Patient Blood Management

State of the Art

Košice CEEA 2017

The Frankfurt PBM Team

Patient Blood Management European Network

Dept. of Anesthesiology, Intensive Care Medicine & Pain Therapy
University Hospital Frankfurt
Director: Professor Kai Zacharowski, MD PhD ML FRCA


INŠTITÚT VZDELÁVANIA

COI

During the last 3 years I have received research grants, consultant/speaker honoria as well as financial support for continuous education of my department :

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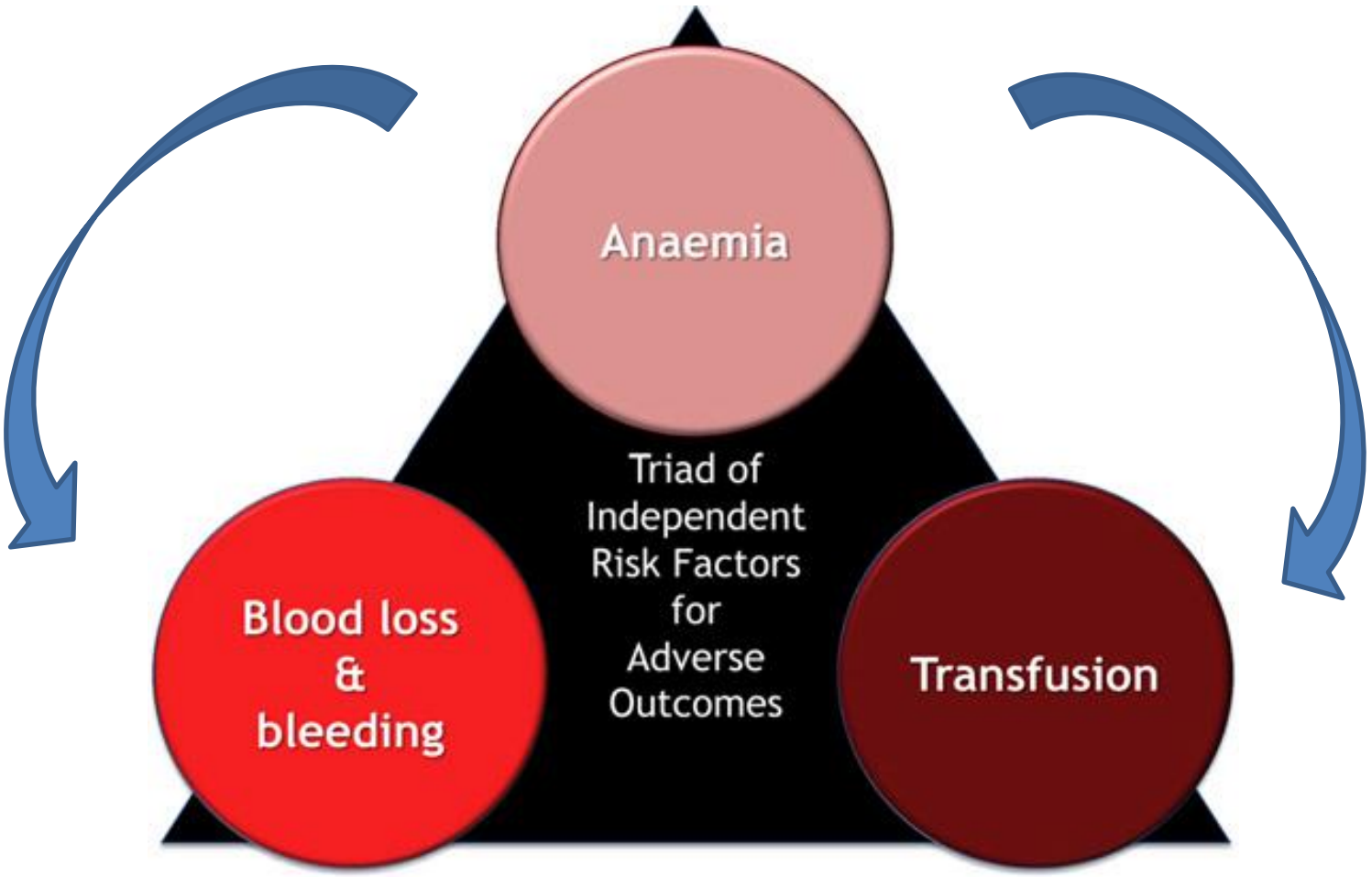
Anemia is a Disease in itself



Farmer et al., 2013 (Best Practice & Research Clinical Anaesthesiolgy)
Meybohm et al. 2016 (Annals of Surgery)
Zacharowski et al. 2016 (Best Practice & Research Clinical Anaesthesiology)

Problem: preoperative anemia

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

Lancet 2011; 378: 1396–407

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See Comment page 1362

Department of Internal Medicine (K M Musallam MD, H M Tamim PhD, A Soweid MD, Prof A T Taher MD), Department of Surgery (A Habbal BSN, M Khreiss MD, F S Dahdaleh MD, P M Sfeir MD, Prof J J Hoballah MD, F R Jamali MD), American University of Beirut Medical Center, Beirut, Lebanon; Angelo Bianchi Bonomi Haemophilia and Thrombosis Centre, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Milan, Italy (K M Musallam); College of Medicine, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia (H M Tamim); Division of Surgery and Interventional Science, University College London Hospital, London, UK

Summary

Background Preoperative anaemia is associated with adverse outcomes after cardiac surgery but outcomes after non-cardiac surgery are not well established. We aimed to assess the effect of preoperative anaemia on 30-day postoperative morbidity and mortality in patients undergoing major non-cardiac surgery.

Methods We analysed data for patients undergoing major non-cardiac surgery in 2008 from The American College of Surgeons' National Surgical Quality Improvement Program database (a prospective validated outcomes registry from 211 hospitals worldwide in 2008). We obtained anonymised data for 30-day mortality and morbidity (cardiac, respiratory, CNS, urinary tract, wound, sepsis, and venous thromboembolism outcomes), demographics, and preoperative and perioperative risk factors. We used multivariate logistic regression to assess the adjusted and modified (nine predefined risk factor subgroups) effect of anaemia, which was defined as mild (haematocrit concentration >29–<39% in men and >29–<36% in women) or moderate-to-severe (≤29% in men and women) on postoperative outcomes.

Findings We obtained data for 227 425 patients, of whom 69 229 (30·44%) had preoperative anaemia. After adjustment, postoperative mortality at 30 days was higher in patients with anaemia than in those without anaemia (odds ratio [OR] 1·42, 95% CI 1·31–1·54); this difference was consistent in mild anaemia (1·41, 1·30–1·53) and moderate-to-severe anaemia (1·44, 1·29–1·60). Composite postoperative morbidity at 30 days was also higher in patients with anaemia than in those without anaemia (adjusted OR 1·35, 1·30–1·40), again consistent in patients with mild anaemia (1·31, 1·26–1·36) and moderate-to-severe anaemia (1·56, 1·47–1·66). When compared with patients without anaemia or a defined risk factor, patients with anaemia and most risk factors had a higher adjusted OR for 30-day mortality and morbidity than did patients with either anaemia or the risk factor alone.

Interpretation Preoperative anaemia, even to a mild degree, is independently associated with an increased risk of 30-day morbidity and mortality in patients undergoing major non-cardiac surgery.

Funding Vifor Pharma.

Musallam K et al. *Lancet 2011;378:1396-407*
Retrospective, 227,425 patients

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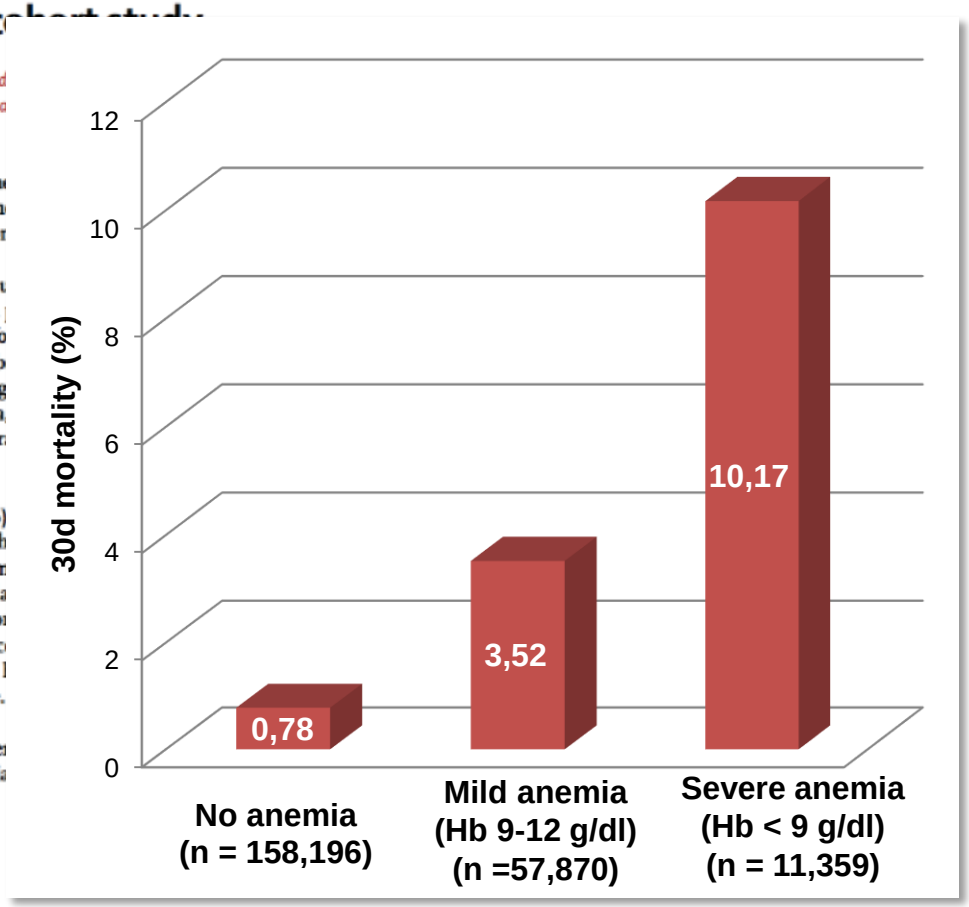
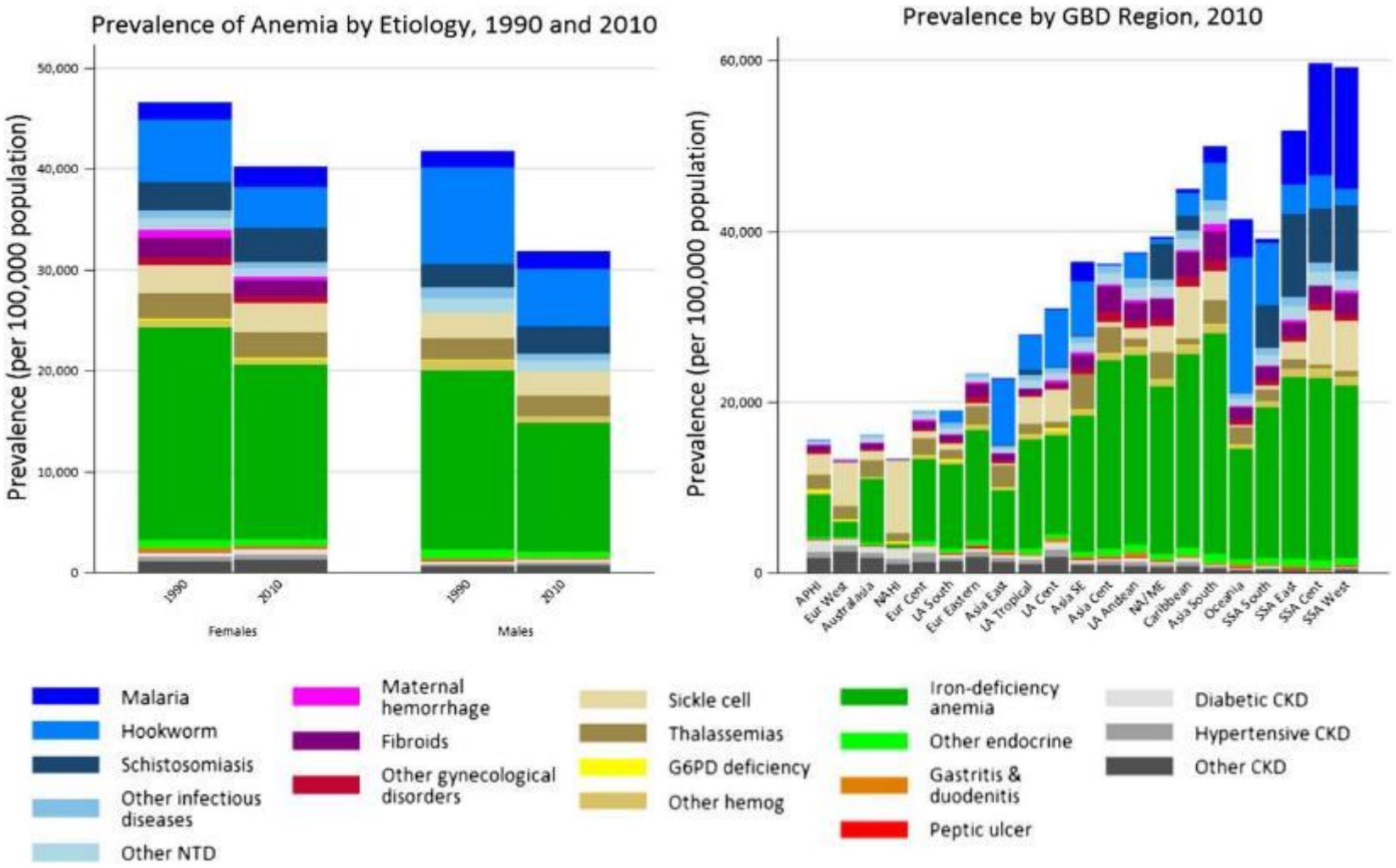


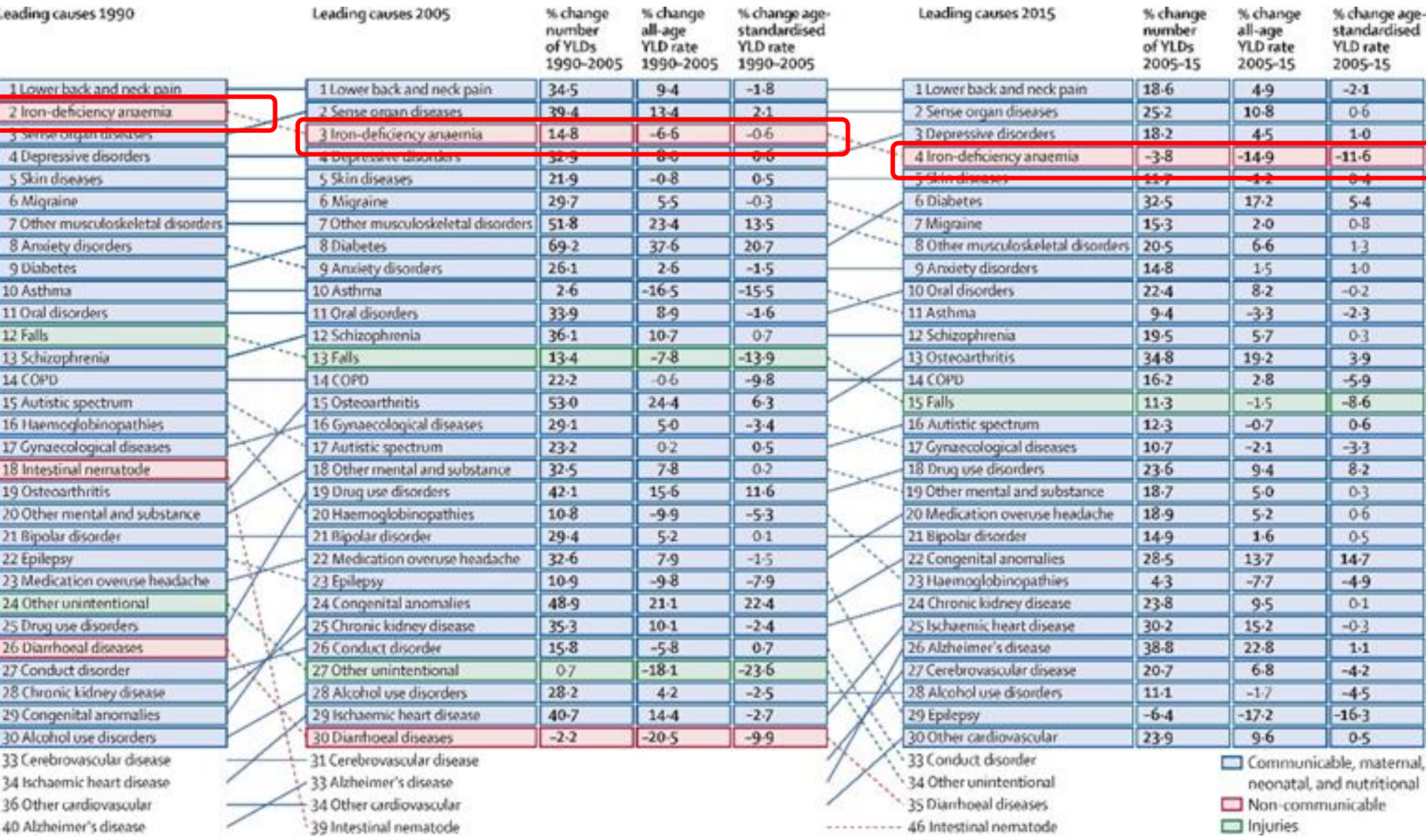
Musallam K et al. *Lancet 2011;378:1396-407*
Retrospective, 227,425 patients

Global and regional cause-specific anemia prevalence for 1990 and 2010



Nicholas J. Kassebaum et al. Blood 2014;123:615-624

Leading 30 global health problems in the years 1990, 2005 & 2015. The Lancet 2016



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Systematic review

Meta-analysis of the association between preoperative anaemia and mortality after surgery

A. J. Fowler, T. Ahmad, M. K. Phull, S. Allard, M. A. Gillies, R. M. Pearse

First published: 9 September 2015 Full publication history

DOI: 10.1002/bjs.9861 View/save citation

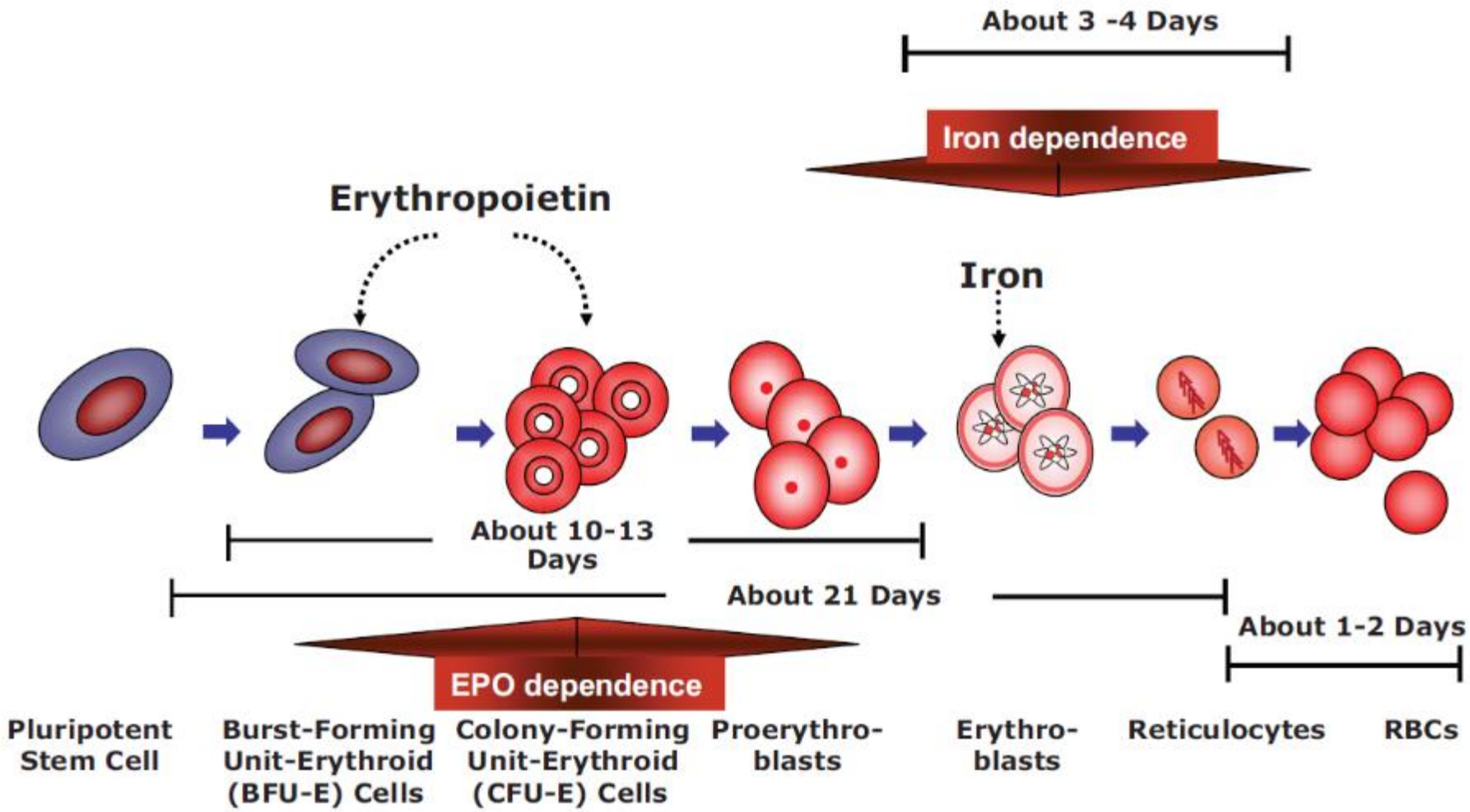
View issue TOC
Volume 102, Issue 11
October 2015
Pages 1314–1324

- 949.449 pts in 24 studies
- 39% anemia (WHO Definition)

→ Anemia was associated with

- RBC transfusion ↑ OR = 5.1 (4.1 – 6.2, $p < 0.001$)
- Periop. Mortality ↑ OR = 2.9 (2.3 – 3.7, $p < 0.001$)
- Acute renal failure ↑ OR = 3.8 (2.9 – 4.8, $p < 0.001$)
- Infections ↑ OR = 1.9 (1.1 – 1.6, $p < 0.01$)

Erythropoesis



Besarab et al. *Oncologist* 2009;14: 22-33

Pre- & postop. anaemia

Ortho/Cardiac/Gyn/ Carcinoma Prostate & Liver [1-3]

Preop. iron def. [1]
66% of anaemic pts.
50% of non-anaemic pts.

Multiple phlebotomies [2]
Reduced iron intake [2]
Low iron absorption due to postop. inflammation [2]
Periop. blood loss[2]

Preop. anaemia [1]
36%

Postop. anaemia [2]
Up to 90%
↗ Hospital LOS [3]
↗ Severe postop. infections [3]

Frankfurt [4]

VS:	55%	VS/Heart/Gyn:	85%
Visc/Thorax:	50%	Thorax:	60-70%
Trauma:	35%	AS & NS:	60%
Uro/NS/ENT:	22-28%	Trauma/Uro:	55%
Obs:	45-65%	Gyn:	55%

1. Munoz M et, al. Pre-operative haemoglobin levels and iron status in a large multicentre cohort of patients undergoing major elective surgery. *Anaesthesia* 2017; 72:826-834.
2. Muñoz M et, al. International consensus statement on the peri-operative management of anaemia and iron deficiency. *Anaesthesia* 2017; 72:233–247.
3. Khalafallah AA, et al. IV ferric carboxymaltose vs standard care in the management of postop. anaemia: a prospective, open-label, RCT. *Lancet Haematol.* 2016;3:e415-25.
4. Meybohm P & Zacharowski K: unpublished data (2012-2017).

