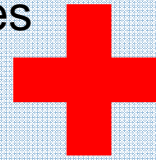


Patient Blood Management  
*Wir sind dabei!*

Deutsches  
Rotes  
Kreuz



UNIVERSITÄTS  
KLINIKUM FRANKFURT



# Patient Blood Management aus der Sicht eines Transfusionsmediziners

Dresden, 18. Oktober 2016

OA Dr. med. Markus M. Müller

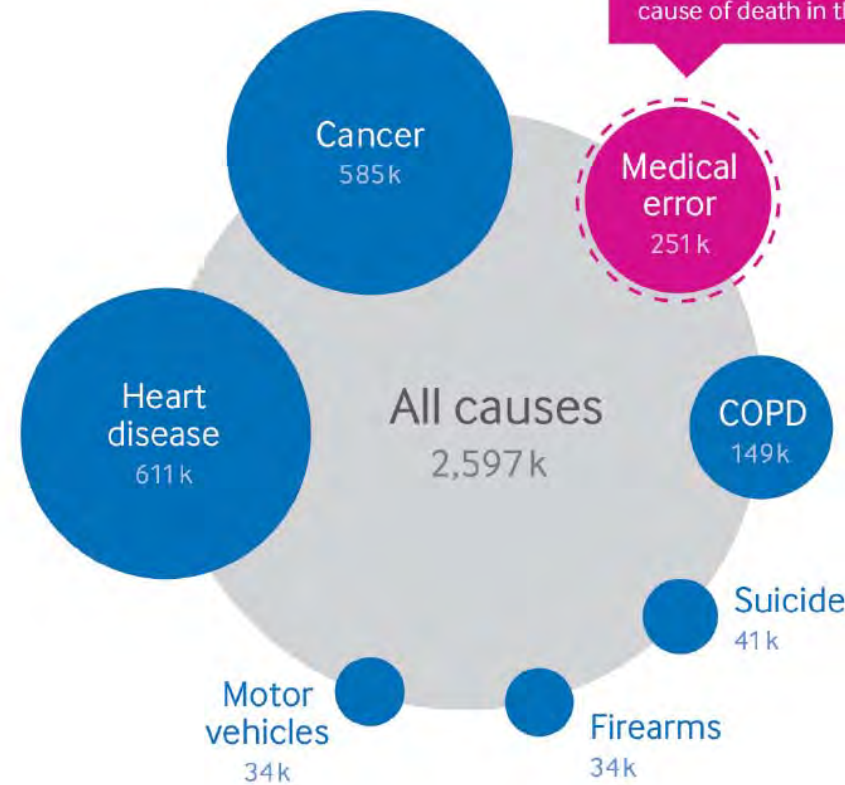


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Direktor: Prof. Dr. Dr. Erhard Seifried



Klinik für Anästhesiologie, Intensivmedizin  
und Schmerztherapie  
Direktor: Prof. Dr. Dr. Kai Zacharowski, FRCA

# Causes of death, US, 2013



Based on our estimate, medical error is the 3rd most common cause of death in the US

Einwohner USA:  
319.000.000 (2014)  
Tod durch med. Fehler:  
251.000/Jahr:  
→ 1 in  
1.271 US-Bürger/Jahr

**Ärztliches Qualitäts-Management**

However, we're not even counting this - medical error is not recorded on US death certificates

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Data source:  
[http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64\\_02.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf)

Quelle: BMJ 2016

Fig 1 Most common causes of death in the United States, 2013<sup>2</sup>



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# Manual of Optimal Blood Use

Support for safe, clinically effective and efficient use of blood in Europe



# Optimal Blood Use

Promoting and sharing best practice across the EU

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## Optimal Blood Use

The Optimal Blood Use website is a resource for the promotion of the effectiveness of the clinical transfusion practice.

*Transfusion of the right unit of blood to the right patient, in the right condition and according to the right practice.*

The content of the website and the accompanying materials from 18 EU countries, named in the Manual, have been translated into a number of languages.

Click on a chapter heading below to browse

- 1. Synopsis
- ▶ 2. Purpose
- ▶ 3. Quality systems
- ▶ 4. Adverse events



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# “Safe transfusion therapy is a process, not only a product!”

