

AN OVERVIEW OF IRON DEFICIENCY ANAEMIA IN THE PERI-OPERATIVE SETTING

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UK-MONF-0320-00003 March 2020
Prescribing Information can be found at the end of this presentation

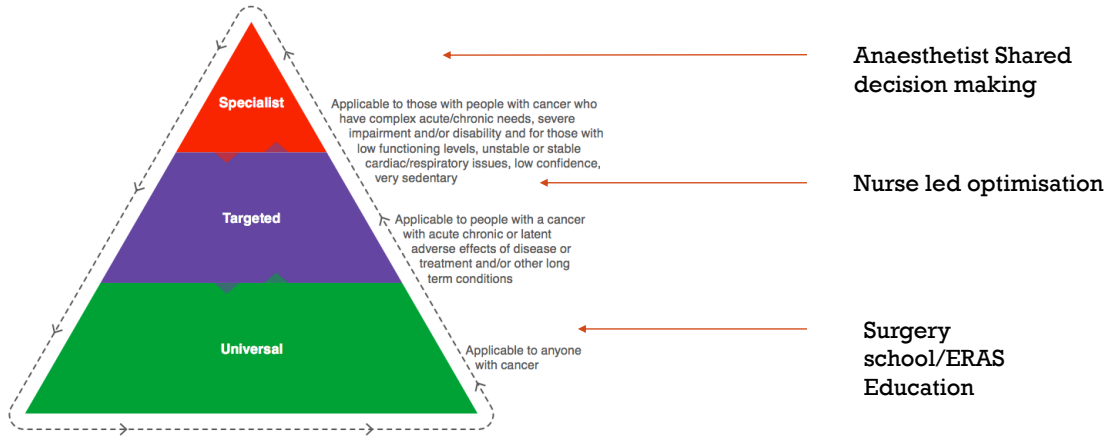
DISCLOSURES

- Pharmacosmos – Honoraria
- Grant from Pfizer for a COPD optimisation nurse specialist
- BMS grant to design materials for newly diagnosed AF

- Can't quite believe as an anaesthetist after all these years I have any
- However, pre-assessment is a massively growing area. It is a new specialty in its own right with its own specific treatments



Figure 3: Prehabilitation interventions



Principles and guidance for prehabilitation within the management and support of people with cancer in partnership with Acknowledgements - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Prehabilitation-interventions_fig2_336617250 [accessed 26 Feb, 2020]



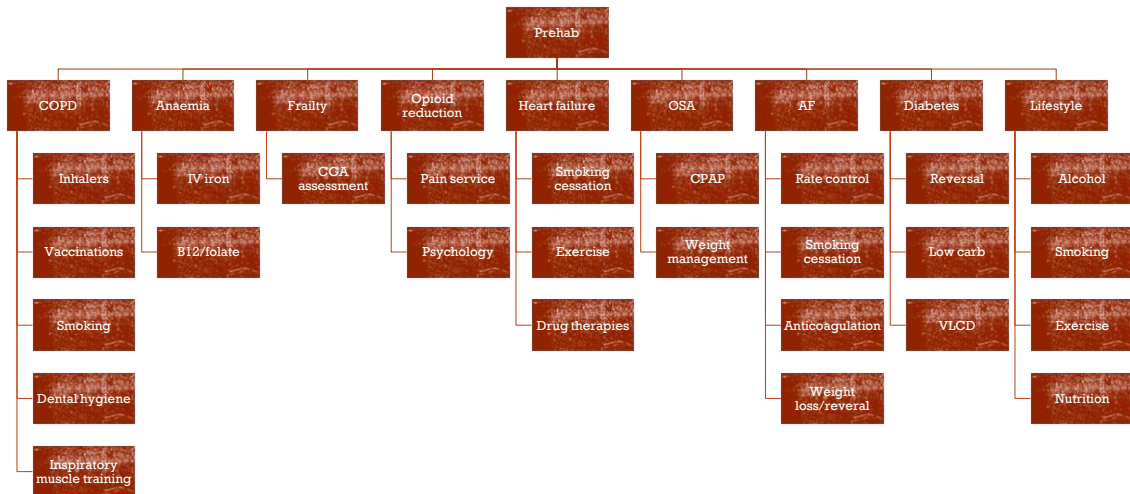
WHAT IS PREHAB

| Always | Often | Sometimes |
|--------------------------|---|---|
| <p>Physical activity</p> | <p>Dietary support</p> <p>Psychological wellbeing</p> | <p>Respiratory exercises</p> <p>Smoking cessation and alcohol reduction</p> <p>Medication and comorbidities review</p> <p>Anaemia management</p> <p>Other (e.g. speech and language therapy, fatigue management, pain management, body image)</p> <p>Lymphoedema management</p> |



WHAT IS PREHAB – WHERE PRE-ASSESSMENT FITS

| Always | Often | Sometimes |
|--|--|---|
|  Physical activity |  Dietary support |  Respiratory exercises |
| | Psychological wellbeing | Smoking cessation and alcohol reduction Medication and comorbidities review Anaemia management Lymphoedema management Other (e.g. speech and language therapy, fatigue management, pain management, body image) |



ANAEMIA

“It’s an easy
win”
Perioperative
GIRFT lead



ANAEMIA

“It’s an easy
win”
Perioperative
GIRFT lead



WHAT IS ANAEMIA



THE WHO DEFINED THRESHOLDS FOR ANAEMIA HAVE NOT BEEN UPDATED SINCE 1968

In 1958 WHO convened a study group to review information available on iron deficiency anaemia

Recommended studies be undertaken to address areas of uncertainty

In 1968 WHO convened a further study group to review progress during which the currently used criteria for diagnosis of anaemia were determined