Preop. anaemia is common in all surgical disciplines

AS	Gyn	Heart	Ortho/Trauma	Visceral	Others
			50% (hip fracture) **25%** (THA/TKA)[16]		
			36% (1956 / 5387 revision hip or knee arthroplasty)[17]		
39.7% (3047 / 7679 patients)[1]			**29.7%** (94 / 317 lumbar decompression and fusion)[18]		
39.1% (371,594 / 949,445 total patients) **29.9%** (WHO-defined anaemia 21,322 / 71,388) **40.3%** (non-cardiac 391,397 / 897,658)[2]		**36%** (1620 / 4494 patients)[10]	**28.1%** (154 / 549 TKA/THA fast-track procedures in >85 y olds)[19]		
33.9% (2127 / 6301 patients)[3]		**32%** (629 / 1972 patients)[11]	**20.4%** (242 / 1187 spinal surgery)[20]		
32% (892 / 2764 neonates)[4]		**29.7%** (1427 / 4804 patients)[12]	**19.6%** (210 / 1142 elective major joint arthroplasty admissions)[21]		
30.4% (69,229 / 227,425 patients)[5]		**28.1%** (200 / 712 patients)[13]	**17.9%** (7 / 39 hindfoot and ankle arthrodesis)[22]		
28.7% (11,295 / 39, 309 patients)[6]	**23.9%** (3071 / 12,836 patients)[8]	**26%** (3500 patients)[14]	**17.6%** (537 / 3050 patients)[23]	**47.4%** (11067 / 23348 elective open and laparoscopic colectomies)[26]	**65.4%** (242 / 370 radical nephrourectomy in UTUC)[29]
19% (3474 patients)[7]	**18.1%** (149 / 824 patients)[9]	**20.9%** (3384 / 16,154 patients)[15]	**16.1%** (6673 / 41,334 TKA)[24]	**32.8%** (4260 / 12,987 elective hepatectomies)[27]	**52%** (174 / 335 cardiac surgery for RHD)[30]
		19.7% (10,197 / 51,787 cardiac patients)[2]	**9.2%** (181 / 2164 ACDF)[25]	**10.2%** (37 / 362 emergency GI surgery)[28]	**51.8%** (257 / 496 abdominal resections in colorectal cancer)[31]

1. Beattie WS et al. Anesthesiology 2009;110:574–581; 2. Fowler AJ et al. Br J Surg 2015;102:1314–1324; 3. Dunne JR et al. J Surg Res 2002;102:237–244; 4. Goobie SM et al. JAMA Pediatr 2016;170:855–862; 5. Musallam K et al. Lancet 2011;378:1396–1407; 6. Baron DM et al. Br J Anaesthesia 2014;113:416–423; 7. Gombotz H et al. Transfusion 2007;47:1468–1480; 8. Richards T et al. PLoSOne 2015;10:e0130861; 9. Browning RM et al. Aus N Zealand J Obs Gyn 2012;52:455–459; 10. von Heymann C et al. J Thorac Cardiovasc Surg 2016;152:1412–1420; 11. Hallward G et al. J Cardiothoracic Vasc Anesthesia 2016;30:901–908; 12. Kulier A et al. Circulation 2007;116:471–479; 13. Kim CJ et al. Perfusion 2015;30:277–283; 14. Karkouti K et al. Circulation 2008;117:478–484; 15. Ranucci M et al. Ann Thorac Surg 2013;96:478–485; 16. Spahn DR. Anesthesiology 2010;113:482–495; 17. Kasivisvanathan R et al. Transfusion Med 2016;26:271–277; 18. Sanoufa M et al. J Perioper Pract 2015;25:267–271; 19. Pitter FT et al. Anesth Analg 2016;122:1807–1815; 20. Khanna R et al. Clin Spine Surg 2016 Jul 14 [Epub ahead of print]; 21. Saleh E et al. Br J Anaesth 2007;99:801–808; 22. Dix B et al. Foot Ankle Spec 2016 Sep 9. pii: 1938640016666921; 23. Smilowitz NR et al. Am J Med 2016;129:315–323; 24. Chamieh JS et al. J Arthroplasty 2016;31:766–770; 25. Gruskay JA et al. Clin Spine Surg 016;29:E34–E42; 26. Leichtle SW et al. J Am Coll Surg 2011;212:187–194; 27. Tohme S et al. HPB (Oxford) 2016;18:255–261; 28. Lee JY et al. Medicine 2016;95:35(e4530); 29. Yeh H-C et al. Urol Oncol 2016;34:337:e1–e9; 30. Deepak B et al. J Cardio Vasc Anes 2016;30:896–900; 31. Mörner MEM et al. Int J Colorectal Dis 2017;32:223–232

Germany vs. Netherlands (van Hoeven et al. 2012)

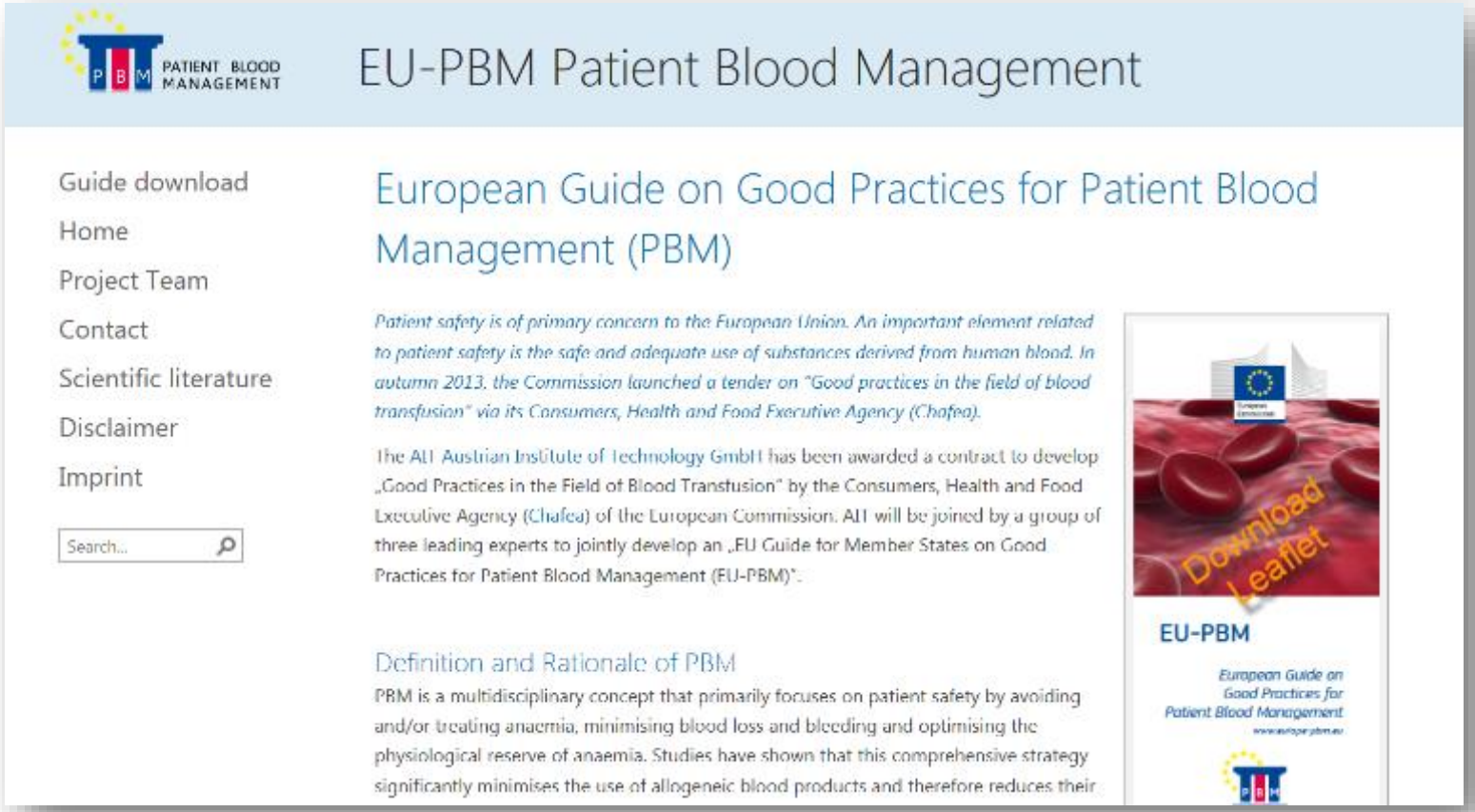
D & NL comparable in terms of population & health system.

D: 57.5 RBCs / 1000 inhabitants

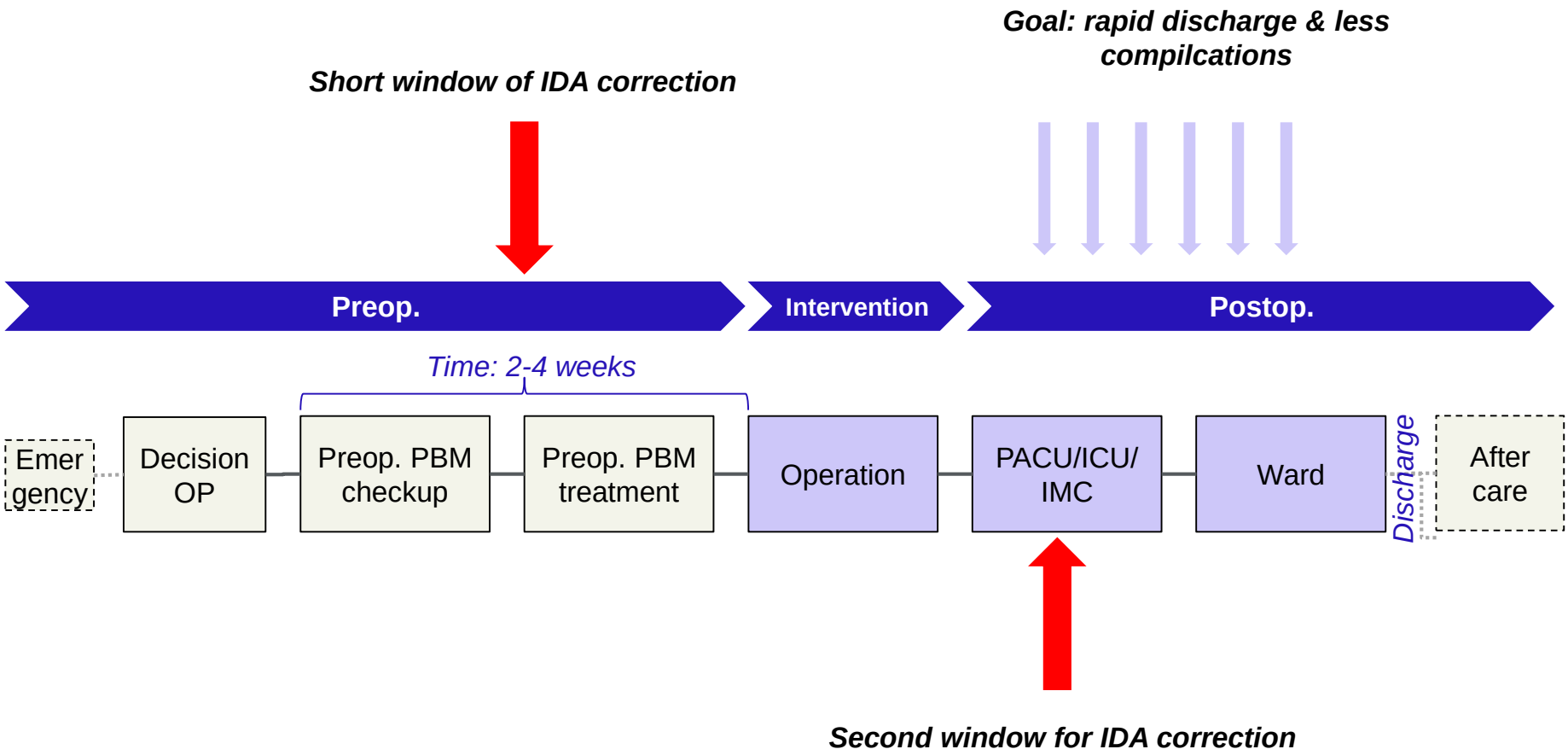
NL: 27.1 RBCs / 1000 inhabitants

2x

Differences not plausible!



Efficient management of IDA



Responsible: GPs, Surgeons & Anaethesists

3 columns of PBM

1. Management of pre-operative anemia

- ►Screening and diagnosis
- ►Treatment

2. Minimising blood loss & bleeding

3. Restrictive use of blood units

Anemia walk-in-clinic

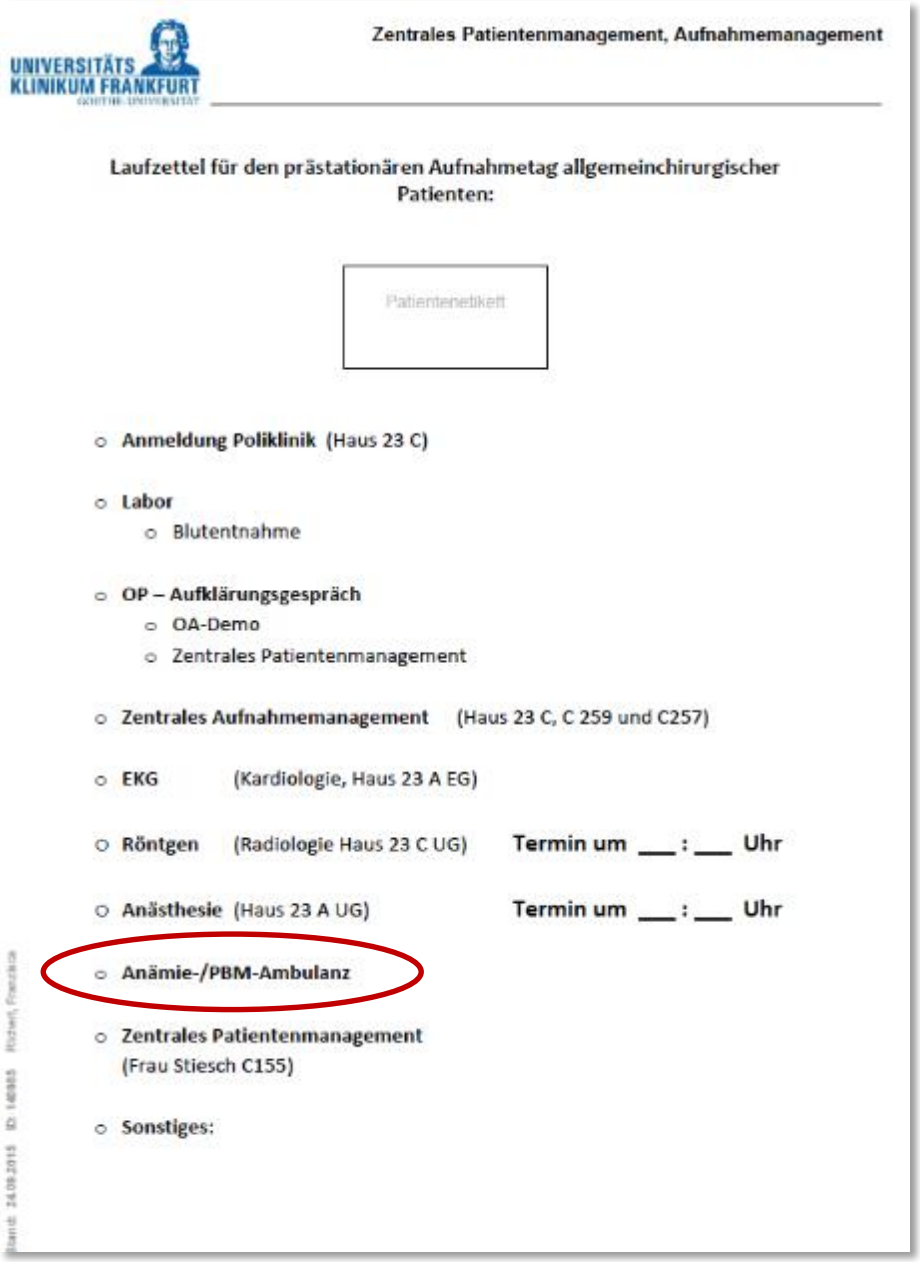
Patient Blood Management
Ambulanz

- Contact: Sabine Isik
- Mo-Fr: 08:00-16:00h
- Tel.: +49 69 6301 – 87461
- E-Mail: patientbloodmanagement@kgu.de

Froessler et al. Ann Surg 2016; 264: 41-6

- RCT i.v. Fe in IDA undergoing abd. surgery
- Ethics: stopped trial after 72 Pat., Fe-group significant better outcome
- 15mg/kg Fe-Carboxymaltose ~ 10d prior surgery
  - cHb ↑
  - RBC transfusions ↓ (75%)
  - Hospital-LOS: 9 to 6d ↓
  - Hb-increase postop. accelerated

SOP – preop. list…



UNIVERSITÄTS KLINIKUM FRANKFURT

Zentrales Patientenmanagement, Aufnahmemanagement

Laufzettel für den prästationären Aufnahmetag allgemeinchirurgischer Patienten:

Patientenetikett

- **Anmeldung Poliklinik** (Haus 23 C)
- **Labor**
  - Blutentnahme
- **OP – Aufklärungsgespräch**
  - OA-Demo
  - Zentrales Patientenmanagement
- **Zentrales Aufnahmemanagement** (Haus 23 C, C 259 und C257)
- **EKG** (Kardiologie, Haus 23 A EG)
- **Röntgen** (Radiologie Haus 23 C UG) **Termin um ___ : ___ Uhr**
- **Anästhesie** (Haus 23 A UG) **Termin um ___ : ___ Uhr**
- **Anämie-/PBM-Ambulanz**
- **Zentrales Patientenmanagement**
  (Frau Stiesch C155)
- **Sonstiges:**

Causes

Absolut ID

lowTransferrin-Satturation[8]
lowFerritin[8]
High sTfR[8]

Blood loss

- strong/ prolonged menstruale bleeding
- Strog uterus bleeding[4]
- Giving birth[5,8]
- GI-diseases[7]
- GI-bleeding[6]
- Operation[6]
- Donation of blood[6]
- Dialysis[6]

Increased iron demand

- Devolepment[1,8]
- Elderly[1,8]
- Pregnancy[1,5,8]
- Endurance sports[7]

Reduced iron absorption

- Nutrition[1]
- Vegetariens[1]
- Anorexia (cancer)[3]
- Eating disorder[2]

Functional ID

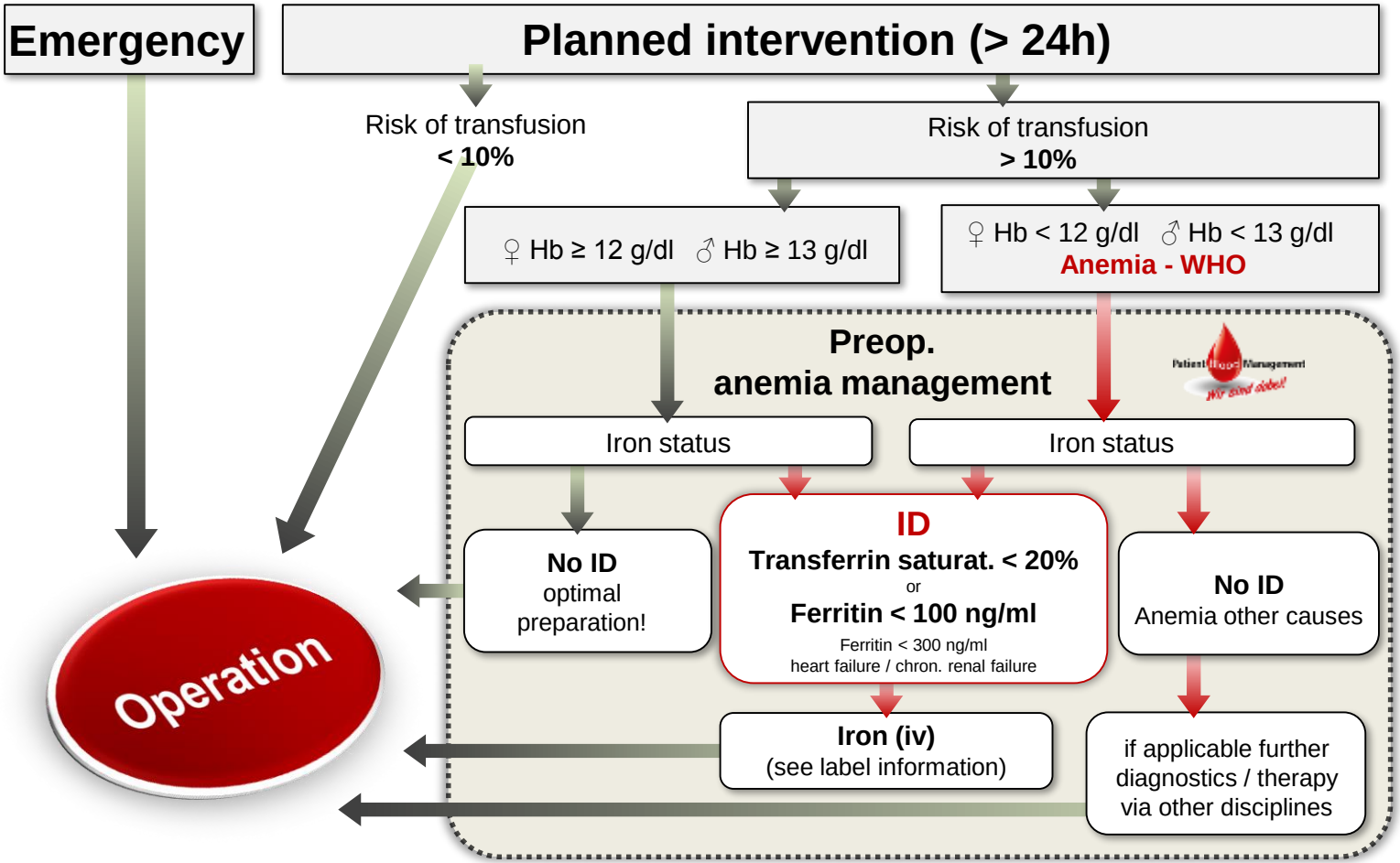
Low Transferrin-satturation[8]
Normal/ high Ferritin[8]
Normal sTfR[8]

Reduced iron absorption and use

- Chronic-inflammatory bowel disease[5]
- Chronic inflammation or cancer[8]
- Interaction with certain food ingedients[8]
- Drugs[8]
- Malabsorption[8]
- Chronic kidney disease
- Heart failure

1. Zimmermann et al. *Lancet* 2007; 370: 511-20. 2. Barton et al. *BMC Blood Disorders* 2010; 10: 9. 3. Aapro et al. *Ann Oncol* 2012; 23: 1954-82. 4. Marret al. *Eur J Obst Gyn Reprod Med* 2010; 152: 133-7. 5. Milman et al. *Ann Hematol* 2006; 85: 869-85. 6. Crichton et al. 2008 Iron therapy – With special emphasis on intravenous administration. UNI-MED Verlag. 7. Stein et al. *Nat Rev Gastroenterol* 2010; 7: 599-610. 8. Weiss et al. *NEJM* 2005; 352: 1011-23.

Preop. algorithm – V3.0



Gründe für die unzureichende Implementierung von Protokollen zur Behandlung der präoperativen Anämie

- Kosten und Zeitaufwand der präoperativen Anämietherapie
- potenzielle Nebenwirkungen einer ESA-Therapie (gastrointestinale Unverträglichkeit, Thrombosen, kardiovaskuläre Komplikationen, Tumorprogression)
- fast ubiquitäre und vermeintlich preiswerte Verfügbarkeit von allogenen Blutprodukten
- fehlendes Bewusstsein der behandelnden Ärzte in Anästhesiologie und operativer Medizin, dass die präoperative Anämie ein behandelbarer Risikofaktor für die Prognose operativer Patienten ist

von Heymann C, et al. *Anästhesiol Intensivmed Notfallmed Schmerzther* 2011; 46: 648–653

Originalien

Anaesthesist
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[3] DRK Blutspendedienst Baden-Württemberg Hessen, Institut für Transfusionsmedizin und Immunhämatologie, Frankfurt am Main, Deutschland

Kostenanalyse eines Patient-Blood-Management-Konzepts

Tab. 1 Patientenbezogene Transfusionskosten

Transfusion eines Erythrozytenkonzentrates		
Sachkosten		
Erythrozytenkonzentrat (EK)	90,50 €	Blutgruppenunabhängiger Preis
Material	0,86 €	2 × S-Monovette (EDTA) für Blutgruppenbestimmung, Antikörpersuchtest und Kreuzprobe; Adapter für Luer-System; Transfusionsset; Bedside-Test
Labordiagnostik		
ABO und Rhesus D AK-Suchtest (AKS) Kreuzprobe	8,16 € 5,83 € 11,66 €	Im Einzelfall kann eine erweiterte Labordiagnostik indiziert sein[a]
Personalkosten		
Vorbereitung, Durchführung	30,42 €	Arzt: 18 min; Pflege: 23 min
Indirekte Kosten (in weiteren Kalkulation unberücksichtigt)		
Verwurf ungenutzter EK (2,6 %)	2,35 €	Kostenumlegung auf transfundierte EK
Zusätzliche Kosten (in der weiteren Kalkulation unberücksichtigt)		
Bestrahlte Produkte (Aufpreis)	5,20 €	z. B. immunkompromittierte Patienten
Erweiterte Labordiagnostik, z. B.		
Rhesusformel und Kell AK-Differenzierung	11,00 € 6,30 €	z. B. Frauen in gebärfähigem Alter z. B. nach positivem AKS (15 %)
Spezielle Laboranforderungen	19,81 €	Schnell; nachts/abends
Lieferung	0,00 €	Logistikservice kostenfrei

Ettwein[2] · M. M. Müller[3] · C. Geisen[3] ·

herapie, Universitätsklinikum Frankfurt,

ratives Controlling, Universitätsklinikum

ut für Transfusionsmedizin und

es Patient-

nt-Konzepts

Kleinerüschkamp A et al. *Anästhesist* 2016 65(6):438-48

Tab. 1 Patientenbezogene Tra

Transfusion eines Erythrozyt
Sachkosten
Erythrozytenkonzentrat (EK)
Material
Labordiagnostik
ABO und Rhesus D AK-Suchtest (AKS) Kreuzprobe
Personalkosten
Vorbereitung, Durchführung
Indirekte Kosten (in weiteren Ka
Verwurf ungenutzter EK (2,6 %)
Zusätzliche Kosten (in der weite
Bestrahlte Produkte (Aufpreis)
Erweiterte Labordiagnostik, z. B
Rhesusformel und Kell AK-Differenzierung
Spezielle Laboranforderungen
Lieferung

Tab. 2 PBM – Präoperatives Anämiemanagement (Säule I)

PBM – Präoperatives Anämiemanagement		
Sachkosten		
Anämiediagnostik		
Materialkosten	0,18 €	2 × S-Monovette: EDTA und Serum (je 0,09 €)
Laborprofil: Standard Laborprofil: Erweitert	33,81 € 109,00 €	(Differenzial-)Blutbild, Retikulozyten, Kreatinin i. S., Eisen i. S., Transferrin i. S., Ferritin i. S. U. a. Leber- und Nierenfunktion, Folsäure i.S.
Anämietherapie (Kosten pro Patient)		
Eisen (Fe 3+) [Ferinject®] 117,59 €/500 mg	117,59 €	Dosis: 500 mg
Folsäure [Folsan®] 0,10 €/5 mg	6,00 €	Dosis: 10 mg/Tag über 30 Tage
Cyanocobalamin [Cytobion®] 0,17 €/1000 µg	2,21 €	Dosis: 1000 µg/Woche über 90 Tage
Epoetin alpha [Erypo®] (optional) 80,00 €/10.000 IE	640,00 €	Dosis: 40.000 IE, 2 × präoperativ
Personalkosten		
Anämiediagnostik		
Anamnese, Bluttest, Ergebnisbeurteilung	14,70 €	Arzt: 12 min; Pflege: 5 min
Anämietherapie		
Medikation, Überwachung	10,40 €	Arzt: 5 min; Pflege: 10 min

Costs

Blood vs. Iron therapy

Blood (2 RBCs)

- RBC 180 €
- Material 60 €
- Personel 90 €
- Complication(s) ??

- Summ 350++ €

Anemia therapy

- Material/Lab 30 €
- Drug 284 €
- Personel 30 €
- Complication(s) --

- Summ 344 €

Gründe für die unzureichende Implementierung von Protokollen zur Behandlung der präoperativen Anämie

- Kosten und Zeitaufwand der präoperativen Anämietherapie
- potenzielle Nebenwirkungen einer ESA-Therapie (gastrointestinale Unverträglichkeit, Thrombosen, kardiovaskuläre Komplikationen, Tumorprogression)
- fast ubiquitäre und vermeintlich preiswerte Verfügbarkeit von allogenen Blutprodukten
- fehlendes Bewusstsein der behandelnden Ärzte in Anästhesiologie und operativer Medizin, dass die präoperative Anämie ein behandelbarer Risikofaktor für die Prognose operativer Patienten ist

von Heymann C, et al. *Anästhesiol Intensivmed Notfallmed Schmerzther* 2011; 46: 648–653

Outcome studies

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Preoperative Intravenous Iron to Treat Anaemia in Major Surgery (PREVENTT)

This study is currently recruiting participants.

Verified January 2014 by University College, London

Sponsor:
University College, London

Information provided by (Responsible Party):
University College, London

ClinicalTrials.gov Identifier:
NCT01692418

First received: September 14, 2012
Last updated: January 23, 2014
Last verified: January 2014
History of Changes

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Impact of Preoperative Treatment of Anemia and Iron Deficiency in Cardiac Surgery on Outcome.

This study is currently recruiting participants.

