





## GUIDELINE

### BSH Guideline

# 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 (<https://b-s-h.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 the 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 September 2014 (date of literature search for previous

guideline) to the 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) 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 The Royal College of Anaesthetists, The Royal College of Physicians, The Association of Anaesthetists and the Centre for Perioperative Care; these organisations do not necessarily approve or endorse the contents.

## INTRODUCTION

The previous version of this guideline was published in 2015<sup>1</sup> 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<sup>2,3</sup> and the use of intravenous iron for patients undergoing major surgery.<sup>4,5</sup>

The SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pandemic has placed extra importance on the appropriate management of preoperative patients, with a now huge number of patients<sup>6</sup> 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.<sup>7-10</sup> A BSH Good Practice Paper published in 2021<sup>11</sup> made recommendations for best patient blood management (PBM) while working within the limitations imposed by the need to minimise hospital attendances to reduce the risk of SARS-CoV-2 infection. Many of the recommendations made at that time remain relevant and where appropriate have been incorporated into the current guideline.

While blood stocks are currently good, the blood supply has been challenging, with NHS Blood and Transplant declaring an Amber alert in October 2022.<sup>12</sup> This unprecedented event led to a rapid push to implement PBM 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 only at an individual patient level but also 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 recently published Centre for Perioperative Care guideline for the management of anaemia in the perioperative pathway.<sup>13</sup> This BSH guideline provides an up-to-date literature review with recommendations. Implementation should be informed by local circumstances and integrated into existing care pathways.

### The association of preoperative anaemia with 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 PBM have evolved over the years since its inception, with the recent publication of a

global definition as follows: 'PBM 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'.<sup>14</sup> 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.<sup>15-17</sup> Studies reviewing the prevalence of anaemia in the preoperative population vary but demonstrate up to 35%–50% of preoperative patients to be anaemic,<sup>18-20</sup> this being influenced by the presenting disease, that is, cancer population, the burden of comorbidities, age, gender and surgical procedure.

The severity of anaemia has also been linked to outcomes.<sup>16</sup> Patients with a haemoglobin (Hb) concentration >100 g/L, classified as mildly anaemic, had a 30% increased relative risk of complications and death.

The identification of links between preoperative anaemia and adverse outcomes has 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.<sup>21</sup> This figure was corroborated in patients undergoing major abdominal surgery in the PREVENTT study where 82% had iron deficiency.<sup>22</sup> Recent perioperative guidelines suggest identifying and managing the underlying cause of anaemia is essential in its management.<sup>13</sup> Transfusing a patient for haematinic 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.<sup>23</sup> Transfusion for haematinic deficiency in the absence of symptoms is therefore reportable to Serious Hazards of Transfusion (SHOT) as an avoidable transfusion.<sup>24</sup> Transfusing without correcting the haematinic 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.

The detection of anaemia as part of the preoperative risk assessment is predictive of higher transfusion rates 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 and potential treatment options to allow for shared decision-making regarding further management (2B).**

## DIAGNOSIS OF ANAEMIA

### Definition of anaemia

The World Health Organization (WHO)<sup>25</sup> defines anaemia as Hb <130 g/L for men and <120 g/L for women, with recent work suggesting further evidence is required to change global disease defining thresholds.<sup>26</sup> A 2017 Europe wide consensus statement<sup>27</sup> proposed a pragmatic threshold of 130 g/L for all, based on the observation that the transfusion rate for non-pregnant women with an Hb of 120 g/L is twice that of men with an Hb of 130 g/L. In addition, this approach allows the identification of non-anaemic iron deficiency that is common in non-pregnant women, often due to heavy menstrual bleeding.<sup>28</sup> The identification of this patient cohort will allow the replenishment of iron stores prior to surgery and associated bleeding. In the preoperative setting, the focus should be on the identification of those who may benefit from the preoperative optimisation of Hb, and those who may have a serious underlying pathology.

