

# Maternal Anaemia Management

A Quality Improvement Journey.

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#### Consultant focus

Cell Salvage and Blood Conservation (UHP Lead)

MOH inc. ROTEM guided hemorrhage management

Perioperative Medicine and Prehabilitation (inc CPET)

I have no declarations of interest



# Objectives

## Setting the scene

- Impact e to Mother and Baby
- Relevant Maternal and Iron Physiology
- International and National Perspective/Morbidity
- UHP Drivers and Timeline

## UHP Strategy

- What are Normal Triggers in 2022
- The Challenges of Iron Management
- Prevention vs Cure. Dividing supplementation from treatment
- UHP Algorithms/ Working with NICE guidance
- Essential requirements to succeed

## Q. What should we accept as “Normal”?

- ▶ IDA 20-30% of pregnancies in UK. (LMICs prevalence 30% to 50%)
- ▶ In 2021.. 82 LMICS (3 million women in study) studied and limited decrease in anaemia (35% vs 32%) over 18 year period (2000-18)
- ▶ Less data on UK iron deficiency . Rates of iron deficiency of 26%, 33.5% and 53% have been documented (1<sup>st</sup> to 3<sup>rd</sup> Trimester respectively) .
- ▶ 80% of women at term are iron deplete in UK
- ▶ 20% of women at BOOKING are iron deplete in UK
- ▶ Ferritin levels are significantly lower in pregnant women over 25, and gravida 3 and above.
- ▶ Women 10 x more likely to have IDA, and 2 x more likely than men to need a transfusion



## Maternal implications

- Reduced physical and mental performance, lethargy, excessive fatigue, sleeping difficulties
- Increased risk of APH and PPH (and Mortality esp LMICs)
- Delayed healing of perineal trauma or LSCS wounds
- Breast milk quality & quantity affected
- Increased LOS/ transfusion requirements increased



## Fetal implications

- Poor uterine growth, decreased liquor, small gestational age
- Premature delivery, low birth weight
- Postpartum: poor weight gain & failure to thrive



## Economic implications

- Physical productivity losses esp in LMICs
- Economic modelling indicate losses of billions per annum worldwide
- Recent analysis suggest gains of \$8 billion lifetime income in LMICs
- Arguably change less impactful in UK of course (salary protection etc)

# Maternal Risk Groups for IDA

<b>During pregnancy</b>	<b>Postpartum</b>
After first trimester	Iron deficiency and iron-deficiency anemia during pregnancy
Iron deficiency in prior pregnancy	High blood loss at delivery
Multiparity	Poor socio-economic status
Short recovery between pregnancies	Poor nutritional status
Multipara	
Poor socio-economic status	
Poor nutritional status	

# Iron requirement during pregnancy

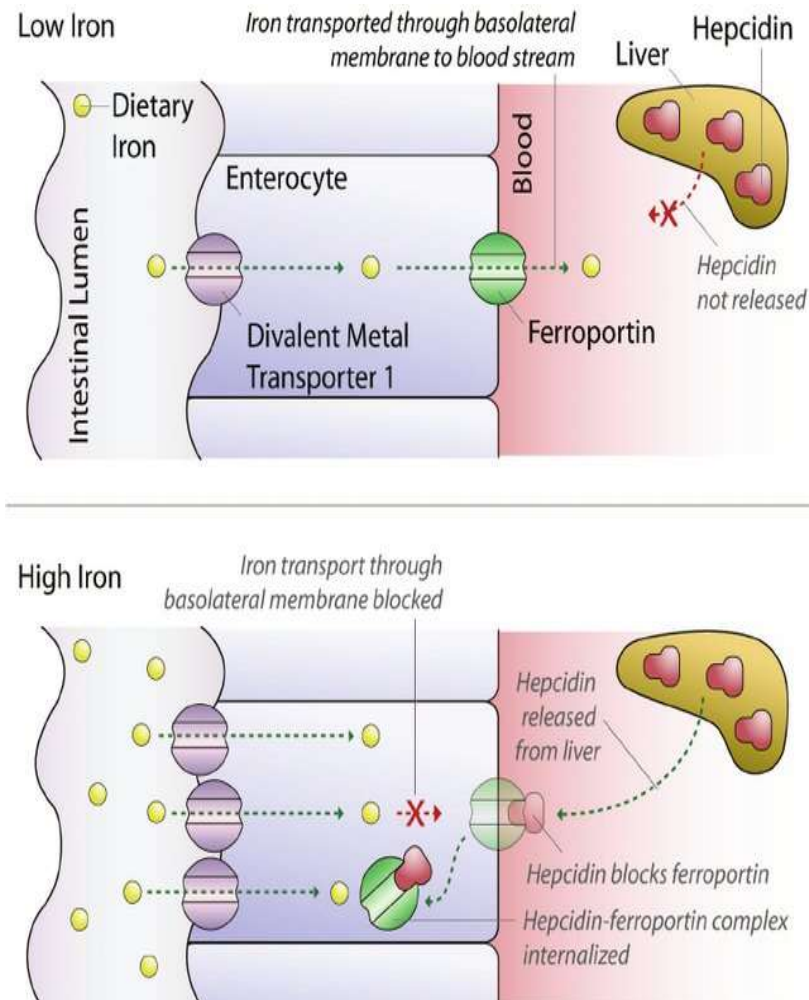
- ▶ Gestational body iron requirement = **1000 mg**
  - ▶ 350mg to foetus and placenta
  - ▶ 450mg maternal red cell mass increase
  - ▶ 250mg basal losses from the body
- ▶ 250mg lost at delivery
- ▶ Total iron needs (1000mg) concentrated in last two trimesters (NOT 1<sup>st</sup>)
- ▶ DAILY elemental iron requirements increase from approx. 20mg to 30mg/day when pregnant
- ▶ FeSO<sub>4</sub> absorption (BNF 60MG elemental iron)

