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Pre-op Correction of Iron Deficiency Anaemia

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Risk of transfusion; SHOT 2016

- Mortality 1 per 100,000, morbidity 5 per 100,000
- Transfusion reactions 3.5 per 100,000
- Transfusion related circulatory overload (TACO) 1.5 per 100,000
- Transfusion associated dyspnoea 0.2 per 100,000
- Viral transmission 10 episodes in 10yrs;
  - <1 in million HIV 1 + 2
  - <1 in million hepatitis C
  - <1 in million hepatitis B.
  - <1 in million hepatitis E
- CJD. None since 1999
- Bacterial infection 10 episodes in 10yrs.
- ?Next new risk

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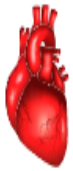
SHOT REPORT 2016

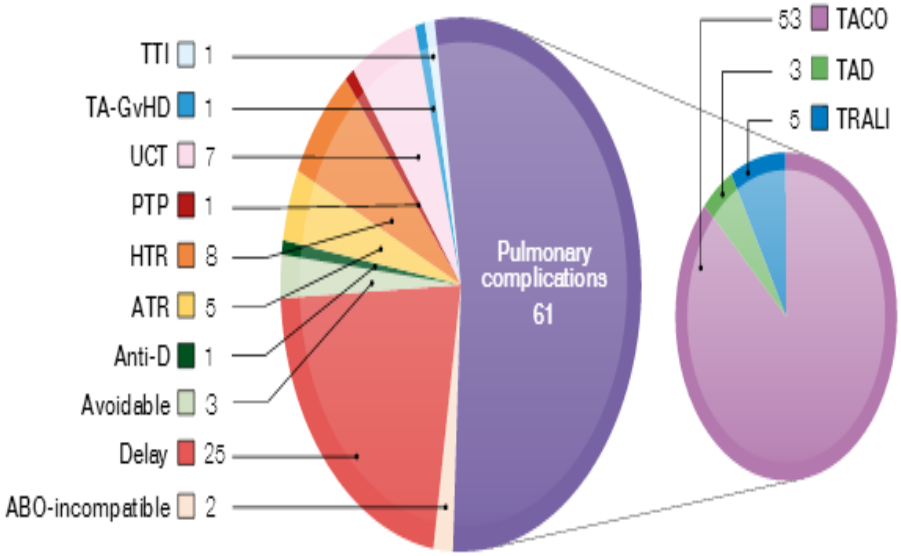
TACO Checklist	Red cell transfusion for non-bleeding patients
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic?
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?
	Is the fluid balance clinically significantly positive? Is the patient on concomitant fluids (or has been in the past 24 hours)? Is there any peripheral oedema? Does the patient have hypoalbuminaemia? Does the patient have significant renal impairment?

If 'yes' to any of these questions

1. Review the need for transfusion (do the benefits outweigh the risks)?
2. Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?
3. Consider body weight dosing for red cells (especially if low body weight)
   - Transfuse one unit (red cells) and review symptoms of anaemia
   - Measure the fluid balance
   - Consider giving a prophylactic diuretic
   - Monitor the vital signs closely, including oxygen saturation

Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.

Pulmonary complications, particularly transfusion-associated circulatory overload (TACO), cause the most deaths and major morbidity. Delayed transfusions are an important cause of death, 25/115 (21.7%) 2010 to 2016



We need to optimise the Haemoglobin pre-op

- To reduce Transfusions
- To reduce Length of Stay
- To reduce Morbidity
- To reduce Mortality
- To improve QOL

- How can we do this?

1. Identify anaemia
2. Identify cause
3. Treat cause

Simples……

Anaemia – a minor detour

- WHO: 130 g/L men, 120 women (1968)

Gender bias?

- Women are smaller than men
- Women have smaller body surface area and less blood
- Women bleed just as much as men!

- **Question** - Should we be aiming for an Hb > 130 g/L in men *and* women?

Anaesthesia 2018 doi:10.1111/anae.14185

Original Article

The association between borderline pre-operative anaemia in women and outcomes after cardiac surgery: a cohort study

G. Blaudszun,[1] K. E. Munting,[1] A. Butchart,[1] C. Gerrard[2] and A. A. Klein[3]

1 Fellow, 2 Information Analyst, 3 Consultant, Department of Anaesthesia and Intensive Care, Papworth Hospital, Cambridge, UK

Answer – Yes, Probably

- Women with Hb 120-130 have ↑ morbidity
  - 24% had Hb <120 g/l "anaemic"
  - 29% had Hb 120–129 g/l "borderline anaemic"
  - 47% had Hb ≥ 130 g/l "not anaemic"
- Blood Transfusion (p=0.0001) RR1.5 (1.4–1.7):
  - "Borderline anaemic" transfused **69%**
  - "Not anaemic" transfused **45%**
- "Borderline anaemia" received more units (p=0.0001)
- LOS significantly longer; p=0.0159.
  - "Borderline anaemic" **8d** (6–12 [3–45])
  - "Not anaemic" **7d** (6–11[4–6])
- No significant difference in long/short term survival

What IS iron deficiency?

