

Anaemia management – putting it into practice.

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- The story so far:
 - Anaemia is associated with transfusion.
 - The more anaemic you are pre op the more likely you are to require a transfusion.
 - Anaemia is associated with increased post op morbidity & mortality – independent of transfusion.

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Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study



Khaled M Musallam, Hani M Tamim, Toby Richards, Donat R Spahn, Frits R Rosendaal, Aida Habbal, Mohammad Khreiss, Fadi S Dahdaleh, Kaivan Khavandi, Pierre M Sfeir, Assaad Soweid, Jamal J Hoballah, Ali T Taher, Faek R Jamali

US Veterans Database (NSQIP) (n=227,425)

Anaemia (n=69,229; 30.4%)

30 day mortality

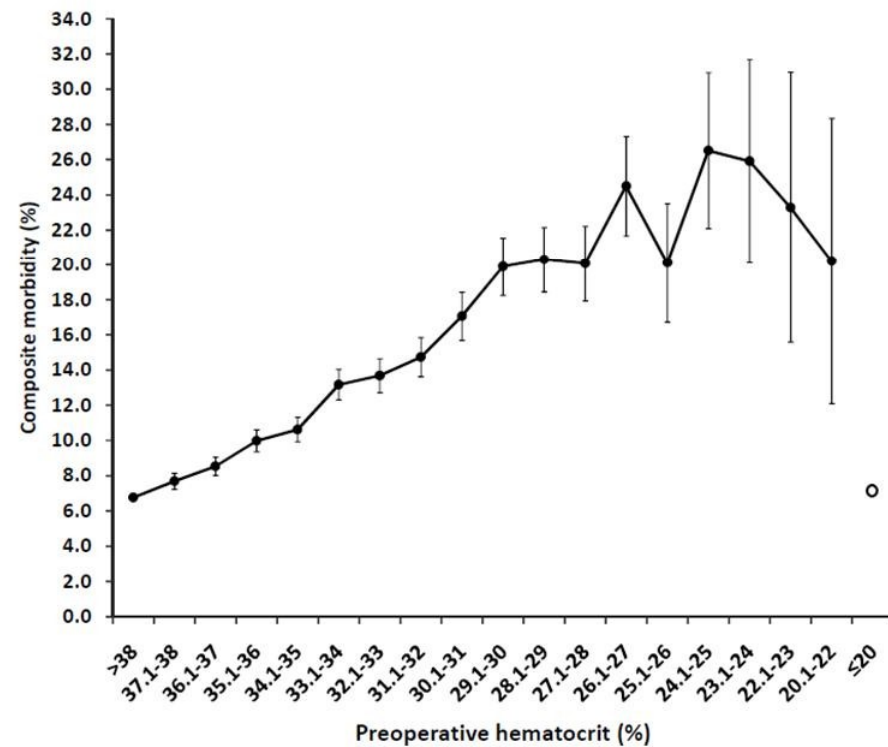
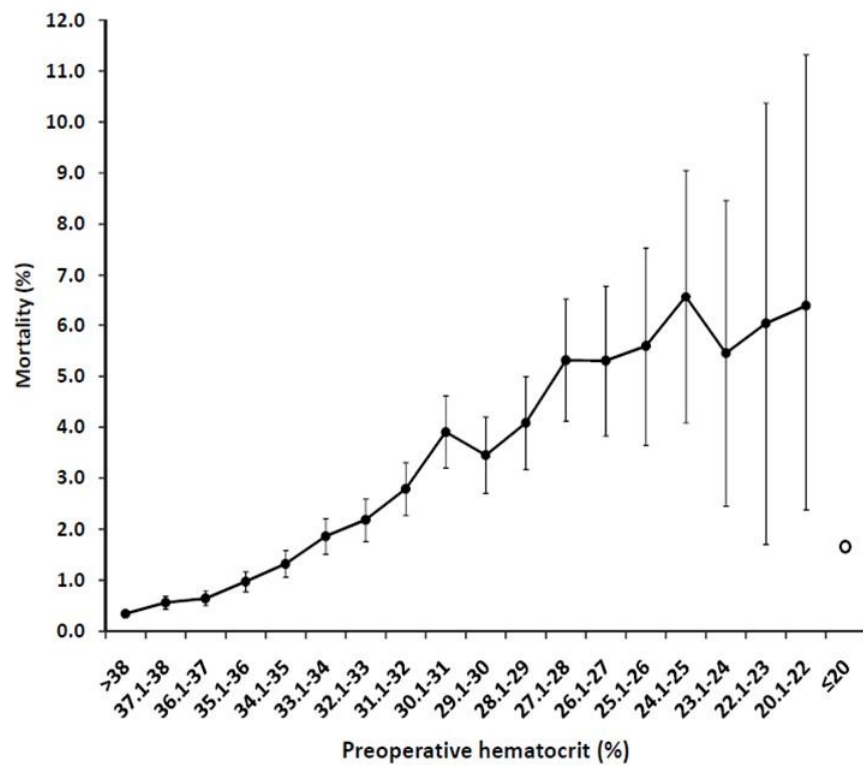
30 day composite morbidities (9 defined areas)

Multivariate regression

(9 defined subgroups)

(56 cofactors)