(Hallberg, 1988).



# Oral Iron absorption

- ▶ Body cannot excrete iron, therefore absorption is tightly regulated
- ▶ Only ferrous ( $\text{Fe}^{2+}$ ) iron absorbed: transported via DMT-1 into enterocyte
- ▶ Enters bloodstream via Ferroportin
- ▶ High iron load luminally: liver produces **HEPCIDIN** - binds to Ferroportin & complex is destroyed
- ▶ Iron does not cross basolateral membrane; enterocyte sloughed



Naigamwala *et al.*,  
(2012)



# Replacement

- ▶ Red meat, may contain up to 2 mg/100 mg.
- ▶ Dietary iron absorption varies from 1-20 % (animal vs plant)
- ▶ For vegetable sources, lacking heme iron, requirements are higher (1000 g soya beans or 5000 g spinach)!
- ▶ Food based strategies unlikely to succeed
- ▶ 3 mg of supplemental iron in addition to dietary iron should be assimilated daily during the second and third trimesters to prevent iron deficiency in most women
- ▶ 60 mg elemental iron from 200mg FeSO<sub>4</sub> OD
- ▶ BUT Lack of compliance high (1 in 5) esp. TDS iron

# Iron Risk in Pregnancy

- ▶ Selection of the iron deficient essential as a strategy (and benefits clearly shown)
- ▶ Risk is in unidentified iron replete patients and may include...
  - ▶ Overload
  - ▶ Free radical formation and oxidative stress (linked to GDM)
  - ▶ Changes in intestinal biome
  - ▶ Proliferation of pathogens eg malaria
  - ▶ Obs specific : iron supplementation in women with **high** Hb concentrations (i.e., >132 g/L) associated with increased rate of maternal preeclampsia and fetal growth restriction

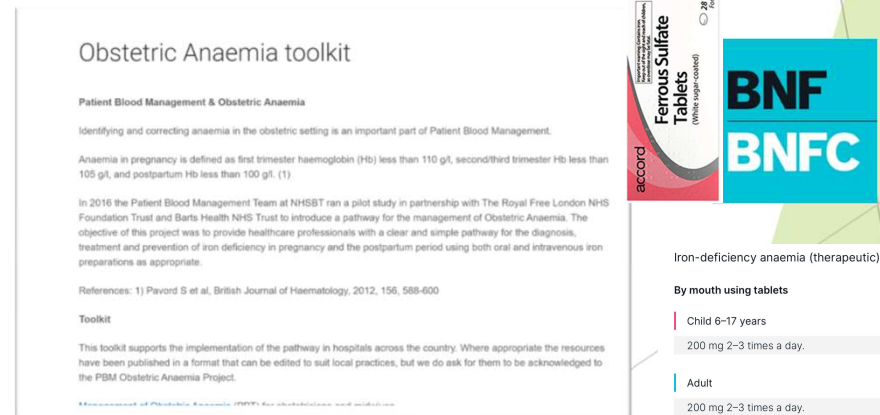
**UHP strategy : Targeted ID treatment with Ferritin essential**