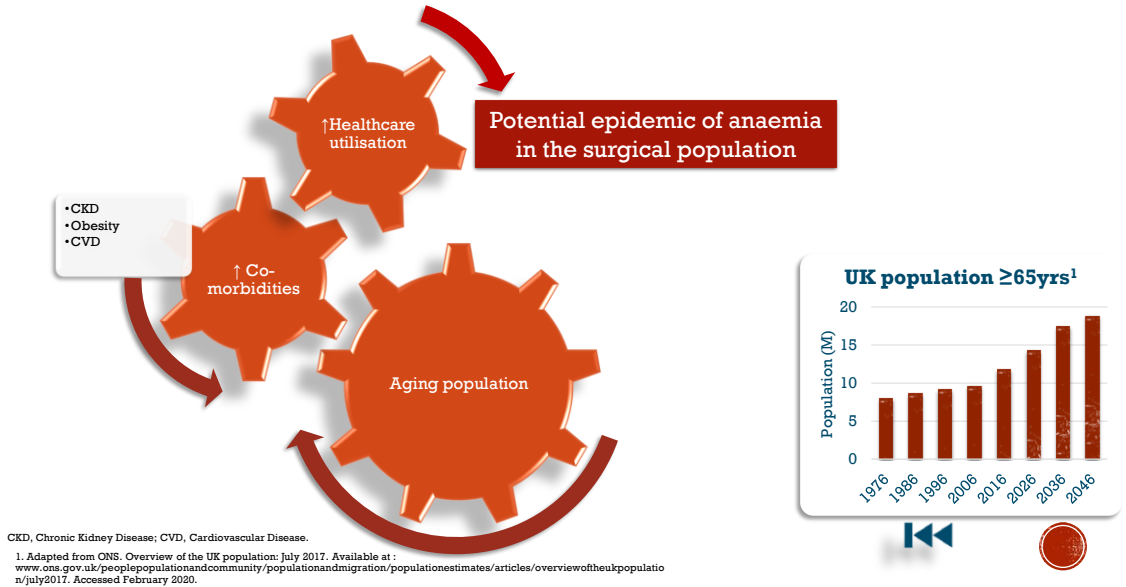
CRITERIA FOR THE DIAGNOSIS OF ANAEMIA

The report of the 1958 WHO Study Group recommended haemoglobin values below which anaemia could be considered to exist. These figures were chosen arbitrarily and it is still not possible to define normality precisely. It is recommended that, in future studies, anaemia should be considered to exist in those whose haemoglobin levels are lower than the figures given below:-

| | Hb g/l |
|------------------------------|--------|
| Children 6mon-6yrs | 110 |
| Children 6-14yrs | 120 |
| Adult Males | 130 |
| Adult Females (non-pregnant) | 120 |
| Adult Females (pregnant) | 110 |



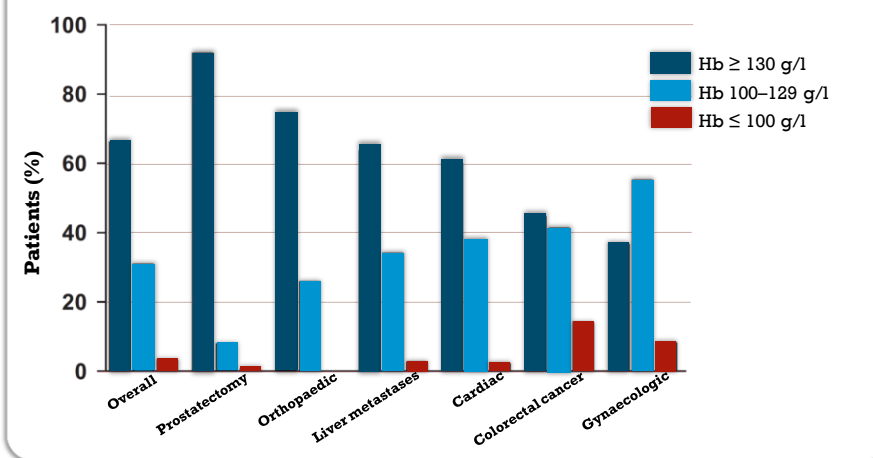
CHANGING DEMOGRAPHICS IMPACT LEVELS OF ANAEMIA IN THE SURGICAL POPULATION



HAEMOGLOBIN LEVELS DIFFER BETWEEN TYPES OF SURGERY

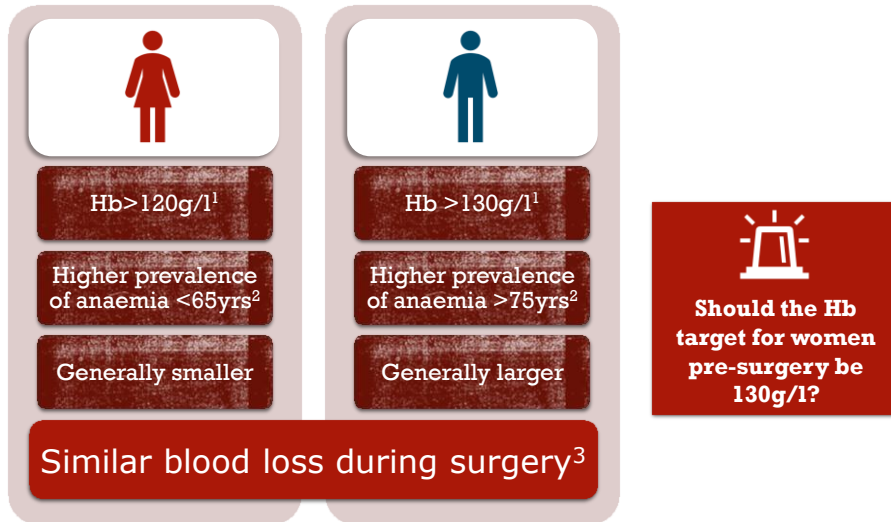
Adapted from: Munoz M, et al. *Anaesthesia* 2017;72:826–834.

• 3342 consecutive patients from 5 centres in Spain (Jan 2008 – Dec 2014)



Hb, haemoglobin.

GENDER BIAS



Hb, haemoglobin.

1. WHO Technical Support Series No. 405, 1968; 2. Patel KV. *Semin Hematol.* 2008;45(4):210-217; 3. Gombotz H, et al. *BMJ Open* 2016;6:e012210.