*Sunny Dzik, 2001*

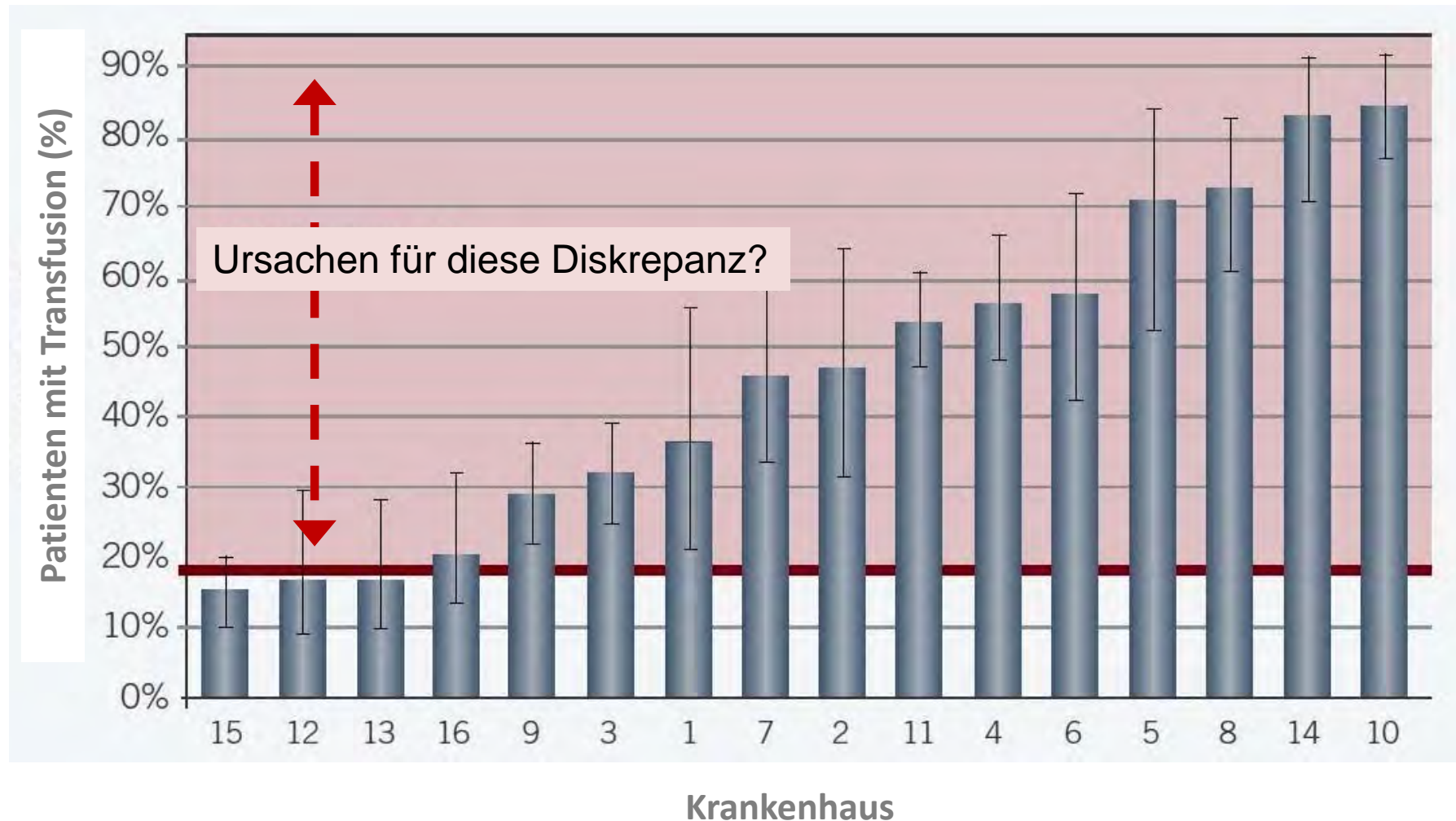


# Drei interessante Ergebnisse aus Voruntersuchungen

---

1.