- Absolute Iron deficiency
  - A condition where there is an inadequate amount of mobilisable iron stores resulting in a compromise in iron supply to tissues.
- Functional Iron deficiency **(Anaemia of chronic disease)**
  - Where there is insufficient iron incorporation into erythroid precursors in the face of adequate iron stores.


bjh guideline

Guideline for the laboratory diagnosis of functional iron deficiency

D. Wayne Thomas,[1] Rod F. Hinchliffe,[2] Carol Briggs,[3] Iain C. Macdougall,[4] Tim Littlewood[5] and Ivor Cavill[6]
on behalf of British Committee for Standards in Haematology

How do I Dx Iron deficiency?

- Simples? NO!
- **Ferritin**
  - LOW
  - EXCEPT in
    - Infection
    - Surgery
    - Inflammation
    - Cancer

  <12=absolute Iron deficiency

  <100=high likelihood of IDA

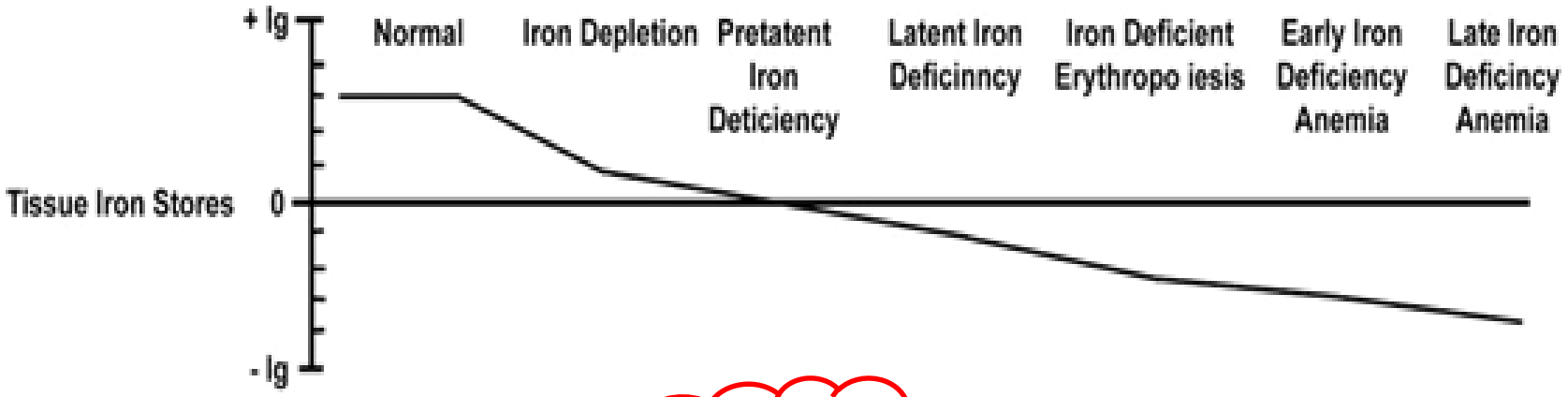
  <200=high likelihood of IDA IF on dialysis

  <1500=cannot exclude functional iron deficiency
- **MCV/MCH**
  - LOW (but only in severe IDA)
  - EXCEPT in
    - Thalassaemia
    - Blood loss (is a very late marker)

Transferrin saturation	• LOW • FALLS in inflammation
TIBC	• HIGH • EXCEPT in inflammation
Reticulocytes	• HIGH in bleeding • LOW in IDA, CKD, BMF
Erythropoietin	• HIGH • EXCEPT in CKD, Cancer • Expensive
Bone marrow iron stores	• Invariably low in true iron deficiency • Unrealistic to use routinely