EFFECT OF ANAEMIA ON OUTCOME



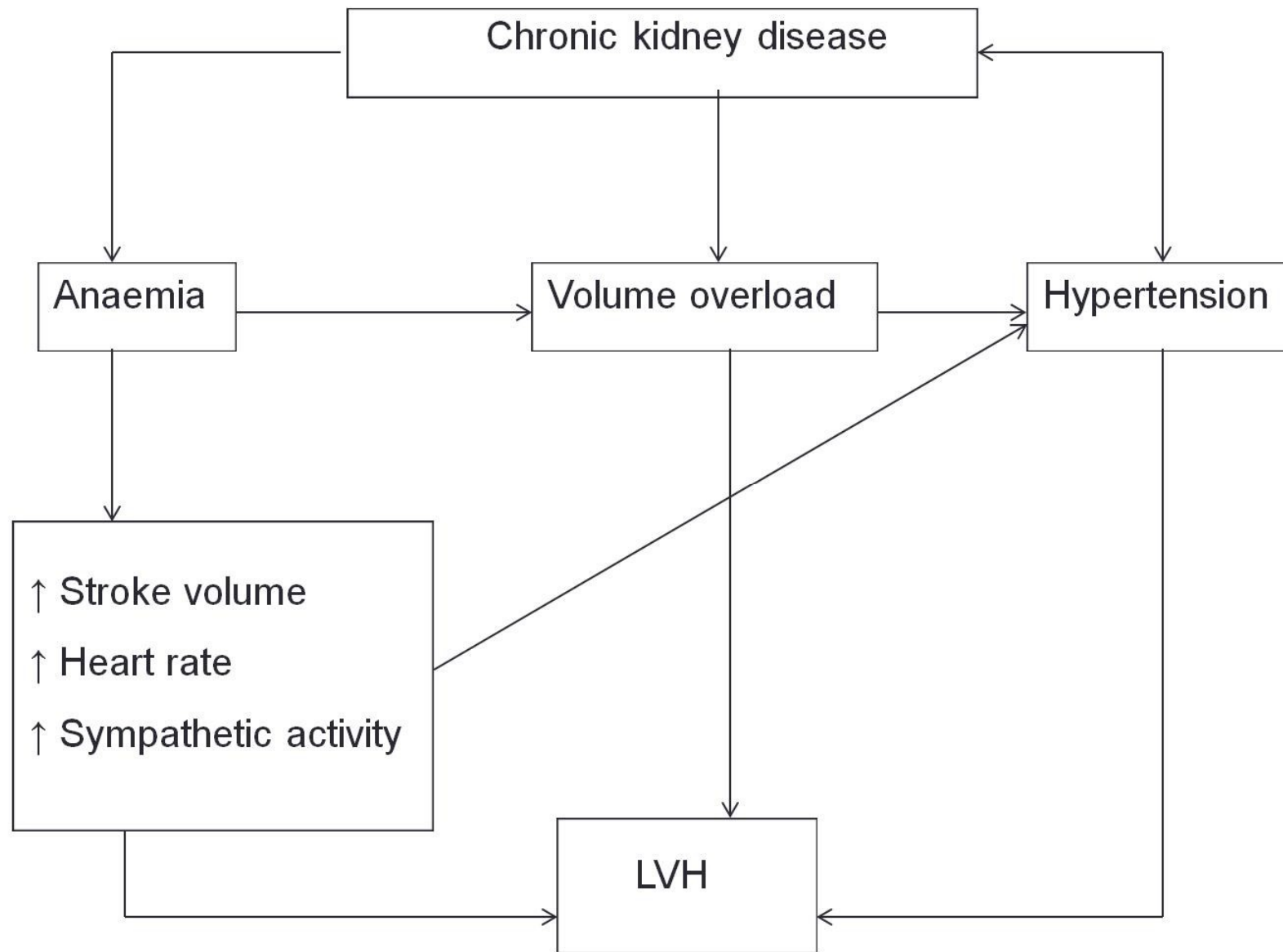
Oxygen delivery

$$DO_2 = C.O. \times [Hb \text{ g/l}] \times SaO_2 \times 1.34 \times 10^{-5}$$

But – how much oxygen do we really need to deliver?

At Hb of 150g/l approx 200ml O₂ per litre of blood.

Only utilise 200ml O₂ at rest



LVH in CKD patients (Mann JF, Nephrol, Dial Transplant 1999;14(Suppl 2):29-36)

- Supposition, correcting pre op anaemia will reduce:
 - Requirement for transfusion
 - Reduce morbidity and mortality
 - Reduce length of stay
 - Reduce cost of health care
 - PREVENTT trial (PREoperative intraVENous iron To Treat anaemia in major surgery)

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- PREVENTT
 - Major surgery
 - Hb >90g/litre <120g/litre
 - Single dose of iv iron
- Logistical problems
 - Infusion 14 – 42 days pre op.

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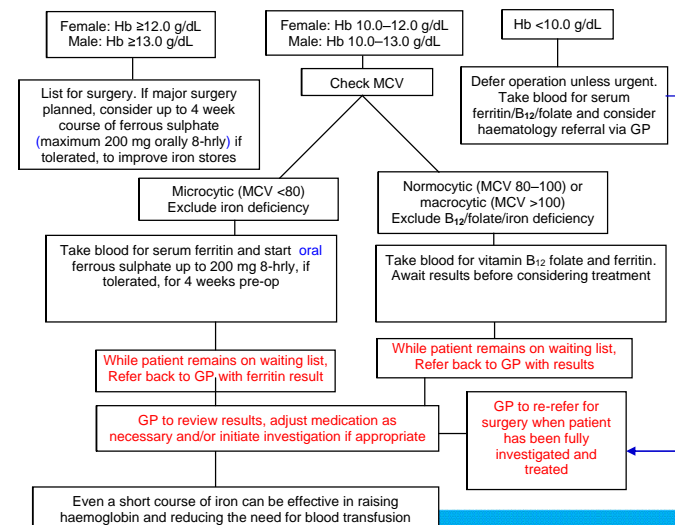
PRE-OPERATIVE MANAGEMENT – HAEMATOLOGY

- We already have guidelines:
 - West Mercia clinical guidelines
 - West Midlands RTC guidelines