GENDER DISPARITIES IN RBC TRANSFUSION IN ELECTIVE SURGERY: A POST HOC MULTICENTER COHORT STUDY

Gombotz *et al.* *BMJ Open* 2016;6:e012210

A post hoc gender comparison of transfusion-related modifiable risk factors among patients undergoing elective surgery

- 23 Austrian centers randomly selected and stratified by region and level of care

6,530 patients enrolled – 3465 women and 3065 men

- 1491 coronary artery bypass graft (CABG)
- 2570 primary unilateral total hip replacement (THR)
- 2469 primary unilateral total knee replacement (TKR)

Primary outcomes

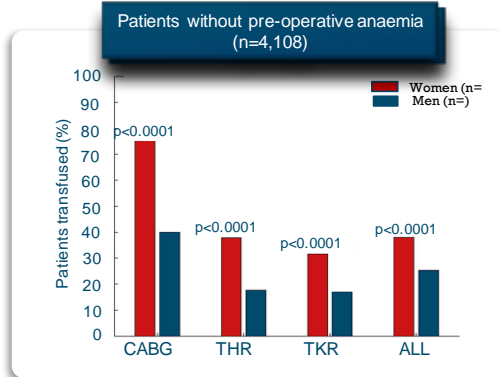
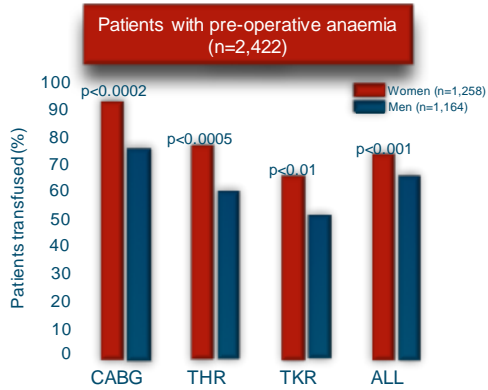
- Number of allogeneic and autologous red blood cell (RBC) units transfused (postoperative day 5)
- Differences in intraoperative and postoperative transfusion rate between men and women.

Secondary outcomes

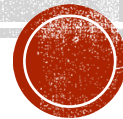
- Perioperative blood loss in transfused and non-transfused
- Volume of RBCs transfused
- Perioperative haemoglobin values and circulating red blood volume on postoperative day 5.

1. Gombotz H, et al. *BMJ Open* 2016;6:e012210.

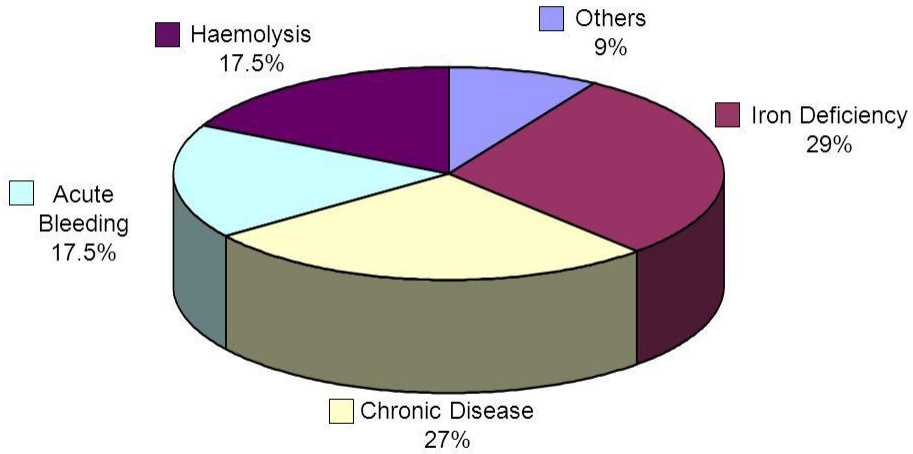
TRANSFUSION RATES HIGHER IN WOMEN



CAUSES OF ANAEMIA



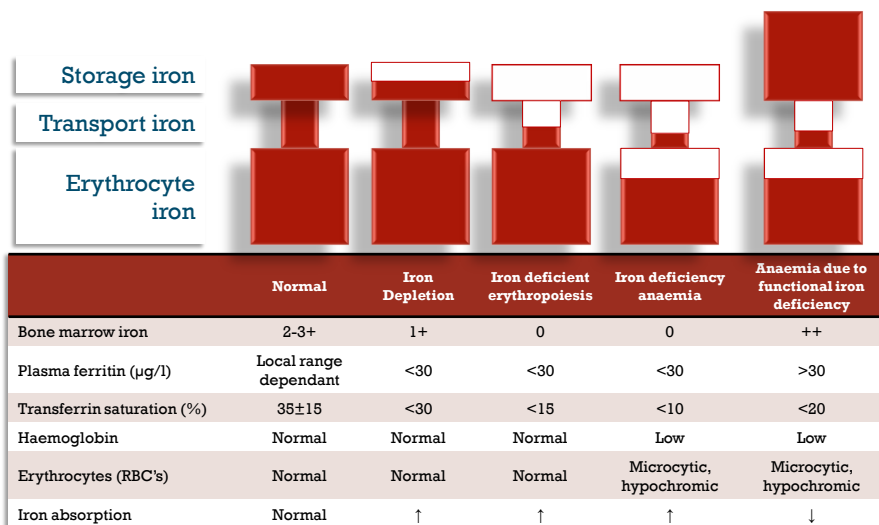
Main Causes of Anaemia



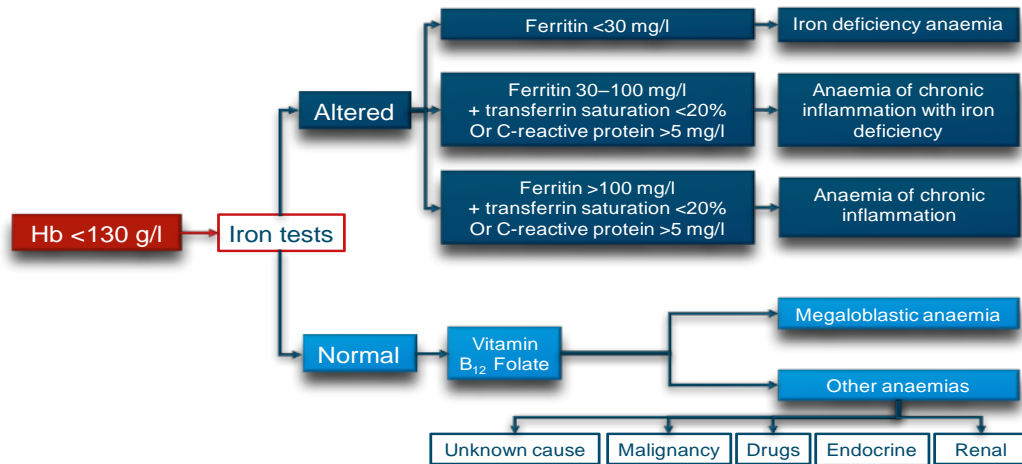
Beris P, Tobler A. *Schweiz Rundsch Med Prax.* 1997;86:1684.