A Plea

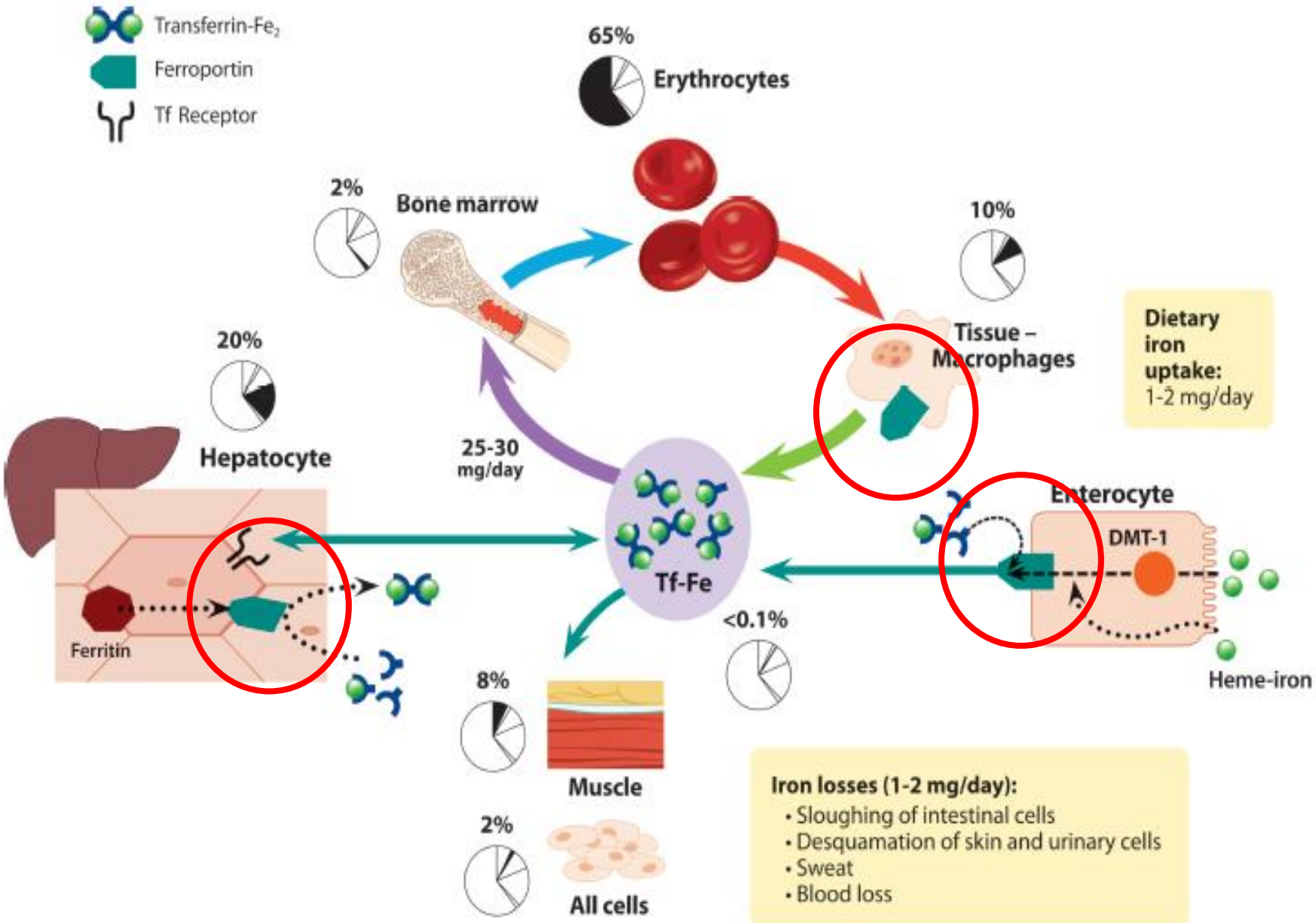
- Don’t EVER look at serum iron



Serum Ferritin (µg/1)	60	20	<12	<12	<12	<12	<12
Transferrin Saturation (%)	35	35	35	20	<16	<16	<16
Hemoglobin (g/dl)	140	140	140	140	130	<120	<120
Mean Corpuscular Volume (μ^3)	90	90	90	90	88	86	<82
Mean Corpuscular Hemoglobin Concentration (0/0)	33	33	33	33	33	31	<28

Why the variablility in results? A brief science interlude….

- ~50mg iron in diet/day
- Absorbed from enterocyte via Ferroportin molecule.
- Transported in blood on Transferrin molecule.
- Stored in hepatocyes, tissue macrophages & BM.
- Transported from blood to storage via Ferroportin.
- Released from storage when required via Ferroportin.



Lasocki et al. Anesthesiology 2011; 114: 688-94

Hepcidin

- A regulator of iron homeostasis
- Amino acid produced mainly in the liver.
- Acts by binding to Ferroportin.
- Blocks Ferroportin absorption of Fe in intestinal cells leading to iron deficiency.
- Blocks Ferroportin release of Fe from macrophages and hepatocytes.