HAEMOGLOBIN

- Investigate and treat unexpected anaemia. Anaemia is defined by WHO as Hb <13 g/dL in men and Hb <12 g/dL in women. See **Algorithm for management of unexpected pre-operative anaemia**
- in patients with shortness of breath or worsening angina caused by anaemia, consider blood transfusion – see **Chronic anaemia – transfusion flowchart** in **Medical** guidelines and postpone operation until asymptomatic
- Prescribe oral iron for patients with surgical conditions known to predispose to ongoing blood loss from time of diagnosis until condition treated
- if surgery urgent (cancer surgery) or operation required within 2 weeks, consider pre-operative use of intravenous iron, vitamin B₁₂ injections and folate as guided by assays; use blood transfusion only when there has been insufficient response to haematinic agents and patient is symptomatic of anaemia
- In patients with anaemia associated with chronic diseases, such as chronic renal failure or rheumatoid arthritis with Hb <12 g/dL, consider intravenous iron to treat functional iron deficiency state
- such patients may subsequently undergo surgery, despite a persistently low Hb, but take into account risk of bleeding during surgery and discuss transfusion requirements with **blood bank** taking in to account the **Maximum surgical blood ordering schedule (MSBOS)** guideline and patient's usual haemoglobin level
- if **pre-operative** patient has iron deficiency or functional iron deficiency state and is unable to take/tolerate oral iron, treat as soon as possible with IV iron **as out-patient after checking with consultant surgeon**

Algorithm for management of unexpected pre-operative anaemia



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Guidelines for the Management of Anaemia in Pre-operative Assessment Clinics (2007)



Some key recommendations:

www.transfusionguidelines.org.uk

The GP should **identify and treat anaemia before referral** wherever possible

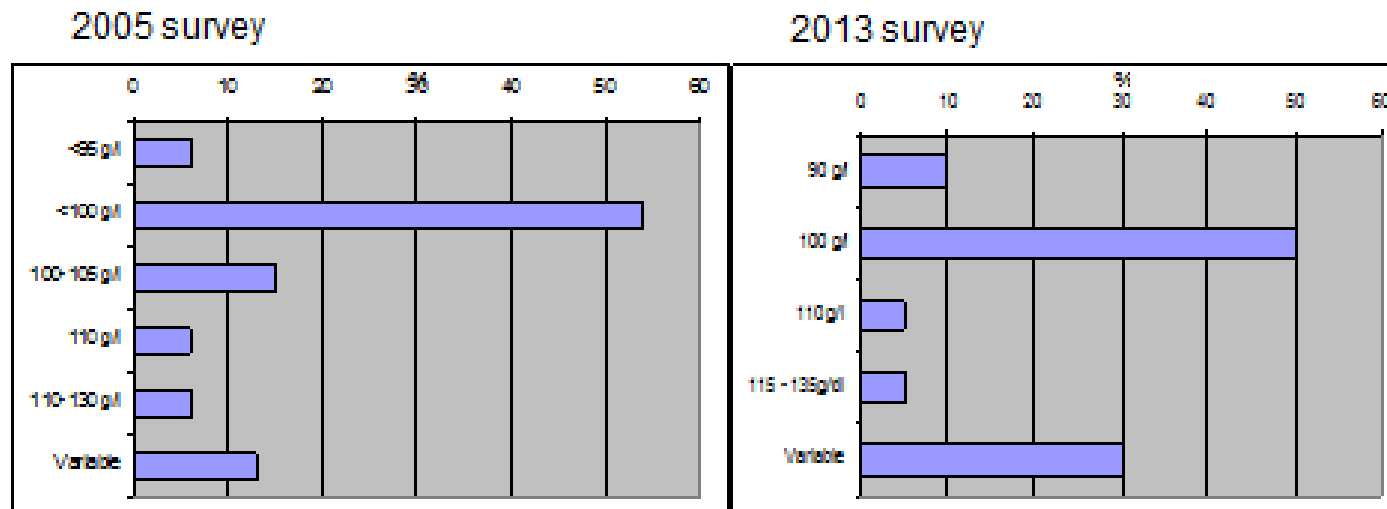
Pre-operative assessment should take place **at least 4 weeks prior to surgery**, and ideally immediately following the decision to operate

All patients who are identified as at risk of requiring a blood transfusion should **have FBC assessed at PAC**. These patients should also be given information about the possibility of requiring a blood transfusion

All FBC results should be reviewed within **2 working days**
The **definition of anaemia** should be based on **WHO classifications**
Male Hb <13g/dl / Female Hb <12g/dl

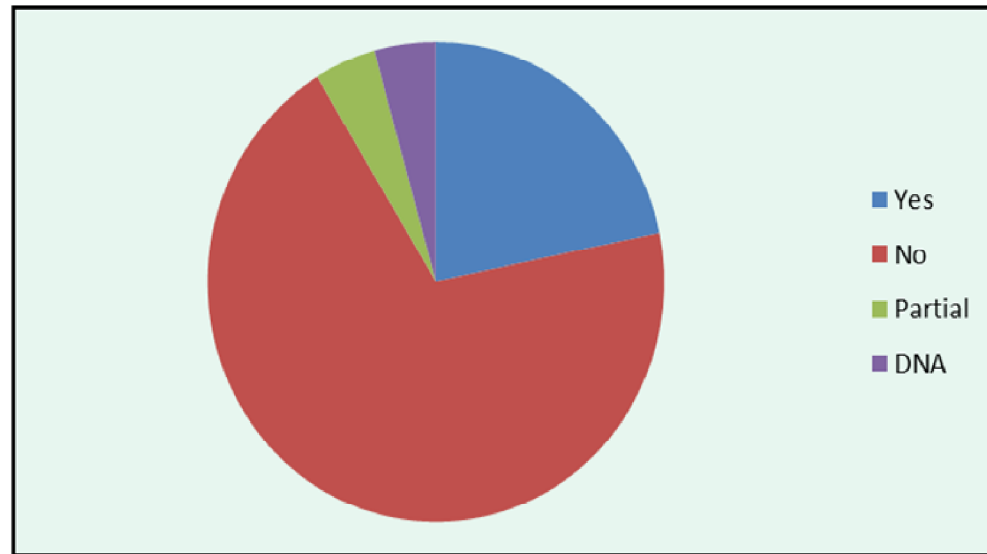
Anaemic results should be seen by a member of the clinical team who has **sufficient authority** to commence treatment, refer for further investigation or delay surgery.