Reprinted from Lambert JF, et al. In C Beaumont, P Beris, Y Beuzard, C Brugnara, eds. *Disorders of iron homeostasis, erythrocytes, erythropoiesis.* Forum service editore, Genoa, Italy, 2006 page 73 figure 1, by permission of European School of Haematology.

STAGES OF IRON DEFICIENCY AND IRON DEFICIENCY ANAEMIA

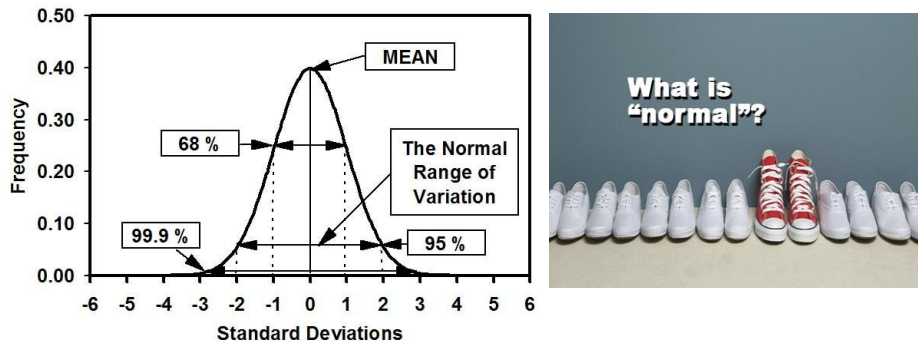


CLASSIFICATION OF ANAEMIA



WHAT IS ANAEMIA IN A SURGICAL POPULATION?

WHAT IS THE DEFINITION OF NORMAL?



Hepatobiliary surgery

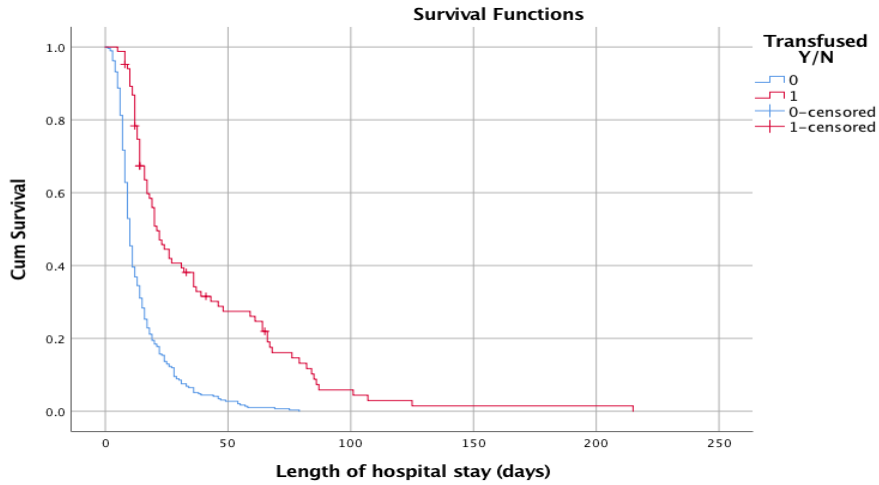
- Whipples and liver resections
1. Highest blood loss surgery
 2. Vast majority open procedures
 3. All cancers

BLOOD TRANSFUSION RATE 22.3%

TRANSFUSION AND PERIOPERATIVE OUTCOMES

| | Not Transfused | Transfused | P= |
|--------------------------------------|----------------|--------------|--------|
| N= | 293 | 84 | |
| Age | 64.1 yrs(11.5) | 63.3 (11.2) | 0.55 |
| Sex | 111f 182m | 35f 48m | 0.52 |
| Preop Hb | 135.75 (14.5) | 118.8 (19.7) | <0.001 |
| Length of surgery mins | 400 (107) | 488 (114) | <0.001 |
| Length of CCU stay | 1.93 (2.0) | 10.2 (14.5) | <0.001 |
| Length of total hospital stay | 14.2 (12.1) | 35.1 (34.1) | <0.001 |
| In hospital Mortality n= | 0 | 7 (8.3%) | |

KAPLEIN-MEIER SURVIVAL CURVE



PRE-OPERATIVE HB AND TRANSFUSION

| Hb | N | Tx | Not Tx | Tx rate | Mean LoS | Median LoS |
|---------|-----|----|--------|---------|----------|------------|
| <100 | 19 | 18 | 1 | 95% | 27 | 20 |
| 100-109 | 14 | 6 | 8 | 43% | 23 | 20 |
| 110-119 | 45 | 15 | 30 | 33% | 21 | 13 |
| 120-129 | 85 | 21 | 64 | 24% | 20 | 11 |
| 130+ | 214 | 24 | 190 | 11.2% | 17 | 10 |



OPTIMAL HB AND TRANSFUSION RATES

| | Hb <125 | Hb =>125 | P= |
|--------------------------------|-------------|-------------|--------|
| N= | 121 | 256 | |
| Transfusion rate | 46.2% | 10.9% | <0.001 |
| Length of CCU stay | 5.8 (10.9) | 3.0 (5.7) | 0.001 |
| Length of hospital stay | 24.5 (27.9) | 16.9 (16.6) | 0.002 |



ORTHOPAEDIC ANAEMIA

- Consecutive patients from 2015 having elective primary hip or knee replacement surgery at Freeman
- Why – prior to a real optimisation process for orthopaedic anaemia
- Told blood transfusion rate extremely low historically
- WHO classification I have real concerns about using this threshold for surgical intervention and male/female differences



TRANSFUSION

- 1094 consecutive patients – blood transfusion rate 6%
- Transfusion associated with:-

| | Transfused | Not transfused | P value |
|---------------|-------------------|-----------------------|----------------|
| Preop Hb | 117.5 (15.9) | 134.4 (13.5) | P<0.001 |
| Hospital LoS | 11.7 (11.2) | 5.4 (12.3) | P<0.001 |
| Surgical time | 153 (53.2) | 124 (39.2) | P<0.001 |