Hepcidin action

INCREASED LEVELS

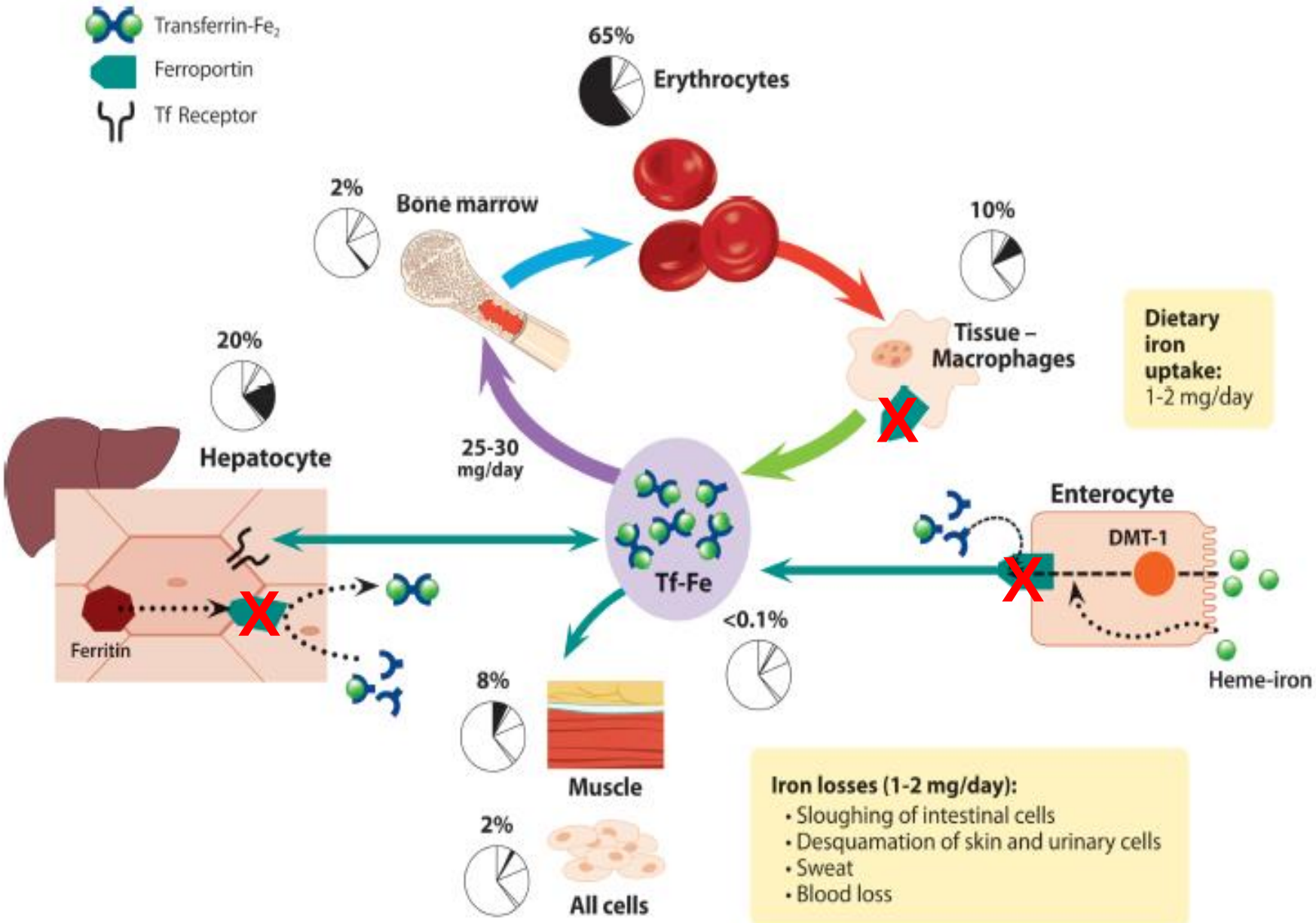
- ↑ Ferroportin blockade
- ↓ Absorption & storage Fe
- ↑ in iron overload
- BUT

REDUCED LEVELS

- ↓ Ferroportin blockade
- ↑ Absorbtion & storage Fe
- ↓ in acute blood loss
- ↓ in iron deficiency,
- ↓ hypoxia

↑ in INFLAMMATION via IL-6
↑ CKD as cleared by the kidney.
Ageing is a pro-inflammatory state,
so ↑ with age.

↓ CLD as produced in liver.



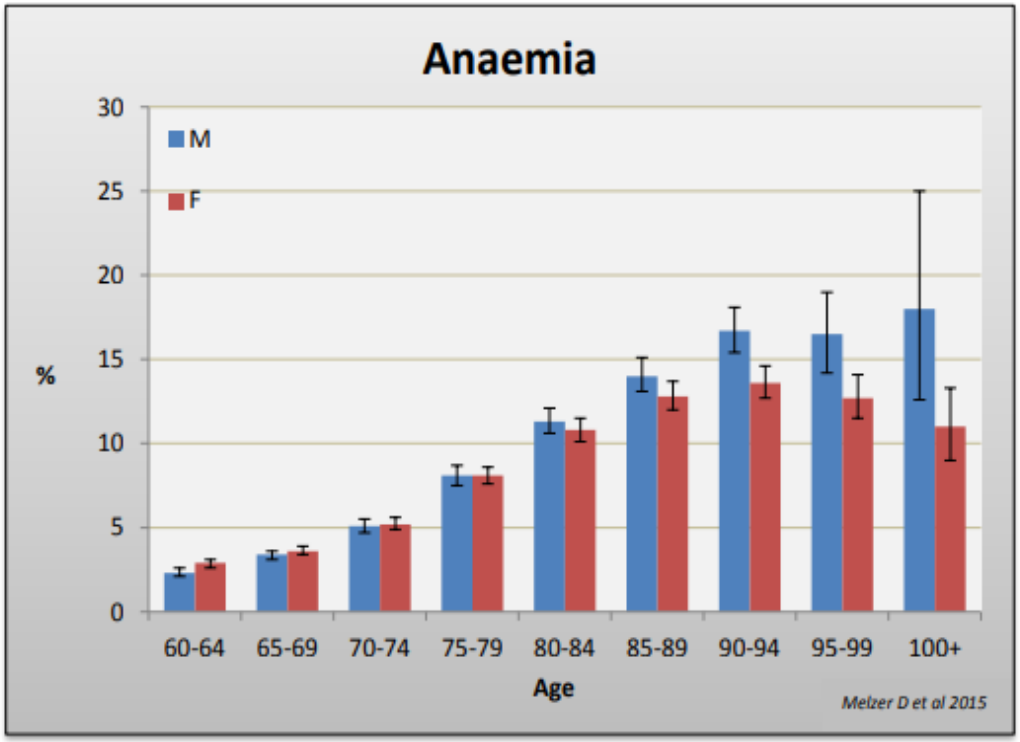
Lasocki et al. Anesthesiology 2011; 114: 688-94

Simples?

