local robust follow up flags for acting on abnormal results</td>
</tr>
<tr>
<td><strong>Patients identified as at risk of requiring a blood transfusion should have RBC assessed at PAC. Information on the following should be offered: possibility of requiring a blood transfusion, and, alternatives to transfusion e.g. intra-operative cell salvage</strong></td>
<td><strong>Assessment &amp; Triage</strong></td>
</tr>
<tr>
<td><strong>Point of care testing can be used if available, but abnormal results should be confirmed by laboratory tests - all results must be fully documented in the patient’s clinical records</strong></td>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td><strong>Assessment of current medication for drugs which increase blood loss considered if these can be stopped pre-operatively</strong></td>
<td><strong>Determination of anaemia are determined by the following thresholds (Hb&gt;135g/l) are locally determined normal ranges</strong></td>
</tr>
<tr>
<td><strong>The diagnosis of anaemia are determined by the following thresholds (Hb&gt;135g/l) are locally determined normal ranges</strong></td>
<td>If assessment and triage carried out in primary care, GP/practice nurse/physician associate to action</td>
</tr>
<tr>
<td><strong>Determining the cause of anaemia: likely IDA - Ferritin &lt;15, or ferritin 15-100 and TSAT &lt;0.2</strong></td>
<td>If assessment in PAC - implement local robust follow up flags for acting on abnormal results</td>
</tr>
<tr>
<td><strong>Likely IDA: where MCV/MCV &lt;80 + MCH &lt;27</strong></td>
<td><strong>Treatment &amp; prevention</strong></td>
</tr>
<tr>
<td><strong>Trial of oral iron for 4 weeks</strong></td>
<td><strong>IV iron should be considered if oral iron is not tolerated/appropriate/restricted time before surgery</strong></td>
</tr>
<tr>
<td><strong>Those patients who were found to have IDA should be re-assessed prior to listing for theatre</strong></td>
<td><strong>Enteral iron should be considered pre-operatively if a rapid rise in Hb is needed due to the urgency of the surgery, or doubling the potential blood savings, and blood transfusion refused</strong></td>
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Appendix 2 Literature Search

The previous search was performed using MEDLINE. The new search has been performed using PubMed.

*Column Details (reading left-right):*

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results (Prior Medline-1894- 01 Sept 2014 unless otherwise stated)</th>
<th>Pubmed search (same parameters as column 3)</th>
<th>Pubmed search (01 Sept 2014-present)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>exp specialties, surgical/ or exp colorectal surgery/ or exp general surgery/ or exp gynecology/ or exp neurosurgery/ or exp obstetrics/ or exp ophthalmology/ or exp orthognathic surgery/ or exp orthopedics/ or exp otolaryngology/ or exp surgery, plastic/ or exp thoracic surgery/ or exp traumatology/ or exp urology/ or exp sports medicine/</td>
<td>70903</td>
<td>22014 1,824,488 1,359,785 (quote marks)</td>
<td>21923 1,339,692 1,080,059 (quote marks)</td>
</tr>
<tr>
<td>2</td>
<td>exp surgical procedures, operative/ or exp ablation techniques/ or exp ambulatory surgical procedures/ or exp anastomosis, surgical/ or exp assisted circulation/ or exp bariatric surgery/ or exp biopsy/ or exp “bloodless medical and surgical procedures”/ or exp body modification, non-therapeutic/ or exp cardiovascular surgical procedures/</td>
<td>1445501</td>
<td>35726 2,738,924 680,394 (quote marks)</td>
<td>13641 1,120,596 302,280 (quote marks)</td>
</tr>
</tbody>
</table>

First value- using exact same terminology from original search in PubMed
Second value- using exact same terminology but with “exp” removed. “Exp” is an explosion function in MEDLINE which is automatically performed in PubMed through its MeSH terms. We found the inclusion of “Exp” to be confusing and limiting our PubMed search, hence the greatly increased values compared to the first value.
Third value- same as second value except any multi word terms were enclosed in quote marks, eg. “colorectal surgery”. This makes the search specific for sources that discuss colorectal surgery, rather than sources that contain just colorectal or surgery.

*I think the third value in these columns will be the most useful.*
See footnotes for further details.
<p>| or exp curettage/ or exp debridement/ or exp decompression, surgical/ or exp deep brain stimulation/ or exp device removal/ or exp digestive system surgical procedures/ or exp dissection/ or exp drainage/ or exp electrocurettage/ or exp endocrine surgical procedures/ or exp extracorporeal circulation/ or exp hemostasis, surgical/ or exp laparotomy/ or exp ligation/ or exp lymph node excision/ or exp mastectomy/ or exp metastasectomy/ or exp microsurgery/ or exp monitoring, intraoperative/ or exp obstetric surgical procedures/ or exp neurosurgical procedures/ or exp ophthalmologic surgical procedures/ or exp oral surgical procedures/ or exp orthopedic procedures/ or exp amputation/ or exp anterior cruciate ligament reconstruction/ or exp arthrodesis/ or exp arthroplasty/ or exp arthroplasty, replacement/ or exp arthroplasty, subchondral/ or exp arthroscopy/ or exp bone lengthening/ or exp bone transplantation/ or exp cementoplasty/ or exp disectomy/ or exp fracture fixation/ or exp joint capsule release/ or exp limb salvage/ or exp osteotomy/ or exp ostomy/ or exp otorhinolaryngologic surgical procedures/ or exp perioperative care/ or exp perioperative period/ or exp prosthesis implantation/ or exp punctures/ or exp reconstructive surgical procedures/ or exp reoperation/ or exp second-look surgery/ or exp splenectomy/ or exp surgery, computer-assisted/ or exp surgical procedures, minimally invasive/ or exp thoracic surgical procedures/ or exp cardiac surgical procedures/ or exp mediastinoscopy/ or exp pulmonary surgical procedures/ or exp sternotomy/ or exp thoracoplasty/ or exp thoracoscopy/ or exp transplantation/ |
| --- | --- | --- | --- |
| 3 | 1 or 2 | 1497296 | 47866 |
|  |  | 3,612,895 | 30435 |
|  |  | 1,938,765 |  |</p>
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<th>exp iron compounds/ or exp ferric compounds/ or exp ferrous compounds/ or exp iron carbonyl compounds/ or exp iron, dietary/</th>
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Exp animals/not humans.sh (not sure what .sh means in the context of translating to pubmed. However, if I understand correctly this step is to get step 21 as human only studies, which PubMed can do via a species filter. I will apply species filter for search 21).

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Footnotes:
#: As the final column is a follow up to the previous literature search, the date range for this search was set to 01/09/2014-present.
References


33. WHO. WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations 2020 [Available from: https://www.who.int/publications/i/item/9789240000124.].