# Regulators of iron absorption

Regulator	Target	Effect	Result
PPI, antacids, antihistamines	Gastric pH	Raise pH, insoluble ferric iron	Reduced iron absorption from duodenal lumen
Polyphenols, dietary fibre, fluoroquinolones	Ferric iron	Chelation: insoluble antinutritional-mineral complex	Reduced iron absorption from duodenal lumen
Lead, cobalt, manganese, zinc, calcium	DMT-1	Competitive inhibition of iron uptake	Reduced iron absorption from duodenal lumen
Ascorbic acid, citrate, amino acids	Ferric iron	Converts to ferrous iron	Increased iron absorption
Oral iron supplementation, IL-6, saturated transferrin	Hepcidin	Increased hepcidin production & destruction of ferroportin	Reduced iron efflux into bloodstream
Anaemia, hypoxia	Hepcidin	Reduced hepcidin production	Increased iron efflux into bloodstream

# Setting the scene (2019 at UHP)

- ▶ Iron deficiency anaemia (IDA) - most common pregnancy-associated anaemia. National focus on treatment following NCA in 2018
- ▶ 2019 Toolkit/NCA solution. 200mg TDS iron, emphasis on Anaemia and BSH Hb triggers
- ▶ UHP approach Reactive rather than proactive (iv ferrinject use at 28 weeks (DAU) and oral 200mg tds iron)
- ▶ Normal Hb values as per BSH/local guidelines:
  - ▶ Non-pregnant women: Hb 120-155g/L
  - ▶ First trimester: Hb >110g/L
  - ▶ Second & Third trimesters: Hb >105g/L
  - ▶ Postpartum: Hb >100g/L



The image shows a document titled 'Obstetric Anaemia toolkit' with the following text:

**Obstetric Anaemia toolkit**

**Patient Blood Management & Obstetric Anaemia**

Identifying and correcting anaemia in the obstetric setting is an important part of Patient Blood Management.

Anaemia in pregnancy is defined as first trimester haemoglobin (Hb) less than 110 g/L, second/third trimester Hb less than 105 g/L, and postpartum Hb less than 100 g/L. (1)

In 2016 the Patient Blood Management Team at NHSBT ran a pilot study in partnership with The Royal Free London NHS Foundation Trust and Barts Health NHS Trust to introduce a pathway for the management of Obstetric Anaemia. The objective of this project was to provide healthcare professionals with a clear and simple pathway for the diagnosis, treatment and prevention of iron deficiency in pregnancy and the postpartum period using both oral and intravenous iron preparations as appropriate.

References: 1) Pavord S et al, British Journal of Haematology, 2012, 156, 588-600

**Toolkit**

This toolkit supports the implementation of the pathway in hospitals across the country. Where appropriate the resources have been published in a format that can be edited to suit local practices, but we do ask for them to be acknowledged to the PBM Obstetric Anaemia Project.

Management of Obstetric Anaemia (PBM) for obstetric settings

Accord Ferrous Sulfate Tablets (White sugar-coated) 200mg 28 tablets For women

**BNF BNFC**

Iron-deficiency anaemia (therapeutic)

**By mouth using tablets**

- Child 6-17 years  
200 mg 2-3 times a day.
- Adult  
200 mg 2-3 times a day.

# National Comparative Audit



Blood and Transplant

## 2018 National Comparative Audit of the Management of Maternal Anaemia (Hb<110g/L)

- ▶ Interim Key Performance Indicator Report
- ▶ Participation: 86 maternity units from around the UK took part and contributed data on 860 births.

### KPI Headliners:

- ▶ 221 women were found to be anaemic in pregnancy across all trimesters. The point prevalence of anaemia in pregnancy was 221/848 (26%).
- ▶ **Trend: more commonly diagnosed at 28 weeks later rather than at booking** (with continuing iron depletion and/or suggest first trimester Hb is commonly nearer “non pregnant” i.e. higher than 110 g/dl)
- ▶ **Nationally only 22% of anaemic patients TREATED!**
- ▶ **Nationally only 1 of 35 eligible women REFERRED for Obs review and iv iron at >34 weeks !**

# Audit results: Pre pandemic UHP LSCS

*Q. Local population: high level of deprivation. What was our likely IDA incidence?*

- ▶ LSCS from 1<sup>st</sup> Jan 2019 to 31<sup>st</sup> Oct 2019
- ▶ 890 cases with pre-delivery Hb on system
- ▶ 342 Category 4 LSCS:
  - ▶ 18% (<110 g/L)
- ▶ 548 Category 1-3 LSCS:
  - ▶ 16% (<110g/L)

# UHP Aims

- ▶ What should be considered anaemic in our local population? What triggers should we consider normal based on evidence
- ▶ How could we **prevent** rather than wait to treat (at cheaper cost)
- ▶ How can we decrease workload on community colleagues (more iron needs more prescription and MDT discussion) and DAU staff (decrease iv iron need)
- ▶ How could we detect iron deficiency and IDA and increase compliance if treatment indicated?
- ▶ **UHP Aspiration: To decrease anaemia at term to 0%**