1. Identify anaemia
2. Identify cause
3. Treat cause

1. Identify Anaemia

Figure 18: Prevalence of recorded anaemia (all types) in English general practice records in 2014. Previous 5 years of GP patient history considered.



Note: Estimate from CPRD records based on clinical codes entered in anonymised GP records up to 5 years previously, with 95% confidence intervals.

•Source Age UK 2015

By Whom?

- GP?
- Pre-assessment clinic?
- Pre-op anaemia clinic?
- How is anaemia communicated between teams….?

2. Identify cause

- 1/3 are nutritional
  - Iron, Folate, B12 deficiency
  - 12% Iron deficient patients have GI malignancy
- 1/3 have functional iron deficiency
  - Inflammatory diseases
  - CKD
  - Cancer
- 1/3 have no cause identified.
  - Bone marrow cause?

3.Treat cause

NICE National Institute for Health and Care Excellence

NICE Quality Statement 138

- **Patients with iron-deficiency anaemia who are having surgery should be offered iron supplementation before and after surgery.**

- Pre-operative anaemia is associated with increased morbidity and mortality, and increased transfusion.
- Treating iron deficiency with iron supplements can reduce the need for blood transfusion.
- This avoids serious risks associated with blood transfusion e.g. infection, fluid overload and mismatch.
- May also reduce the length of hospital stays and cost to the NHS.
- Depending on the circumstances, the cause of the iron deficiency should be investigated before or after surgery.