# Es war einmal im OP ...



Österreichische Benchmark Studie I: n=2.600 Knie- oder Hüft-Totalendoprothese



Gombotz H et al. *Transfusion* 2007;47:1468-1480



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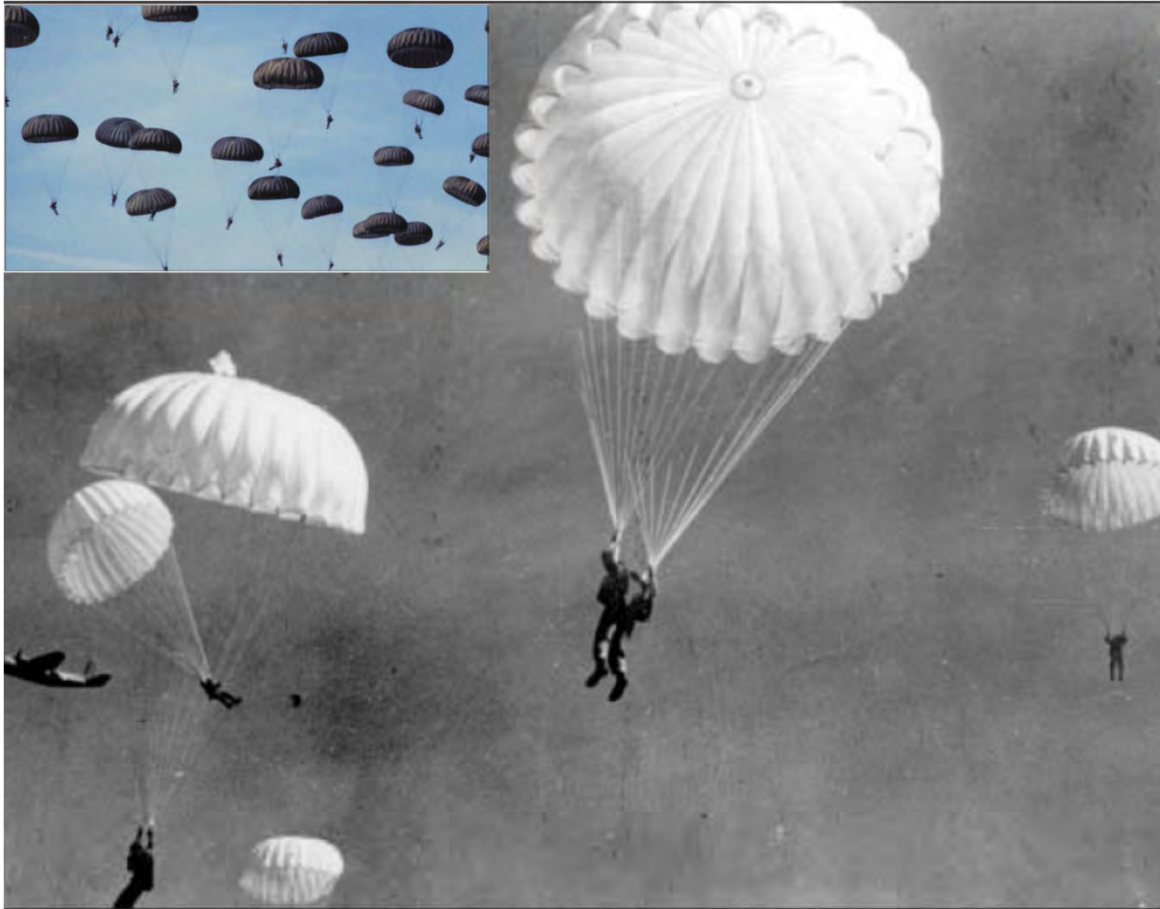
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# Drei interessante Ergebnisse aus Voruntersuchungen

---

2.

# Evidence Based Medicine



Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials



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## What is already known about this topic

Parachutes are widely used to prevent death and major injury after gravitational challenge

Parachute use is associated with adverse effects due to failure of the intervention and iatrogenic injury

Studies of free fall do not show 100% mortality

## What this study adds

No randomised controlled trials of parachute use have been undertaken

The basis for parachute use is purely observational, and its apparent efficacy could potentially be explained by a “healthy cohort” effect

Individuals who insist that all interventions need to be validated by a randomised controlled trial need to come down to earth with a bump