- **In the preoperative context, Hb <130 g/L should be considered the threshold at which patients are likely to benefit from screening for iron and/or other nutrient deficiencies and enhanced PBM measures (1B).**

### Iron deficiency anaemia and iron metabolism

The prevalence and causes of preoperative anaemia vary in differing surgical populations; however, the most common cause overall is iron deficiency anaemia (IDA). In early IDA, mean cell volume (MCV) may be normal, but a declining MCV on serial blood tests (even within the normal range) may indicate iron deficiency. When present, a low MCV and a low mean cell haemoglobin are suggestive of iron deficiency which may be due to blood loss related to the presenting surgical problem (e.g. gastrointestinal cancer) or unrelated (e.g. heavy menstrual bleeding). Iron depletion results in iron-restricted erythropoiesis progressing to IDA.<sup>29</sup> Iron-restricted erythropoiesis occurs in non-pregnant women as the ferritin falls to <25 µg/L.<sup>30</sup>

### Diagnosing iron deficiency

The single most useful test to diagnose iron deficiency is the serum ferritin, with a ferritin of <15 µg/L (with or without evidence of inflammation) indicative of absolute iron deficiency (AID).<sup>31</sup> In the preoperative setting, a ferritin <30 µg/L has been suggested as a sensitive and specific marker of absolute

iron depletion or deficiency,<sup>27</sup> regardless of gender or the presence or absence of anaemia. This is the same threshold advised for the diagnosis of iron deficiency in pregnancy.<sup>32</sup> Ferritin behaves as an acute-phase reactant. In the presence of inflammation, anaemia with moderately reduced ferritin levels remains strongly suggestive of iron deficiency. The WHO suggests a ferritin threshold of 70 µg/L be used to diagnose iron deficiency in patients with concomitant inflammation (as evidenced by elevated levels of C-reactive protein for example).<sup>33</sup>

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, both serum iron and transferrin saturation (TSAT) decline. 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 on clinical trial data.<sup>31</sup> Other tests such as reticulocyte haemoglobin content may be helpful, where available, in cases where initial tests are inconclusive.<sup>31</sup> Future studies examining the impact of inflammation and comorbidities on iron homeostasis may help further define the appropriate measures of iron depletion/deficiency going forward.

- **Ferritin <30 µg/L suggests absolute iron depletion/deficiency likely to benefit from iron supplementation (1B).**
- **Ferritin 30–100 µg/L with a low TSAT (<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 premenopausal women.<sup>34,35</sup> Hypoferritinaemia in the absence of anaemia (<15 µg/L) is associated with a cancer prevalence of 0.9% in men and postmenopausal women and referral is also indicated in this context.<sup>34</sup> The decision as to whether such investigations are undertaken prior to, or after surgery will depend on the indication for and urgency of surgery and the degree of anaemia.

- **Patients with unexplained AID 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 vitamin 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.<sup>36</sup>

### Chronic kidney disease

In the presence of an estimated glomerular filtration rate of  $<30 \text{ mL/min/1.73 m}^2$ , anaemia is likely to be due to chronic kidney disease, particularly if other causes are excluded.<sup>37,38</sup>

### 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 microcytosis or 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 presents specific challenges for surgery requiring specialist collaboration.<sup>39</sup>

### Multimorbidity and frailty syndromes

Anaemia is often a marker of multimorbidity, and patients identified as anaemic who have multimorbidity and a frailty syndrome may benefit from referral to geriatricians with expertise in perioperative medicine such as such as a peri-operative care for older people undergoing surgery service for the consideration of investigation and preoperative optimisation.

- **In unexplained anaemia without iron deficiency, referral to haematology should be considered according to the severity of anaemia (e.g. men with Hb  $<120 \text{ g/L}$ , women with Hb  $<100 \text{ g/L}$ , 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<sup>27</sup> 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 United Kingdom, general practitioners are the gate keepers to this pathway, and it is important that they are involved from the outset. Such pathways may benefit from the reflex testing (the addition of predetermined additional tests to the index sample) 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](#), which 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 IDA predominantly include oral or intravenous (IV) iron.<sup>40,41</sup> However, in randomised trials of preoperative IV iron, the treatment effect to increase haemoglobin levels<sup>42</sup> has not consistently translated into reduced allogeneic transfusion or improved end-points of patient benefit such complications or length of hospital stay.<sup>43,44</sup> The perioperative population is highly heterogeneous and while there are individual groups for whom perioperative optimisation with IV rather than oral iron may be beneficial, the Cochrane reviews published to date do not recommend this across the board.<sup>45,46</sup> As a result, in this guideline we are unable to recommend for or against this.