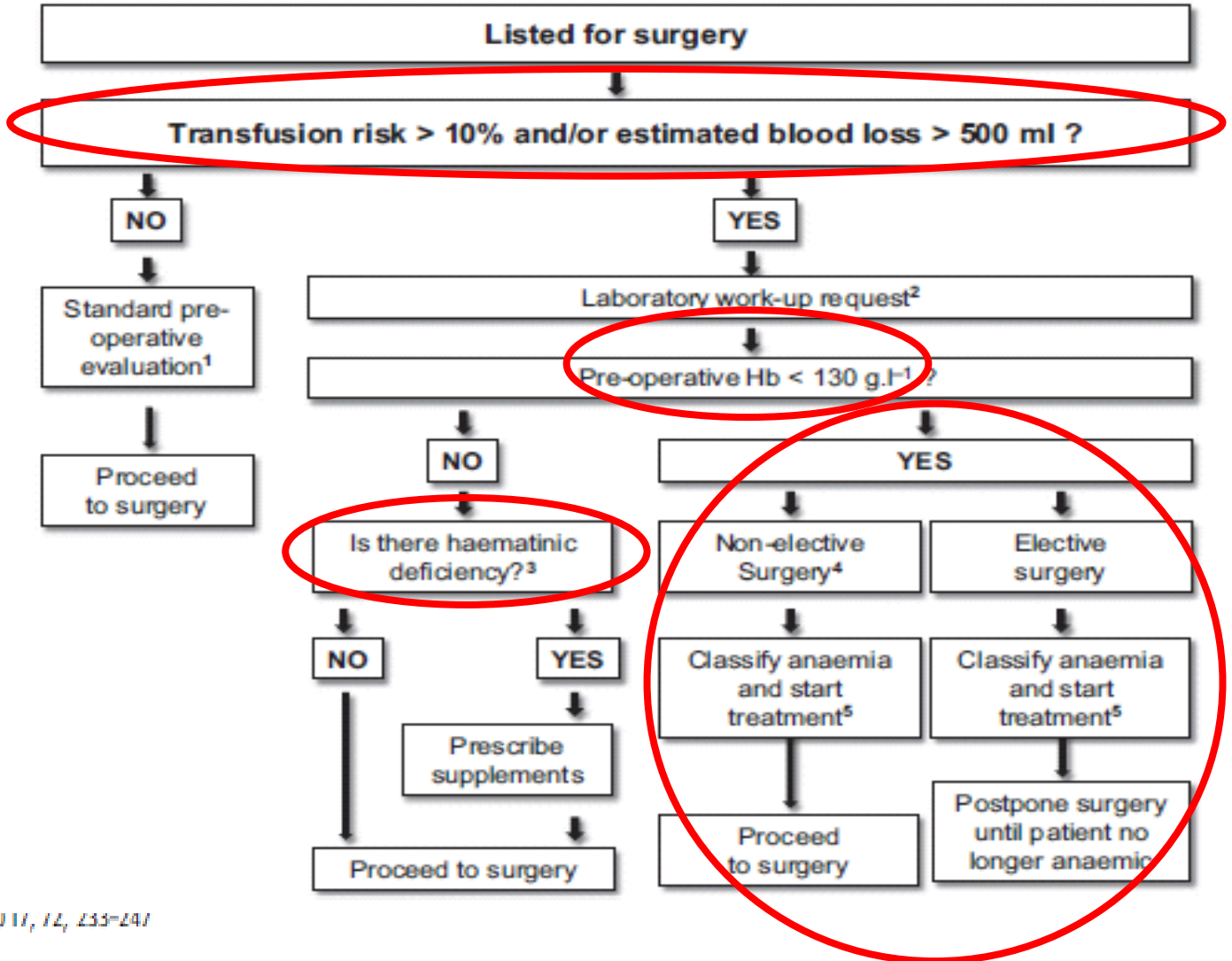
Anaesthesia 2017 doi:10.1111/anae.13773

Consensus Statement

International consensus statement on the peri-operative management of anaemia and iron deficiency

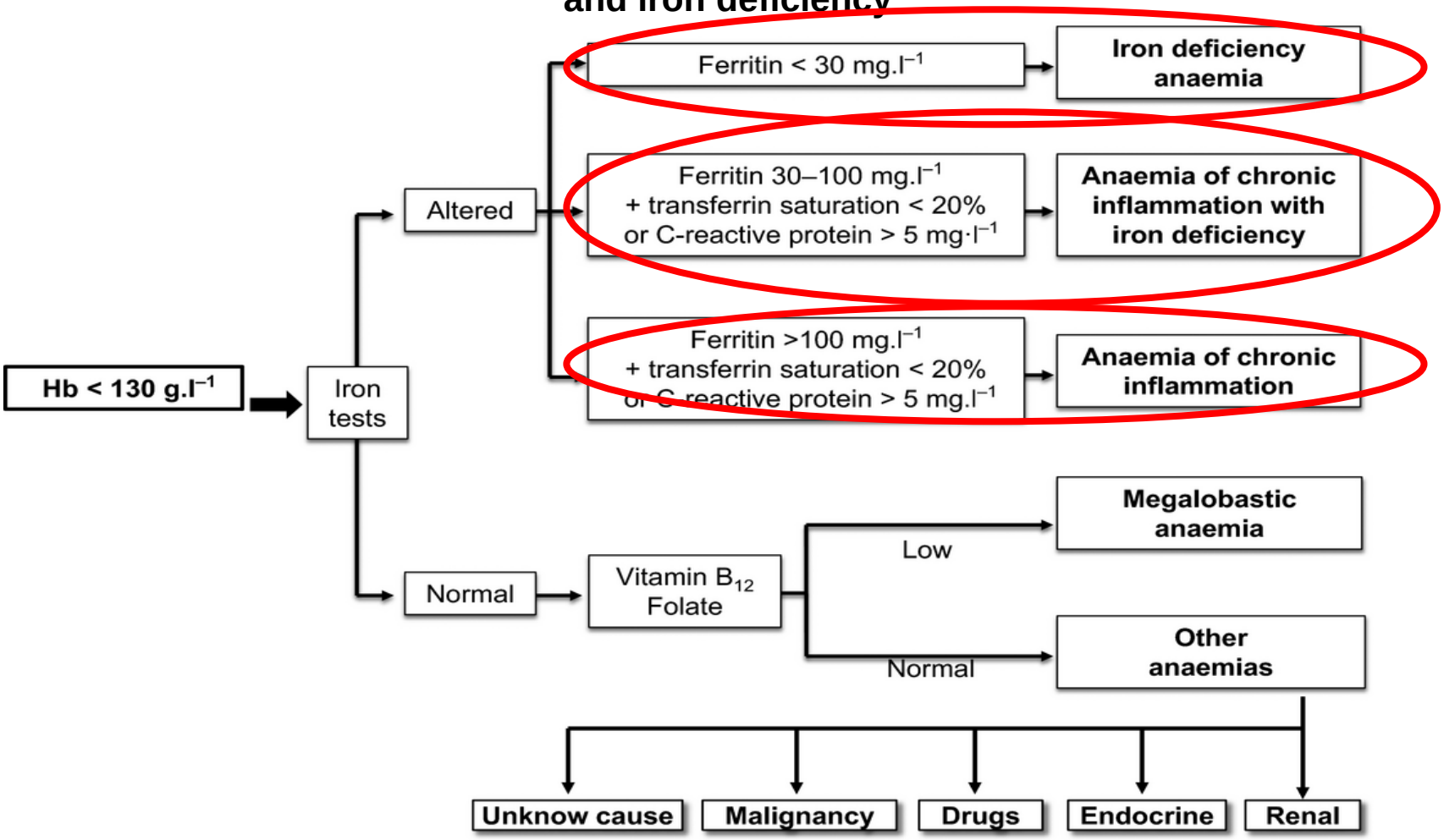
M. Muñoz,[1] A. G. Acheson,[2] M. Auerbach,[3] M. Besser,[4] O. Habler,[5] H. Kehlet,[6] G. M. Liumbruno,[7] S. Lasocki,[8] P. Meybohm,[9] R. Rao Baikady,[10] T. Richards,[11] A. Shander,[12] C. So-Osman,[13] D. R. Spahn[14] and A. A. Klein[15]