**BMJ** Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith and Jill P Pell

*BMJ* 2003;327:1459-1461  
doi:10.1136/bmj.327.7429.1459

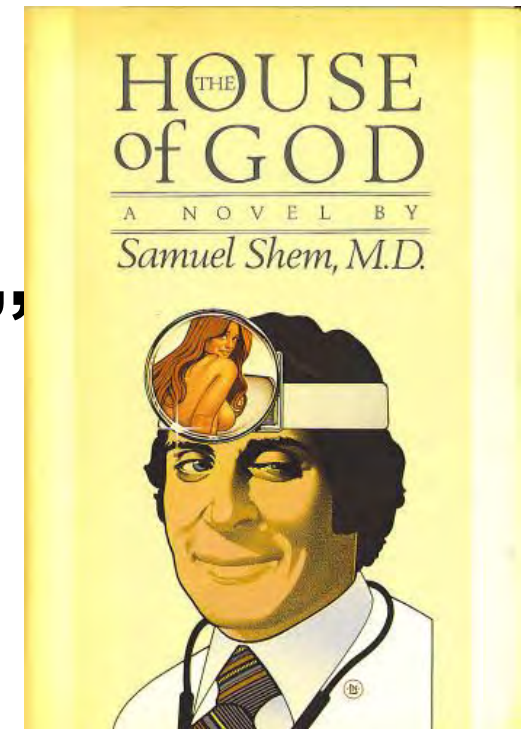


# LAWS OF THE HOUSE OF GOD: XIII

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**“THE DELIVERY OF  
MEDICAL CARE  
IS TO DO AS MUCH  
NOTHING AS POSSIBLE.”**

*Samuel Shem, M.D., 1978*



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# Randomisierte Transfusions- Trigger-Studien für EK (n>40)

**TRICC**

**TRIPICU**

**FOCUS**

**Villanueva**

**FOCUS**

3yr follow up

**TRISS**

**MINT**

(pilot)

**TRACS**

**TITRe2**

**Almeida**

**usw, usf, ....**

# Empfehlungen zur Transfusion von EK bei akuter Anämie (normovolämischer Patient!)

Hämoglobin-Bereich	Kompensation/ Risikofaktoren	Transfusion: JA/NEIN	Be- wertung
≤ 6 g/dL (≤ 3,7 mmol/L)	–	<b>JA</b> (in Einzelfällen niedrigere Hb-Werte tolerabel)	<b>1 C+</b>
> 6 g/dL – 8 g/dL (> 3,7 – 5,0 mmol/L)	Gute Kompensation/ keine Risiken	<b>NEIN</b>	<b>1 C+</b>
	Eingeschr. Kompens. / Risikofaktoren vorh.	<b>JA</b>	<b>1 C+</b>
	Zeichen anämischer Hypoxie	<b>JA</b>	<b>1 C+</b>
> 8 g/dL – 10 g/dL (> 5,0 – 6,2 mmol/L)	Zeichen anämischer Hypoxie	<b>JA</b>	<b>2 C</b>
> 10 g/dL (> 6,2 mmol/L)	–	<b>NEIN</b> (in Einzelfällen auch Transfusion bei Hb-Werten > 10 g/dL)	<b>1 A</b>

# The New England Journal of Medicine

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VOLUME 340

FEBRUARY 11, 1999

NUMBER 6



## A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D.,  
CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.Sc.,  
ELIZABETH YETISIR, M.Sc., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS  
FOR THE CANADIAN CRITICAL CARE TRIALS GROUP\*

# TRICC



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# TRICC Trial (Hebert et al., 1999)

**Methods** We enrolled 838 critically ill patients with euvolemia after initial treatment who had hemoglobin concentrations of less than 9.0 g per deciliter within 72 hours after admission to the intensive care unit and randomly assigned 418 patients to a restrictive strategy of transfusion, in which red cells were transfused if the hemoglobin concentration dropped below 7.0 g per deciliter and hemoglobin concentrations were maintained at 7.0 to 9.0 g per deciliter, and 420 patients to a liberal strategy, in which transfusions were given when the hemoglobin concentration fell below 10.0 g per deciliter and hemoglobin concentrations were maintained at 10.0 to 12.0 g per deciliter.