ORTHOPAEDIC ANAEMIA

| | n | LoS | % transfused |
|-----------------------------------|----------|-------------|---------------------|
| Consensus guide anaemia | 442 | 6.4 (7.2) | 10.8% |
| Consensus guide no anaemia | 652 | 4.7 (4.4) | 2.0% |
| Hb<115 | 99 | 9.35 (11.6) | 27% |
| 115 - 130 | 343 | 5.5 (5.1) | 6.1% |
| >130 | 652 | 4.7 (4.4) | 2.0% |



WHAT I BELIEVE FOR PREOPERATIVE ANAEMIA

- Extremely common – even if just add ferritin it is a start
- There should be no difference between men and women
- Don't believe in WHO classification of anaemia – continuous variable. So where do we intervene
 1. We are not primary care
 2. We can overwhelm services – including our own
 3. We are a new specialty and have to start small and build
 4. Start by looking at LOS and Hb in your own hospital – data is key



CHANGING THE PROCESS

Emma McCone

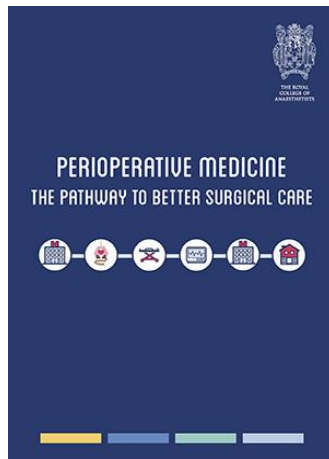
Pre-operative assessment lead nurse

MY DISTORTED VIEW

- What's in a number – 10 ok!
- Didn't know about Peri op anaemia and its affect on post op complications!
- Treating anaemia pre op isn't something we did routinely
- Pathways wouldn't facilitate changes so wasn't our issue



THE 5 YEAR PERI OPERATIVE MEDICINE PROGRAMME RCOA (2016)

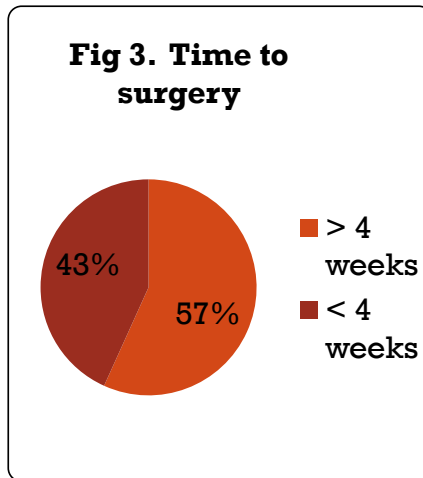


- Focus on optimisation of long term conditions Pre operatively
- Multiple studies of correlation between Anaemia and poorer outcomes post surgery
- Huge focus on treating anaemia PRE surgery

<https://www.rcoa.ac.uk/sites/default/files/documentis/2019-09/Perioperative%20Medicine%20-%20The%20Pathway%20to%20Better%20Care.pdf> [Accessed February 2020]



RESULTS : TIME BETWEEN PRE-ASSESSMENT AND SURGICAL DATE



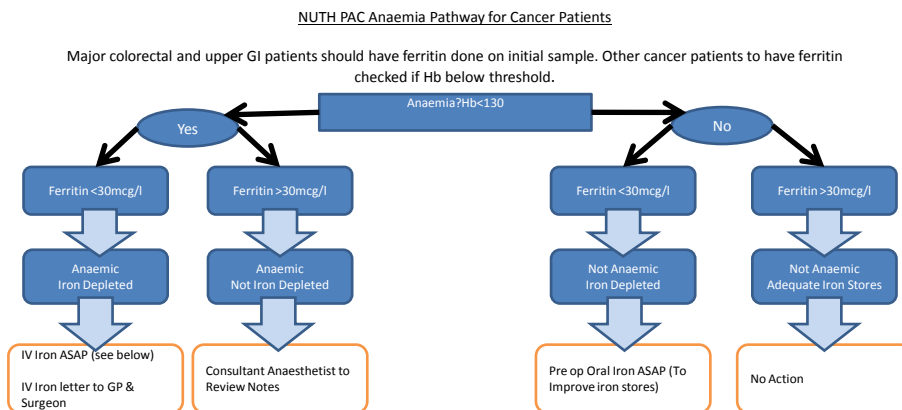
- Iron deficiency anaemia can take up to 6 weeks to correct
- Absorption is iron status dependent
- In severely deficient anaemia can expect 10g/l increase per week on 100mg elemental iron

SUMMARY OF RESULTS - 2016

- High incidence of anaemia in pre-assessment
- Poor at identifying iron deficiency
- Should be offering oral iron to elective cases
- Should consider iv iron where cases are urgent or patients are intolerant
- Start with a patient subgroup rather than trying to implement a change for all specialties
- Surgical backing needed to make this work
- Haematology support needed

WHERE DO YOU START?

- A bunch of enthused individual's.....
- Some sample patient groups
- Sharing the regional work via TEPOT and learning from each other
- Service change/ audit and improvement
- Support
- Admitting that we may make mistakes!



Oesophageal Cancer

Please Inform Upper GI specialist nurse (Claire Sedgewick or Maria Bliss) who will arrange for IV iron to be given on ward 45
Do not delay treatment.

Contact
Claire.sedgewick@nuth.nhs.uk
Maria.bliss@nuth.nhs.uk
 Dect 29437

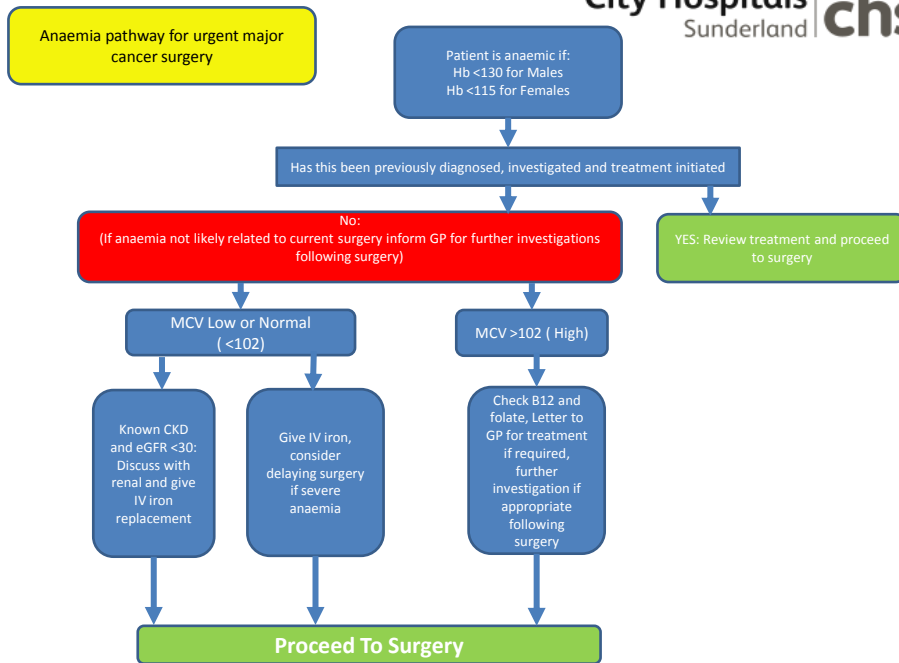
Colorectal/Anal Cancer (and inflammatory bowel disease)