# UHP PLAN OF ACTION

- ▶ **CURRENT GUIDELINES:** scrutinise - what can be improved?
- ▶ **AUDIT:** five months of antenatal blood results at booking and 28-weeks to assess the scale of the problem and define Hb **normal** range in local Obstetric population
- ▶ **LITERATURE REVIEW:** prevention and treatment of maternal anaemia
- ▶ **NEW GUIDELINES:** generated on audit results & literature review findings
- ▶ **IMPLEMENTATION & RE-AUDIT**



# Normal Range: Local population (UHP)

- ▶ Two audits performed using electronic blood results:
  1. All women (1715) at booking and 28-weeks over a five month period, assessing Hb values & if ferritin requested
  2. LSCS patients over 10 months and assessing pre-op Hb
  3. Now published

Implementation of early management of iron deficiency in pregnancy during the SARS-CoV-2 pandemic

Tessa Stewart<sup>1</sup>, Joanna Lambourne<sup>2</sup>, Daryl Thorp-Jones<sup>1</sup>, and Wayne Thomas<sup>1</sup>

<sup>1</sup>University Hospitals Plymouth NHS Trust

<sup>2</sup>William Harvey Hospital

October 14, 2020

*Title: Implementation of early management of iron deficiency in pregnancy during the SARS-CoV-2 pandemic*

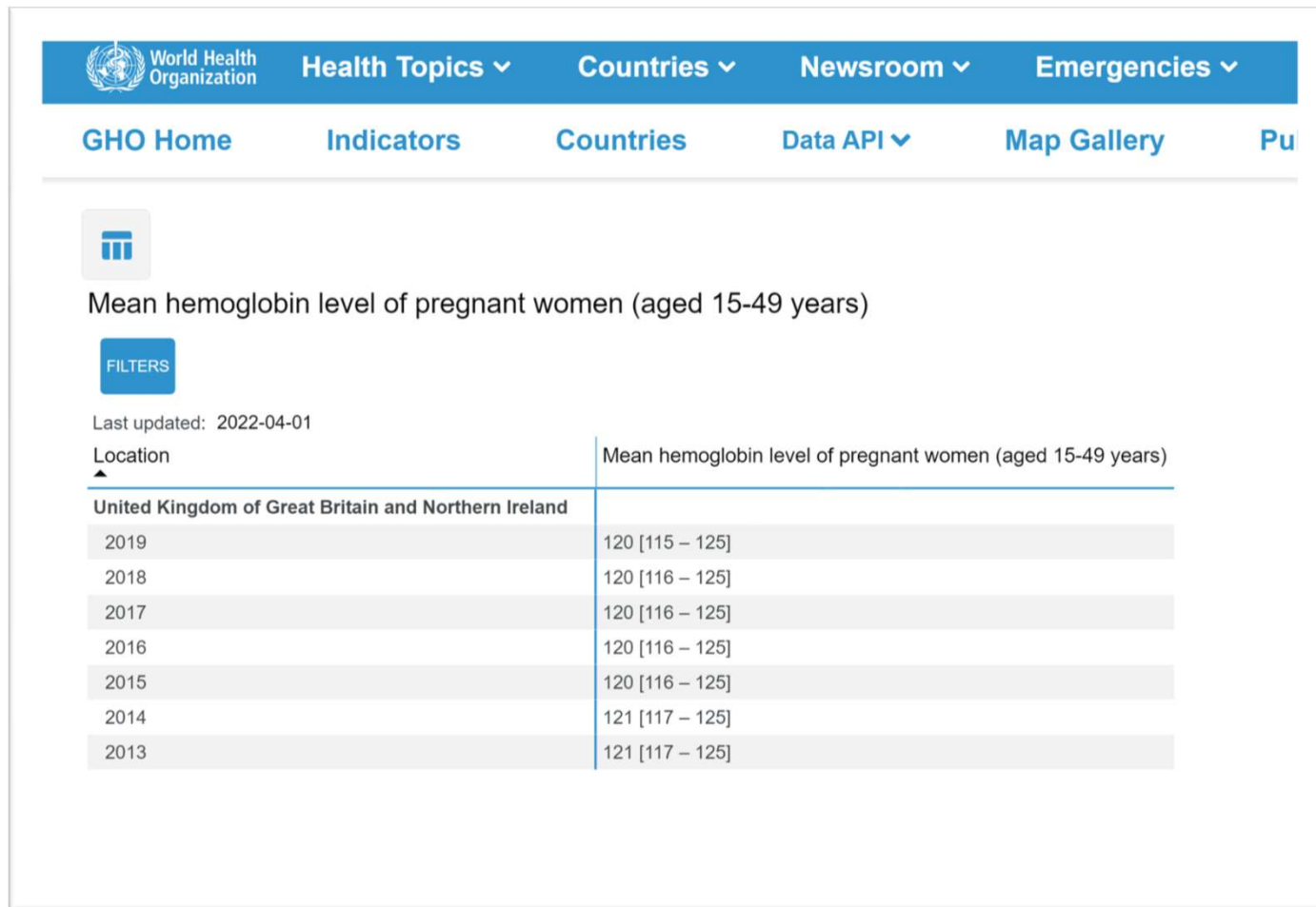
Stewart T<sup>1</sup>, Lambourne J<sup>2</sup>, Thorpe-Jones D<sup>1</sup>, Thomas DW<sup>1</sup>.<sup>1</sup>University Hospitals Plymouth NHS Trust, Plymouth, Devon, PL6 8DH. <sup>2</sup>East Kent Hospitals NHS Foundation Trust, William Harvey Hospital, Kennington Road, Willesborough, Ashford, Kent, TN24 0LZ