Verified March 2014 by University of Zurich

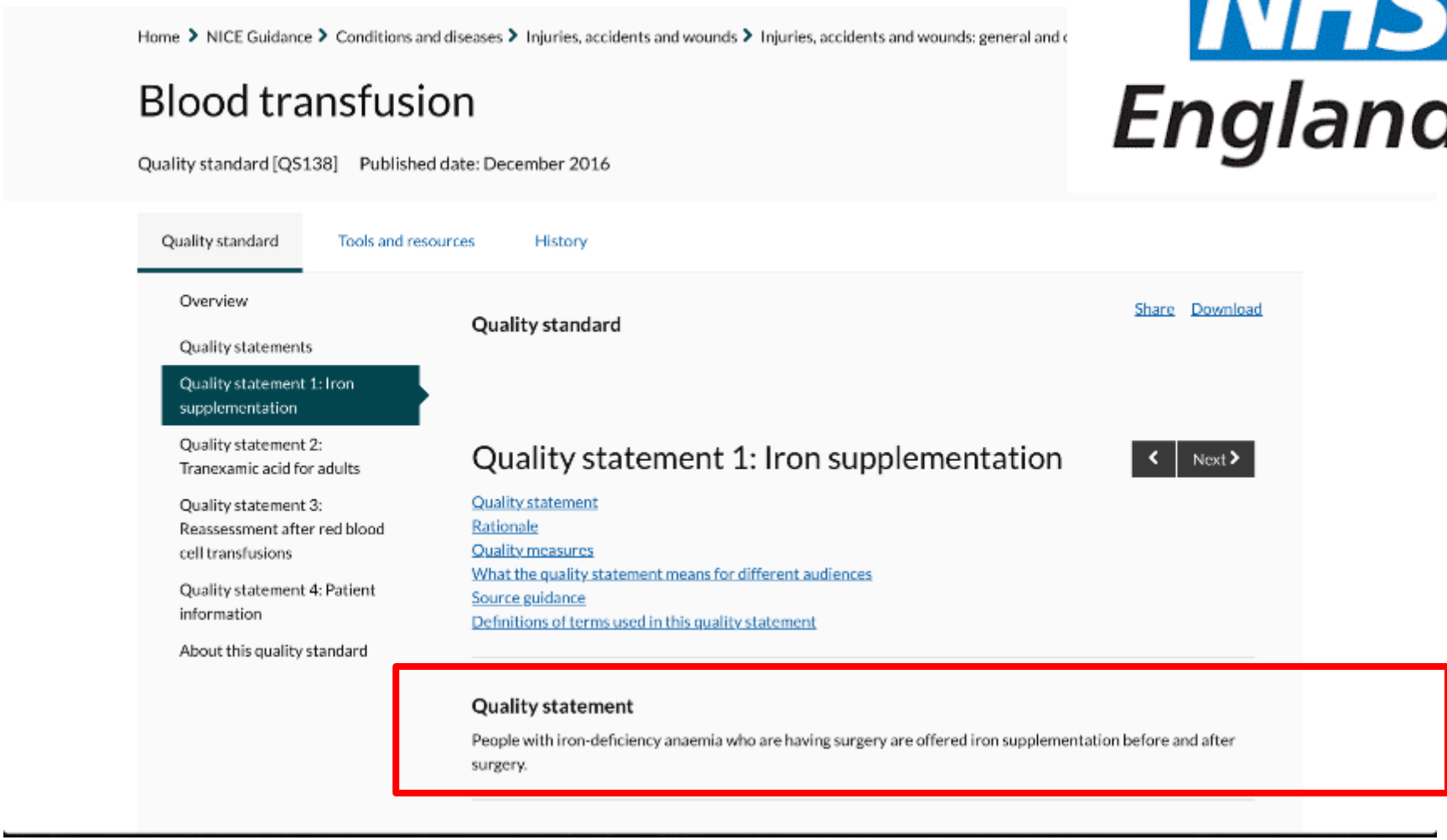
Sponsor:
University of Zurich

Information provided by (Responsible Party):
University of Zurich

ClinicalTrials.gov Identifier:
NCT02031289

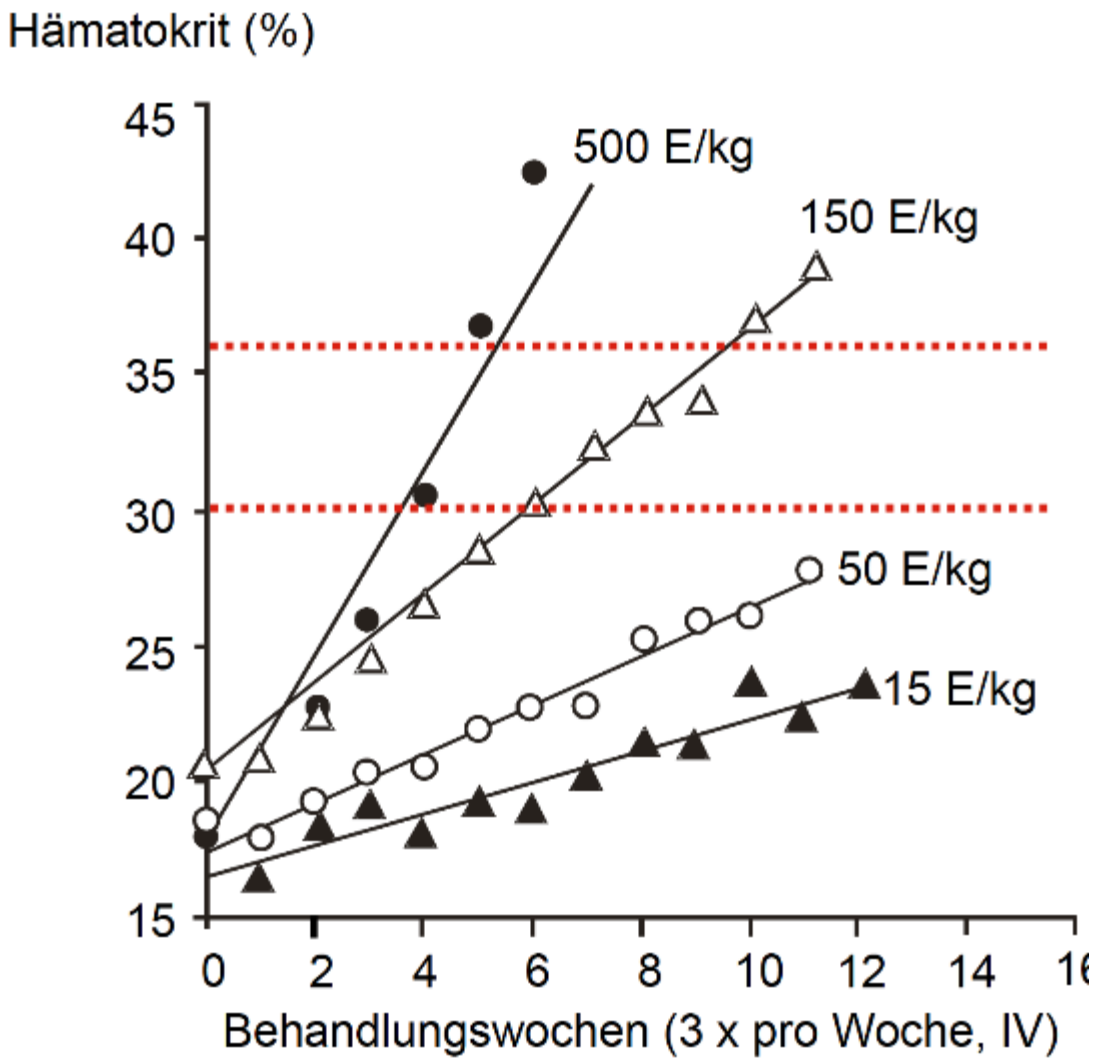
First received: December 16, 2013
Last updated: March 3, 2014
Last verified: March 2014
History of Changes

NICE Quality Standard [QS138] – Feb 2017



https://www.nice.org.uk/guidance/QS138/chapter/Quality-statement-1-Iron-supplementation

Erythropoietin



Nach: Eschbach J et al, *N Engl J Med* 316: 73-8, 1987

Erythropoietin

EU-zugelassene Epoetine (ESA) u. Indikationen

NEU 2007 - 2010

Präparat	Epoetin alfa [Erypo®]	Epoetin beta [NeoRecormon®]	Darbepoetin alfa [Aranesp®]	PEG-Epoetin beta [Mircera®]	Epoetin alfa-/zeta-Biosimilars [HEXAL®, Abseamed®, Binocrit®/ Silapo®, Retacrit®]	Epoetin theta: [Biopoin®, Eporatio®]
Indikation	Renale Anämie; Solide Tumoren/ MM/Non-Hodgkin-L/ CLL + Chemotherapie; Autologe Transfusion; Orthopäd. Op.	Renale Anämie; Solide Tumoren/ MM/Non-Hodgkin-L/ CLL + Chemotherapie; Autologe Transfusion; Anämie von Frühchen	Renale Anämie; Solide Tumoren + Chemotherapie	Renale Anämie	Renale Anämie; Solide Tumoren + Chemotherapie; Orthopäd. Op. (alfa) Autologe Transfusion (zeta)	Renale Anämie; Nicht-myeloide maligne Erkrankungen + Chemotherapie

Literatur: Jelkmann W. *Brit J Haematol* 141: 287-97, 2008;
Jelkmann W. *Am J Hematol* 85: 771-80, 2010

Erythropoietin

EU-zugelassene Epoetine (ESA) u. Indikationen

NEU 2007 - 2010

Präparat	Epoetin alfa [Erypo®]	Epoetin beta [NeoRe-	Darbepoetin alfa	PEG-	Epoetin	
	therapie; Autologe Transfusion; Orthopäd. Op.	Chemo-therapie; Autologe Transfusion; Anämie von Frühchen	Chemo-therapie		tumoren + Chemo-Therapie; Orthopäd. Op. (alfa) Autologe Transfusion (zeta)	Nicht-myeloide maligne Erkrankungen + Chemo-therapie

Literatur: Jelkmann W. *Brit J Haematol* 141: 287-97, 2008;
Jelkmann W. *Am J Hematol* 85: 771-80, 2010

EPO alfa / beta (kurzwirksam): 1-2x 40.000 (i.v./s.c.)

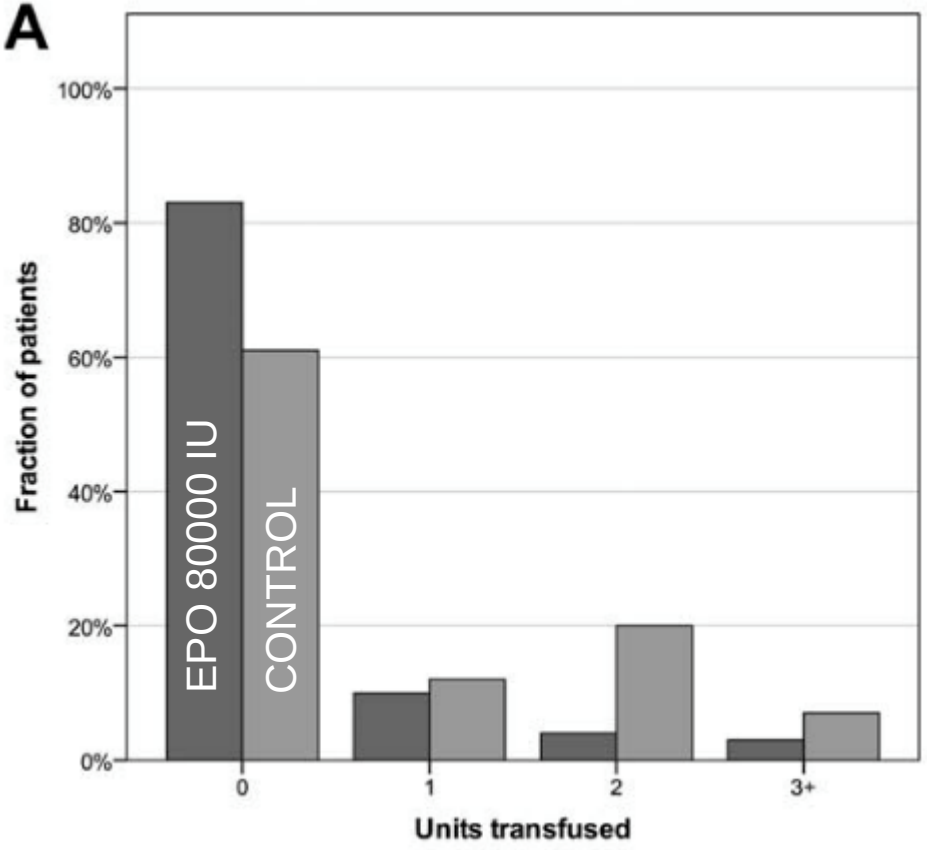
Darbepoetin (14d): Start mit 50 µg (s.c./i.v.)

Erythropoietin

A single dose of erythropoietin reduces perioperative transfusions in cardiac surgery: results of a prospective single-blind randomized controlled trial

Luca Weltert,[1] Beatrice Rondinelli,[2] Ricardo Bello,[3] Mauro Falco,[4] Alessandro Bellisario,[1] Daniele Maselli,[1] Franco Turani,[4] Ruggero De Paulis,[1] and Luca Pierelli[2,5]

- N = 600 randomized to
  - Epoetin alfa 2 days before surgery
  - Control



Hentze et al. *Transfusion* 2015; 55: 1644-54

Erythropoietin

VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2016)

REVIEW ARTICLE

Vox Sanguinis published by John Wiley & Sons Ltd on behalf of International Society of Blood Transfusion
DOI: 10.1111/vox.12412

Erythropoietin to reduce allogeneic red blood cell transfusion in patients undergoing total hip or knee arthroplasty

Study or Subgroup	Erythropoietin Events	Total	Control/Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Canadian Study group 1993	35	130	36	78	14·6%	0·58 [0·40, 0·85]	1993
de Andrade 1996	20	193	22	96	10·8%	0·45 [0·26, 0·79]	1996
Faris 1996	27	121	36	67	13·9%	0·42 [0·28, 0·62]	1996
Feagan 2000	23	123	35	78	13·0%	0·42 [0·27, 0·65]	2000
Wurnig 2001	41	124	28	51	15·0%	0·60 [0·42, 0·86]	2001
Weber 2005	56	460	107	235	16·6%	0·27 [0·20, 0·35]	2005
So-Osman 2014	53	339	91	344	16·1%	0·59 [0·44, 0·80]	2014
Total (95% CI)		**1490**		**949**	**100·0%**	**0·46 [0·35, 0·60]**	
Total events	255		355				

Heterogeneity: $Tau^2 = 0·09$; $Chi^2 = 20·97$, $df = 6$ ($P = 0·002$); $I^2 = 71\%$
Test for overall effect: $Z = 5·81$ ($P < 0·00001$)

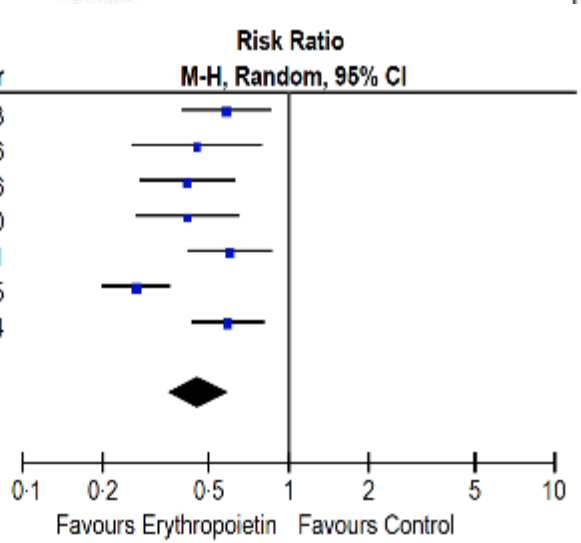
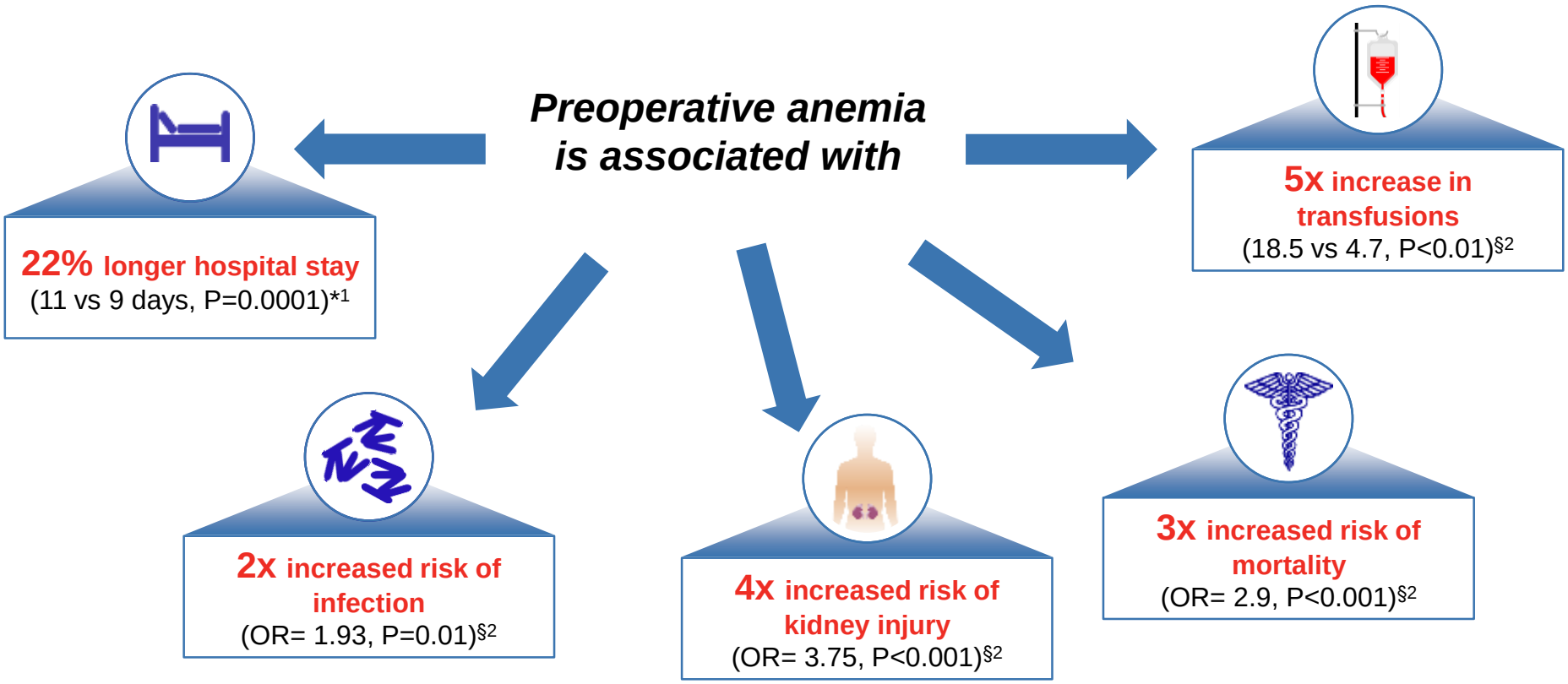


Fig 2 Patients exposed to allogeneic RBC transfusion.

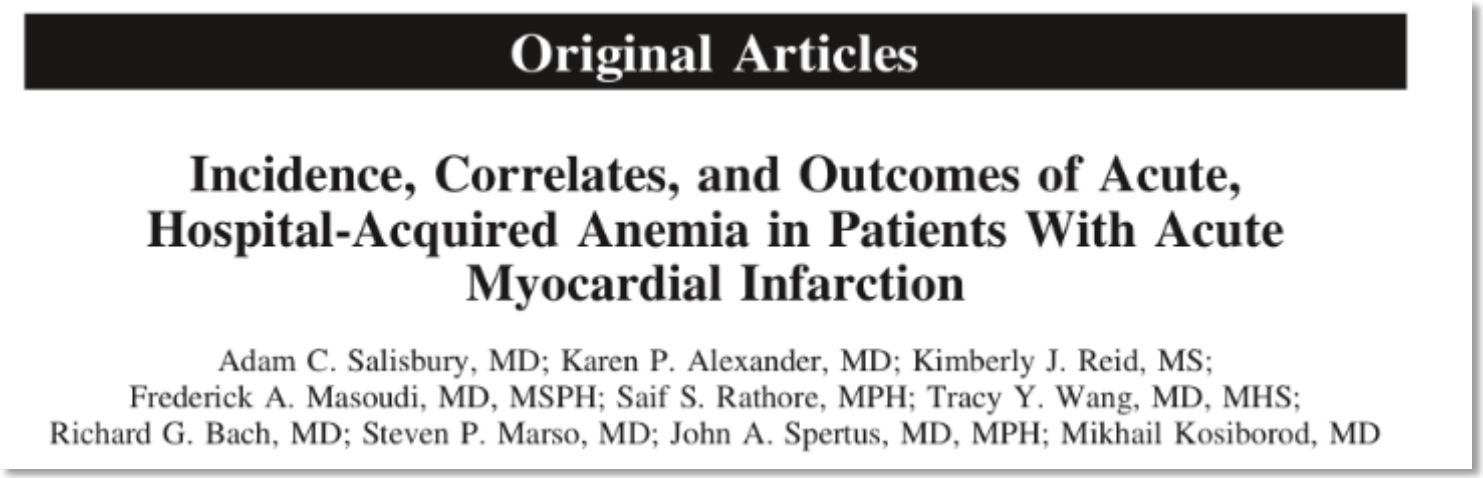
Preoperative anemia



* Retrospective single-centre cohort study of consecutive patients >18 years undergoing non-cardiac surgery between March 2003 and June 2006 (N= 7,759). Shown are the propensity-matched values for variables that are potential confounders in the relationship between anaemia and postoperative mortality (N=2,090).[1] § Systematic review and meta-analysis of observational studies exploring associations between preoperative anaemia and postoperative outcomes (24 studies N=949,445).[2] † Retrospective cohort study of major non-cardiac surgery in 2008 (a prospective validated outcomes registry from 211 hospitals worldwide, N=227,425). OR presented had an extended adjustment for a large number of clinically relevant variables.[3]

1. Beattie WS et al. Anesthesiology. 2009;110:574–81; 2. Fowler AJ et al. Br J Surg. 2015;102:1314–24; 3. Musallam KM et al. Lancet. 2011;378:1396–1407

Hospital-aquired anemia



Original Articles

Incidence, Correlates, and Outcomes of Acute, Hospital-Acquired Anemia in Patients With Acute Myocardial Infarction

Adam C. Salisbury, MD; Karen P. Alexander, MD; Kimberly J. Reid, MS; Frederick A. Masoudi, MD, MSPH; Saif S. Rathore, MPH; Tracy Y. Wang, MD, MHS; Richard G. Bach, MD; Steven P. Marso, MD; John A. Spertus, MD, MPH; Mikhail Kosiborod, MD

Retrospective analysis (n= 2902 MI and Hb > 12g/dl) at admission

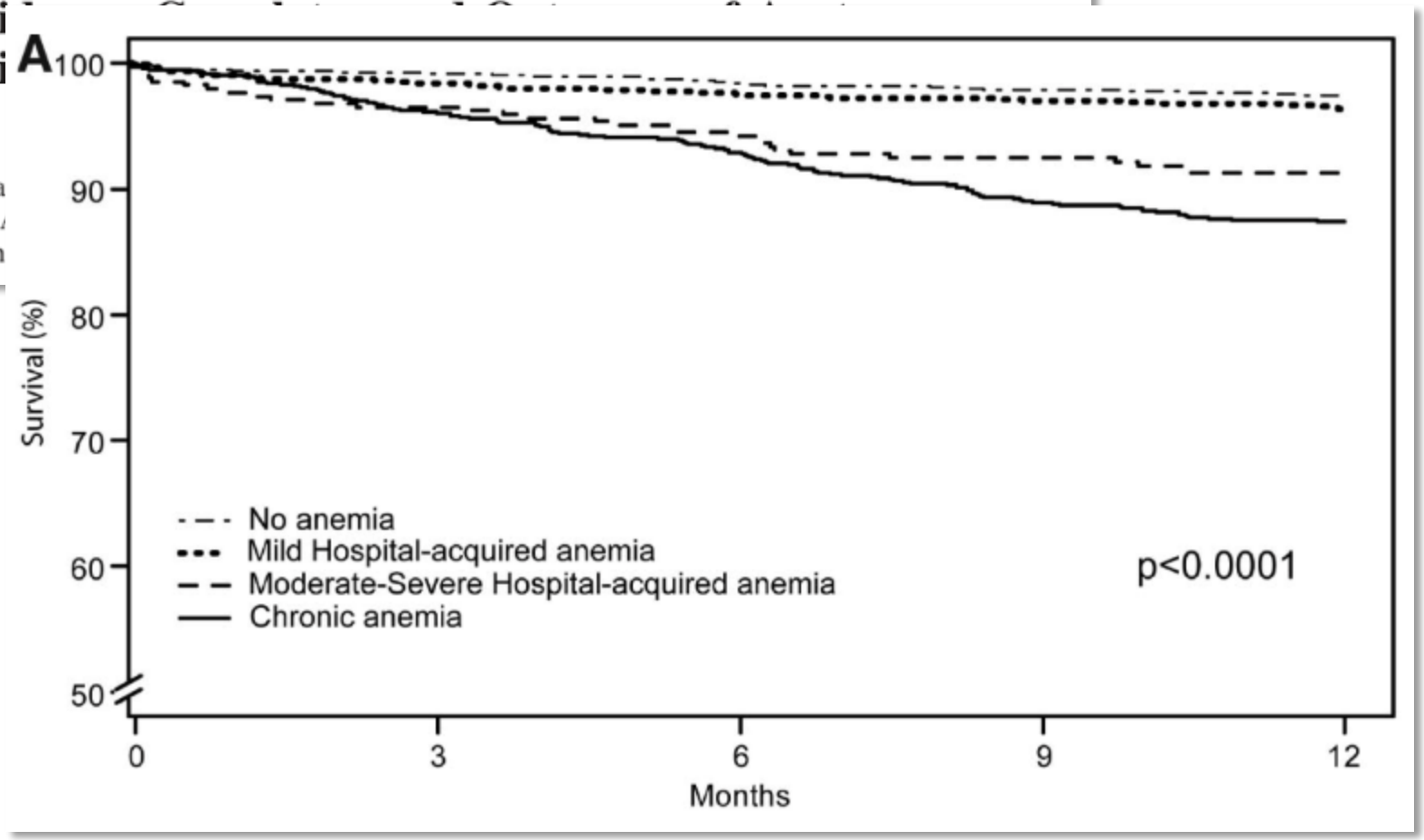
Salisbury et al. *Circ Cardiovasc Qual Outcomes. 2010;3:337-346*

Hospital-aquired anemia

Original Articles

Inci
Hospi

Ada
Frederick
Richard G. Bach

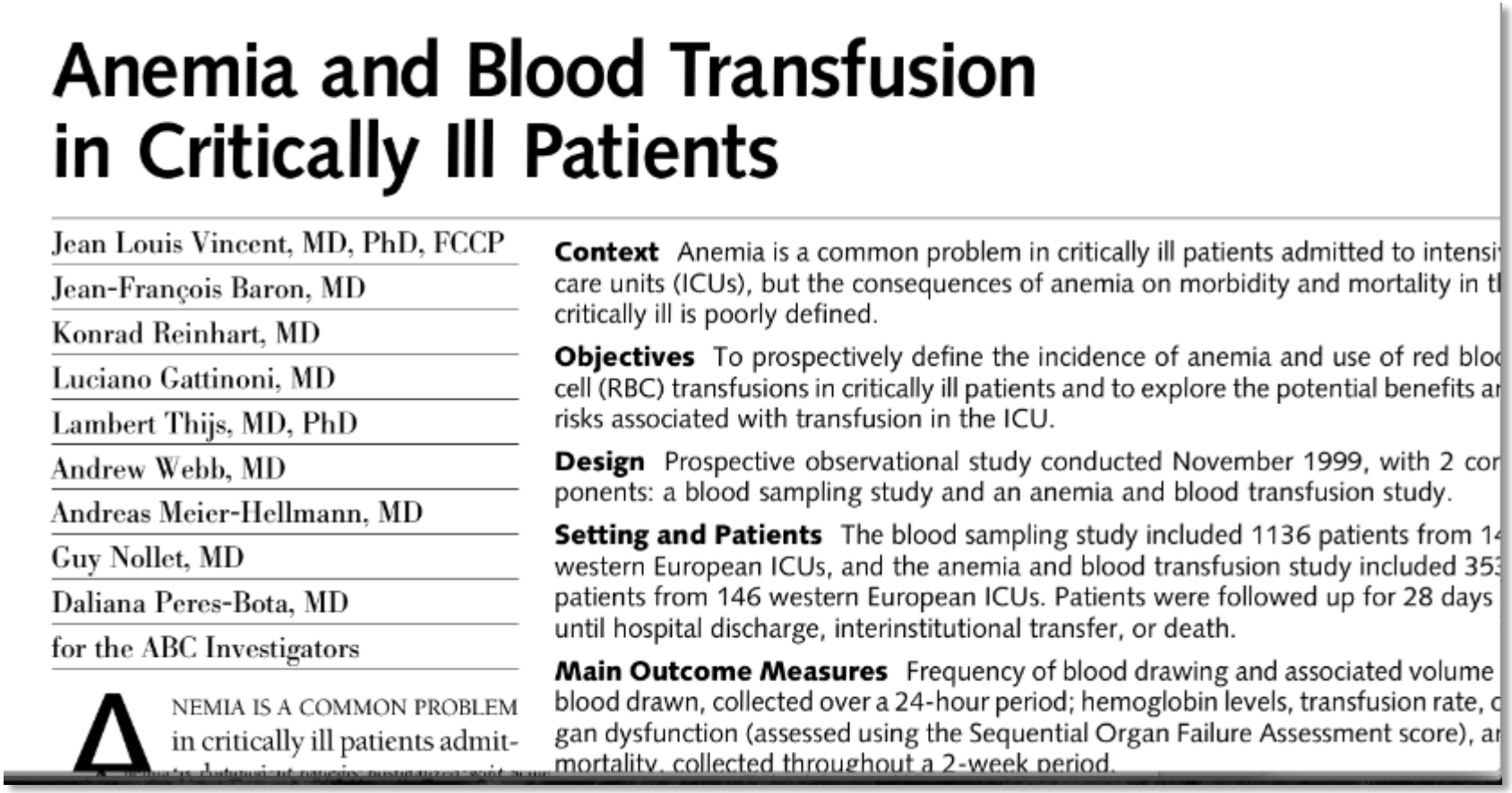


Retrospective analysis (n= 2902 MI and Hb > 12g/dl) at admission

Salisbury et al. *Circ Cardiovasc Qual Outcomes. 2010;3:337-346*

Anemia on ICU

Anemia on ICU



Anemia and Blood Transfusion in Critically Ill Patients

Jean Louis Vincent, MD, PhD, FCCP
Jean-François Baron, MD
Konrad Reinhart, MD
Luciano Gattinoni, MD
Lambert Thijs, MD, PhD
Andrew Webb, MD
Andreas Meier-Hellmann, MD
Guy Nollet, MD
Daliana Peres-Bota, MD
for the ABC Investigators

Context Anemia is a common problem in critically ill patients admitted to intensi care units (ICUs), but the consequences of anemia on morbidity and mortality in tl critically ill is poorly defined.