The definition of IDA in the surgical patient has been heterogeneous in clinical trials.<sup>47</sup> The reanalysis of the PREVENTT trial suggested that a greater preoperative haemoglobin response appears in those with AID (ferritin  $<30 \mu\text{g/L}$ ) and less so in those with functional iron deficiency (FID) (ferritin  $<100 \mu\text{g/L} \pm \text{TSATS} <20\%$ ).<sup>22</sup> Similar results were seen in the cardiac surgery population, with improved peak oxygen uptake following IV iron only seen in patients with ferritin  $<30 \mu\text{g/L}$  in a reanalysis of the IronIC trial.<sup>48,49</sup> 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.<sup>5</sup> 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 established indications are likely to represent low-value care.

Oral iron is a safe, cheap and effective as the first-line treatment for correcting IDA and is recommended as first-line treatment by the National Institute for Health and Care Excellence (NICE).<sup>23</sup> Iron is better absorbed into an empty stomach, and compliance is improved with once daily dosing.<sup>50</sup> Early phase studies suggest gastrointestinal absorption of iron is similar in patients on twice daily or alternate day dosing schedules.<sup>2,3</sup> Taken together, these data support the use of administration of intermittent oral iron regimens (every other day or three times per week) rather than twice daily dosing to improve tolerability without compromising efficacy. 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 45–65 mg and no more than 100 mg of elemental iron is recommended.

Oral iron should be started as soon as iron deficiency is identified. A Hb rise of 10 g/L within 4 weeks of starting treatment with an increase in serum ferritin to above 30 µg/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.<sup>34</sup> Current lengthy waiting lists for surgery mean early identification of iron deficiency in primary care may mean effective treatment can be completed prior to formal preoperative assessment.

For patients unable to tolerate oral iron or where there is no response, IV iron is indicated. Modern IV iron preparations are safe and effective treatments for IDA with side effect profiles comparable to other intravenous therapies.<sup>27,34</sup> Dosage should be obtained from the dosage tables in the product literature or by using the Ganzoni equation.<sup>51,52</sup> 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. Monitoring for side effects should be undertaken as described in the relevant summary of product characteristics. Staff and patient education are vital.

**TABLE 1** Oral iron preparations.

Iron salt	Strength	Elemental iron
Ferrous fumarate	210 mg	68 mg
Ferrous fumarate	305 mg	100 mg
Ferrous fumarate liquid	140 mg/5 mL	45 mg/5 mL
Ferrous gluconate	300 mg	35 mg
Ferrous sulphate, dried	200 mg	65 mg
Sodium feredetate liquid	190 mg/5 mL	27.5 mg/5 mL

## Timing of iron therapy

The optimum time to administer an IV iron intervention in relation to the time of surgery is not well-defined, and given the paucity of evidence, the writing group do not make a recommendation regarding the 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 a robust system for IV treatment is already in place before surgery that is patient focused and convenient, its use in patients with AID 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 is 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 postsurgical period. Data are encouraging in terms of improvement in Hb and reduction in transfusion rates with postoperative IV iron therapy.<sup>53–55</sup> A 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 IDA 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, or where there is insufficient time in the surgical pathway to assess 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 vitamin B12 or folate deficiency

Where vitamin 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.<sup>56</sup> Intramuscular may be preferred when rapid replenishment is desired. 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 to ensure a timely response to therapy. This is in line with the current BSH guidance for the diagnosis and treatment of cobalamin

and folate disorders.<sup>36</sup> Folate deficiency should be treated with oral folic acid 5 mg daily.<sup>57</sup>

## Erythropoiesis-stimulating agent 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.<sup>58</sup> Trial data in this setting have raised concerns regarding cardiovascular risk associated with using these agents to correct Hb to normal or near normal levels.<sup>59</sup> Patients must be iron replete when considering the use of ESA to ensure efficacy, with the correction of AID 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 120 g/L for adult patients.<sup>38</sup>

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 (e.g. highly alloimmunised patients or patients who decline transfusion) was desirable.<sup>1</sup> This approach was also endorsed by the NICE transfusion guideline published in 2015.<sup>23</sup>

The primary focus of trials investigating the use of ESA preoperatively has been the impact on transfusion rates.<sup>60,61</sup> 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 600 units/kg once weekly for 3 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.<sup>62</sup> A further study found no additional benefit of an increased number of doses of preoperative ESA when compared with the standard of care of four doses.<sup>63</sup> 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 levels in the treatment group.<sup>64</sup> 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.