# Summary of UHP paper and Local Normal Ranges

- ▶ 1715 cases
- ▶ Booking: 148 (8.6%) women had Hb concentrations  $<120$  g/L with 25 (1.5%)  $<110$  g/L
- ▶ Hb values: Median Hb 132 g/L, minimum 90 g/L, and maximum Hb 160 g/L The 95% lower limit confidence level was 116 g/L
- ▶ 81 cases: Hb fell from booking to 28 weeks' gestation by a median of 8 g/L (range +39 to -27 g/L) with 33 (41%) dropping by 10 g/L or more

Conventional standards accept Hb 110g/L by 13 weeks gestation as normal, but our lower limit of normal for the first trimester was 116g/L?

# Normal range: WHO Maternal HB Data




The screenshot shows the WHO data interface for 'Mean hemoglobin level of pregnant women (aged 15-49 years)'. It includes a navigation bar with 'Health Topics', 'Countries', 'Newsroom', and 'Emergencies'. Below the navigation, there are links for 'GHO Home', 'Indicators', 'Countries', 'Data API', 'Map Gallery', and 'Pu'. A 'FILTERS' button is visible. The data is presented in a table for the 'United Kingdom of Great Britain and Northern Ireland' from 2013 to 2019, showing a value of 120 g/L with a normal range of [115 - 125] g/L for 2019-2016, and 121 g/L with a normal range of [117 - 125] g/L for 2014-2013.

World Health Organization

Health Topics ▾ Countries ▾ Newsroom ▾ Emergencies ▾

GHO Home Indicators Countries Data API ▾ Map Gallery Pu



Mean hemoglobin level of pregnant women (aged 15-49 years)

[FILTERS](#)

Last updated: 2022-04-01

Location	Mean hemoglobin level of pregnant women (aged 15-49 years)
<b>United Kingdom of Great Britain and Northern Ireland</b>	
2019	120 [115 – 125]
2018	120 [116 – 125]
2017	120 [116 – 125]
2016	120 [116 – 125]
2015	120 [116 – 125]
2014	121 [117 – 125]
2013	121 [117 – 125]

INVISIBLE  
WOMEN

EXPOSING  
DATA BIAS  
IN A WORLD  
DESIGNED  
FOR MEN

MAROLIN  
RIADO  
PEREZ

## Triggers for Surgical Pre-optimisation (at UHP)

- ▶ Anaemia is defined by the WHO as an Hb concentration <130 g/l for men, <120 g/l for non-pregnant women and <110 g/l for pregnant women
- ▶ Historically, sex specific definitions for anaemia were the norm as the higher prevalence of iron-deficiency due to pregnancy and menstruation was often noted as a “physiological”
- ▶ 2017 international consensus statement on the Peri-operative management of anaemia and iron-deficiency (Anaesthesia) noted that women are twice as likely to receive a transfusion compared with men
- ▶ In addition, a 10 g/l decrease in Hb has been shown to be independently associated with increased transfusion requirements, increased mortality and prolonged hospital stay
- ▶ ..... Hence we feel **gender specific definitions are unhelpful.....**

First trimester	Haemoglobin (Hb) <120g/L
Second and third trimester	Hb <120g/L
Term/ Postpartum	Hb <110g/L

## UHP Triggers

# Logistical challenges faced BY MIDWIVES

- ▶ Challenges when implementing guidelines:
  - ▶ Manually check bloods after booking
  - ▶ Contact women if low Hb
  - ▶ Organise FeSO<sub>4</sub> prescription from GP or Obstetrician (supplementation vs NICE TDS)
  - ▶ Retest Hb after 2-4 weeks, manually check results
  - ▶ If Hb not improved or even lower: contact pregnant woman to say another blood test required (ferritin)
  - ▶ Organise blood test, manually check result
  - ▶ If ferritin low, requesting parenteral iron infusion from Obstetrician
  - ▶ Perhaps pregnant person is busy that week with other childcare commitments so can't attend hospital for first IV infusion
  - ▶ Delayed by another week or two...