Objectives To prospectively define the incidence of anemia and use of red bloc cell (RBC) transfusions in critically ill patients and to explore the potential benefits ar risks associated with transfusion in the ICU.

Design Prospective observational study conducted November 1999, with 2 cor ponents: a blood sampling study and an anemia and blood transfusion study.

Setting and Patients The blood sampling study included 1136 patients from 14 western European ICUs, and the anemia and blood transfusion study included 353 patients from 146 western European ICUs. Patients were followed up for 28 days until hospital discharge, interinstitutional transfer, or death.

Main Outcome Measures Frequency of blood drawing and associated volume blood drawn, collected over a 24-hour period; hemoglobin levels, transfusion rate, c gan dysfunction (assessed using the Sequential Organ Failure Assessment score), ar mortality, collected throughout a 2-week period.

ANEMIA IS A COMMON PROBLEM in critically ill patients admit-

(n= 1136 ICU patients in 146 Westeuropean ICU units)

Vincent JL et al. *JAMA 2012;288:1499-1507*

Anemia on ICU

Anemia and Blood Transfusion in Critically Ill Patients

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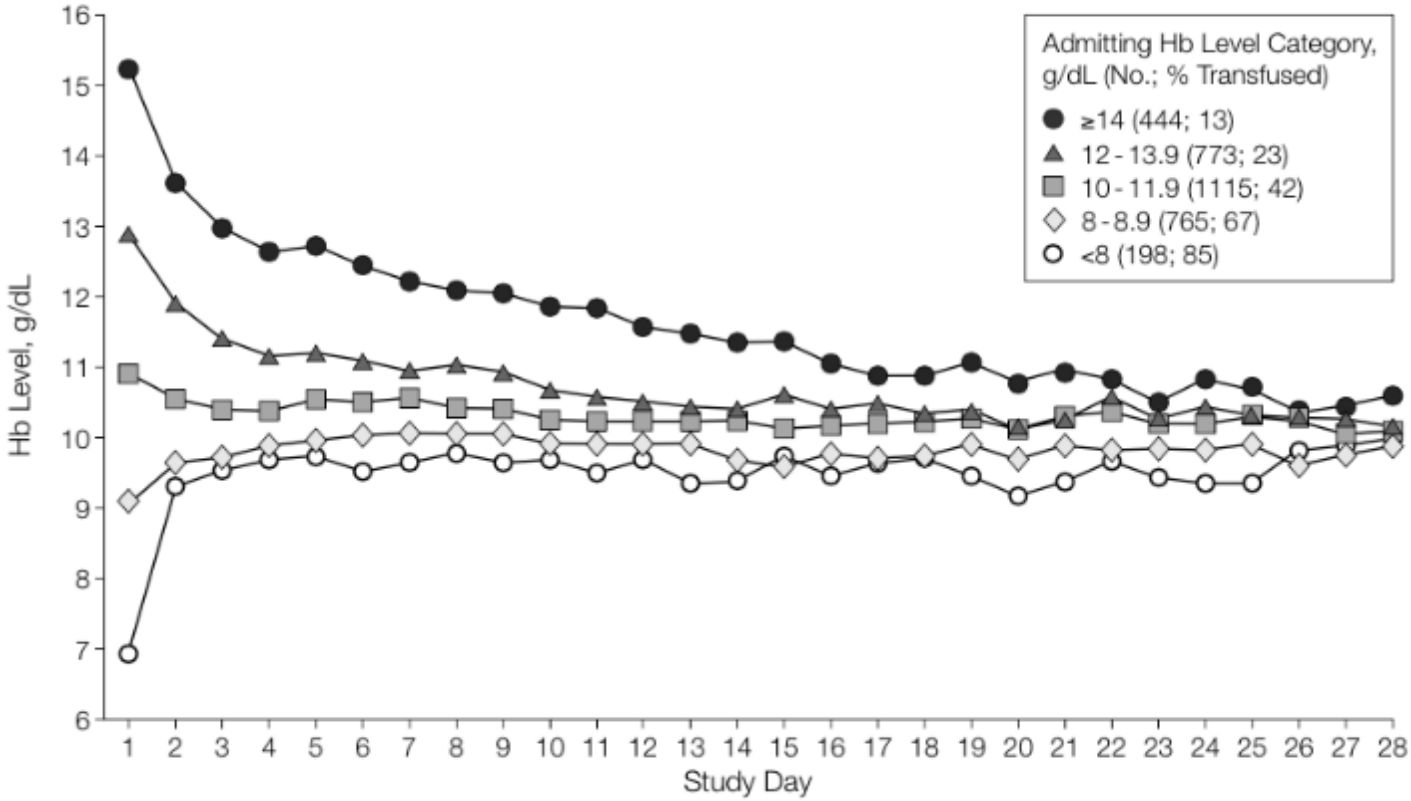
ANEMIA IS A COM
in critically ill

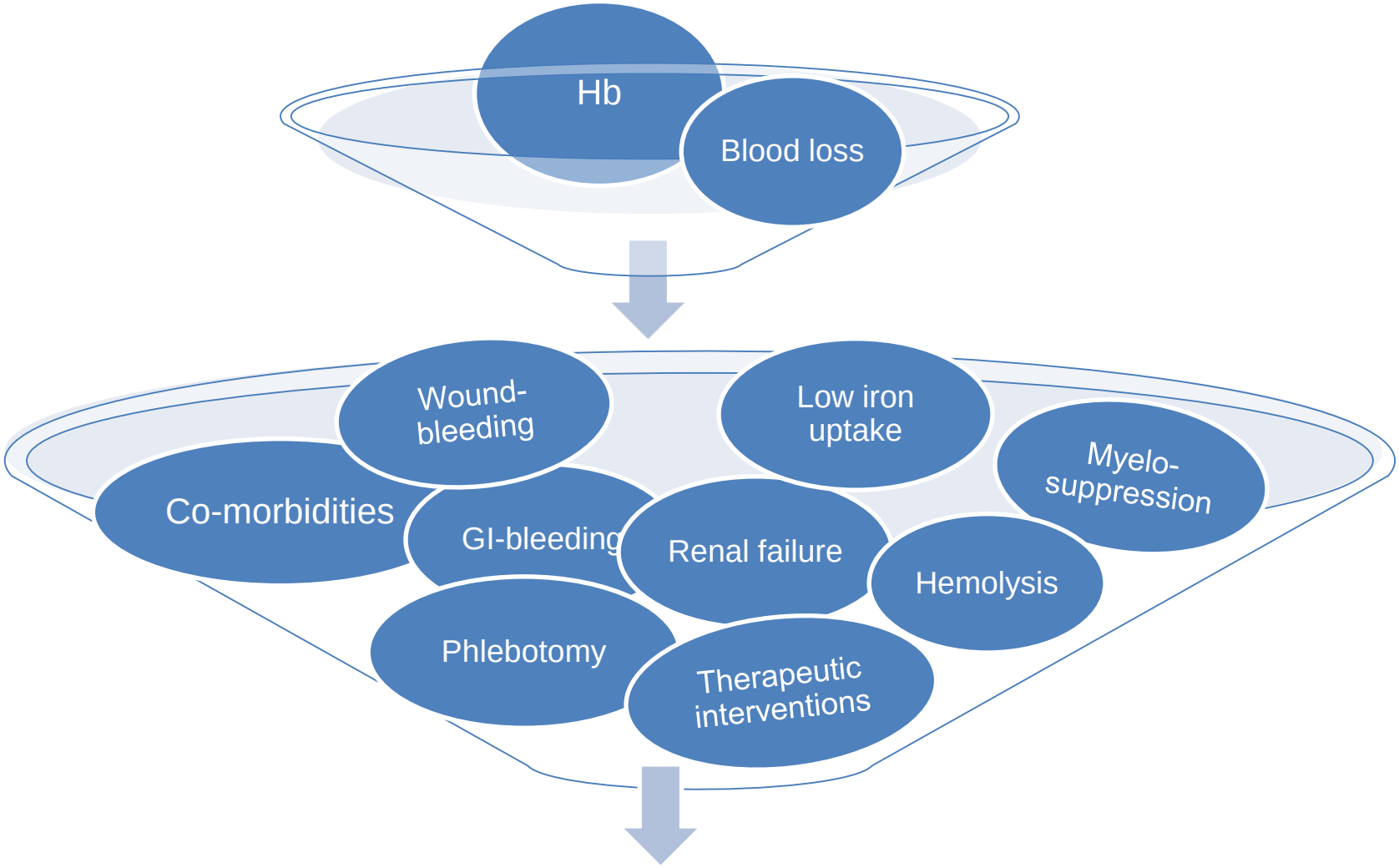
Figure 1. Course of Hemoglobin (Hb) Patterns by Admitting Hb Level Category



(n= 1136 ICU patients in 146 Westeuropean ICU units)

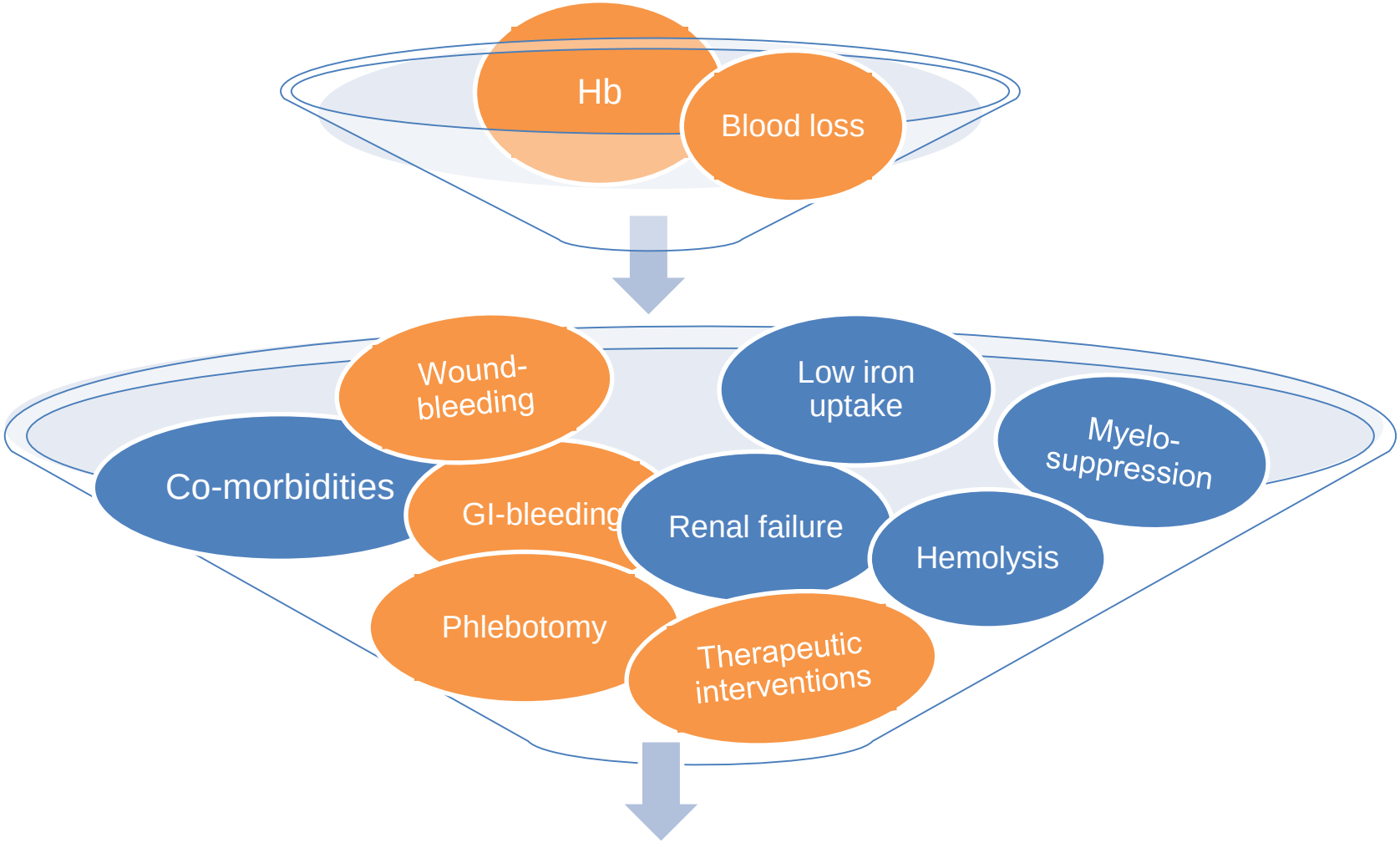
Vincent JL et al. *JAMA 2012;288:1499-1507*

Risk factors



Anemia in ICU-patients ↑↑↑

Blood conservation



Anemia in ICU-patients ↓↓↓

Khalafallah et al. The Lancet Haematology 2016

- Postop. IDA can be treated with i.v. Fe
- 201 pts: 1. postop. day IDA
- Placebo vs 1g Fe-Carboxymaltose i.v.
- Fe-group:
  - Faster Hb-recovery
  - RBC-transfusion: 6 to 1% ↓
  - postop. infections: 14 to 2% ↓
  - Hospital-LOS: 12 to 8d ↓

Causes for anemia

Disease:

‘Anemia’

‚Nutrion‘-related

- Iron
- Vitamin B12
- Folic acid

Acquired

- Hemato-onkological
- Renale anemie
- Chronic Inflammation
- Cander-assosiated
- Parasites
- Hemolysis
- Toxins/ Drugs
- Autoimmunological

Hospital acquired

- Blood loss diagnostic
- Bloodloss Intervention
- Blood loss Operation
- Reduced Erythropoesis

Congenital

- Hemoglobin

Unknown

- Age-related reduced Erythropoesis
- Erythropoetin defiency

Example from Frankfurt

- 42J, female Anaesthesist, 3 kids, „tired“

	11.01.2016
Lab	
Hb (11,6-15,5 g/dl)	10,0
MCH (26-33 pg)	21,7
MCV (80-95 fl)	70
Thrombozyten (182-369/nl)	383

Beispiel

- 42J, female Anaesthesist, 3 kids, „tired“

	11.01.2016
Kleines Blutbild	
Hb (11,6-15,5 g/dl)	**10,0**
MCH (26-33 pg)	**21,7**
MCV (80-95 fl)	**70**
Thrombozyten (182-369/nl)	383
Eisen-/Vitaminstatus	
Ferritin (9-140 ng/ml)	**7**
Transferrinsättigung (16-45%)	**6**
Vitamin B_{12} (197-771 pg/ml)	329
Folsäure (2-9 ng/ml)	5,5
Entzündungsparameter	
C-reaktives Protein (<0,5 mg/dl)	0,14

Beispiel

- 42J, female Anaesthesist, 3 kids, „tired“

	11.01.2016
Kleines Blutbild	
Hb (11,6-15,5 g/dl)	**10,0**
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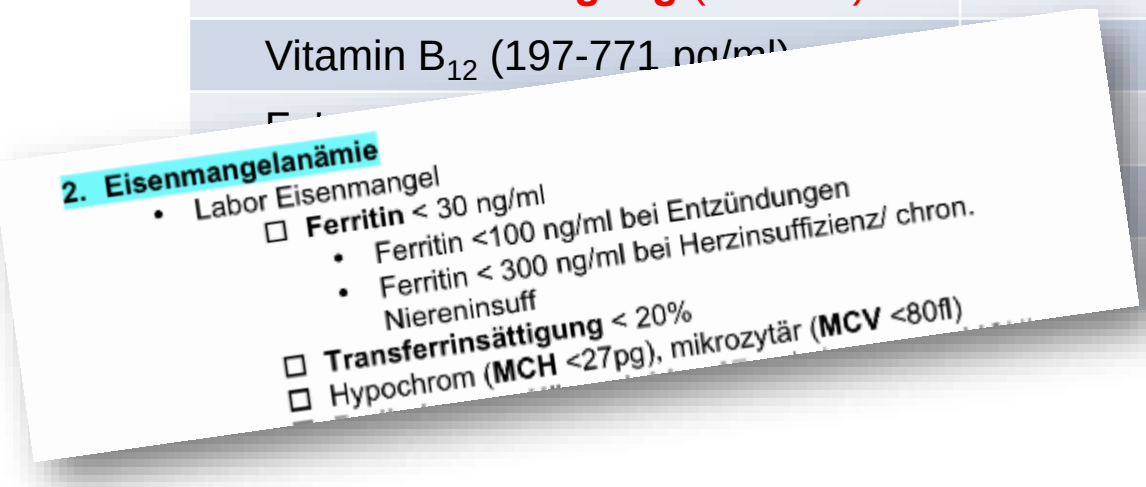
	5,5
	0,14



Pre- & postop. anaemia

Ortho/Cardiac/Gyn/ Carcinoma Prostate & Liver [1-3]

Preop. iron def. [1]
66% of anaemic pts.
50% of non-anaemic pts.

Multiple phlebotomies [2]
Reduced iron intake [2]
Low iron absorption due to postop. inflammation [2]
Periop. blood loss[2]

Preop. anaemia [1]
36%

Postop. anaemia [2]
Up to 90%
↗ Hospital LOS [3]
↗ Severe postop. infections [3]

Frankfurt [4]

VS:	55%	VS/Heart/Gyn:	85%
Visc/Thorax:	50%	Thorax:	60-70%
Trauma:	35%	AS & NS:	60%
Uro/NS/ENT:	22-28%	Trauma/Uro:	55%
Obs:	45-65%	Gyn:	55%

1. Munoz M et, al. Pre-operative haemoglobin levels and iron status in a large multicentre cohort of patients undergoing major elective surgery. *Anaesthesia* 2017; 72:826-834.
2. Muñoz M et, al. International consensus statement on the peri-operative management of anaemia and iron deficiency. *Anaesthesia* 2017; 72:233–247.
3. Khalafallah AA, et al. IV ferric carboxymaltose vs standard care in the management of postop. anaemia: a prospective, open-label, RCT. *Lancet Haematol.* 2016;3:e415-25.
4. Meybohm P & Zacharowski K: unpublished data (2012-2017).

Preop. anaemia is common in all surgical disciplines

AS	Gyn	Heart	Ortho/Trauma	Visceral	Others
			50% (hip fracture) **25%** (THA/TKA)[16]		
			36% (1956 / 5387 revision hip or knee arthroplasty)[17]		
39.7% (3047 / 7679 patients)[1]			**29.7%** (94 / 317 lumbar decompression and fusion)[18]		
39.1% (371,594 / 949,445 total patients) **29.9%** (WHO-defined anaemia 21,322 / 71,388) **40.3%** (non-cardiac 391,397 / 897,658)[2]		**36%** (1620 / 4494 patients)[10]	**28.1%** (154 / 549 TKA/THA fast-track procedures in >85 y olds)[19]		
33.9% (2127 / 6301 patients)[3]		**32%** (629 / 1972 patients)[11]	**20.4%** (242 / 1187 spinal surgery)[20]		
32% (892 / 2764 neonates)[4]		**29.7%** (1427 / 4804 patients)[12]	**19.6%** (210 / 1142 elective major joint arthroplasty admissions)[21]		
30.4% (69,229 / 227,425 patients)[5]		**28.1%** (200 / 712 patients)[13]	**17.9%** (7 / 39 hindfoot and ankle arthrodesis)[22]		
28.7% (11,295 / 39, 309 patients)[6]	**23.9%** (3071 / 12,836 patients)[8]	**26%** (3500 patients)[14]	**17.6%** (537 / 3050 patients)[23]	**47.4%** (11067 / 23348 elective open and laparoscopic colectomies)[26]	**65.4%** (242 / 370 radical nephrourectomy in UTUC)[29]
19% (3474 patients)[7]	**18.1%** (149 / 824 patients)[9]	**20.9%** (3384 / 16,154 patients)[15]	**16.1%** (6673 / 41,334 TKA)[24]	**32.8%** (4260 / 12,987 elective hepatectomies)[27]	**52%** (174 / 335 cardiac surgery for RHD)[30]
		19.7% (10,197 / 51,787 cardiac patients)[2]	**9.2%** (181 / 2164 ACDF)[25]	**10.2%** (37 / 362 emergency GI surgery)[28]	**51.8%** (257 / 496 abdominal resections in colorectal cancer)[31]

1. Beattie WS et al. Anesthesiology 2009;110:574–581; 2. Fowler AJ et al. Br J Surg 2015;102:1314–1324; 3. Dunne JR et al. J Surg Res 2002;102:237–244; 4. Goobie SM et al. JAMA Pediatr 2016;170:855–862; 5. Musallam K et al. Lancet 2011;378:1396–1407; 6. Baron DM et al. Br J Anaesthesia 2014;113:416–423; 7. Gombotz H et al. Transfusion 2007;47:1468–1480; 8. Richards T et al. PLoSOne 2015;10:e0130861; 9. Browning RM et al. Aus N Zealand J Obs Gyn 2012;52:455–459; 10. von Heymann C et al. J Thorac Cardiovasc Surg 2016;152:1412–1420; 11. Hallward G et al. J Cardiothoracic Vasc Anesthesia 2016;30:901–908; 12. Kulier A et al. Circulation 2007;116:471–479; 13. Kim CJ et al. Perfusion 2015;30:277–283; 14. Karkouti K et al. Circulation 2008;117:478–484; 15. Ranucci M et al. Ann Thorac Surg 2013;96:478–485; 16. Spahn DR. Anesthesiology 2010;113:482–495; 17. Kasivisvanathan R et al. Transfusion Med 2016;26:271–277; 18. Sanoufa M et al. J Perioper Pract 2015;25:267–271; 19. Pitter FT et al. Anesth Analg 2016;122:1807–1815; 20. Khanna R et al. Clin Spine Surg 2016 Jul 14 [Epub ahead of print]; 21. Saleh E et al. Br J Anaesth 2007;99:801–808; 22. Dix B et al. Foot Ankle Spec 2016 Sep 9. pii: 1938640016666921; 23. Smilowitz NR et al. Am J Med 2016;129:315–323; 24. Chamieh JS et al. J Arthroplasty 2016;31:766–770; 25. Gruskay JA et al. Clin Spine Surg 016;29:E34–E42; 26. Leichtle SW et al. J Am Coll Surg 2011;212:187–194; 27. Tohme S et al. HPB (Oxford) 2016;18:255–261; 28. Lee JY et al. Medicine 2016;95:35(e4530); 29. Yeh H-C et al. Urol Oncol 2016;34:337:e1–e9; 30. Deepak B et al. J Cardio Vasc Anes 2016;30:896–900; 31. Mörner MEM et al. Int J Colorectal Dis 2017;32:223–232

Germany vs. Netherlands (van Hoeven et al. 2012)

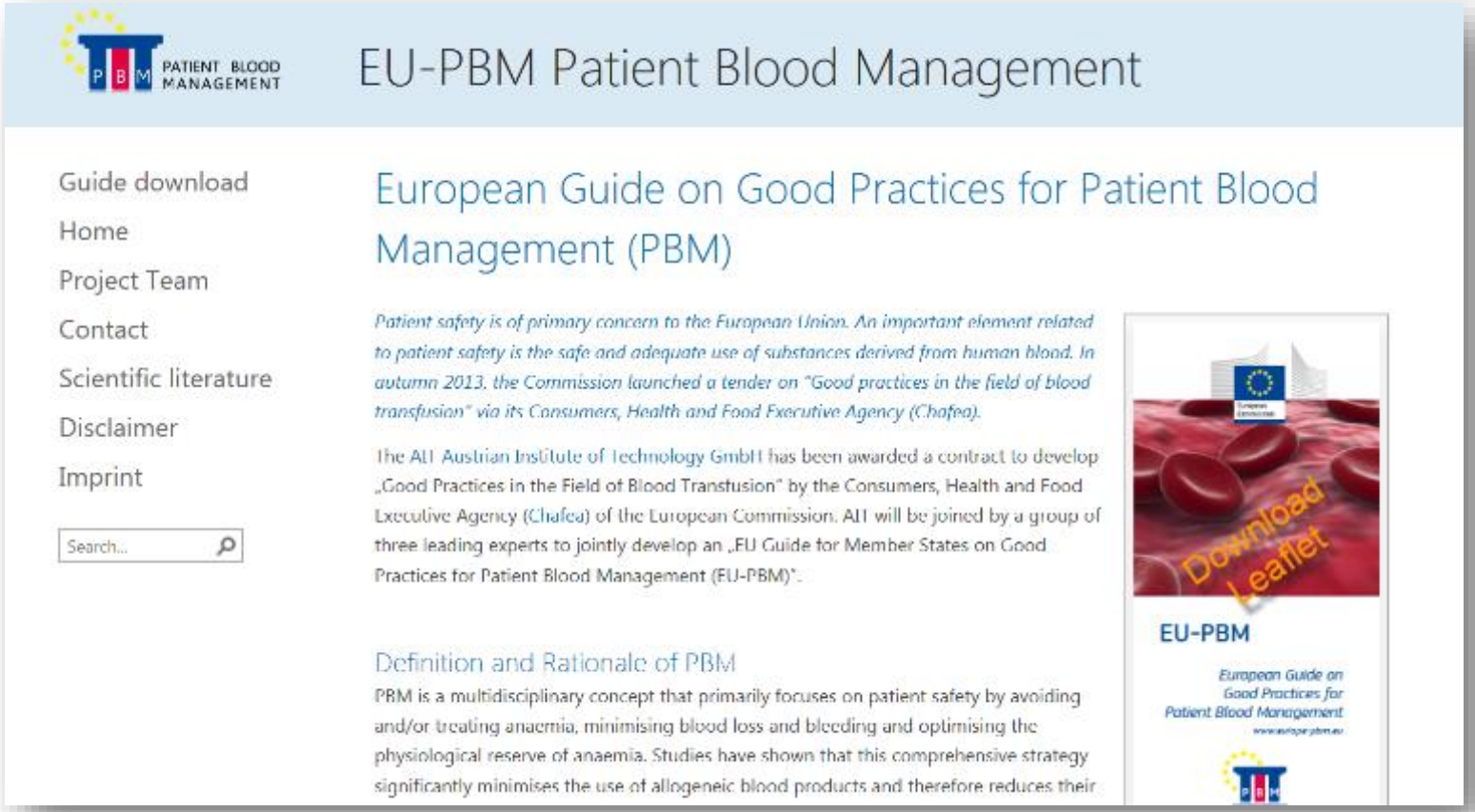
D & NL comparable in terms of population & health system.