Hb level at which action is taken in fit patients under the age of 65



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Is treatment of anaemia initiated by the POAC – 2013 survey results only



If yes – what treatments are initiated?

	Routinely	Regularly	Rarely	Never
Oral Iron	2	1	2	0
IV iron	0	1	0	3
Transfusion	1	2	2	0

- Battles to be fought:
 - Availability of suitable iv iron preparation
 - Selection of appropriate treatment once anaemia identified
 - Recognition of anaemia
 - Somewhere to give iv iron
 - Someone to give iv iron
 - Control of the waiting lists

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Formulation	Iron Dextran	Iron Sucrose	Ferric Carboxymaltose	Iron Isomaltoside
Maximum single dose	20mg/kg body weight	200mg	20mg/kg body weight, maximum 1000mg per dose	20mg/kg body weight
Dosage regimen	Single total dose infusion possible	Repeated doses up to 3 times per week	Single total dose infusion possible	Single total dose infusion possible
Incidence of adverse reactions	5% non-serious Anaphylactoid reactions 1:100-1:1000 Anaphylaxis <1:10 000	0.5 -1.5% non-serious Anaphylactoid Reactions 1:1000 – 1:10 000	3% non-serious Anaphylactoid reactions 1:100 – 1:1000	>1% non-serious Anaphylactoid reactions 1:100 – 1:1000 Anaphylaxis <1:10 000
Test dose required?	Yes	First treatment only	No	No
Duration of infusion	4-6 hours	2-5 minutes	15 minutes	30 minutes (up to 10mg/kg) 60 minutes (up to 20mg/kg)
Cost per gram of elemental iron	£79.70	£93.50	£191.00	£169.50

Equivalence of delivering 1000mg of iron to a non compromised patient

	Oral iron	Intravenous iron	Blood transfusion
Background	Commonly ferrous sulphate or fumarate.	Traditionally bound to dextran, newer compounds bound to Carbohydrates	Blood is donated by volunteers, it is screened for a number of diseases.
Risks	Upset tummy, diarrhoea, constipation	Skin staining if extravasates, <1 in 10,000 risk of anaphylaxis	Transfusion reactions, wrong blood, infections, immunomodulation, can no longer donate.
Benefits	Will feel better over a few weeks	Will feel better over a few weeks	Will feel better very soon
Time taken	6 months	As little as 30mins	9-12 hours
Costs	£10	Up to £200	Over £375
comments	Outpatient treatment	Outpatient treatment	In/outpatient treatment

- Recognition of anaemia
 - Talk to the pre operative assessment nurses
 - Referrals made to me
 - Treatment initiated – Consultants advised
 - Talk on stat & mandatory training to Consultant staff

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Investigations for anaemia

- FBC
 - Hb >120g/l for women, >130g/l for men
 - MCV 80 – 100fl
 - MCHb 26.5 – 31.5pg
- B12 200-900pg/ml
- Folate 3-12pg/ml
- Ferritin 20-300µg/L
- Serum iron 13 - 32µmol/L
- Transferrin 1.68-3.36g/L
- Transferrin saturation 20-40%
- Reticulocyte count (analyser dependent)
- %hypochromic red cells normal <2.5%. If >10% definitely iron deficient (sample needs to be <4 hours old)

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Why do patients bleed? Causes of anaemia

- Not enough substrate (dietary deficiency)
- Losing it faster than you can make it (Cancer / menorrhagia)
- Functional iron deficiency
- Losing it faster than you can make it (massive haemorrhage)
- Bone marrow failure

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Lady with menorrhagia (1)

Item Name	24/07/2013 10:58				
Ferritin.					
Haemoglobin	96				
White Cell Count	5.7				
Platelet Count	359				
Red Blood Cell	4.28				
Haematocrit	0.32				
Mean Cell Volume	74.8				
Mean Cell Haemoglobin	22.5				
Absolute Neutrophil Count	3.8				
Absolute Lymphocyte Count	1.4				
Absolute Monocyte Count	0.2				
Absolute Eosinphil Count	0.1				
Absolute Basophil Count	0				
Absolute Large Unstained Cell Count	0.1				
ESR.	5				
Prothrombin INR					
APTT Ratio					

Lady with menorrhagia (2)

Item Name	24/07/2013 10:58	19/02/2014 13:15			
Ferritin.			4		
Haemoglobin	96	97			
White Cell Count	5.7	6.7			
Platelet Count	359	388			
Red Blood Cell	4.28	4.19			
Haematocrit	0.32	0.31			
Mean Cell Volume	74.8	74.3			
Mean Cell Haemoglobin	22.5	23.2			
Absolute Neutrophil Count	3.8	4			
Absolute Lymphocyte Count	1.4	2			
Absolute Monocyte Count	0.2	0.3			
Absolute Eosinphil Count	0.1	0.2			
Absolute Basophil Count	0	0			
Absolute Large Unstained Cell Count	0.1	0.1			
ESR.	5	2			
Prothrombin INR					
APTT Ratio					

Lady with menorrhagia (3)