Easy to see how it is difficult to implement timely and adequate treatment & delayed to the point where women remain anaemic at term



# Optimal dosing regimen (decrease hepcidin)

## Dosing >OD:

- Increase hepcidin
- Reduce iron absorption
- Increase side effects

## Daily dosing vs alternate day dosing:

- Hepcidin reduced in alternate day dosing
- No difference in maternal or fetal outcomes
- Fewer side effects in alternate day dosing
- Better patient adherence
- Less likely to have high Hb (>150) in alternate day dosing



Cochrane Database of Systematic Reviews

## Intermittent oral iron supplementation during pregnancy (Review)

Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T

THE LANCET  
Haematology

ARTICLES | VOLUME 4, ISSUE 11, PE524-E533, NOVEMBER 01, 2017



Purchase

Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials

Nicole U Stoffel, MSc · Colin I Cercamondi, PhD · Prof Gary Brittenham, MD · Christophe Zeder, MSc · Anneke J Geurts-Moespot, BSc · Prof Dorine W Swinkels, PhD · et al. [Show all authors](#) · [Show footnotes](#)

Published: October 09, 2017 · DOI: [https://doi.org/10.1016/S2352-3026\(17\)30182-5](https://doi.org/10.1016/S2352-3026(17)30182-5) · [Check for updates](#)

# “Prevention is better than Cure”

- ▶ The phrase 'prevention is better than cure' is often attributed to the Dutch philosopher **Desiderius Erasmus** in around 1500.
- ▶ **It is now a fundamental principle of modern health care and inherent within health and social care strategies across the UK**
- ▶ Economic advantage probable especially when interventions are **cheap and low risk**
- ▶ \*28 x 200mg Ferrous Sulphate costs £1.11



# Proposed changes to anaemia pathway

## Different protocols for booking & 28 weeks

- Anaemia: target Hb <120g/L until term/post partum (then <110 g/L)
- Treat iron deficiency without anaemia (Prevent rather than cure)

## Check Ferritin

- Targeted treatment in all women - Ferritin at booking & 28 weeks

## More nuanced approach to treatment

- Stratify patients according to MCHr at 28 weeks

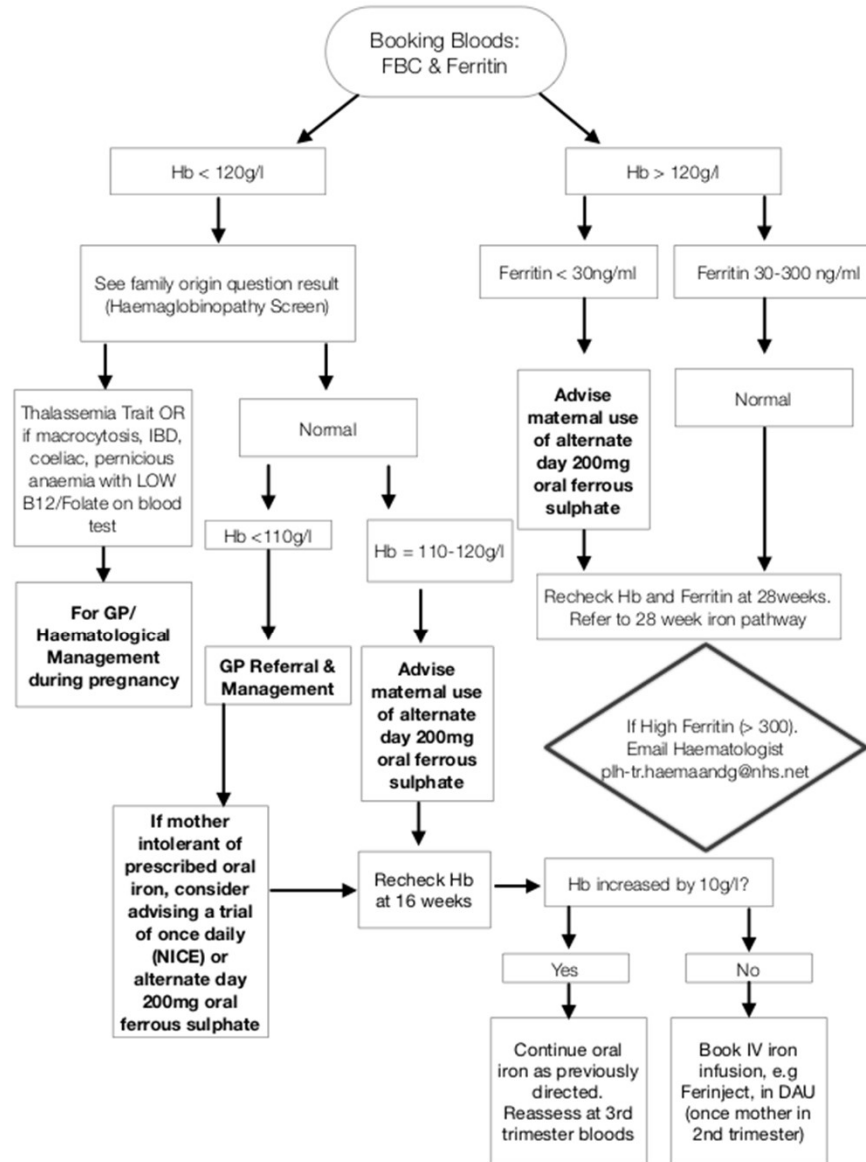
## Targeted supplementation as emphasis : Alternate day dosing of oral iron