D: 57.5 RBCs / 1000 inhabitants

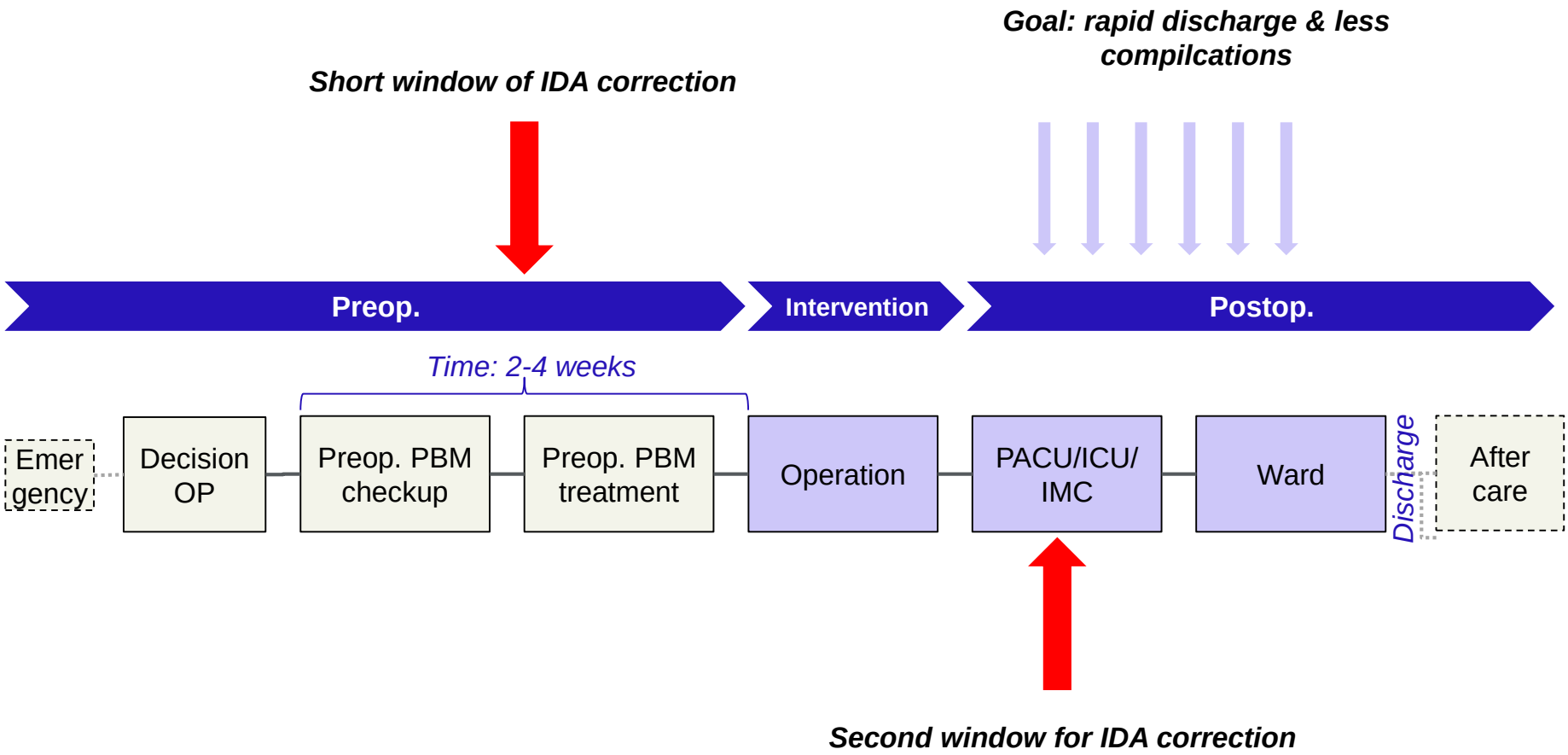
NL: 27.1 RBCs / 1000 inhabitants

2x

Differences not plausible!



Efficient management of IDA



Responsible: GPs, Surgeons & Anaethesists

Minimising Blood Loss & Bleeding

1. Management of pre-operative anemia

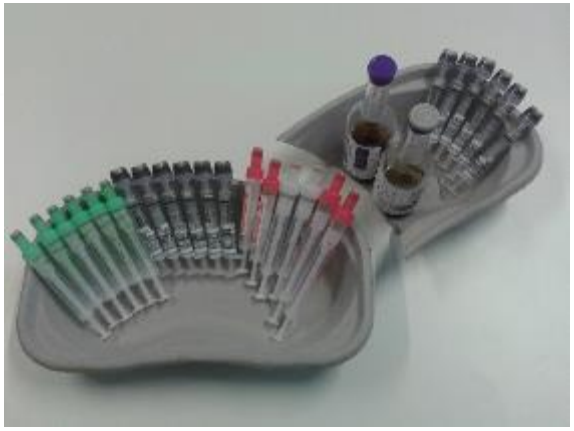
2. Minimising blood loss & bleeding

- ►Blood sparing techniques
- ►Hemostasis
- ►Intraoperative blood salvage
- ►Coagulation management

3. Restrictive use of blood units

Phlebotomy on ICU

D1: 188.2 ml (2x lab. + 3x BK + 12x BGA + cross-match)
D2: 79.2 ml (2x lab. + 10 BGA)
D3: 69.2 ml (2x lab. + 8x BGA)
D4: 129.2 ml (2x lab. + 8x BGA + 3x BK)
D5: 59.2 ml (2x lab. + 6x BGA)
D6: 59.2 ml (2x lab. + 6x BGA)
D7: 59.2 ml (2x lab. + 6x BGA) = **643.4 ml**



15 g/dl
(6L BV)

13.4 g/dl

11 g/dl
(2.8L BV)

8.5 g/dl

Phlebotomy on ICU

Septic shock + Acut cardial-, pulmonary- & kidney dysfunction
→ ECMO & RRT

→ cumulative in 1 week: 9x blood culture, 14x lab, 84x Blood gases, 1x ECMO-Clot, 3x RRT-Clot

→1623 ml in 1 Week

15 g/dl
(6L BV)

↓

10.9 g/dl

11 g/dl
(2.8L BV)

↓

4.8 g/dl

Hospital-acquired Anemia

Contemporary Bloodletting in Cardiac Surgical Care

Colleen G. Koch, MD, MS, Edmunds Z. Reineks, MD, PhD, Anne S. Tang, MS, Eric D. Hixson, PhD, MBA, Shannon Phillips, MD, Joseph F. Sabik, III, MD, J. Michael Henderson, MD, and Eugene H. Blackstone, MD

Department of Cardiothoracic Anesthesia, Heart and Vascular Institute; Quality and Patient Safety Institute; Robert J. Tomsich Pathology & Laboratory Medicine Institute; Department of Quantitative Health Sciences, Research Institute; Business Intelligence, Medical Operations; Department of Thoracic and Cardiovascular Surgery, Heart & Vascular Institute; and Department of General Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, Ohio

Background. Health care providers are seldom aware of the frequency and volume of phlebotomy for laboratory testing, bloodletting that often leads to hospital-acquired anemia. Our objectives were to examine the frequency of laboratory testing in patients undergoing cardiac surgery, calculate cumulative phlebotomy volume from time of initial surgical consultation to hospital discharge, and propose strategies to reduce phlebotomy volume.

Methods. From January 1, 2012 to June 30, 2012, 1,894 patients underwent cardiac surgery at Cleveland Clinic; 1,867 had 1 hospitalization and 27 had 2. Each laboratory test differed between ICU and hospital floors, with median volumes of 332 mL and 118 mL, respectively. Cumulative median volume for the entire hospital stay was 454 mL. More complex procedures were associated with higher overall phlebotomy volume than isolated procedures; eg, combined coronary artery bypass grafting (CABG) and valve procedure median volume was 653 mL (25th/75th percentiles, 428 of 1,065 mL) versus 448 mL (284 of 658 mL) for isolated CABG and 338 mL (237 of 619) for isolated valve procedures.

Conclusions. We were astonished by the extent of

Data (n= 1867 cardiac surgery patients: 221,498 lab tests)

Koch CG et al. *Ann Thorac Surg 2015*

Hospital-acquired Anemia

Contemporary Bloodletting in Cardiac Surgical Care

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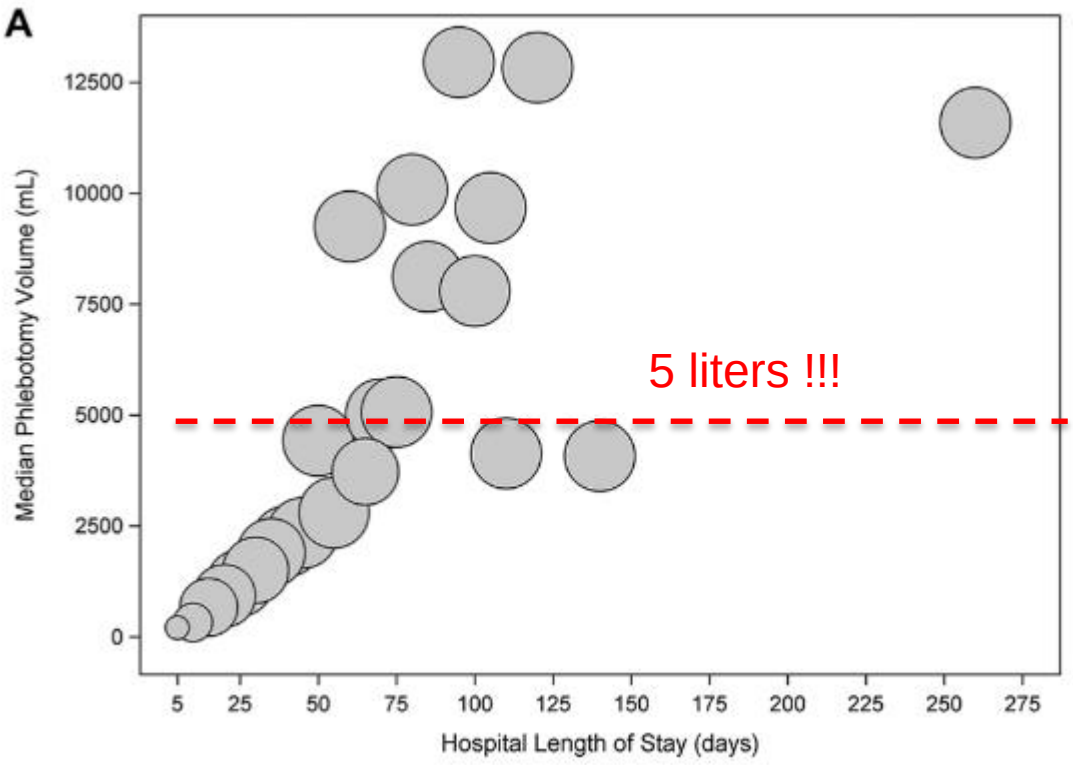


Data (n= 1867 cardiac surgery patients: 221,498 lab tests)

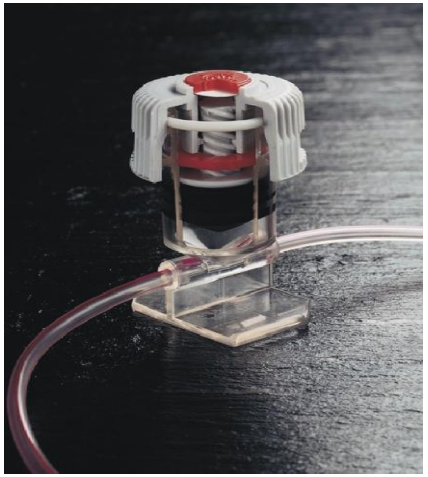
Koch CG et al. *Ann Thorac Surg 2015*

Restrictive blood sampling

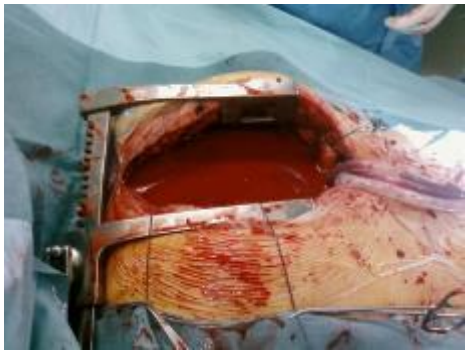
Patient Blood Management .de /en

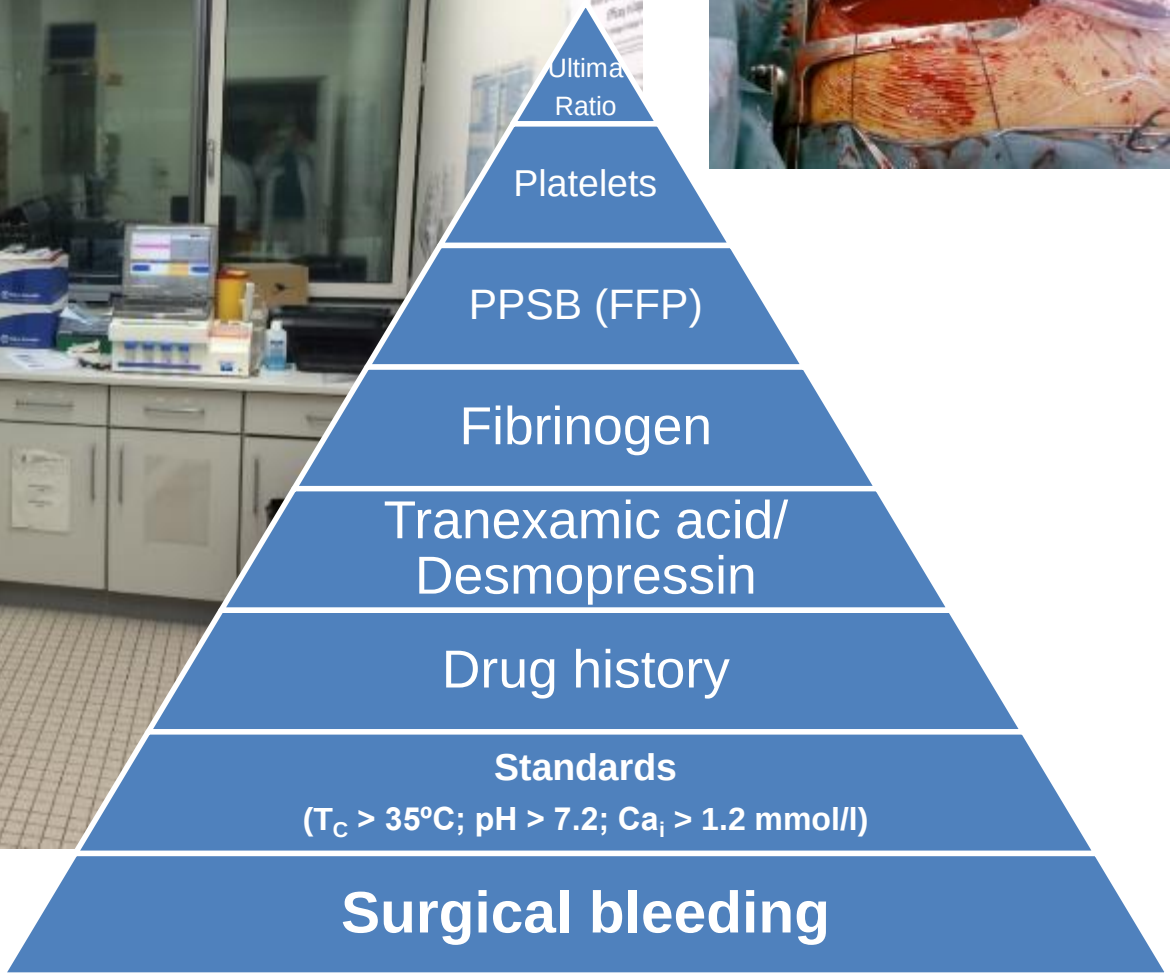
Fischer D, et al. Crit Care. 2014

Restrictive blood loss



Management of bleeding





Weber CF et al., Anesthesiology. 2012 Sep;117(3):531-47.

Restrictive use of blood units

1. Management of pre-operative anemia

2. Minimising blood loss and bleeding

3. Restrictive use of blood units
   - ► Monitoring tolerance of anemia
   - ► Restrictive transfusion trigger

Guideline – whiche? (p50 – PMB ☺)

BUNDESÄRZTEKAMMER

Richtlinie
zur Gewinnung von Blut und Blutbestandteilen und zur Anwendung von Blutprodukten (Richtlinie Hämotherapie)

Aufgestellt gemäß §§ 12a und 18 Transfusionsgesetz von der Bundesärztekammer im Einvernehmen mit dem Paul-Ehrlich-Institut

Querschnitts-Leitlinien (BÄK) „Hämotherapie“
2017; 103 Seiten

Patient Blood Management

dations for the Implementation of Patient

.A. Klein, M. Muñoz, M.F. Murphy, T. Richards, A.

ination of PBM-related metrics

ative anemia

-/surgery-related blood loss

patient-centered clinical decision support

Meybohm et al. 2017 (Periop Medicine)

Gesamtnovelle 2017

in der vom Vorstand der Bundesärztekammer auf Empfehlung seines Wissenschaftlichen Beirats am 17.02.2017 verabschiedeten Fassung.
Das Einvernehmen des Paul-Ehrlich-Instituts wurde am 26.06.2017 hergestellt.

International guidelines

1. Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, et al. Red blood cell transfusion: a clinical practice guideline from the AABB*. Annals of internal medicine. 2012;157(1):49-58
2. Guidelines of the German Medical Association regarding the use of blood and blood components 2014; 1-137
3. Retter A, Wyncoll D, Pearse R, Carson D, McKechnie S, Stanworth S, et al. Guidelines on the management of anaemia and red cell transfusion in adult critically ill patients. British journal of haematology. 2013;160(4):445-64
4. Padhi S, Kemmis-Betty S, Rajesh S, Hill J, Murphy MF, Guideline Development G. Blood transfusion: summary of NICE guidance. BMJ (Clinical research ed. 2015;351:h5832.
5. …
6. …

Transfusion trigger checklist

List has to be filled for each RBC!!!!!

(Exception: massive bleeding)

Hb < 6 g/dl

- ☐ **Independent of any compensation possibilty**

Hb 6 - 8 g/dl

- ☐ **Clinical symptoms for Anemic hypoxia** (tachycardia, hypotension, ischemic ECG changes, lactate acidosis)
- ☐ **Limited compensation, existing risk factors** (e.g. coronary artery disease, heart failure, cerebrovascular insufficiency)
- ☐ **(Other indication: .....)**

Transfusion in case of Hb > 8 g/dl are related to an unclear risk-benefit balance

- ☐ Hb > 8 g/dl (only indicated in indiviual cases; **Very low recommendation level (2 C)**)

Riks and side-effects

META-ANALYSIS

Effects of Allogeneic Red Blood Cell Transfusions on Clinical Outcomes in Patients Undergoing Colorectal Cancer Surgery

A Systematic Review and Meta-Analysis

Austin G. Acheson, MD, Matthew J. Brookes, PhD,† and Donat R. Spahn, MD, FRCA‡*

TABLE 2. Clinical Outcomes of Transfused Patients Undergoing CRC Surgery Versus NonTransfused Controls

Clinical Outcome	No. Studies	Odds Ratio (95% CI, *P*)	I^2 (95% CI) for OR (%)	Incidence Rate Ratio (95%CI, *P*)	I^2 (95% CI) for IRR (%)
All-cause mortality	29	1.72 (1.55–1.91, <0.001)	23.3 (0–51.1)	1.31 (1.23–1.39, <0.001)	0.0 (0–37.0)
Cancer-related mortality	17	1.71 (1.43–2.05, <0.001)	45.0 (0–67.6)	1.45 (1.26–1.66, <0.001)	35.0 (0–62.7)
Recurrence—metastasis–death	19	1.66 (1.41–1.97, <0.001)	50.8 (3.5–69.8)	1.32 (1.19–1.46, <0.001)	28.2 (0–58.1)
Postoperative infection	12	3.27 (2.05–5.20, <0.001)	78.1 (59.1–86.1)	NA	NA
Surgical reintervention	2	4.08 (2.18–7.62, <0.001)	NA	NA	NA

NA indicates not available.

Metaanalyse von 55 Studien (n=20.795 Patienten mit Kolon-Ca)

Acheson AG et al. *Ann Surg 2012;256: 235–244*

Riks and side-effects

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Transfusion of 1-2 RBCs is associated with higher re-ocurrence of colon cancer…

Perioperative Checklist

Preoperative

- Transfusion risk > 10 %:
  - Detection, evaluation and management of anaemia
  - Crossmatch RBC units
- Discontinue anti-coagulation
- Discontinue antiplatelet drugs

Intraoperative

- Restrictive transfusion triggers
- Normothermia
- Coagulation management (pH > 7.2, Ca^{2+} > 1.2)
- Point-of-Care diagnostics: ROTEM, Multiplate
- Tranexamic acid, desmopressin
- Cell saver
- Normovolemia
- Optimize cardiac output
- Minimize blood samples
- Cardiac surgery: Hemokoncentration? Postfiltration?

Postoperative

- Restrictive transfusion triggers
- Normothermia
- Coagulation management (pH > 7.2, Ca2+ > 1.2)
- Cell Saver
- Tranexamic acid, desmopressin
- Normovolemia
- Optimize cardiac output
- Minimize the frequency and volume of blood sampling for laboratory testing

Patient Blood Management

We're part of it!

Hip surgery

N Engl J Med. 2011 Dec 29;365(26):2453-62. doi: 10.1056/NEJMoa1012452. Epub 2011 Dec 14.

Liberal or restrictive transfusion in high-risk patients after hip surgery.

Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, Nemo G, Dragert K, Beaupre L, Hildebrand K, Macaulay W, Lewis C, Cook DR, Dobbin G, Zakriya KJ, Apple FS, Horney RA, Magaziner J; FOCUS Investigators.

- 2,016 patients
- Prospective, randomized, controlled
- Hb > 10 g/dl vs. >8 g/dl

RBCs transfused: 2 vs. 0 units

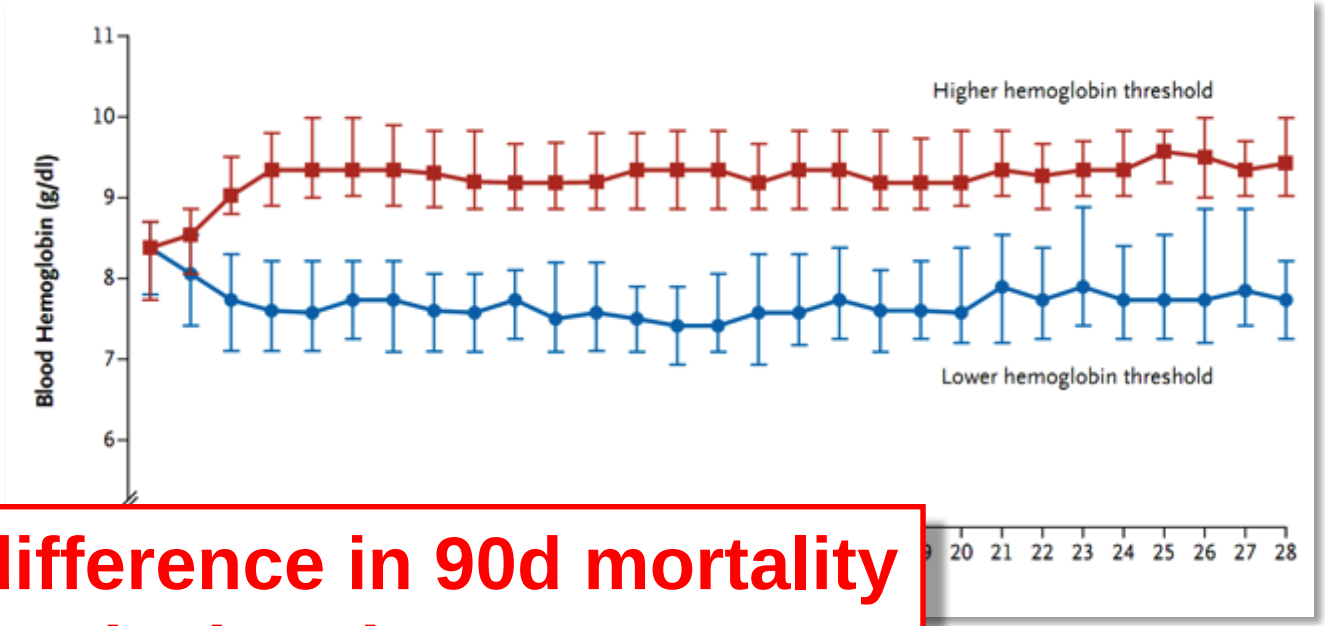
NO difference in mortality or mobility at 30 or 60 days!

Septic shock

N Engl J Med. 2014 Oct 9;371(15):1381-91. doi: 10.1056/NEJMoa1406617. Epub 2014 Oct 1.

Lower versus higher hemoglobin threshold for transfusion in septic shock.

Holst LB[1], Haase N, Wetterslev J, Wernerman J, Guttormsen AB, Karlsson S, Johansson PI, Aneman A, Vang ML, Winding R, Nebrich L, Nibro HL



NO difference in 90d mortality or ischemic events !