Algorithm for the Management of a Surgical Patient



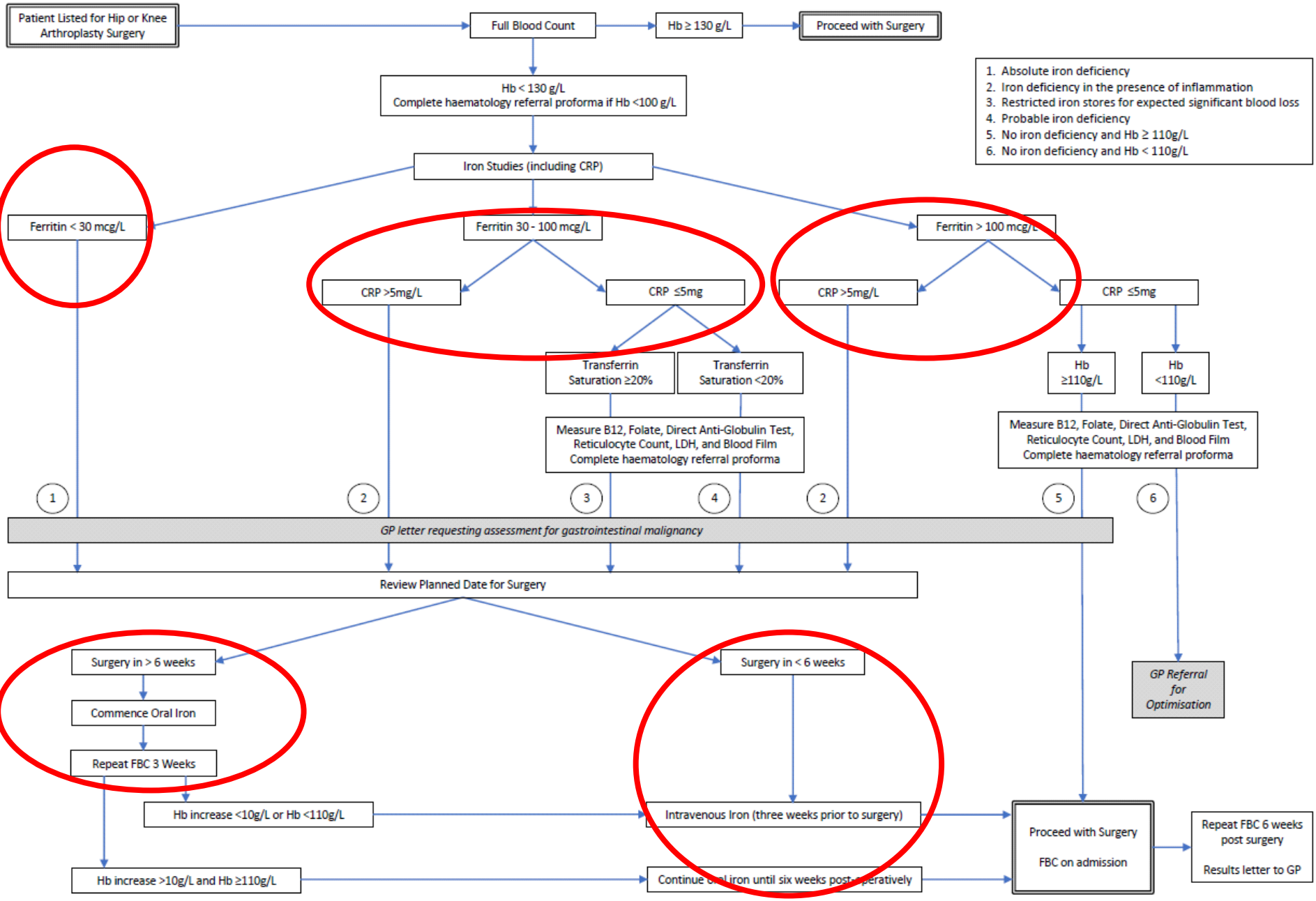
Anaesthesia 2017, 72, 233–247

International consensus statement on the peri-operative management of anaemia and iron deficiency



Anaesthesia
Volume 72, Issue 2, pages 233-247, 20 DEC 2016 DOI: 10.1111/anae.13773
http://onlinelibrary.wiley.com/doi/10.1111/anae.13773/full#

Pre-Operative Anaemia Algorithm for Males and Females
Hip and Knee Arthroplasty Surgery: Nuffield Orthopaedic Centre



UIBC	^58	umol/L		Auth
TIBC	60	umol/L	(45 to 70)	Auth
% saturation	3	%	(25 to 56)	Auth
Ferritin	9	ug/L	(30 to 400)	Auth
Vitamin B12	341	ng/L	(197 to 771)	Auth
Folate	19.5	ug/L		Auth

Comments :

Folate Reference Range: > 3.8 ug/L

WBC	7.7	10^9/L	(3.7 to 11.1)	Auth
RBC	3.14	10^12/L	(4.32 to 5.6)	Auth
Hb	68	g/l	(130 to 170)	Auth

Iron	4	umol/L	(5.8 to 34.5)	Auth
UIBC	^69	umol/L		Auth
TIBC	73	umol/L	(45 to 70)	Auth
% saturation	5	%	(14 to 51)	Auth
Ferritin	3	ug/L	(13 to 150)	Auth
Vitamin B12	563	ng/L	(197 to 771)	Auth
Folate	6.6	ug/L		Auth

Comments :

But?