Item Name	24/07/2013 10:58	19/02/2014 13:15	25/07/2014 00:00
Ferritin.		4	5
Hæmoglobin	96	97	67
White Cell Count	5.7	6.7	5.8
Platelet Count	359	388	415
Red Blood Cell	4.28	4.19	3.57
Hæmatocrit	0.32	0.31	0.23
Mean Cell Volume	74.8	74.3	65.3
Mean Cell Hæmoglobin	22.5	23.2	18.9
Absolute Neutrophil Count	3.8	4	3.9
Absolute Lymphocyte Count	1.4	2	1.4
Absolute Monocyte Count	0.2	0.3	0.3
Absolute Eosinphil Count	0.1	0.2	0.1
Absolute Basophil Count	0	0	0
Absolute Large Unstained Cell Count	0.1	0.1	0.1

Lady with menorrhagia (4)

Item Name	24/07/2013 10:58	19/02/2014 13:15	25/07/2014 00:00	29/07/2014 16:10	24/10/2014 15:42
Ferritin.		4	5		6
Haemoglobin	96	97	67	68	110
White Cell Count	5.7	6.7	5.8	7.3	5.4
Platelet Count	359	388	415	483	299
Red Blood Cell	4.28	4.19	3.57	3.69	4.36
Haematocrit	0.32	0.31	0.23	0.25	0.36
Mean Cell Volume	74.8	74.3	65.3	66.8	82.4
Mean Cell Haemoglobin	22.5	23.2	18.9	18.5	25.3
Absolute Neutrophil Count	3.8	4	3.9	5.2	2.8
Absolute Lymphocyte Count	1.4	2	1.4	1.5	2
Absolute Monocyte Count	0.2	0.3	0.3	0.3	0.3
Absolute Eosinphil Count	0.1	0.2	0.1	0.1	0.2
Absolute Basophil Count	0	0	0	0	0
Absolute Large Unstained Cell Count	0.1	0.1	0.1	0.1	0.1
ESR.	5	2			
Prothrombin INR				1	1.1
APTT Ratio				0.88	1.12

Man with SOBOE (1)

Item Name	20/06/2014 11:13				
Magnesium.					
Serum B12.					
Serum Folate.					
Ferritin.					
Transferrin.					
Serum Iron.					
Transferrin Saturation.					
Aspartate Transaminase.					
CRP - Wide Range.					
Prothrombin INR					
Haemoglobin	107				
White Cell Count	7				
Platelet Count	240				
Red Blood Cell	4.61				
Haematocrit	0.33				
Mean Cell Volume	71.8				
Mean Cell Haemoglobin	23.3				
Absolute Neutrophil Count	4.9				
Absolute Lymphocyte Count	1.1				
Absolute Monocyte Count	0.6				
Absolute Eosinophil Count	0.2				
Absolute Basophil Count	0.1				
Absolute Large Unstained Cell Count	0.2				
Percentage Reticulocyte Count					
Absolute Reticulocyte Count					
Direct Antiglobulin Test.					
APTT Ratio					

Man with SOBOE (2)

Item Name	14/03/2013 08:50	20/06/2014 11:13				
Magnesium.						
Serum B12.						
Serum Folate.						
Ferritin.						
Transferrin.						
Serum Iron.						
Transferrin Saturation.						
Aspartate Transaminase.						
CRP - Wide Range.						
Prothrombin INR						
Haemoglobin	15.3	107				
White Cell Count	8.5	7				
Platelet Count	223	240				
Red Blood Cell	5.35	4.61				
Haematocrit	0.45	0.33				
Mean Cell Volume	84.4	71.8				
Mean Cell Haemoglobin	28.5	23.3				
Absolute Neutrophil Count	5.8	4.9				
Absolute Lymphocyte Count	1.4	1.1				
Absolute Monocyte Count	0.5	0.6				
Absolute Eosinphil Count	0.2	0.2				
Absolute Basophil Count	0.1	0.1				
Absolute Large Unstained Cell Count	0.3	0.2				
Percentage Reticulocyte Count						
Absolute Reticulocyte Count						
Direct Antiglobulin Test.						
APTT Ratio						

Man with SOBOE (3)

Item Name	14/03/2013 08:50	20/06/2014 11:13	14/11/2014 11:30		
Magnesium.					
Serum B12.			477		
Serum Folate.			6.8		
Ferritin.			Result was 7 ng/mL 17 days ago		
Transferrin.			3.38		
Serum Iron.			5		
Transferrin Saturation.			5.7		
Aspartate Transaminase.					
CRP - Wide Range.					
Prothrombin INR					
Haemoglobin	15.3	107	90		
White Cell Count	8.5	7	10.7		
Platelet Count	223	240	276		
Red Blood Cell	5.35	4.61	4.56		
Haematocrit	0.45	0.33	0.32		
Mean Cell Volume	84.4	71.8	71.1		
Mean Cell Haemoglobin	28.5	23.3	19.8		
Absolute Neutrophil Count	5.8	4.9	8.2		
Absolute Lymphocyte Count	1.4	1.1	1.3		
Absolute Monocyte Count	0.5	0.6	0.7		
Absolute Eosinphil Count	0.2	0.2	0.2		
Absolute Basophil Count	0.1	0.1	0.1		
Absolute Large Unstained Cell Count	0.3	0.2	0.2		
Percentage Reticulocyte Count					
Absolute Reticulocyte Count					
Direct Antiglobulin Test.					
APTT Ratio					

Man with SOBOE (4)