- 998 patients in septic shock
- Prospective, randomized, controlled
- **Transfused RBCs (Median): 1 vs. 4**

RCTs !!!

	Date / Journal	Hb – threshhold (mg/dl)		Patients transfused (%)		Results
ICU	1999 / NEJM	**7**	10	67	99	Safe (Survival trend ↑)
Cardiac surgery	2010 / JAMA	**8**	10	47	78	Safe (Survival →)
HIP replacement	2013 / NEJM	**8**	10	41	97	Safe (Survival trend ↑) Mobilisation →
Upper GI-bleeding	2013 / NEJM	**7**	9	49	86	Advantage (Survival ↑)
Head Injury	2014 / JAMA	**7**	10	52	73	Advantage (Neurological outcome ↑)
Septic shock	2014 / NEJM	**7**	9	64	99	Safe (Survival →)
Cardiac surgery	2015 / NEJM	**7.5**	9	53	92	Safe (30d-Survival→ 90d-Survival (not powered) ↓

Concepts of blood transfusion in adults

Lawrence T Goodnough, Jerrold H Levy, Michael F Murphy

Goodnough LT et al. Lancet 2013;381:1845-54

10?

	Recommendations
NIH Consensus Conference,[42] 1988	<70 g/L (acute)
American College of Physicians,[43] 1992	No number
American Society of Anesthesiologists,[44] 1996	<60 g/L (acute)
American Society of Anesthesiologists,[45] 2006	No number
Canadian Medical Association,[26] 1997	No number
Canadian Medical Association,[46] 1998	No number
College of American Pathologists,[47] 1998	60 g/L (acute)
British Committee for Standards in Haematology,[48] 2001	No number
British Committee for Standards in Haematology,[49] 2012	70 g/L*
Australasian Society of Blood Transfusion,[50] 2001	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[51] 2007	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[52] 2011	80 g/L*
American College of Critical Care Medicine, Society of Critical Care Medicine,[53] 2009	70 g/L
American College of Critical Care Medicine, Society of Critical Care Medicine,[54] 2009	70 g/L
Society for the Advancement of Blood Management,[55] 2011	80 g/L
National Blood Authority, Australia,[13] 2012	No number
AABB,[56] 2012	70–80 g/L or 80 g/L†
Kidney Disease: Improving Global Outcomes,[57] 2012	No number
National Cancer Center Network,[58] 2012	70 g/L

*For patients with acute blood loss. †For patients with symptoms of end-organ ischaemia.

Table 3: **Medical society clinical practice guidelines for red blood cell transfusion**

TRICS – NEJM 2017 November 13th

ORIGINAL ARTICLE

7.5g/dl (n=2430) **9.5g/dl (n=2430)**

Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery

C.D. Mazer, R.P. Whitlock, D.A. Fergusson, J. Hall, E. Belley-Cote, K. Connolly, B. Khanykin, A.J. Gregory, É. de Médicis, S. McGuinness, A. Royse, F.M. Carrier, P.J. Young, J.C. Villar, H.P. Grocott, M.D. Seeberger, S. Fremes, F. Lellouche, S. Syed, K. Byrne, S.M. Bagshaw, N.C. Hwang, C. Mehta, T.W. Painter, C. Royse, S. Verma, G.M.T. Hare, A. Cohen, K.E. Thorpe, P. Jüni, and N. Shehata, for the TRICS Investigators and Perioperative Anesthesia Clinical Trials Group*

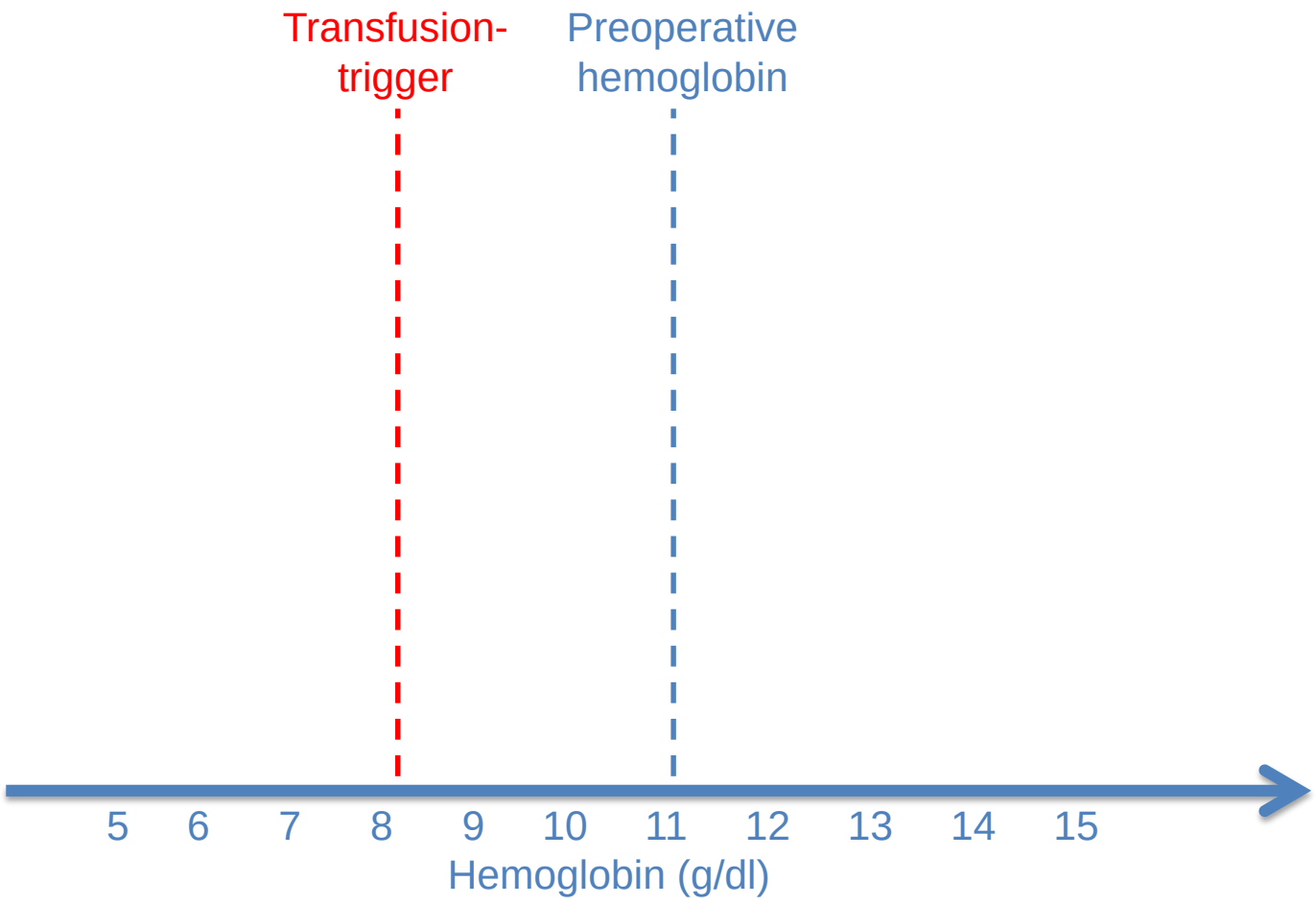
Primary composite outcome

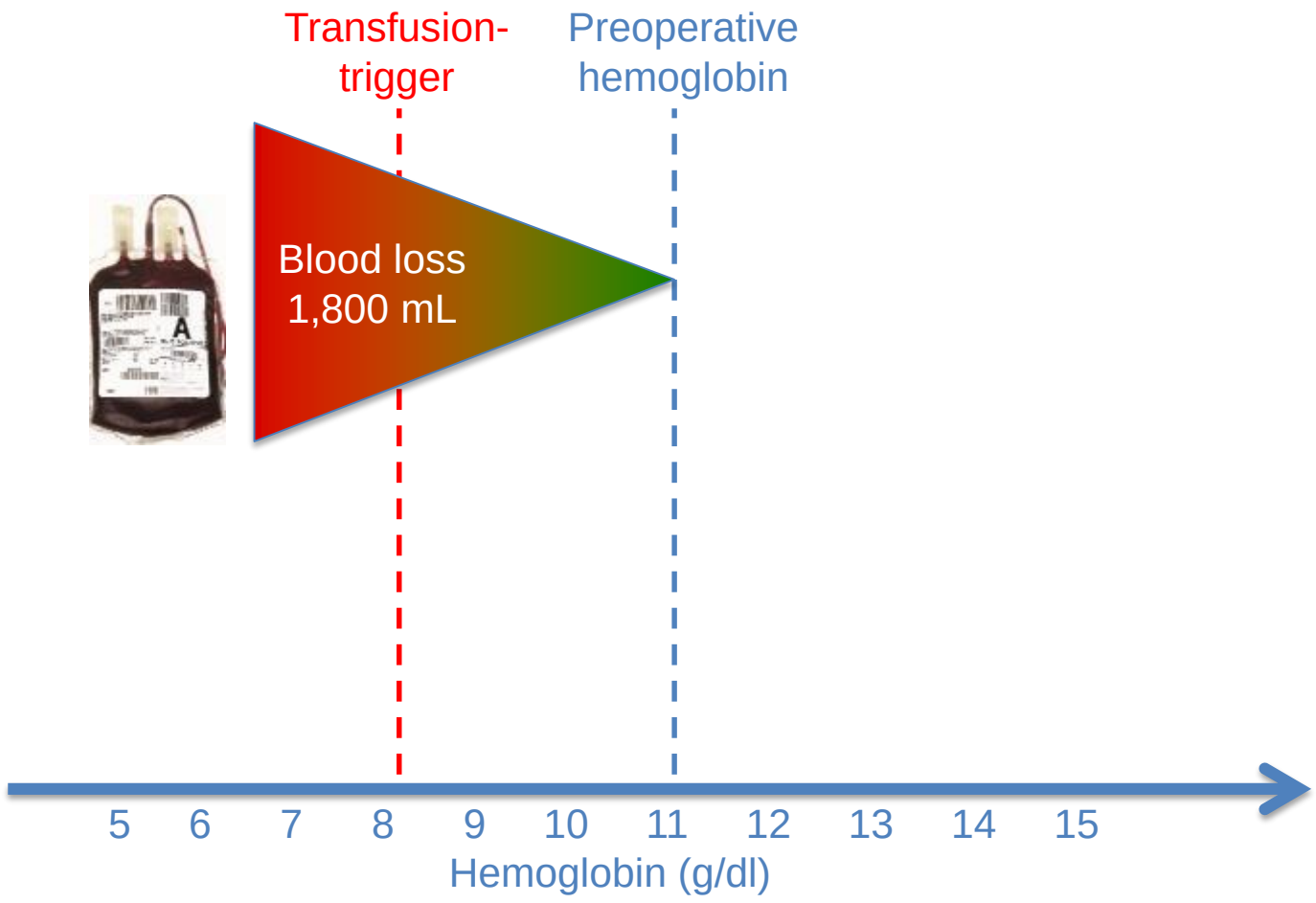
Death, MI, stroke, or new onset RF with dialysis at discharge or 28d:
11.4% vs **12.5%**: absolute risk difference, −1.11 percentage points; 95% confidence interval [CI], −2.93 to 0.72; OR, 0.90; 95% CI, 0.76 to 1.07; P<0.001 for non-inferiority).
Mortality was **3.0%** vs. **3.6%**: OR 0.85; 95% CI, 0.62 to 1.16

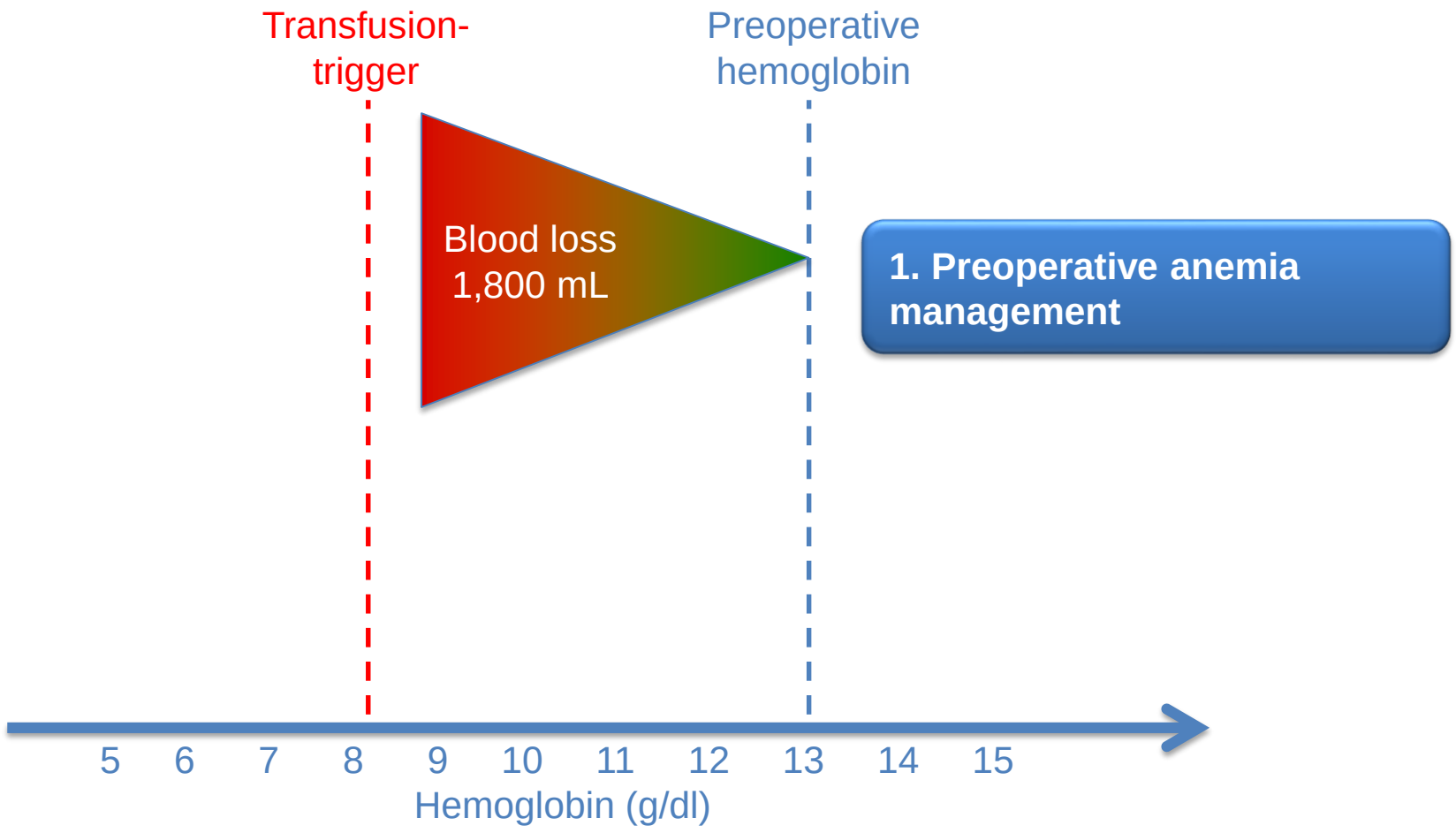
Secondary outcome

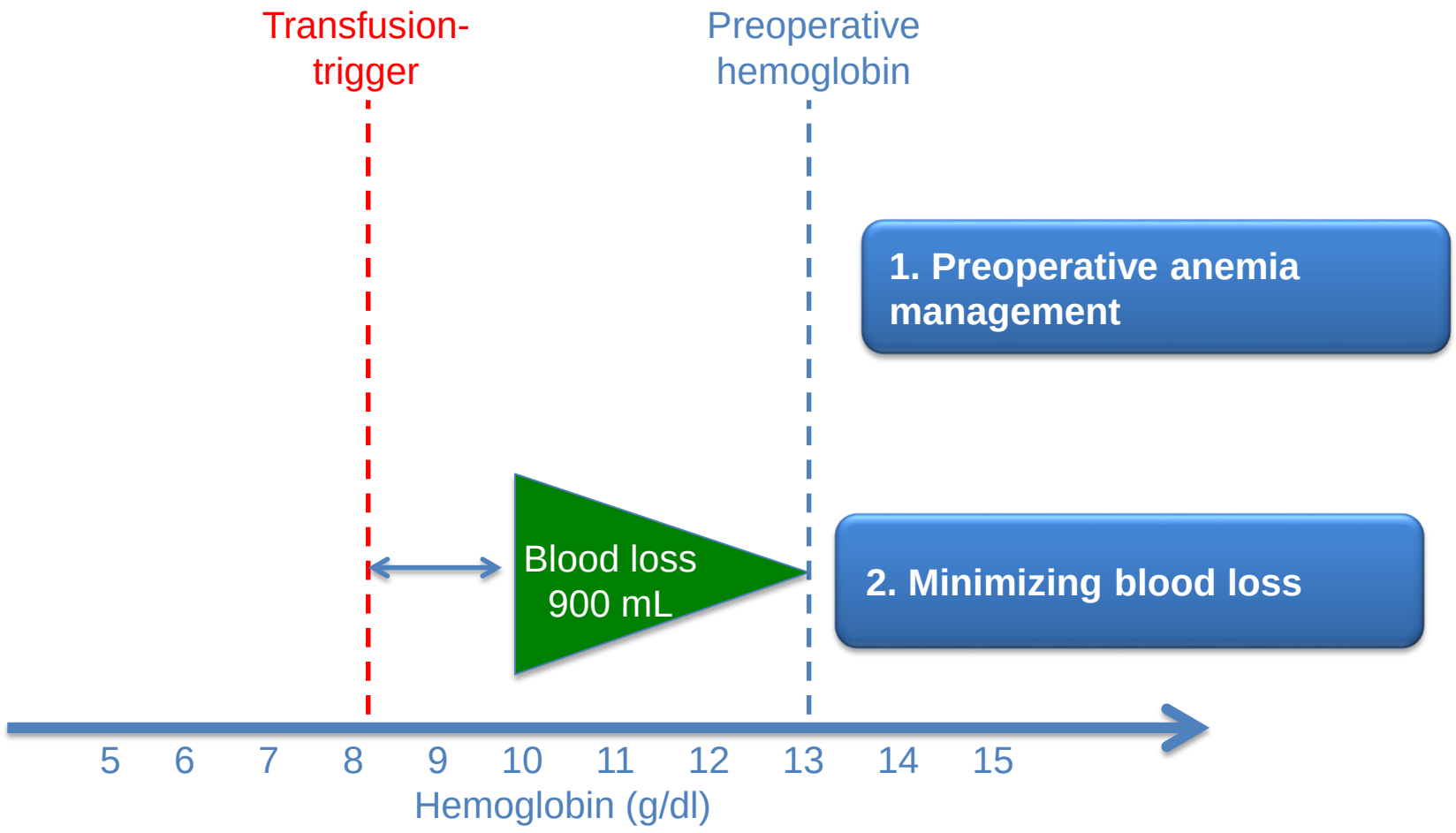
RBC: **52.3%** vs **72.6%** OR, 0.41; 95% CI, 0.37 to 0.47

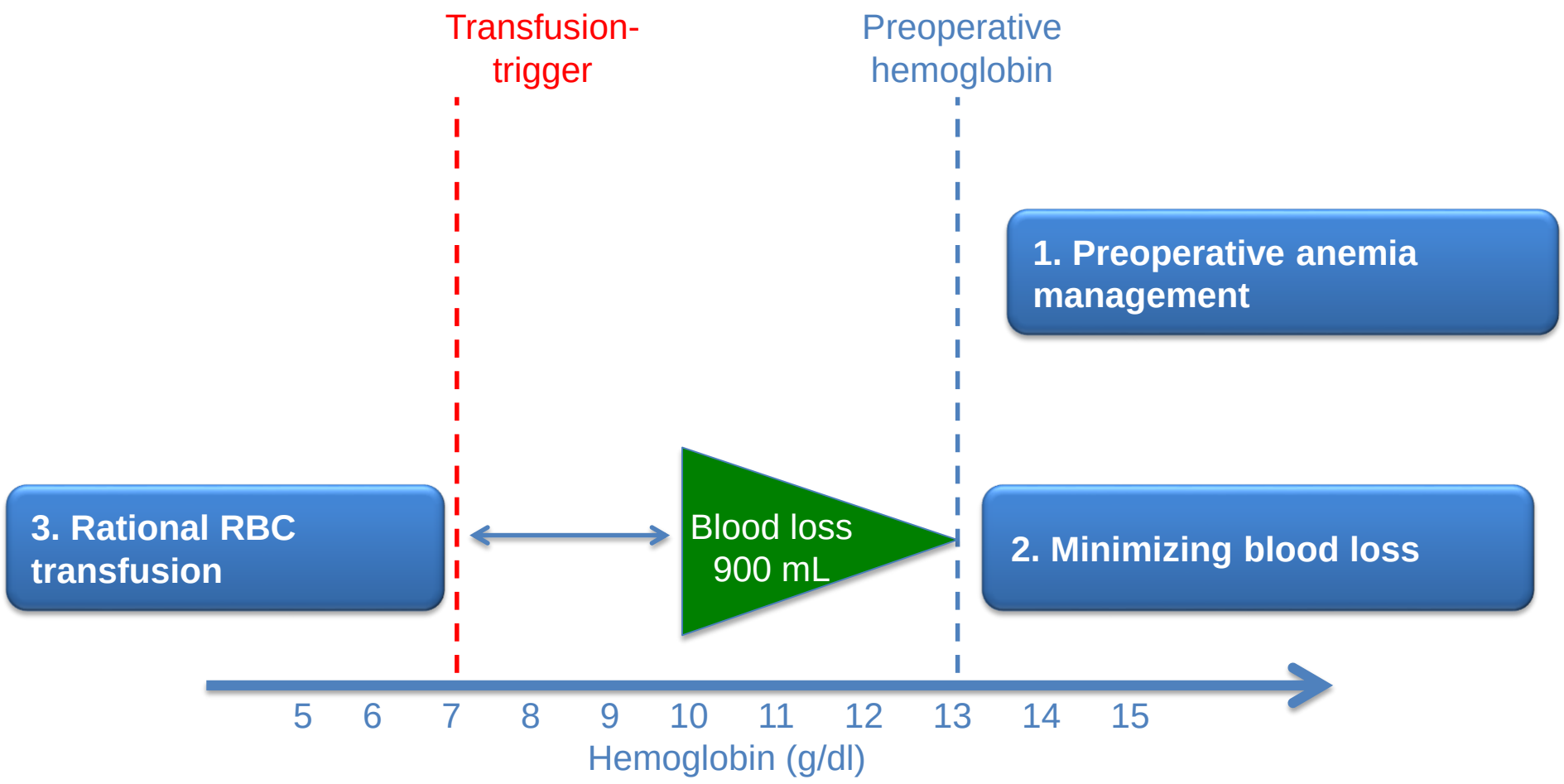
Implementation


Transfusion-trigger
Preoperative hemoglobin
5 6 7 8 9 10 11 12 13 14 15
Hemoglobin (g/dl)

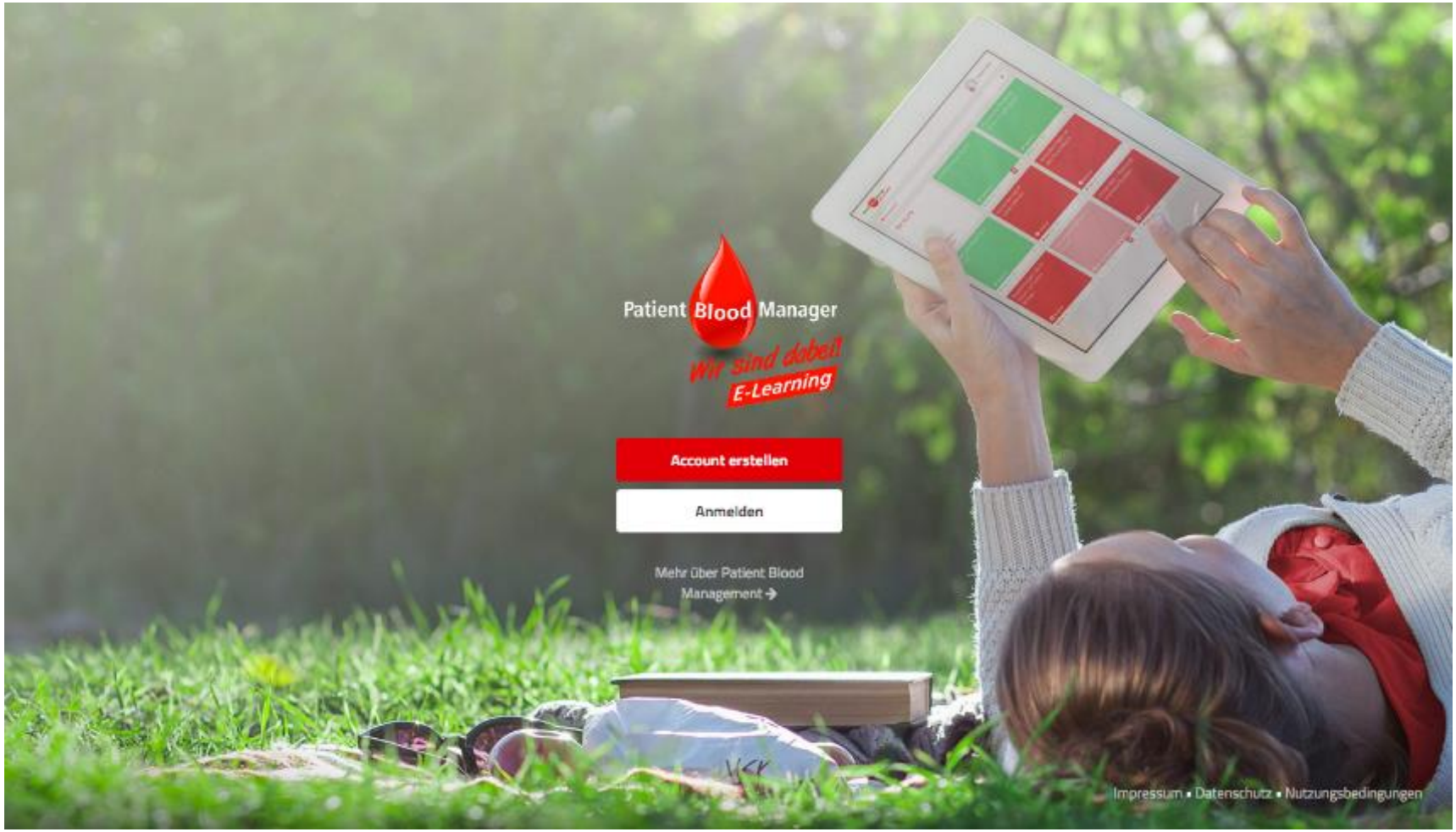

Transfusion-trigger
Preoperative hemoglobin
Blood loss 1,800 mL
5 6 7 8 9 10 11 12 13 14 15
Hemoglobin (g/dl)


Transfusion-trigger
Preoperative hemoglobin
Blood loss 1,800 mL
1. Preoperative anemia management
5 6 7 8 9 10 11 12 13 14 15
Hemoglobin (g/dl)


Transfusion-trigger
Preoperative hemoglobin
1. Preoperative anemia management
Blood loss 900 mL
2. Minimizing blood loss
5 6 7 8 9 10 11 12 13 14 15
Hemoglobin (g/dl)


Transfusion-trigger
Preoperative hemoglobin
1. Preoperative anemia management
3. Rational RBC transfusion
Blood loss 900 mL
2. Minimizing blood loss
5 6 7 8 9 10 11 12 13 14 15
Hemoglobin (g/dl)

www.patientbloodmanager.de



www.patientbloodmanager.de

Patient Blood Management .eu DO it!