- **ESA therapy may be indicated to treat preoperative anaemia in patients who decline transfusion therapy or in patients who have complex red cell antibodies (2B).**

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

## Role of preoperative transfusion

Red cell transfusion plays a very 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 level. 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 six obstetric and one 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.<sup>65</sup>

In some circumstances, preoperative assessment may not have occurred, or there may have been a suboptimal response to anaemia treatment, in which case transfusion may be considered, particularly if there is an urgency for surgery. Correction of anaemia using transfusion has not been demonstrated to improve surgical outcomes for anaemic patients. A recent, retrospective review<sup>66</sup> 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.<sup>67</sup> However, a recent study in this patient group<sup>68</sup> identified preoperative anaemia itself as an independent prognostic factor for overall survival, which was not impacted by preoperative transfusion.

National guidance<sup>23</sup> 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 70 g/L and only when there is an urgency for surgery which cannot wait for the correction of anaemia by other means.

- **Preoperative transfusion should only be considered for the correction of preoperative anaemia in very anaemic patients when an urgency for 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 the treatment of preoperative anaemia with iron and other PBM interventions to reduced blood transfusion rates.
3. The mechanism of FID in surgical patients to further inform how best to manage it.
4. The effect of iron supplementation on postoperative outcomes.
5. The impact of the 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 newer iron preparations (Sucrosomial iron, Ferracru and iron hydroxide adipate tartrate) and it will be interesting to understand whether these have potential in this setting.

## AUTHOR CONTRIBUTIONS

KH chaired the writing group. All the authors contributed to the writing and revision of the manuscript.

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## CONFLICT OF INTEREST STATEMENT

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 speaker roles from Pharmacosmos. AK has received consultancy fees from Pharmacosmos and

speaker fees from Vifor Pharma. AW has received honoraria for presentations from Takeda, AbbVie and Pharmacosmos. ST received consultancy fees from Pharmacosmos for support of an experienced practice group for the management of IDA. TR has received departmental reimbursement from BioAge Labs and Viatrix. The following members of the writing group: KH, SN and 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 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 3 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](http://www.b-s-h.org.uk/guidelines)).

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**APPENDIX 1**

**Framework for preoperative anaemia pathway**

<b>Identification</b>	GPs / referring physician should consider the possibility of anaemia prior to surgical referral and consider investigating and treating those at risk	<b>Accountability</b>  General Practitioner/ practice nurse/physician associate to act on blood results and escalate concerns
	Referral letter should include all relevant clinical information	
<b>Assessment &amp; Triage</b>	Preoperative assessment should take place at a minimum of 4 weeks from the decision to operate and prior to listing for theatre.	If assessment and triage carried out in primary care, GP/practice nurse/physician associate to action  If assessment in PAC- implement local robust follow up flags for actioning abnormal results
	Patients identified as at risk of requiring a blood transfusion should have FBC 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	
	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 patients' clinical records	
	Assessment of current medication for drugs which increase blood loss consider if these can be stopped preoperatively	
<b>Diagnosis</b>	Further investigation should be undertaken if Hb<130g/L or at locally determined thresholds	If assessment and triage carried out in primary care, GP/practice nurse/physician associate to action  If assessment in PAC- implement local robust follow up flags for actioning abnormal results
	Determine the cause of anaemia: likely IDA – Ferritin <30, or ferritin 30-100 and TSAT<20 Likely ID: where MCV < 80 +/- MCH <27 Trial of oral iron for 4 weeks	
	Patients found to have IDA should be re-assessed prior to listing for theatre.	
<b>Treatment &amp; prevention</b>	If poor response to oral iron, consider IV iron if appropriate and/ or restricted time before surgery	If no response to oral or IV iron, and/or considering erythropoietin, discuss with haematology
	Erythropoietin should only be considered preoperatively if patient declines transfusion or patient has multiple alloantibodies meaning it is difficult to source donor blood	

FBC, full blood count; ID, iron deficiency; IDA, iron deficiency anaemia; IV, intravenous; MCH, mean cell haemoglobin; MCV, mean cell volume; PAC, preassessment clinic; TSAT, transferrin saturation.

## APPENDIX 2

### Literature search

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

*Column Details (reading left–right):*

*Column 1:* search number.

*Column 2:* search terms.

*Column 3:* results from prior MEDLINE search. Search was performed up until September 2014.

*Column 4:* matching search as in *Column 3* using PubMed. Publication date parameters were set as 1897 (first dates on database) to 1 September 2014.

*Column 5:* PubMed search using date range of 1 September 2014 to the present.

Three different values are shown in Columns 4 and 5.