Please Inform Colorectal specialist nurse (Allison Sharpe) who will arrange for IV iron to be given on ward 45.
Do not delay treatment.

Contact
Allison.sharpe@nuth.nhs.uk
 Dect 29552

**FRH
All Major Cancer**

Consultant Anaesthetist to write prescription for IV iron.
Make appointment for IV iron at day treatment centre ASAP.
Proceed with surgery 2 weeks following IV iron



THE ANAEMIA MDT TEAM

- Anaesthetists
- Haematologists
- Pharmacists
- Nurses
- League of friends
- HCAs
- Transfusion team
- GPs
- Pharmaceutical support for education



BREACH DATES AND PATHWAYS!



Cancer Patients

Day 1 – GP Referral

Day 10-14 Out Patients

Secondary Referral to NUTH

Day 14-21 –Diagnostics

Secondary Referral to NUTH

Day 21 –28 – More diagnostics

Day 31

ADMIT/ PROCEED DO NOT
BREACH!!



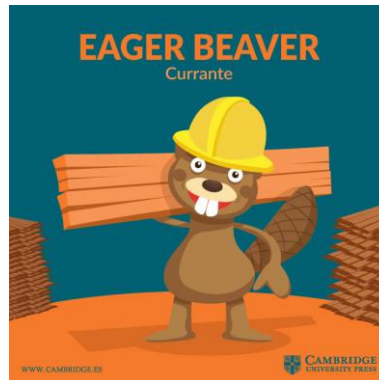
Where
do you
Pac and
treat?



THE SERVICE

- Did we write a business case? No
- Should we have? YES!!

- Too eager and didn't want to wait!!!



THE STEPS TO CHANGE....

- Picking the right product – what did we want it to do?
- Getting the prescription right and on formulary
- Talking to the units who would be involved (we couldn't do it in PAC)
- Informing the patients
- Being careful of the pathways
- Closing the loop!
- Auditing the change
- Cost effectiveness!



WHY WE CHOSE MONOFER (IRON ISOMALTOSIDE 1000) ▼ ?

1. DOSE

- We have one chance to give and can't bring patients back easily
- The administration of high doses were able to be achieved

2. HYPOPHOSPHATAEMIA

- The incidence of hypophosphatemia is known to be associated with the use of IV iron preparations
- Acts on kidney to increase excretion
- Critical care doctors were keen to minimise the risk of hypophosphatemia



AIMS OF THE PATHWAY

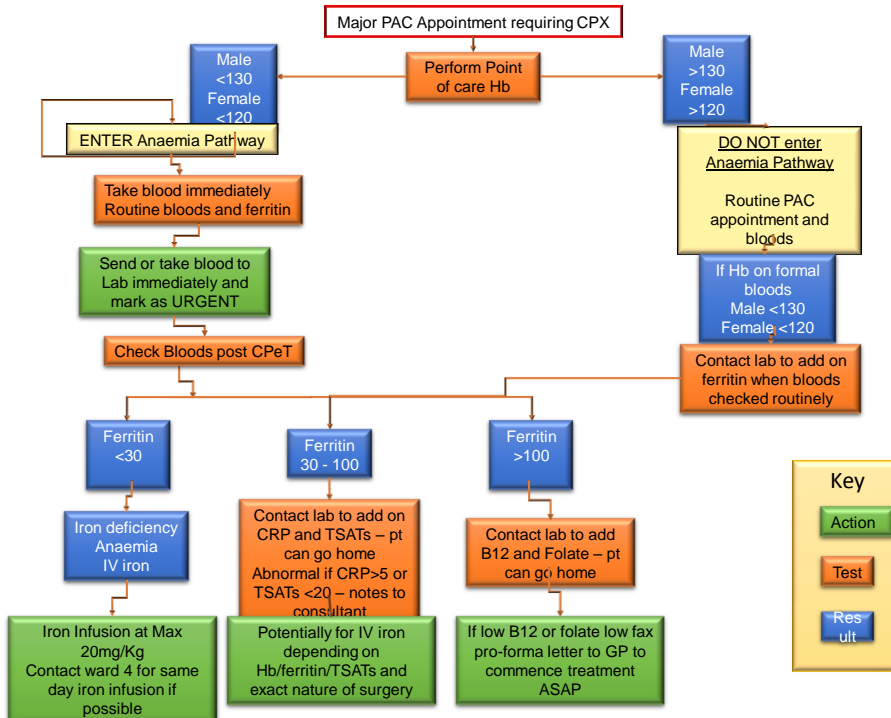
- Reduce the number of ferritin tests being conducted
 - Creating a nurse led triage service at initial PAC appointment
- Increase haematinic tests on anaemia patients
 - Ensure tests are only conducted on patients who are identified as being anaemic
 - No unnecessary tests on patients peri operatively
- Develop a 'one stop shop' for anaemia treatment
 - Reduce patient journeys
 - Reduce clinic visits
 - Provide best practice care for all anaemia patients requiring surgery



INCLUSION CRITERIA – SURGERY TYPE

| FREEMAN SITE | RVI SITE |
|---|---|
| Hepatobiliary Whipples, liver resections, intra-abdominal sarcomas | Upper GI Oesophagectomy, gastrectomy, subtotal gastrectomy |
| Major urology Nephrectomy, cystectomy, prostatectomy | Lower GI Cancer surgery, laparotomies, intestinal failure, Anorectal resections and pelvic exenteration Abdominal wall repairs – Rives stoppa and other component separation surgeries |
| Major vascular AAA repair, aortobifemoral grafts | Gynae open or laparoscopic myomectomy (fibroids +/- hysterectomy) |
| Major ENT/Max-fax cancer operations | Plastics involving thoracotomy, large flap reconstruction, head and neck surgery, sarcoma resections |
| Lower GI Cancer surgery, laparotomies, intestinal failure, Anorectal resections and pelvic exenteration | Major spine surgery scoliosis surgery, deformity correction and >2 level spinal fixations |
| Major orthopaedic oncology | |





AN HONEST COST ANALYSIS..