Annals of Surgery • Volume 264, Number 2, August 2016

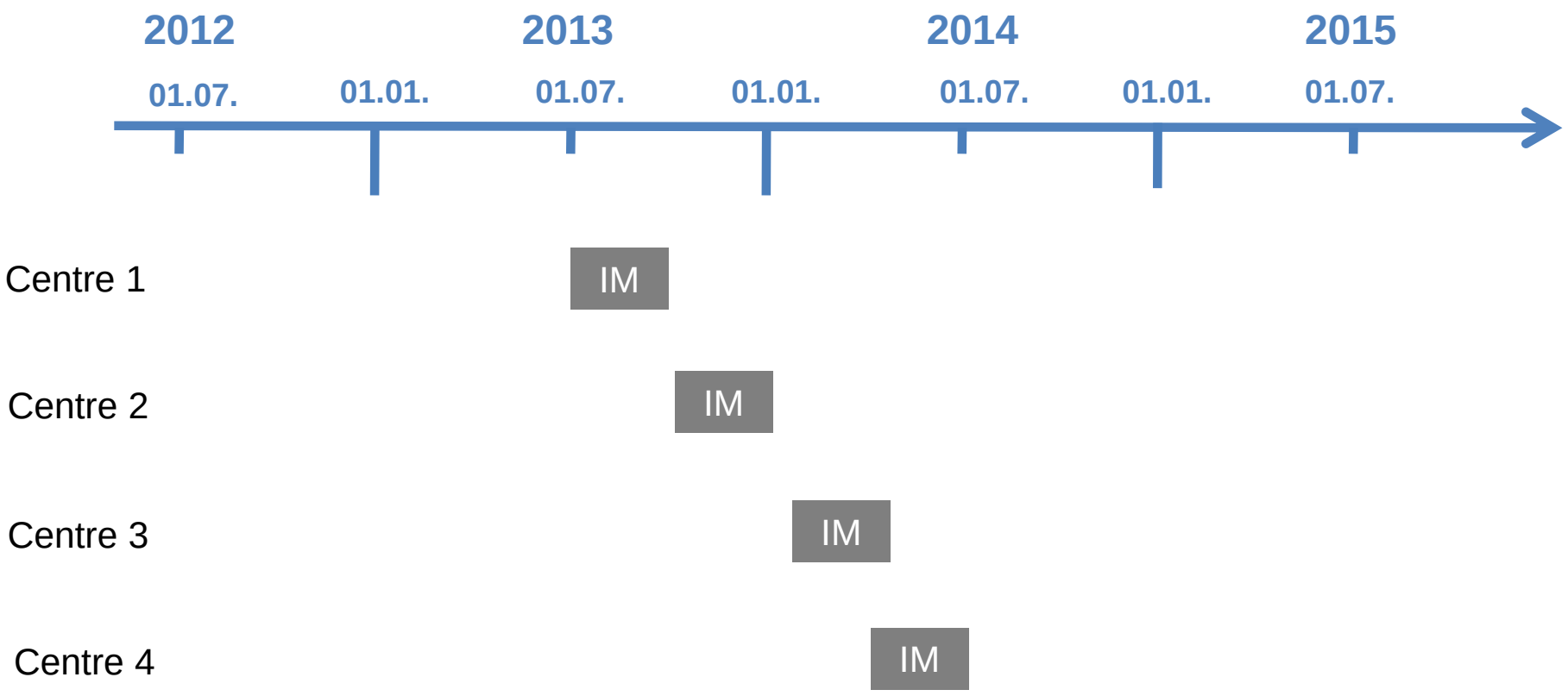
ORIGINAL ARTICLE

Patient Blood Management is Associated With a Substantial Reduction of Red Blood Cell Utilization and Safe for Patient's Outcome

A Prospective, Multicenter Cohort Study With a Noninferiority Design

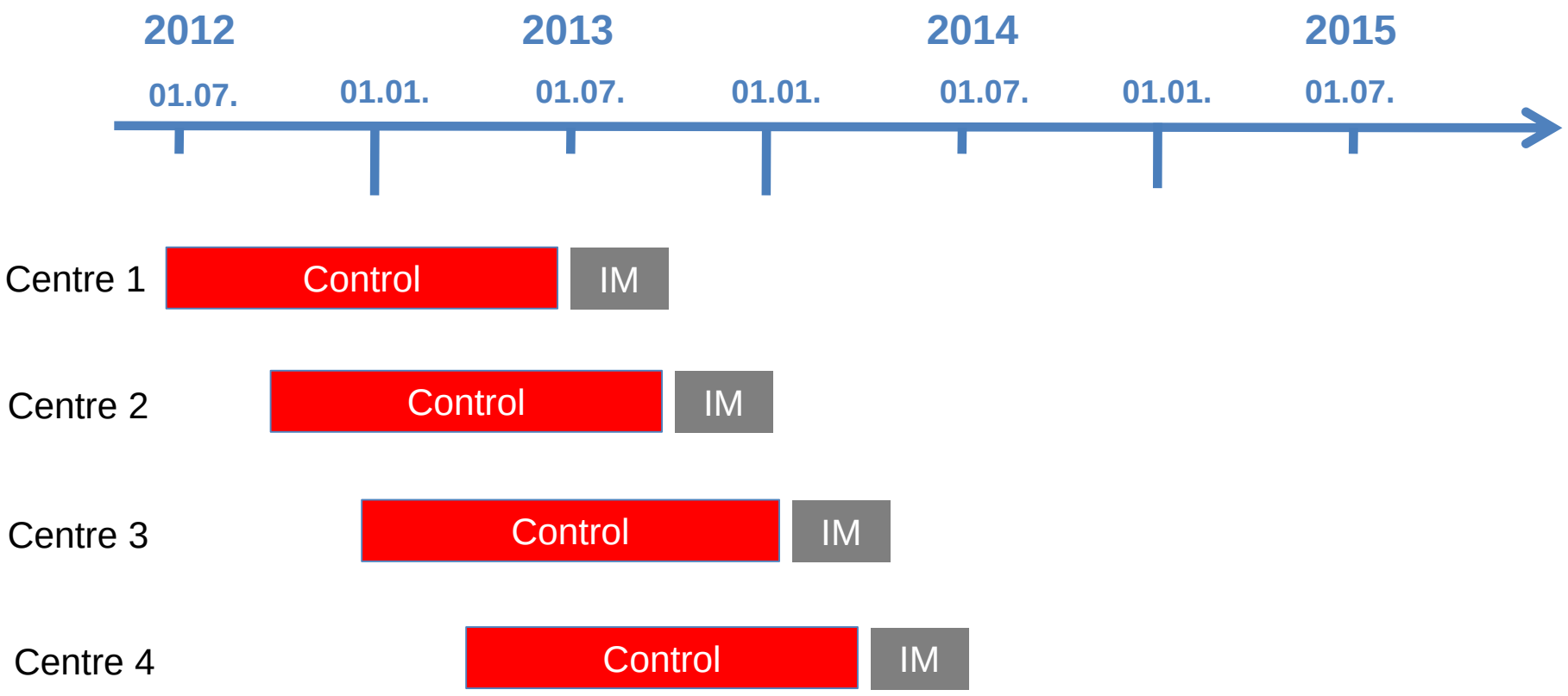
Patrick Meybohm, MD, Eva Herrmann, PhD,† Andrea U. Steinbicker, MD, MPH,‡ Maria Wittmann, MD,§ Matthias Gruenewald, MD,¶ Dania Fischer, MD,* Georg Baumgarten, MD,§ Jochen Renner, MD,¶ Hugo K. Van Aken, MD, PhD, FRCA, FANZCA,‡ Christian F. Weber, MD,* Markus M. Mueller, MD,|| Christof Geisen, MD,|| Julia Rey, PhD,† Dimitra Bon, MS,† Gudrun Hintereder, MD,** Suma Choorapoikayil, PhD,* Johannes Oldenburg, MD,†† Christian Brockmann, MD,‡‡ Raoul G. Geissler, MD,§§ Erhard Seifried, MD,|| and Kai Zacharowski, MD, PhD, FRCA*, and the PBM-study Collaborators*

PBM Study



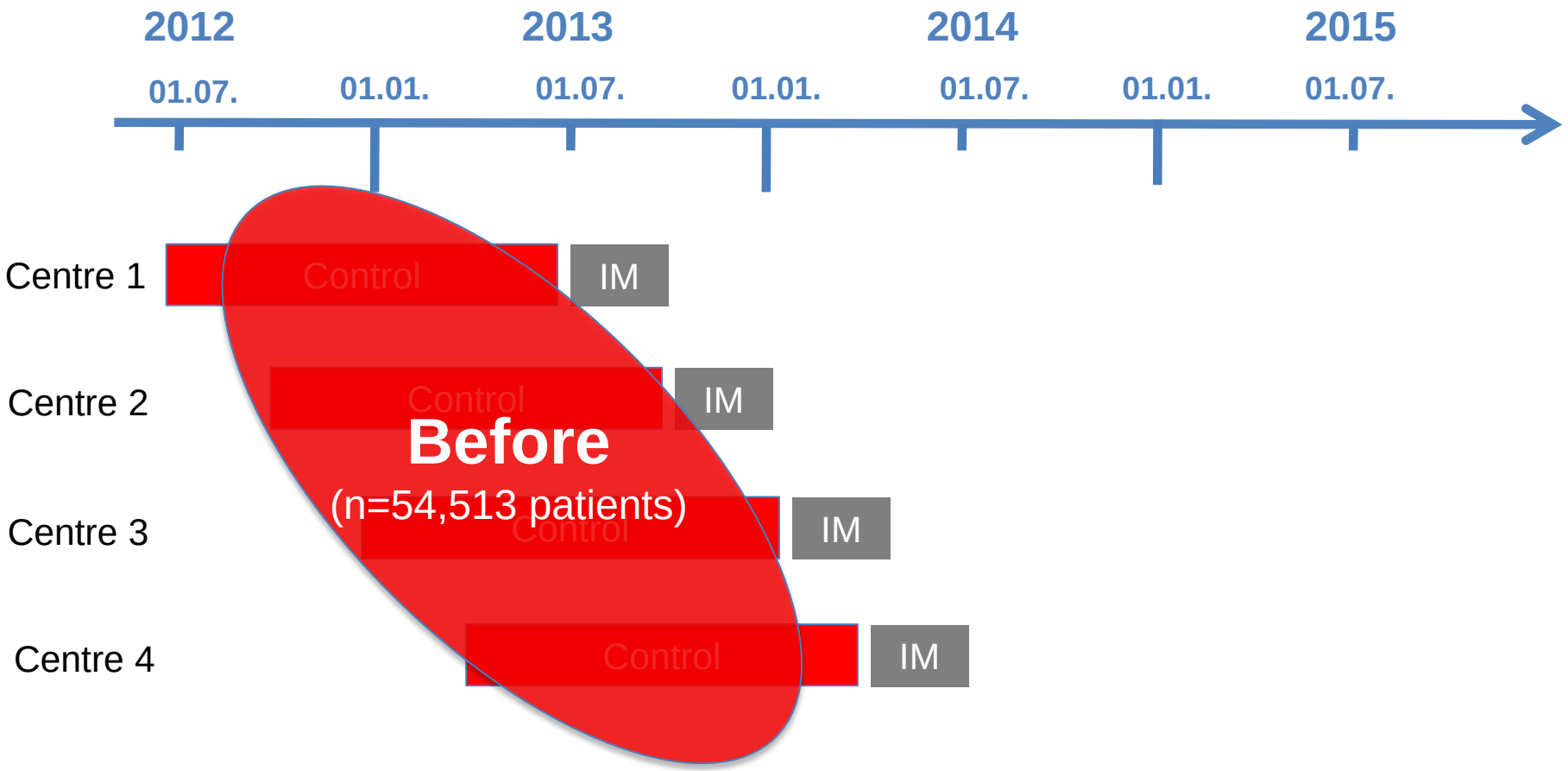
Meybohm P et al. *Ann Surg* 2016

PBM Study



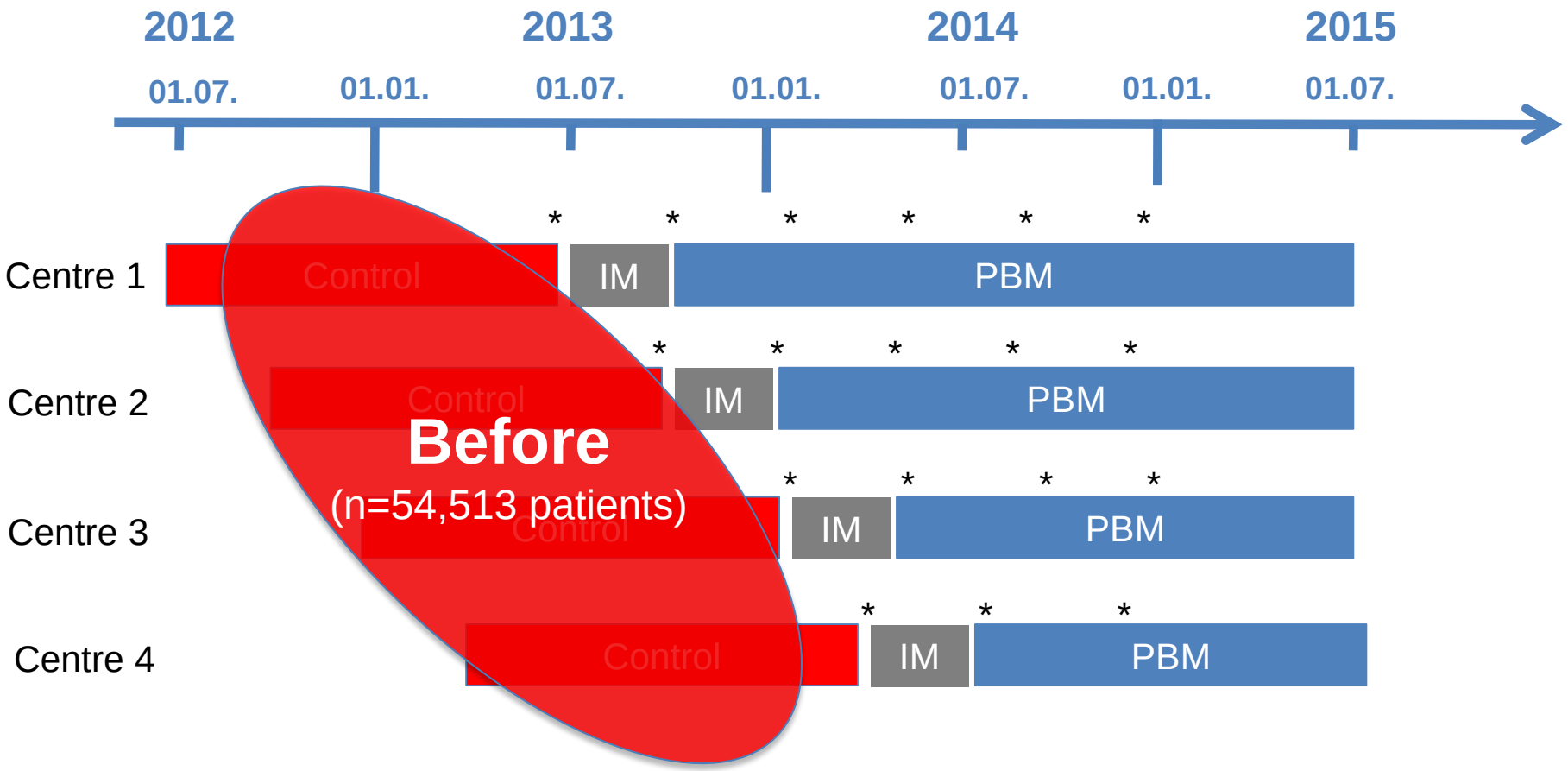
Meybohm P et al. *Ann Surg* 2016

PBM Study



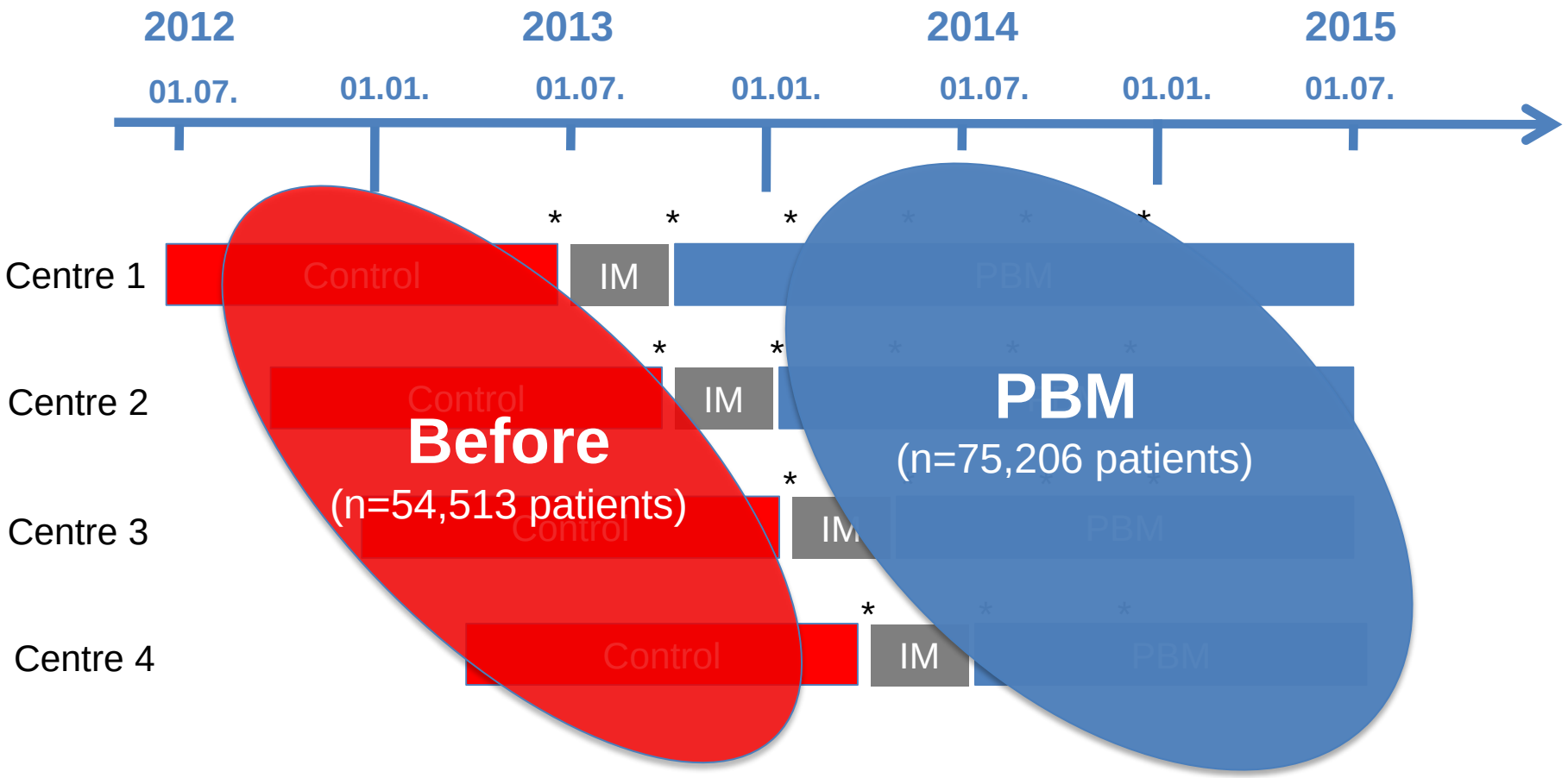
Meybohm P et al. *Ann Surg* 2016

PBM Study



Meybohm P et al. *Ann Surg* 2016

PBM Study



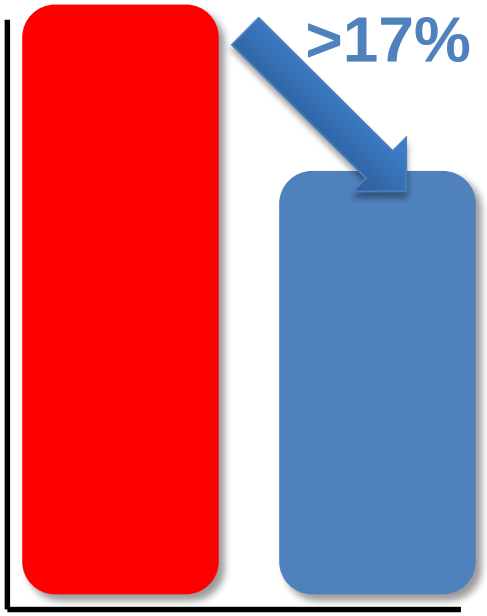
Meybohm P et al. *Ann Surg* 2016

Patient Characteristics of the Two Cohorts

Variable	Pre-PBM (n=54,513)	PBM (n=75,206)
Age (yrs)*	55.7±0.8	55.6±0.8
Male sex (%)	51.6	51.7
Hemoglobin (g/dL)		
First value after admission* /determined (%)	12.9±0.2 / 81.6	12.9±0.1 / 80.8
Last value before discharge* /determined (%)	11.3±0.1 / 66.9	11.2±0.1 / 68.2
Subtypes of surgery†		
Neurosurgery	7135	9886
Otorhinolaryngology	9257	11,701
Thoracic	1951	2609
Cardiac	5630	7904
Vascular	4377	5823
Visceral and endocrine	9164	13,649
Urology	4791	7243
Gynecology	4029	5174
Obstetric	4145	6308
Oral and maxillofacial	2361	3105
Trauma/Orthopedic	12,633	16,298
Others	2844	3830

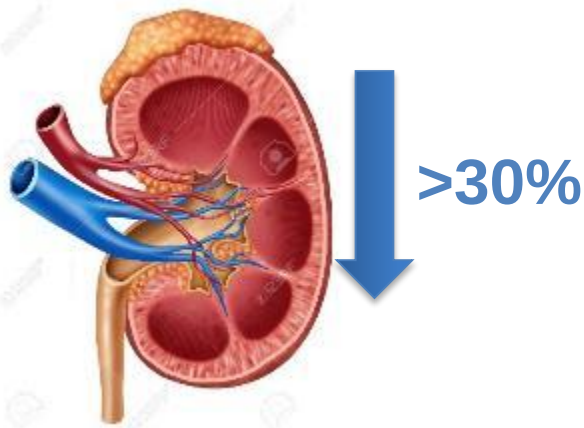
PBM Study Results I

Transfusion



Complications

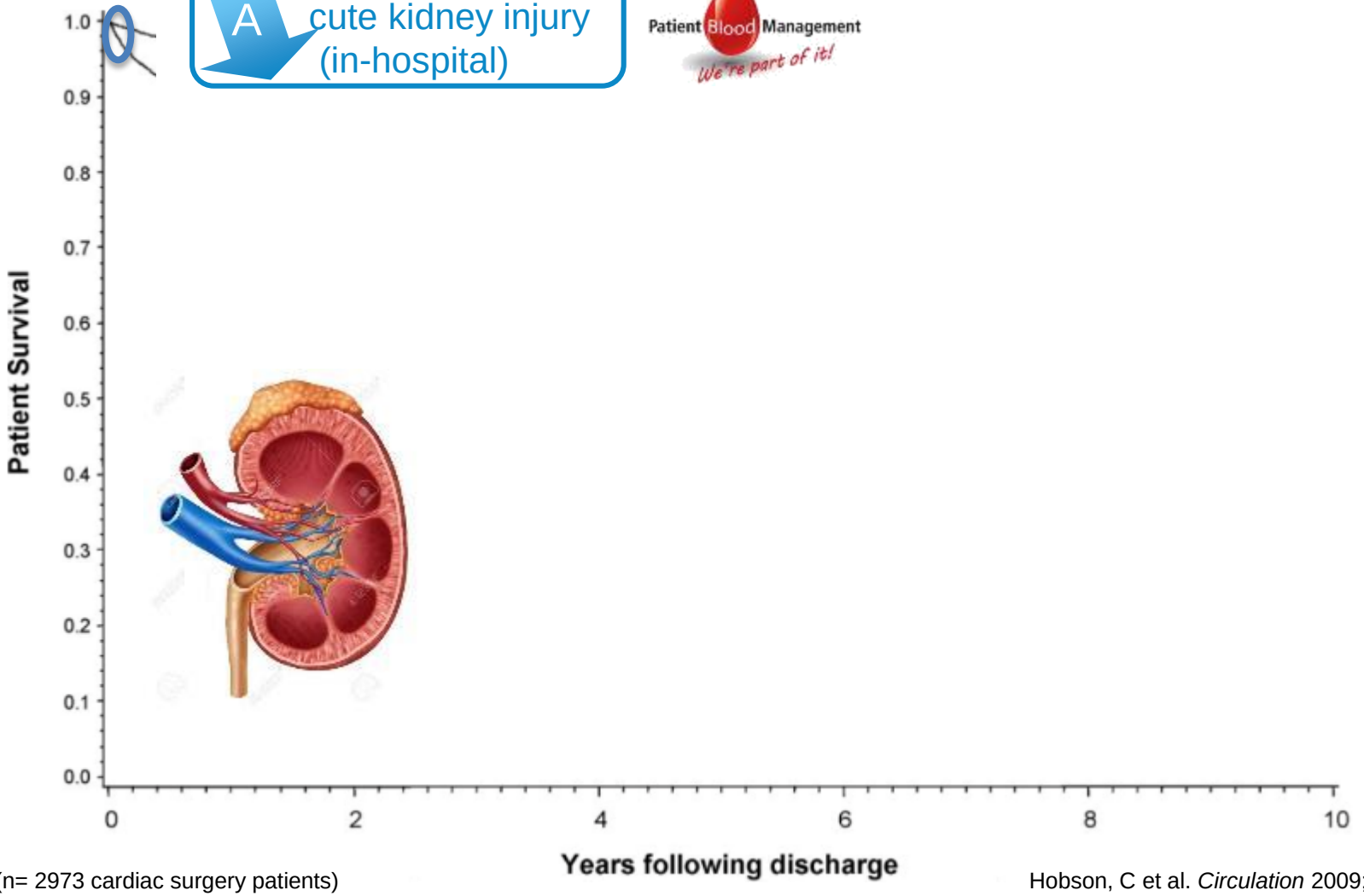
Acute kidney injury (in-hospital)



Meybohm et al. 2016 (Annals of Surgery)

Acute kidney injury (AKI)

Acute kidney injury (in-hospital)

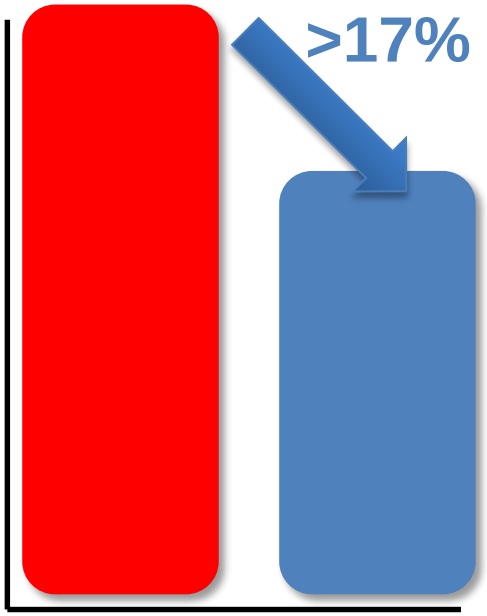


Data (n= 2973 cardiac surgery patients)