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 multiword terms were enclosed in quote marks, for example, ‘colorectal surgery’. This makes the search specific for sources that discuss colorectal surgery, rather than sources that contain just colorectal or surgery.

*The authors believe the third value in these columns will be the most useful.*

See footnotes for further details.

#	Searches	Results (prior Medline—1894—01 Sept 2014 unless otherwise stated)	PubMed search (same parameters as Column 3)	PubMed search (01 Sept 2014 to the present)
1	exp specialties, surgical/ or exp colorectal surgery/ or exp general surgery/ or exp gynaecology/ or exp neurosurgery/ or exp obstetrics/ or exp ophthalmology/ or exp orthognathic surgery/ or exp orthopaedics/ or exp otolaryngology/ or exp surgery, plastic/ or exp thoracic surgery/ or exp traumatology/ or exp urology/ or exp sports medicine/	70 903	22 014 1 824 488 1 359 785 (quote marks)	21 923 1 339 692 1 080 059 (quote marks)
2	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/ 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 electrosurgery/ or exp endocrine surgical procedures/ or exp extracorporeal circulation/ or exp haemostasis, 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 orthopaedic 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 discectomy/ 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/	1 445 501	35 726 2 738 924 680 394 (quote marks)	13 641 1 120 596 302 280 (quote marks)

#	Searches	Results (prior Medline—1894—01 Sept 2014 unless otherwise stated)	PubMed search (same parameters as Column 3)	PubMed search (01 Sept 2014 to the present)
3	1 or 2	1 497 296	47 866 3 612 895 1 967 032 ( <i>quote marks</i> )	30 435 1 938 765 1 324 303 ( <i>quote marks</i> )
4	exp iron compounds/ or exp ferric compounds/ or exp ferrous compounds/ or exp iron carbonyl compounds/ or exp iron, dietary/	36 111	1190 70 424 26 220 ( <i>quote marks</i> )	208 27 619 11 588 ( <i>quote marks</i> )
5	exp Vitamin B12/	6807	581 23 719 22 786 ( <i>quote marks</i> )	41 4416 4226
6	exp Folic Acid/	17 745	938 41 682 33 101 ( <i>quote marks</i> )	119 13 126 10 605 ( <i>quote marks</i> )
7	exp Haematinics/ or exp Erythropoietin/	40 154	2516 74 574 74 360 ( <i>quote marks</i> )	340 22 075 21 935 ( <i>quote marks</i> )
8	4 or 5 or 6 or 7	71 132	4090 158 867 109 383 ( <i>quote marks</i> )	569 149 525 11 588 ( <i>quote marks</i> )
9	3 and 8	5299	373 17 804 7157 ( <i>quote marks</i> )	123 3461 615 ( <i>quote marks</i> )
10	9	5299	373 17 804 7157 ( <i>quote marks</i> )	123 3461 615 ( <i>quote marks</i> )
11	limit 9 to English language and humans and yr '2009–current'	1316	56 3152 1468 ( <i>quote marks</i> )	62 <sup>*</sup> 2408 437 ( <i>quote marks</i> )
12	randomised controlled trial.pt	294 171	392 904	174 661
13	controlled clinical trial.pt	44 550	477 398	180 414
14	randomised.ab	241 270	327 583 <sup>*</sup>	280 438 <sup>*</sup>
15	placebo.ab	108 669	161 105 <sup>*</sup>	73 355 <sup>*</sup>
16	clinical trials as topic.sh	91 172	703 139 <sup>+</sup>	236 060 <sup>+</sup>
17	randomly.ab	163 746	223 203 <sup>*</sup>	158 788 <sup>*</sup>
18	trial.ti	93 985	130 418	129 686
19	12 or 13 or 14 or 15 or 16 or 17 or 18	654 569	1 022 162 <sup>*</sup>	540 918 <sup>*</sup>
20	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)	1 891 498	N/A	N/A
21	19 not 20 (for our searches we have done 19 with Humans filter)	595 530	894 563 <sup>§</sup>	389 037 <sup>§</sup>
22	11 and 21	245	10 629 241	12 433 91

\* PubMed "Title/Abstract" used for these searches.

<sup>+</sup> PubMed "Clinical Trial" filter applied as the publication type here.

<sup>§</sup> #19 Search run through the "Humans Only" PubMed filter.

<sup>¶</sup> As the final column is a follow-up to the previous literature search, the date range for this search was set to 1 September 2014 to the present.