- Haemacues – League of friends
- Adapted HCA role – Free
- Reduction in ferritin tests as targeted but balanced with additional haematinics (cost neutral)
- Cost of product/ time to give/ resource/ materials
- Coded as non theatre admission
- Treatment on the day – best practice tariff (incentivised)
- Reduction in blood transfusion
- Reduction in LoS



EVIDENCE IT WORKED.....



UPPER GI, RESULTS RVI (SINCLAIR, 2018)

| | 2013-14 | | 2017 | |
|--------------------------------------|-------------|----------|------------|----------|
| Total units blood transfused post-op | 33 | | 18 | |
| No patients receiving transfusion | 15/88 (17%) | | 7/62 (11%) | |
| When are these given? | | | | |
| | Units | Patients | Units | Patients |
| Day 0 (surgery) | 8 | 3 | 4 | 2 |
| Day 1-7 | 6 | 3 | 9 (5,4) | 2 |
| Days 8-14 | 13 | 6 | 0 | 0 |
| Days 15-21 | 4 | 2 | 0 | 0 |
| Days 22-28 | 2 | 1 | 5 (2,2,1) | 3 |

MAJORS, FRH (PRENTIS, 2019)

- !!!!VERY EARLY DATA!!!!
- Freeman only – lower rate of anaemia compared to RVI as they have UGI and gynae services

Late 2016 to present – 156 patients

- 18 patients Ferrinject
- 60 Monofer ▼ (iron isomaltoside 1000) (max dose 1.5g)
- 78 higher dose Monofer – now 20mg/kg
- Numbers rapidly rising



SEVERELY ANAEMIC GROUP GOING FOR MAJOR SURGERY WHO HAD IV IRON

- Data on 112 patients – incomplete data due to Hb on day of surgery or didn't have surgery
- Mean Hb at pre-assessment = 101.6 (SD 13.4)
- Mean Hb on day of surgery = 117.5 (SD 15.5)
- Highly significant $p < 0.0001$



TIMELINES

- One stop shop not working yet – issues with infrastructure at Freeman
- Has been a drive and nurses/medical staff more aware
- 17 days from PAC bloods to administration to IV iron down to 10 days from initial Ferrinject/lower dose Monofer vs higher dose Monofer
- However, also seen a drop in time from IV iron to surgery
- Initial group 51 days (SD=65.9) vs 37 days (SD=38.9) NS



OPTIMAL TIME OF IV IRON – AT LEAST 2 WEEKS

| Time from IV iron to surgery | N= | Rise in Hb mean (SD) | Blood transfusion rates |
|------------------------------|----|----------------------|-------------------------|
| < 14 days | 41 | 10.35 (9.26) | 41.3% |
| 14- 28 days | 15 | 17.9 (17.1) | 13.3% |
| >28 days | 67 | 18.2 (14.8) | 11.9% |

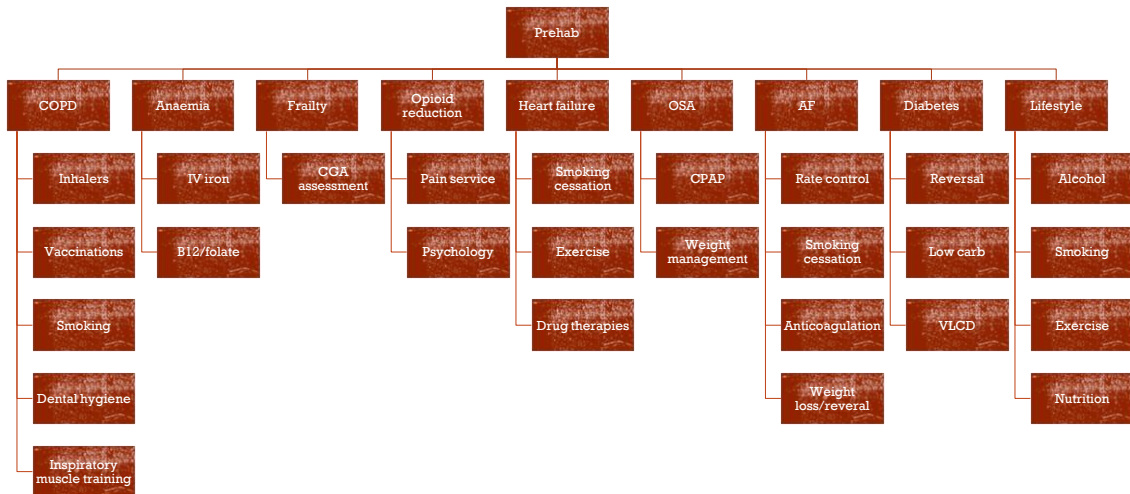
Group 1 vs group 3 p=0.016
Group 1 vs group 2 p=0.08 due to small numbers.