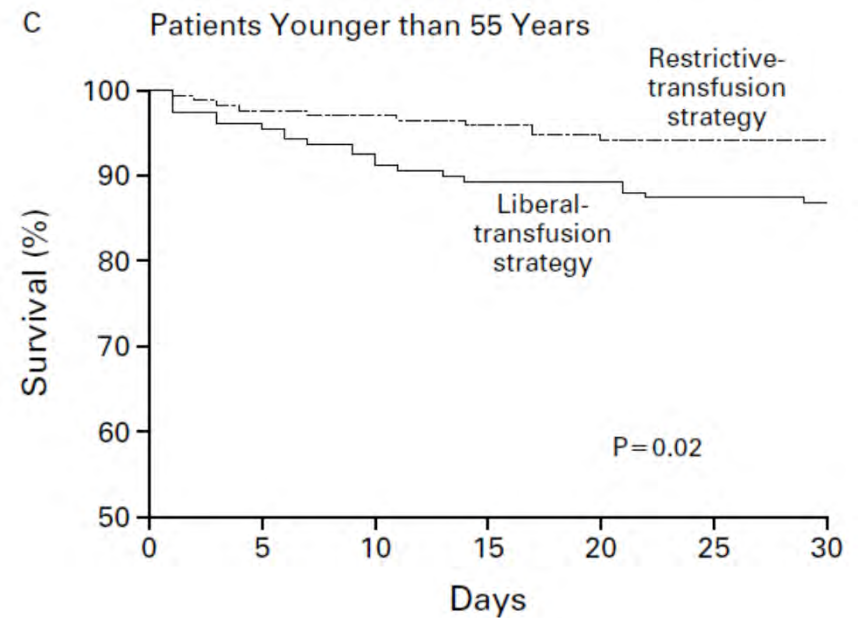
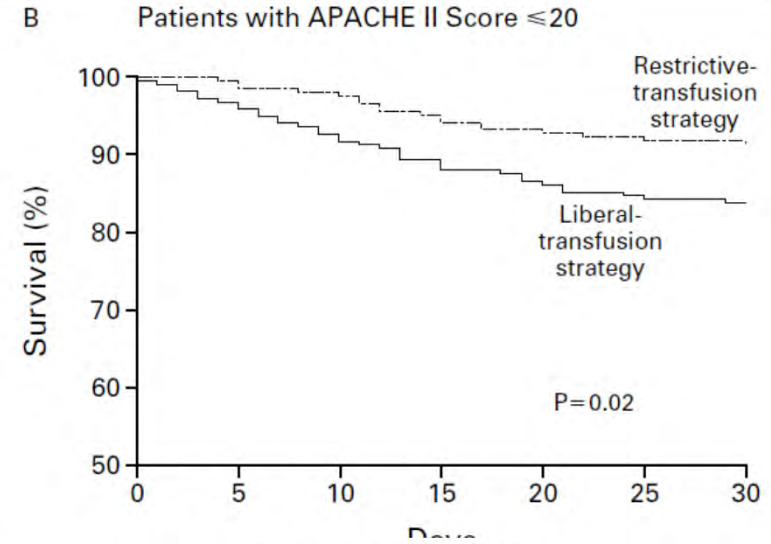
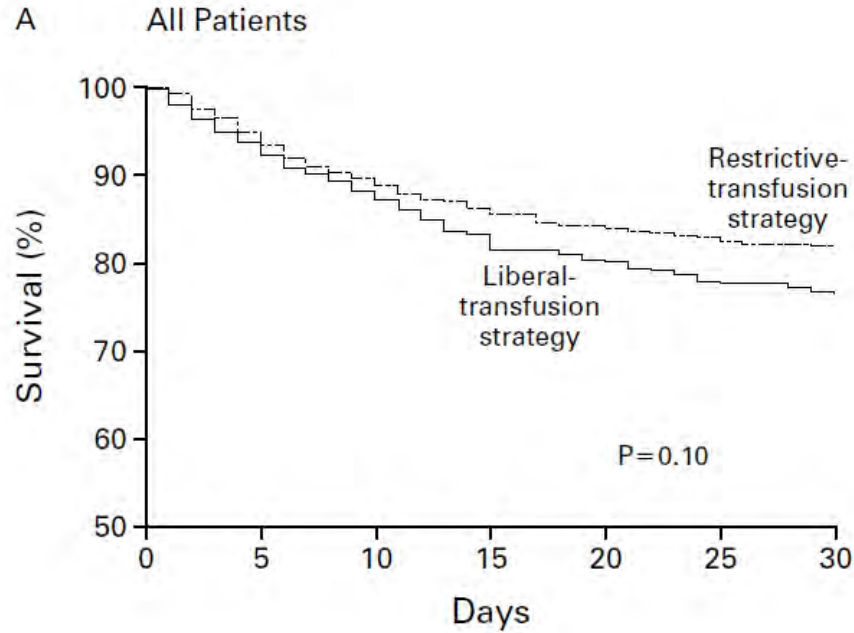
**Conclusions** A restrictive strategy of red-cell transfusion is at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction and unstable angina. (N Engl J Med 1999;340:409-17.)