Hobson, C et al. *Circulation* 2009;119;2444-2453

PBM Study Results II

Transfusion



Complications

Costs

Meybohm et al. 2016 (Annals of Surgery)

Interesting…

TABLE 2. Primary and Secondary Endpoints (Results of Stratified and Adjusted Outcome Analyses)

Variable	Pre-PBM n=54,513)	PBM (n=75,206)	OR Mantel-Haenszel (95% CI)	OR Regression* (95% CI)	*P* #	*P**
Primary endpoint						
Composite endpoint† (at least one of the following six primary endpoints was positive)	6.53%	6.34%	0.96 (0.92–1.00)	0.98 (0.90–1.08)	0.079 and <0.001 for noninferiority	0.74
Death	2.34%	2.37%	1.01 (0.94–1.08)	1.02 (0.95–1.10)	0.89	0.64
Myocardial infarction‡	0.40%	0.41%	1.05 (0.91–1.23)	1.07 (0.92–1.25)	0.52	0.37
Ischemic stroke§	0.54%	0.46%	0.86 (0.74–1.00)	0.88 (0.76–1.03)	0.055	0.12
Acute renal failure	2.39%	1.67%	0.69 (0.64–0.74)	1.03 (0.85–1.24)	<0.001	0.77
Pneumonia	2.51%	2.59%	1.00 (0.93–1.07)	1.02 (0.95–1.10)	0.99	0.56
Sepsis	1.72%	1.86%	1.06 (0.97–1.15)	1.08 (0.99–1.18)	0.21	0.070
Secondary endpoints						
RBC utilization						
Patients receiving RBC	17.23%	15.20%	0.86 (0.83–0.88)	0.91 (0.84–0.99)	<0.001	0.037
RBC units per patient	1.21±0.05	1.00±0.05			<0.001	0.021
Intensive care unit/ hospital stay						
Stay in ICU	20.36%	19.93%	0.98 (0.95–1.00)	0.95 (0.92–0.99)	0.083	0.009
Length of stay in ICU (days)	1.4±0.24	1.5±0.24			0.16	0.40
Hospital length of stay (days)	10.4±0.17	10.2±0.17			<0.001	0.13
Anemia¶						
Anemia at admission	34.35%	36.16%	1.07 (1.03–1.14)	1.08 (1.03–1.14)	<0.001	0.001
Anemia at discharge	70.55%	71.97%	1.07 (1.03–1.10)	1.12 (1.00–1.27)	<0.001	0.058

Meybohm P et al. *Ann Surg* 2016

TABLE 2. Primary and Secondary Endpoints (Results of Stratified and Adjusted Outcome Analyses)

Variable	Pre-PBM (n=54,513)	PBM (n=75,206)	OR Mantel-Haenszel (95% CI)	OR Regression* (95% CI)	*P* #
Primary endpoint					
Composite endpoint† (at least one of the following six primary endpoints was positive)	6.53%	6.34%	0.96 (0.92–1.00)	0.98 (0.90–1.08)	0.079 and <0.001 for noninferiority
Death	2.34%	2.37%	1.01 (0.94–1.08)	1.02 (0.95–1.10)	0.89
Myocardial infarction‡	0.40%	0.41%	1.05 (0.91–1.23)	1.07 (0.92–1.25)	0.52
Ischemic stroke§	0.54%	0.46%	0.86 (0.74–1.00)	0.88 (0.76–1.03)	0.055
Acute renal failure	2.39%	1.67%	0.69 (0.64–0.74)	1.03 (0.85–1.24)	<0.001
Pneumonia	2.51%	2.59%	1.00 (0.93–1.07)	1.02 (0.95–1.10)	0.99
Sepsis	1.72%	1.86%	1.06 (0.97–1.15)	1.08 (0.99–1.18)	0.21
Secondary endpoints					
RBC utilization					
Patients receiving RBC	17.23%	15.20%	0.86 (0.83–0.88)	0.91 (0.84–0.99)	<0.001
RBC units per patient	1.21±0.05	1.00±0.05			<0.001
Intensive care unit/ hospital stay					
Stay in ICU	20.36%	19.93%	0.98 (0.95–1.00)	0.95 (0.92–0.99)	0.083
Length of stay in ICU (days)	1.4±0.24	1.5±0.24			0.16
Hospital length of stay (days)	10.4±0.17	10.2±0.17			<0.001
Anemia¶					
Anemia at admission	34.35%	36.16%	1.07 (1.03–1.14)	1.08 (1.03–1.14)	<0.001
Anemia at discharge	70.55%	71.97%	1.07 (1.03–1.10)	1.12 (1.00–1.27)	<0.001

Meybohm P et al. *Ann Surg* 2016

TABLE 3. RBC Utilization Per Quarter of the Year

Year	2012		2013				2014				2015	
Quarter	Q3_12	Q4_12	Q1_13	Q2_13	Q3_13	Q4_13	Q1_14	Q2_14	Q3_14	Q4_14	Q1_15	Q2_15
Patients transfused (%) (no./total no.)												
Center 1	17.6 (577/3287)	18.7 (640/3427)	18.1 (602/3329)	18.2 (610/3351)	IM	16.4 (559/3409)	15.2 (510/3355)	14.6 (478/3276)	14.5 (478/3407)	14.2 (474/3335)	12.7 (425/3339)	14.5 (478/3293)
Center 2	/	18.0 (582/3242)	16.4 (532/3250)	17.3 (559/3225)	14.1 (542/3365)	IM	15.9 (547/3441)	15.5 (523/3369)	16.2 (534/3287)	15.8 (519/3294)	15.7 (521/3325)	15.0 (492/3287)
Center 3	/	/	18.2 (620/3400)	20.4 (690/3379)	17.8 (654/3684)	17.9 (628/3515)	IM	16.9 (591/3502)	17.4 (614/3531)	17.2 (594/3455)	15.6 (510/3265)	15.7 (497/3162)
Center 4	/	/	/	15.6 (525/3372)	15.5 (558/3592)	15.8 (554/3512)	14.9 (534/3583)	IM	15.1 (558/3697)	15.1 (547/3633)	13.1 (497/3784)	13.0 (487/3760)
Patients transfused (%) relative changes compared with pre-PBM*												
Center 1	Reference (100%; mean=18.2%)				IM	−9.6%	−16.3%	−19.6%	−20.1%	−21.8%	−30.0%	−20.1%
Center 2	/	Reference (100%; mean=16.5%)				IM	−3.3%	−5.8%	−1.5%	−4.0%	−4.6%	−8.8%
Center 3	/	/	Reference (100%; mean=18.6%)				IM	−9.0%	−6.3%	−7.4%	−16.0%	−15.5%
Center 4	/	/	/	Reference (100%; mean=15.5%)				IM	−2.3%	−2.3%	−15.2%	−15.9%
Number of RBC units per center (no.)												
Center 1	4015	4435	4312	4558	IM	4335	3678	3444	3319	2814	2621	3107
Center 2	/	4237	3985	4112	3752	IM	3788	3787	3552	3391	3446	3223
Center 3	/	/	4068	4728	4474	3977	IM	3857	3989	3951	3399	3410
Center 4	/	/	/	3960	4065	3723	3527	IM	3799	3446	2948	2780
RBC units per center (%) relative changes compared with pre-PBM*												
Center 1	Reference (100%; mean=4330)				IM	0.1%	−15.1%	−20.5%	−23.3%	−35.0%	−39.5%	−28.2%
Center 2	/	Reference (100%; mean=4022)				IM	−5.8%	−5.8%	−11.7%	−15.7%	−14.3%	−19.9%
Center 3	/	/	Reference (100%; mean=4312)				IM	−10.5%	−7.5%	−8.4%	−21.2%	−20.9%
Center 4	/	/	/	Reference (100%; mean=3819)				IM	−0.5%	−9.8%	−22.8%	−27.2%
Number of RBC units per patient (no.)												
Center 1	1.22	1.29	1.30	1.36	IM	1.27	1.10	1.05	0.97	0.84	0.78	0.94
Center 2	/	1.31	1.23	1.28	1.12	IM	1.10	1.12	1.08	1.03	1.04	0.98
Center 3	/	/	1.20	1.40	1.21	1.13	IM	1.10	1.13	1.14	1.04	1.08
Center 4	/	/	/	1.17	1.13	1.06	0.98	IM	1.02	0.95	0.78	0.74
RBC units per patient (%) relative changes compared with pre-PBM*												
Center 1	Reference (100%; mean=1.29)				IM	−1.6%	−15.2%	−18.7%	−24.6%	−34.7%	−39.3%	−27.0%
Center 2	/	Reference (100%; mean=1.23)				IM	−10.6%	−8.7%	−12.2%	−16.4%	−15.8%	−20.3%
Center 3	/	/	Reference (100%; mean=1.24)				IM	−10.8%	−8.6%	−7.4%	−15.7%	−12.7%
Center 4	/	/	/	Reference (100%; mean=1.09)				IM	−5.5%	−12.8%	−28.4%	−32.0%

Table: 13 x 24 = 312 cells

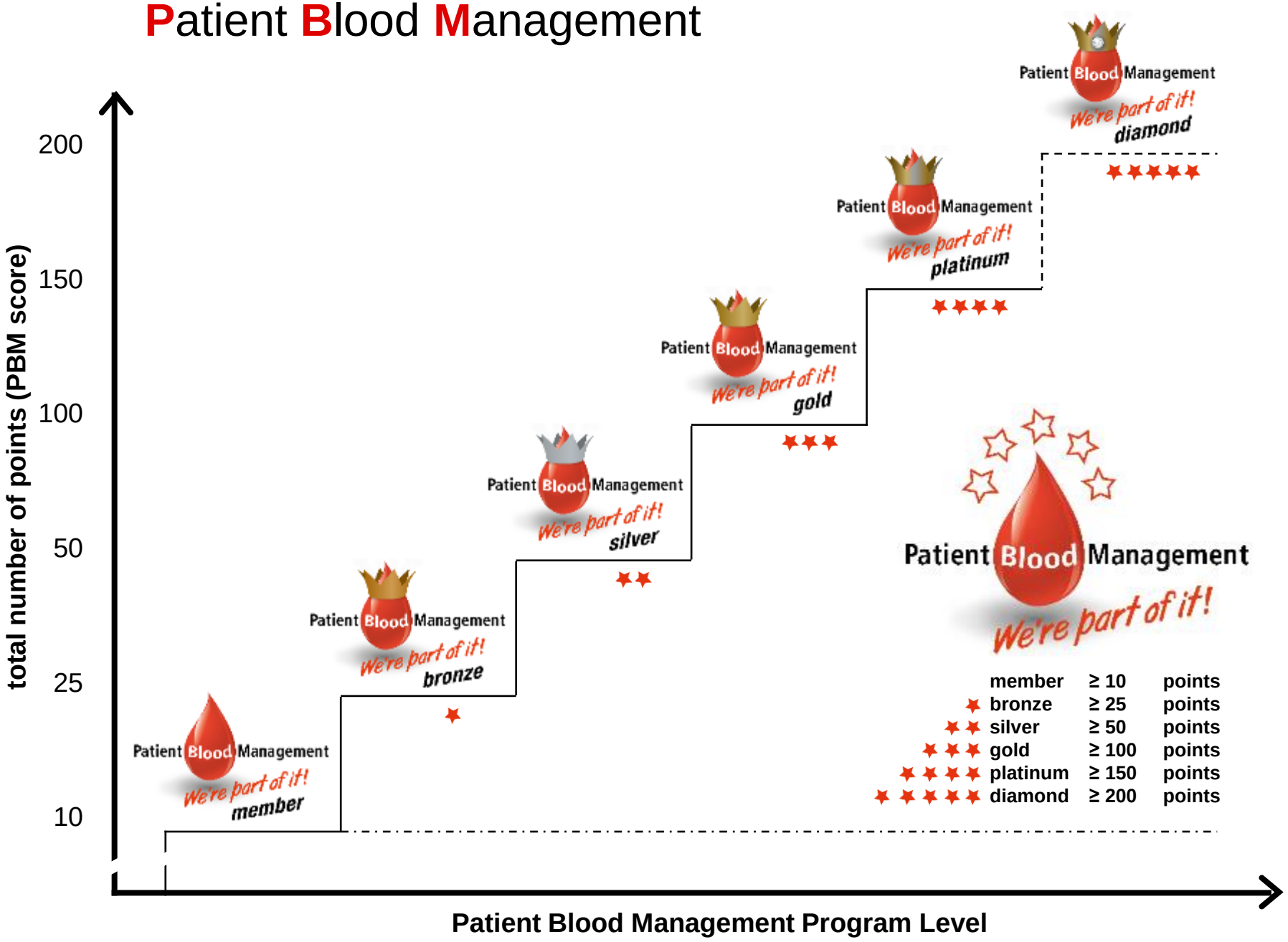
Meybohm P et al. *Ann Surg* 2016

PBM Study Results - Bundles

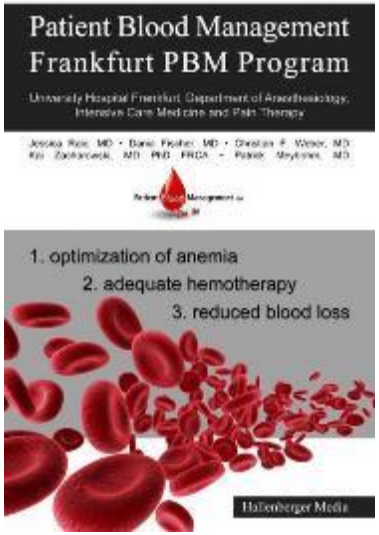
Block 1: General PBM project management			
Involvement of key PBM stakeholders [role]			
PBM coordinator with protected time [central role for communication, networking, education, documentation, and benchmarking]	0	1	2 ✓
Hospital board of directors (e.g. chief medical officer, chief executive officer, chief nursing officer) [support; official directive]	0	1 ✓	2
Surgeons (e.g. orthopaedic/trauma, cardiac, vascular, visceral, trauma, urology, neurosurgery) [interdisciplinary consensus]	0	1	2 ✓
Anaesthesiologists/ intensive care specialists [central role for perioperative care]	0 ✓	1	2
Transfusion medicine specialists / transfusion committee [prevention of blood wastage; optimal blood use; changes in donor blood management]	0	1 ✓	2
Internists/ gastroenterologists/ haematologists/cardiologists/nephrologists [anaemia management; optimal blood use]	0	1	2 ✓
General practitioners/ family doctors [determine the necessity for elective surgery; assign patients to a hospital; preoperative anaemia management]	0	1 ✓	2
Patient's representative [need to be informed about the different alternatives to treat anaemia/ create awareness]	0	1	2 ✓
Paediatrics [mainly refers to blood conservation strategies]	0	1	2 ✓
Central laboratory/ laboratory scientists [smaller blood collecting tubes]	0	1	2
Pharmacists/ purchasing department [introduction of new drugs for the management of anaemia and coagulopathy]	0	1	2
Information technology department [sampling of routine data and key performance metrics]	0	1	2
Finance department [finance experience for program budget plan, initial project costs; hospital-wide cost savings]	0	1	2
Quality management [project management experience; PBM as a fixed part of a quality improvement initiative]	0	1	2
Public affairs [dissemination channels/ marketing of the PBM project (e.g. via journals/ intranet/ emails/ posters/ roll-ups/ press conferences)]	0	1	2
Under- and postgraduate education			
Undergraduate education (nursing school/ medical school)	0	1	2
Post-graduate education of physicians/clinicians (lectures, workshops; initial and once a year)	0	1	2
Post-graduate education of nurses (intensive care unit, normal ward (initial and once a year)	0	1	2
Certificate (e.g. by online E-Learning courses) – to enhance PBM education and knowledge transfer	0	1	2
Local Standard Operating Procedures/ protocols			
Standard operating procedures for Patient Blood Management -			
Anaemia management	0	1	2
Coagulation management	0	1	2
Blood conservation	0	1	2
Optimal blood use/ transfusion of blood products (list of index-procedures for 'type and screen' or 'type and crossmatch (and supply)')	0	1	2
Massive haemorrhage protocols (including such as damage controlled surgery, arterial embolisation, haemotherapy algorithm)			
Massive haemorrhage (in general)	0	1	2
Postpartum haemorrhage	0	1	2
Trauma associated haemorrhage	0	1	2
Cardiac surgery associated haemorrhage	0	1	2

Meybohm et al. 2016 Transfusion Medicine Reviews

Patient Blood Management



Meybohm et al. 2016 Transfusion Medicine Reviews



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PBM international – Patient Safety

Patient Blood Management
We're part of it!

Humanitarian Award

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2017

PBM Europe

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PBM PATIENT BLOOD MANAGEMENT

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

Deutscher Preis für Patientensicherheit 2016

Gefördert durch:
Bundesministerium für Gesundheit
aufgrund eines Beschlusses des Deutschen Bundestages

AKTIONSBÜNDNIS PATIENTENSICHERHEIT

World PBM Network – start 04.02.2017

- World-wide PBM Hospitals
- Data collection
- Numbers of lifes saved!

DGAInfo

The Patient Blood Management Concept[1]*

Joint recommendation of the German Society of Anaesthesiology and Intensive Care Medicine and the German Society of Surgery

Oct 2017

▶ **Citation:** The Patient Blood Management Concept. Joint recommendation of the German Society of Anaesthesiology and Intensive Care Medicine and the German Society of Surgery. Anästh Intensivmed 2017;58:568-571. DOI: 10.19224/ai2017.568

Summary

Patient blood management is a multimodal concept that aims to detect, prevent and treat anaemia, optimise haemostasis, minimise iatrogenic blood loss, and support a patient-centred decision to provide optimal use of allogeneic blood products. Although the World Health Organization has already recommended Patient Blood Management as a new standard in 2010, many hospitals have not implemented it at all or only in part in clinical practice. The German Society of Anaesthesiology and Intensive Care Medicine and the German Society

diagnostic methods. Still the transfusion of cellular blood preparations means "transplanting blood as a liquid organ". Undesired effects of RBCs include, among others, the allergic, the febrile non-haemolytic and acute haemolytic transfusion reaction and the transfusion-associated pulmonary insufficiency. In addition, mistransfusions can happen and, although extremely seldom despite high security efforts, the transmission of viruses, parasites or prions [1].

In the future, demographic changes including an increase of elderly citizens will lead to a further increase of diseases requiring treatment and an increasing

With essential contributions by:

German Society of Anaesthesiology and Intensive Care Medicine (DGAI):

P. Meybohm, Klinik für Anästhesiologie, Intensivmedizin und Schmerztherapie, Universitätsklinikum Frankfurt

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German Society of Surgery (DGCH):

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LIBERAL Trial (2017 - 2019)

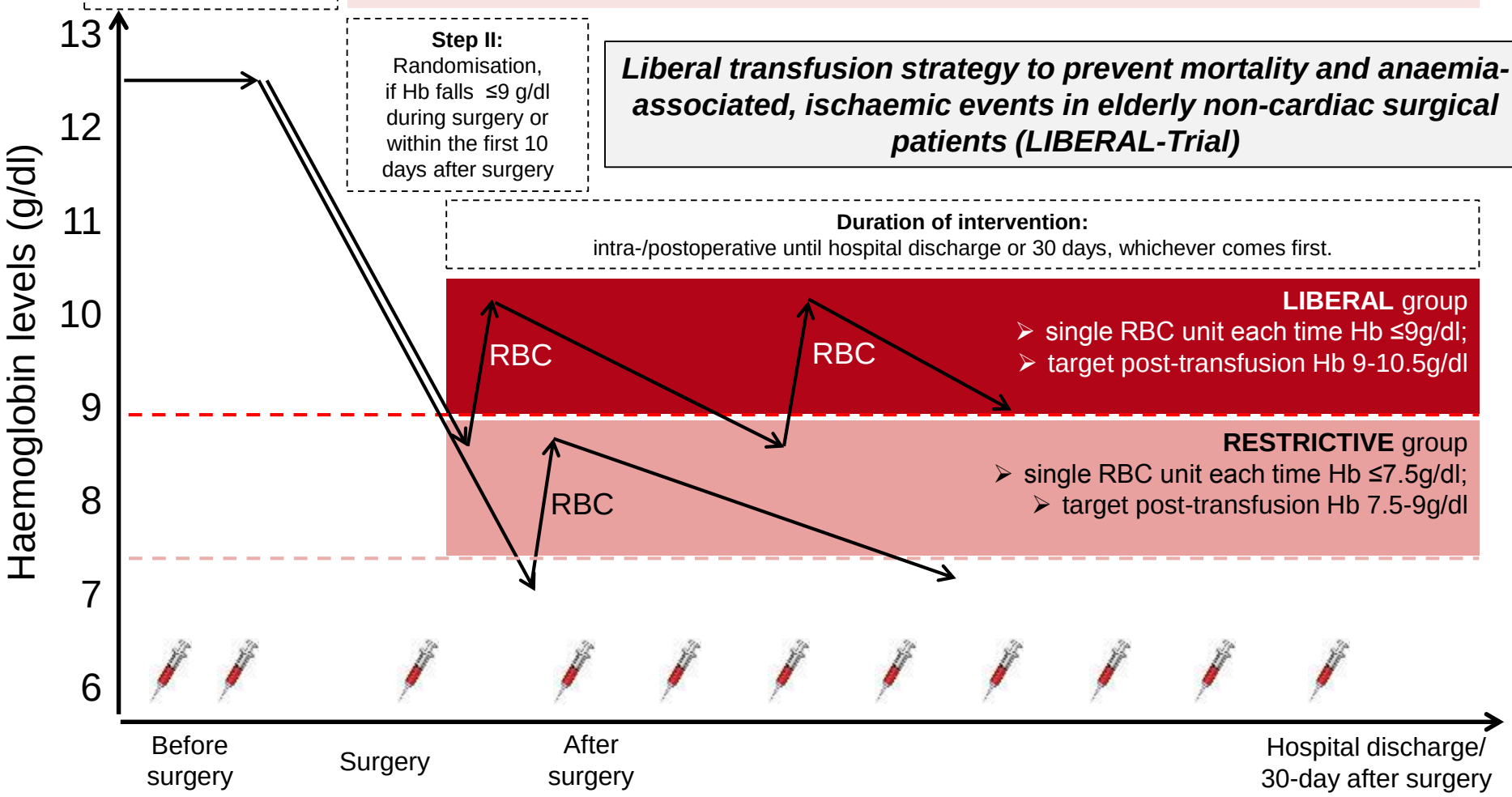
Step I: Registration (age ≥70 years, non-cardiac surgery, informed consent)

No transfusion group

Step II: Randomisation, if Hb falls ≤9 g/dl during surgery or within the first 10 days after surgery

Liberal transfusion strategy to prevent mortality and anaemia-associated, ischaemic events in elderly non-cardiac surgical patients (LIBERAL-Trial)

Duration of intervention:
intra-/postoperative until hospital discharge or 30 days, whichever comes first.



RCT (n=2,470)
Restrictive (RBC if Hb<7.5g/dl) vs.
Liberal (RBC if Hb<9.0g/dl)

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Do it!

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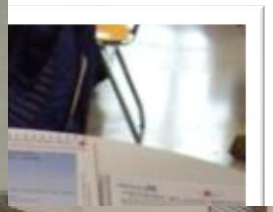
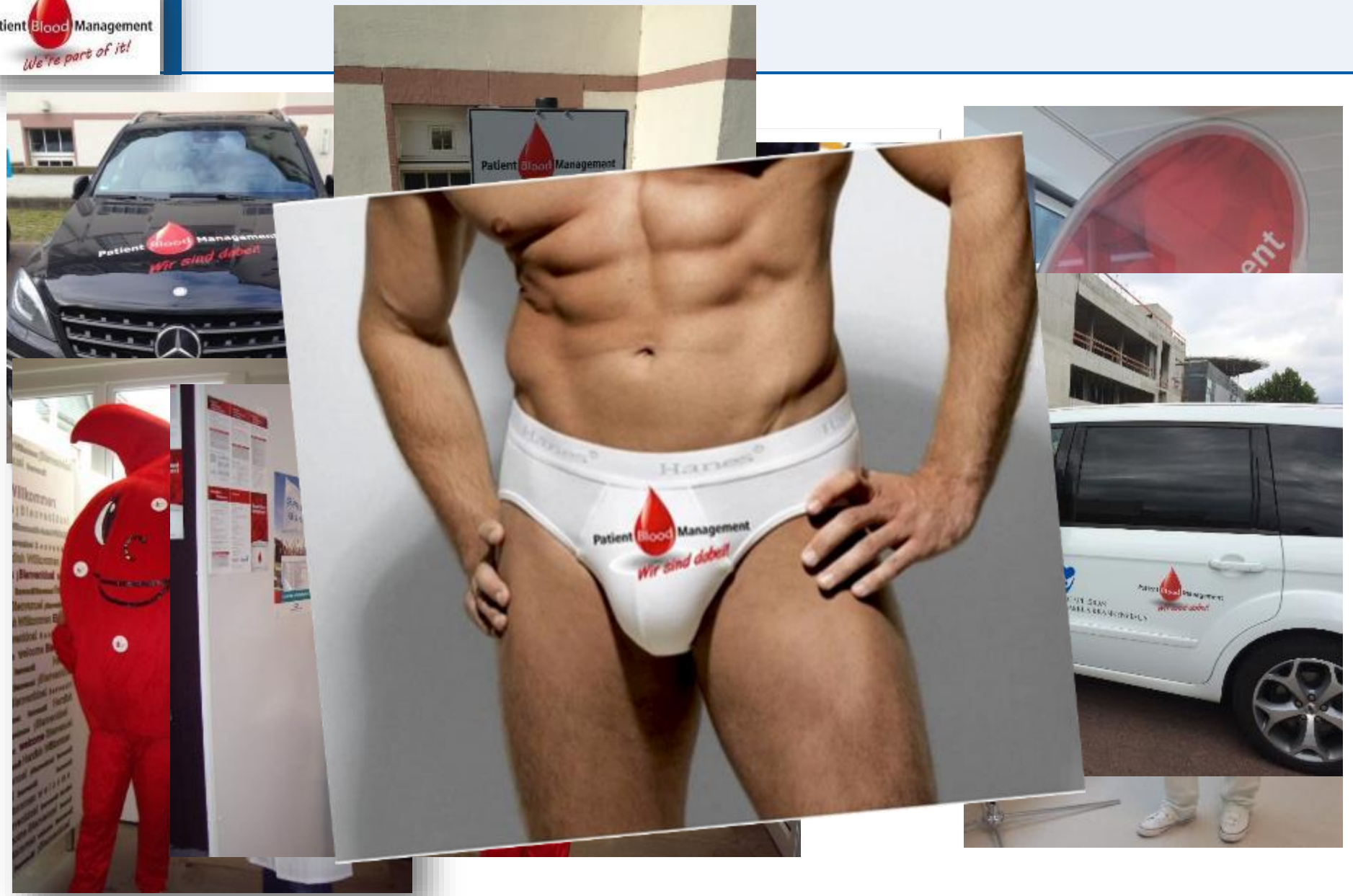
DO it!




Patient Blood Management
We're part of it!
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