CCG10: Screening and treatment of iron deficiency anaemia in patients listed for major elective blood loss surgery

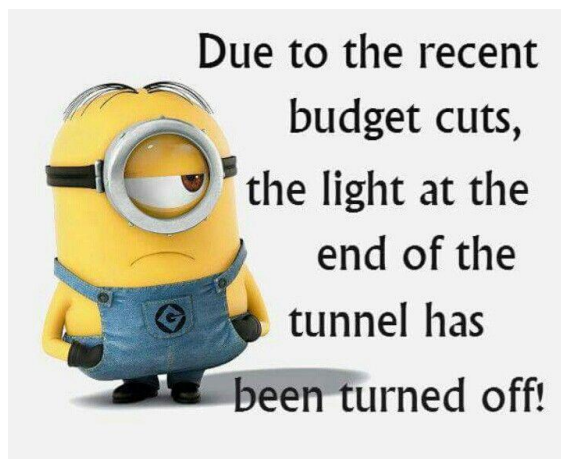


| | |
|---|---|
| <p>Scope Services: Acute (relevant surgical wards) Period: Q1 Q2 Q3 Q4</p> | <p>Data reporting & performance Quarterly submission via National CQUIN collection – see section 4 for details about auditing as well as data collection and reporting. Data will be made available approximately 6 weeks after each quarter. Performance basis: Whole period. The need to allow for screening to take place 6 weeks prior to the procedure requires the denominator to be restricted to only include procedures taking place more than 6 weeks after the start of the 20/21 year. This restriction supports 'whole period', rather than 'quarterly' performance assessment. See section 3 for details about the basis for performance and payment.</p> |
| <p>Payment basis Minimum: 45% Maximum: 60% Calculation: Whole period %</p> | <p>Description Ensuring that 60% of major elective blood loss surgery patients are treated in line with NICE Guideline NG24.</p> |
| <p>Accessing support NHSE&I policy lead Matthew Barker m.barker1@nhs.net</p> | <p>Numerator Of the denominator, all admissions where the following actions were applied within the 6 week period prior to the procedure:</p> <ul style="list-style-type: none"> • Haemoglobin (Hb) measured; and, • If anaemia present, have serum ferritin level tested; and, • If diagnosed with iron-deficiency anaemia offered appropriate iron treatment (oral and/or IV iron). |
| <p>Supporting documents NICE Guideline NG24 The pre-operative anaemia management CQUIN code table will be available on the 'associated projects' section of the GIRFT website. 2016 Audit of Patient Blood Management in adults undergoing elective, scheduled surgery</p> | <p>Denominator Total elective inpatient admissions, within the period 13 May 2020 – 31 March 2021, with a primary procedure in the following groups: Coronary Artery Bypass Graft, Cardiac Valve Procedures, Colorectal Resection, Cystectomy, Hysterectomy, Primary Hip Replacement, Hip Replacement Revision, Primary Knee Replacement, Knee Replacement Revision, Nephrectomy, Carotid Artery (open procedure), Other Aortic/Iliac Occlusive Disease (open procedure). OPCS procedure codes are provided in the pre-operative anaemia management CQUIN code table.</p> |



END THOUGHTS.....

- What made this work was involving a team
- Educating everyone about anaemia
- Looking at small groups of patients and undertaking audits
- Not doing the big bang - uncontrollable
- Service improvement to take this forward locally and nationally
- Sharing ideas, results and using the TEPOT network
- Bringing it into pre-operative assessment



Monofer® (iron isomaltoside 1000) prescribing information

▼ This medicinal product is subject to additional monitoring, and healthcare professionals are asked to report any suspected adverse reaction

Note: Before prescribing please read full Summary of Product Characteristics. **Pharmaceutical form:** Iron isomaltoside 1000 is a dark brown, non-transparent solution for injection/infusion. **Presentations:** Iron in the form of iron isomaltoside 1000; 100 mg/ml available in vials of 100 mg/ml, 500 mg/5 ml and 1,000 mg/10 ml. **Indications:** Monofer® is indicated in patients ≥18 years for treatment of iron deficiency when oral iron preparations are ineffective or cannot be used or when there is a need to deliver iron rapidly. The diagnosis must be based on laboratory tests. **Administration:** Each IV iron administration is associated with a risk of a hypersensitivity reaction. Thus, to minimise risk, the number of single IV iron administrations should be kept to a minimum. The cumulative iron need can be determined using either the Simplified Table or the Ganzoni formula, please consult full Summary of Product Characteristics. Monofer® may be administered as an IV bolus injection of up to 500 mg at an administration rate of up to 250 mg iron/minute up to three times a week, during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as outlined for IV bolus injection, or as an up to 20 mg iron per kg body weight infusion. If the cumulative iron dose exceeds 20 mg iron per kg body weight, the dose must be split into two administrations with an interval of at least one week. It is recommended whenever possible to give 20 mg iron/kg body weight in the first administration. Dependent on clinical judgement the second administration could await follow-up laboratory tests. Doses up to 1,000 mg must be administered over >15 minutes; dose above 1,000 mg must be administered over ≥30 minutes. In case of infusion, Monofer® should be added to maximum 500 ml sterile 0.9% sodium chloride. **Contraindications:** Non-iron deficiency anaemia, iron overload or disturbances in utilisation of iron, hypersensitivity to any of the ingredients, decompensated liver disease, or known serious hypersensitivity to other parental iron products. **Warnings/Precautions:**

Parenterally administered iron preparations can cause potentially fatal anaphylactic/anaphylactoid reactions. The risk is enhanced for patients with known allergies, a history of severe asthma, eczema or other atopic allergy, and in patients with immune or inflammatory conditions. Monofer® should only be administered in the presence of staff trained to manage anaphylactic reactions where full resuscitation facilities are available (including 1:1000 adrenaline solution). Each patient should be observed for at least 30 minutes following administration. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. In patients with compensated liver dysfunction, parenteral iron should only be administered after careful benefit/risk assessment. Careful monitoring of iron status is recommended to avoid iron overload. Parenteral iron should be used with caution in case of acute or chronic infection. Monofer® should not be used in patients with ongoing bacteraemia. Hypotensive episodes may occur if intravenous injection is administered too rapidly. Caution should be exercised to avoid paravenous leakage when administering Monofer®. **Pregnancy:** Monofer® should not be used during pregnancy unless clearly necessary. The treatment should be confined to second and third trimester. In rare cases, foetal bradycardia has been observed in pregnant women with hypersensitivity reactions. **Undesirable effects:** No very common (≥10 %) undesirable effects listed. Common undesirable effects (1 % to 10 %): nausea; injection site reactions. For information on other undesirable effects, please consult full Summary of Product Characteristics. **Legal Category:** POM. **Package Quantities and basic Prices:** 5 vials of 1 ml, £24.75; 5 vials of 5 ml, £423.75; 2 vials of 10 ml, £339.00. **Marketing Authorisation Number/Holder:** PL 18380/001, Pharmacosmos A/S, Roervangsvvej 30, DK-4300 Holbaek, Denmark. **Date of preparation:** June 2017. Further information is available on request to Pharmacosmos UK. **Date of Revision:** January 2018

Adverse events should be reported. Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk>. Adverse events should also be reported to Pharmacosmos UK Ltd.
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