- 200mg ferrous sulfate - **midwife exemption**
- Increased compliance
- Supplementation rather than treatment
- Treatment as per Nov 21 NICE update

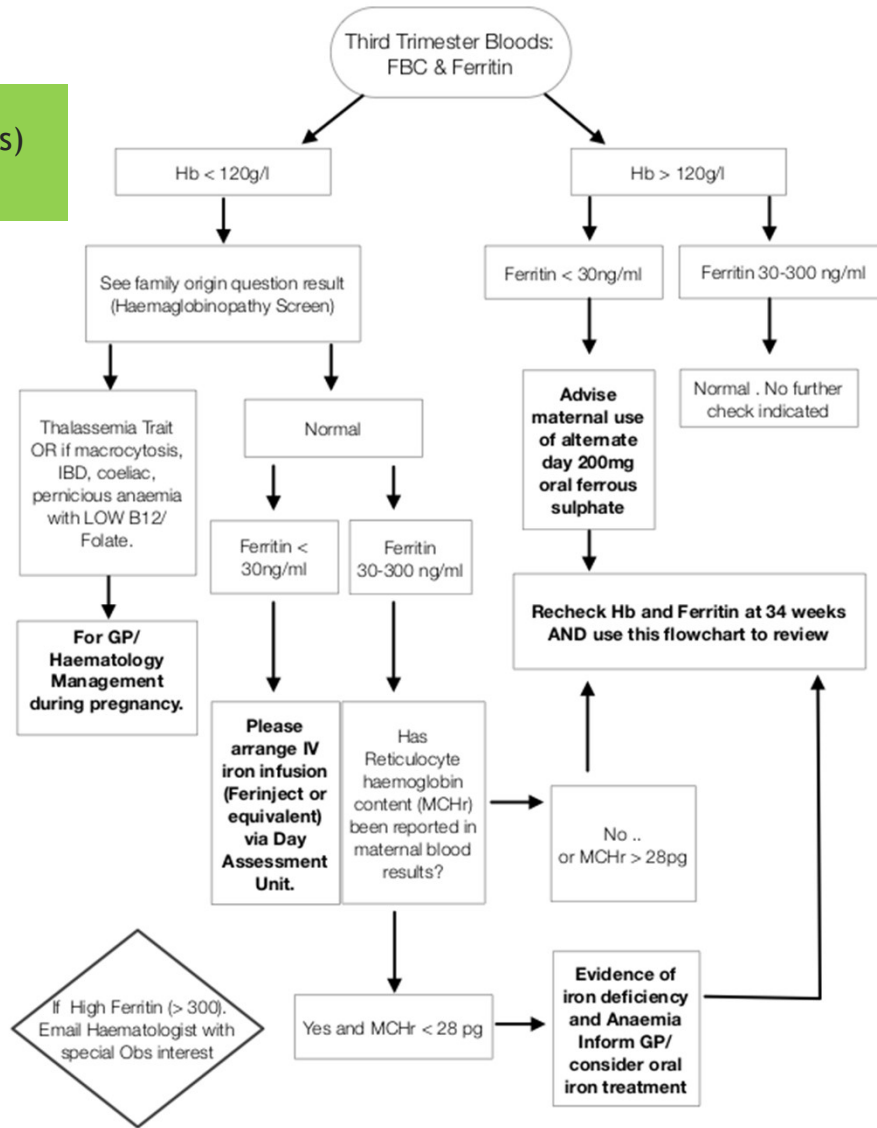
## Recheck Hb after starting PO iron

- Expect 10g/L rise in Hb at 2 weeks
- PO iron should continue for 2-3 months or 6 weeks postpartum