- HOW?
- WHO?
- WHERE?
- COST?

- Hopefully we have convinced you of why?

Business Case: Anaemia Clinic

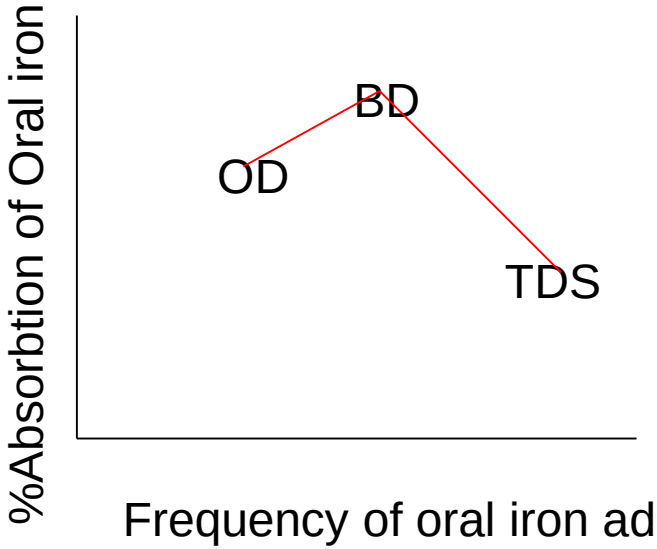
- **Advantages:**
- Reduction in pre-operative anaemia
- Reduction in blood transfusion
- Potential for reduction in post operative morbidity and mortality
- Economic benefits associated with reduced length of stay in hospital
- Potential for income generation in the form of tariff for treatment of pre-operative anaemia

- **Disadvantages:**
- Requirement for additional staffing
- Requirement for training of staff

Example – Colorectal pre-op anaemia clinic. 2000pts/yr
£324.00 expenditure per patient
£255.00 overall savings per patient -> TOTAL SAVING £510,000

Oral Iron

- Use if >6 weeks pre-surgery, test at 3 weeks to confirm response
- Takes ~4 weeks to have an effect
- Frequently poorly tolerated – GI side effects, poor compliance.
- Evidence presented at BSH 2017



- Takes 3 months to fully replace iron stores
- Absorption best if
  - On an empty stomach (advice often to take on full stomach to reduce SE)
  - With acidic drink (Vitamin C)
  - Avoid tannins (tea) Calcium and PPI's to optimise absorption

Intravenous Iron

- Can't or won't take oral iron
- Fail to respond to oral iron in 4 weeks
- < 4 weeks to surgery
- Average 6.6g/L better Hb increase with IV than PO, and 18% average reduction in transfusion **Litton et al. BMJ 2013**
- Single dose – as much as possible in one visit (20 mg/kg)*
- Ferrinject max dose 1000mg/dose (2 doses)
- Monofer max dose 2000mg/dose (1 dose)

*Dose limitations per single administration vary between different IV iron preparations, please refer to the product SPC for full prescribing information

NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Costing statement: Blood transfusion

Implementing the NICE guideline on blood transfusion (NG24)

IV iron vs transfusion

- Blood costs £170-1st unit, £162 2nd/3rd units
- Ferrinject used at SASH £154/1000mg
- 15 min infusion vs overnight stay for blood
- Low risk (IV iron) vs mod risk (blood)
- Blood gives symptomatic relief at 24-48hrs, but doesn't treat cause.
- IV iron gives improvement HB within 7 days. Maximum Hb seen 4-6weeks

Side Effects of Ferrinject

- Mild side effects 1 to 10%
  - headache, arthralgia
  - dizziness,
  - rash,
  - nausea and vomiting,
  - abdominal pain,
  - muscle cramps,
  - diarrhoea,
  - constipation,
  - abnormal liver function,
  - low or high blood pressure
  - injection site reactions.
  - Increased infections
- Anaphylaxis(1/10000 to 1/1000)

To Summarise

- Use 130g/L as cutoff for anaemia in male and female patients
- Use Ferritin <100 Transferrin% <20% and CRP >5 in diagnosis of IDA (=normal range in APEX)
- DON'T LOOK AT SERUM IRON
- GP referral for ?GI malignancy is recommended for all uninvestigated IDA
- Use PO Iron if there is >6 weeks pre-op, OD with dietary advice.
- Recheck FBC after 3 weeks to ensure response
- If intolerant or unresponsive to PO, or there is <4 weeks to surgery, use IV iron.
- If there is functional Iron deficiency with ferritin >100 but CRP<5, further investigation may be required, but IV iron may help.
- Consider pre-op anaemia flowchart for your specific population needs and consider a business case for a pre op anaemia clinic.

Thank You!

- Any Questions?