Item Name	14/03/2013 08:50	20/06/2014 11:13	14/11/2014 11:30	20/11/2014 14:40	21/11/2014 19:24	27/11/2014 09:12
Magnesium.						
Serum B12.			477			
Serum Folate.			6.8			
Ferritin.			Result was 7 ng/ mL 17 days ago			
Transferrin.			3.38			
Serum Iron.			5			103
Transferrin Saturation.			5.7			
Aspartate Transaminase.				19		
CRP - Wide Range.					<4.0	<4.0
Prothrombin INR				1.1	1.1	
Haemoglobin	15.3	107	90	69	62	107
White Cell Count	8.5	7	10.7	10.6	10.8	19.6
Platelet Count	223	240	276	294	322	263
Red Blood Cell	5.35	4.61	4.56	3.42	3.01	4.3
Haematocrit	0.45	0.33	0.32	0.24	0.21	0.34
Mean Cell Volume	84.4	71.8	71.1	71.4	71	80
Mean Cell Haemoglobin	28.5	23.3	19.8	20.3	20.5	24.8
Absolute Neutrophil Count	5.8	4.9	8.2	8.3	8.2	17.3
Absolute Lymphocyte Count	1.4	1.1	1.3	1.2	1.4	0.9
Absolute Monocyte Count	0.5	0.6	0.7	0.6	0.6	0.9
Absolute Eosinophil Count	0.2	0.2	0.2	0.1	0.1	0
Absolute Basophil Count	0.1	0.1	0.1	0.1	0.1	0
Absolute Large Unstained Cell Count	0.3	0.2	0.2	0.3	0.4	0.3
Percentage Reticulocyte Count				3.2		
Absolute Reticulocyte Count				107.9		
Direct Antiglobulin Test.				Negative		
APTT Ratio				0.95		

- Failures

- Time to surgery. CT PET scan but no bloods
- Last Thursday
- Control of waiting lists

- Success

- Upper GI interested in prehabilitation now
- Last Friday

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- Achievements to date:
 - Education of PREAMS staff
 - Referrals from them
 - Referrals from some surgeons
 - >50 iv iron infusions to date
 - No adverse reactions – even in a patient who had previously reacted to iron dextran
 - iv iron given in PREAMS clinics both in County site and Royal site (by me)

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Payments for anaemia management

SA03D	Haemolytic Anaemia with CC	-	400	-	-	18	2,586	18	236	No	-	-	1	HRG
SA03F	Haemolytic Anaemia without CC	-	400	-	-	5	1,807	12	236	No	-	-	1	HRG
SA04D	Iron Deficiency Anaemia with CC	-	417	-	-	5	1,929	22	236	No	-	-	1	HRG
SA04F	Iron Deficiency Anaemia without CC	-	294	-	-	5	813	6	236	No	-	-	1	HRG
SA05D	Megaloblastic Anaemia with CC	-	565	-	-	5	1,830	22	236	No	-	-	1	HRG
SA05F	Megaloblastic Anaemia without CC	-	274	-	-	5	1,124	16	236	No	-	-	1	HRG

• Best practice tariff

SA03D	Haemolytic Anaemia with CC	Anaemia	2,828	2,586	HRG	BP54
SA03F	Haemolytic Anaemia without CC		2,050	1,807		
SA04D	Iron Deficiency Anaemia with CC		2,171	1,929		
SA04F	Iron Deficiency Anaemia without CC		1,055	813		
SA05D	Megaloblastic Anaemia with CC		2,072	1,830		
SA05F	Megaloblastic Anaemia without CC		1,366	1,124		

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51 yr old lady
 1st infusion on 6th March
 2nd infusion 20th March,
 TAH on 29th April LOS 4 days

Item Name	04/02/2013 11:53	20/03/2013 00:00	16/04/2013 13:39	30/04/2013 10:35
Ferritin.		235	241	
Transferrin.		2.47		
Serum Iron.		38		
Transferrin Saturation.		59.1		
Haemoglobin	8.9	11.6	131	128
White Cell Count	6.8	6.9	6.2	10.3
Platelet Count	338	261	245	243
Red Blood Cell	4.26	5.12	4.8	4.54
Haematocrit	0.29	0.37	0.39	0.39
Mean Cell Volume	68	72.8	82	84.9
Mean Cell Haemoglobin	20.9	22.7	27.3	28.2