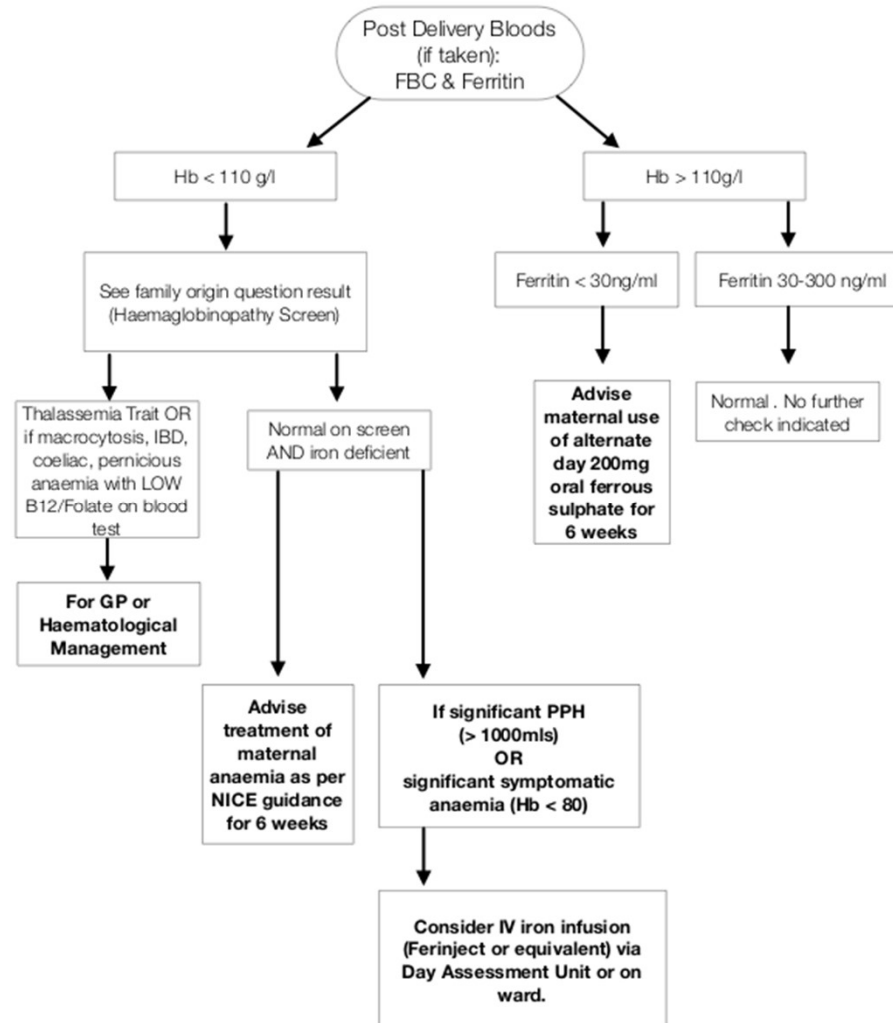
# Booking Pathway



# 3<sup>rd</sup> trimester (28 weeks bloods)



## Term and Post Delivery







Dr Wayne Thomas  
Consultant  
Haematologist



Dr Stuart Cleland  
Obs Anaesthetist and  
RTC/HTC chair



Clara Southby  
Maternity  
Services  
Matron



BJA Education, 19(12): 390–397 (2019)  
doi: 10.1016/j.bjae.2019.09.003  
Advance Access Publication Date: 24 October 2019

### Iron homeostasis and perioperative management of iron deficiency

S.R. Cleland and W. Thomas\*

University Hospitals Plymouth NHS Trust, Plymouth, UK



# Conclusion

- ▶ Evidence-based approach to pathway design
- ▶ Suggest Hb <120g/L until term (then <110g/L) after deriving normal ranges in our local population
- ▶ Separate guidance for booking & 28-week appointments
- ▶ Testing of ferritin with Hb at booking & 28 weeks
- ▶ Treatment of iron deficiency with and without anaemia
- ▶ Midwife exemption to prescribe & dispense ferrous sulphate
- ▶ Reduction in IV iron need
- ▶ Change in dosing regimen:
  - ▶ Alternate day OD dosing to optimise absorption

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- ▶ Stoffel *et al.* Iron absorption from supplements is greater with alternate day than with consecutive day dosing in iron-deficient anemic women. *Haematologica* 2020;**105**(5):1232-1239; <https://doi.org/10.3324/haematol.2019.220830>.



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