94 yr old man

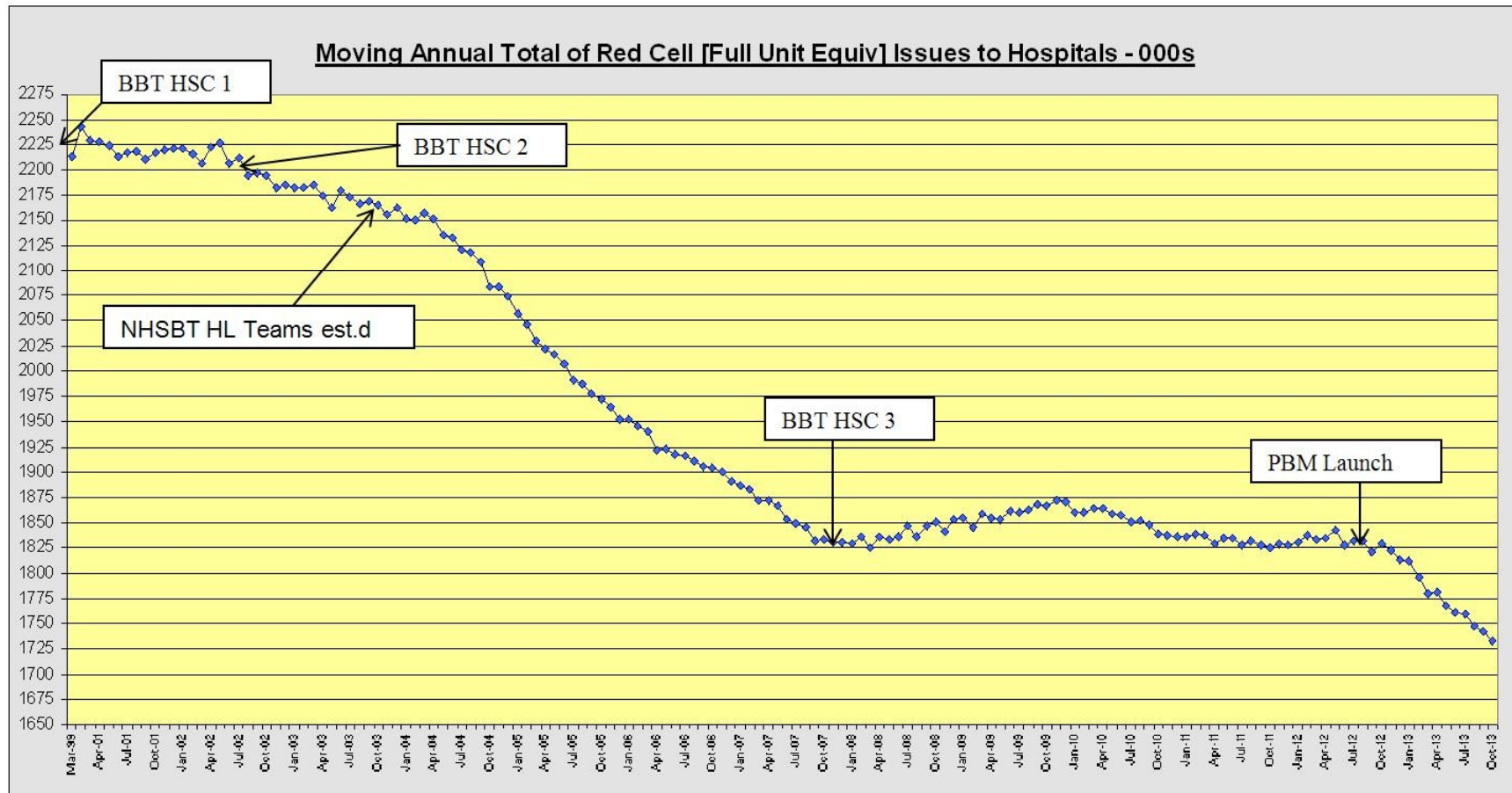
1st infusion 4th December 2013

2nd infusion 11th December 2013

open Rt hemicolectomy, 10th Feb 14 LOS 4 days

Name	28/11/2013	11/12/2013	10/02/2014	11/02/2014	13/02/2014	31/07/2014
Transferrin.		2.99				
Serum Iron.		13				
Transferrin Saturation.		16.7				
Ferritin.		592				
Haemoglobin	68	85	129	90	107	143
Haematocrit	0.25	0.3	0.41	0.29	0.33	0.46
Mean Cell Volume	71.2	79.9	94.7	93.7	94.5	95.6
Mean Cell Haemoglobin	19.8	23.1	29.6	29.7	30.3	30

CHANGE IN RED CELL USAGE 1999-2013



- What will improve anaemia management?
 - Editorials and journal articles (BMJ & BJA)
 - Peer pressure
 - Systems approach

BJA Advance Access published April 15, 2015

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Editorial

Editorial

Non-treatment of preoperative anaemia is substandard clinical practice

It is well known that preoperative anaemia is frequent and associated with increased mortality and morbidity, even if only mild anaemia is present.^{1,2} In addition, preoperative anaemia is one of the most significant risk factors in subsequent red blood cell transfusion,³ which in itself has adverse effects on mortality and morbidity.⁴ Therefore, unmanaged preoperative anaemia is a contraindication for elective surgery.⁵

In this edition of the *British Journal of Anaesthesia*, Muñoz and colleagues⁶ rightly alerted the medical community, reporting that preoperative anaemia is often left untreated. The paradox of known negative consequences of untreated anaemia and current practice is explained by the presentation of 10 widely held misconceptions. Moreover, we identified two additional reasons why physicians are still hesitating to treat preoperative anaemia systematically. First, the World Health Organization's definition of anaemia with a haemoglobin concentration of <120 g litre⁻¹ in women and <130 g litre⁻¹ in men is not sufficiently known by the majority of physicians. Furthermore, the notion that very mild forms of anaemia (haemoglobin values between 100–120 and 100–130 g litre⁻¹, respectively) result in adverse clinical outcomes, such as increased mortality and a long list of complications,^{7,8} is also not well known. Second, there may be reluctance by some physicians to treat preoperative anaemia actively, because of the fact that they themselves will be held responsible for any adverse events occurring thereafter. In contrast, a perioperative transfusion in a patient who is anaemic before surgery is considered by most an inevitable event, for which medical staff cannot be held responsible. Therefore, some physicians prefer not to be involved in treating preoperative anaemia. We hope that the refuting by Muñoz and colleagues⁶ of 10 widely held misconceptions helps pave the way to widespread treatment of preoperative anaemia.

A consortium of four large German University Hospitals (Frankfurt, Münster, Bonn, and Kiel) is engaged in the concept of patient blood management (PBM). The Frankfurt group has shown how to target and implement treatment of preoperative anaemia (ClinicalTrials.gov identifiers: NCT01820949 and NCT02147795). Their investigation clearly highlights five key success factors (Table 1) for implementing a comprehensive preoperative anaemia treatment programme. The first factor, which is clearly the most important, was establishing a dedicated

interdisciplinary PBM steering committee, with preoperative anaemia treatment being the first pillar of PBM.⁹ Second, the inclusion and support of senior hospital management is of utmost importance. Only with this support can the necessary reorganization of the preclinical procedures and structures be implemented. Additionally, the understanding of surgical and medical disciplines is crucial to the management and treatment of preoperative anaemia. Last, but not least, focusing our efforts on the knowledge of how operations are regularly performed in anaemic patients, who frequently require allogeneic red blood cell transfusions, is also essential (www.patientbloodmanagement.eu). Such favourable hospital conditions and improvements can be achieved only by continuous education over years and through the coordination of a dedicated interdisciplinary PBM steering committee. Should your hospital not yet have the aforementioned structure, then becoming a leader in PBM and establishing a steering committee is the way forwards.

Other centres have also succeeded in implementing treatment of preoperative anaemia. Theusinger and colleagues¹⁰ contacted the primary physician of each patient found to be anaemic before surgery. These patients were to undergo major orthopaedic surgery ($n=887$), with suggested treatment of anaemia using erythropoietin α , i.v. iron, vitamin B₁₂, and folic acid. Despite the fact that not all patients who were anaemic before surgery were treated, the incidence of anaemia on the day of operation decreased from 15 to 10% ($P<0.01$) and total allogeneic transfusion rate reduced from 20 to 10% ($P<0.01$). Short-term treatment of preoperative anaemia with erythropoietin and i.v. iron has also been shown to be successful in orthopaedic¹¹ and cardiac surgery.¹² Likewise, a group of four Spanish hospitals recently published their success in short-term preoperative treatment of anaemia with erythropoietin and i.v. iron in 2547 patients undergoing hip and knee arthroplasty or surgery for hip fracture.¹³ They could decrease the allogeneic transfusion rate from 37 to 24% ($P<0.01$), the postoperative infection rate from 12 to 8% ($P<0.01$), and the length of hospital stay from 12 to 11 days ($P<0.01$). In patients undergoing surgery for hip fracture, the 30-day mortality was reduced from 9 to 5% ($P<0.01$).

Through sound scientific evidence, they disproved 10 misconceptions of perioperative anaemia treatment. Moreover, this medical need can be met with successful treatment options.

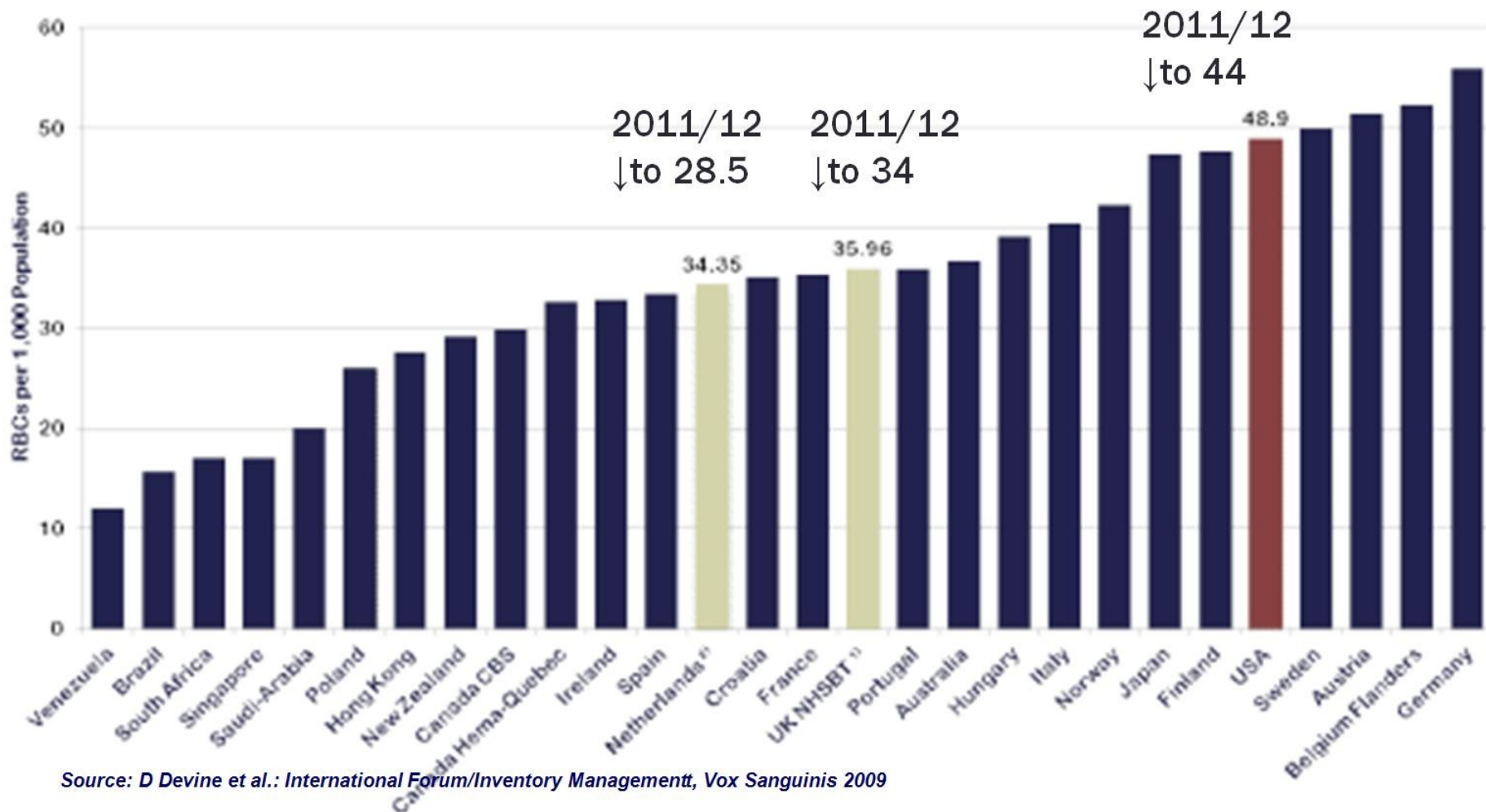
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GLOBAL RED CELL UTILIZATION RATES: 2008 - 09



Source: D Devine et al.: International Forum/Inventory Management, Vox Sanguinis 2009

- Our mission
 - To be un-noticed
 - To ensure all patients turn up in theatre non-anaemic
 - As a consequence – improve outcomes, reduce lengths of stay
 - Let the surgeons take the glory – but be self satisfied that we have made the difference!
 - Ensure that blood is transfused appropriately in all specialties – 25 unit ptp

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