TABLE 2. OUTCOMES.\*

OUTCOME MEASURE	RESTRICTIVE-TRANSFUSION STRATEGY (N=418)	LIBERAL-TRANSFUSION STRATEGY (N=420)	ABSOLUTE DIFFERENCE BETWEEN GROUPS	95% CONFIDENCE INTERVAL	P VALUE
				percent	
Death — no. (%)					
30-day	78 (18.7)	98 (23.3)	4.7	−0.84 to 10.2	0.11
60-day†	95 (22.7)	111 (26.5)	3.7	−2.1 to 9.5	0.23
ICU	56 (13.4)	68 (16.2)	2.3	−2.0 to 7.6	0.29
Hospital	93 (22.2)	118 (28.1)	5.8	−0.3 to 11.7	0.05
Multiple-organ-dysfunction score					
Unadjusted score	8.3±4.6	8.8±4.4	0.5	−0.1 to 1.1	0.10
Adjusted score‡	10.7±7.5	11.8±7.7	1.1	0.8 to 2.2	0.03
Change from base-line score§	3.2±7.0	4.2±7.4	1.0	0.1 to 2.0	0.04
No. of organs failing — no. (%)					
0	100 (23.9)	82 (19.5)			
1	136 (32.5)	149 (35.5)			
2	109 (26.1)	108 (26.0)			
3	51 (12.2)	63 (15.0)			
>3	22 (5.3)	18 (4.3)	1.8¶	−3.4 to 7.1¶	0.53¶
Length of stay — days					
ICU	11.0±10.7	11.5±11.3	0.5	−1.0 to 2.1	0.53
Hospital	34.8±19.5	35.5±19.4	0.7	−1.9 to 3.4	0.58



# TRICC Trial (Hebert et al., 1999)



# The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2007;356:1609-19.

APRIL 19, 2007

VOL. 356 NO. 16

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## TRIPICU Transfusion Strategies for Patients in Pediatric Intensive Care Units

Jacques Lacroix, M.D., Paul C. Hébert, M.D., James S. Hutchison, M.D., Heather A. Hume, M.D.,  
Marisa Tucci, M.D., Thierry Ducruet, M.Sc., France Gauvin, M.D., Jean-Paul Collet, M.D., Ph.D.,  
Baruch J. Toledano, M.D., Pierre Robillard, M.D., Ari Joffe, M.D., Dominique Biarent, M.D.,  
Kathleen Meert, M.D., and Mark J. Peters, M.D., for the TRIPICU Investigators,\* the Canadian Critical Care  
Trials Group, and the Pediatric Acute Lung Injury and Sepsis Investigators Network

### CONCLUSIONS

In stable, critically ill children a hemoglobin threshold of 7 g per deciliter for red-cell transfusion can decrease transfusion requirements without increasing adverse outcomes. (Controlled-trials.com number, ISRCTN37246456.)



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# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

DECEMBER 29, 2011

VOL. 365 NO. 26

## Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

Jeffrey L. Carson, M.D., Michael L. Terrin, M.D., M.P.H., Helaine Noveck, M.P.H., David W. Sanders, M.D., Bernard R. Chaitman, M.D., George G. Rhoads, M.D., M.P.H., George Nemo, Ph.D., Karen Dragert, R.N., Lauren Beaupre, P.T., Ph.D., Kevin Hildebrand, M.D., William Macaulay, M.D., Courtland Lewis, M.D., Donald Richard Cook, B.M.Sc., M.D., Gwendolyn Dobbin, C.C.R.P., Khwaja J. Zakriya, M.D., Fred S. Apple, Ph.D., Rebecca A. Horney, B.A., and Jay Magaziner, Ph.D., M.S.Hyg., for the FOCUS Investigators\*



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# FOCUS *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

DECEMBER 29, 2011

## Liberal or Restrictive Transfusion in after Hip Surgery

Jeffrey L. Carson, M.D., Michael L. Terrin, M.D., M.P.H., Helaine Novack, M.D.,  
Bernard R. Chaitman, M.D., George G. Rhoads, M.D., M.P.H., George M. Vercoutre, M.D.,  
Lauren Beaupre, P.T., Ph.D., Kevin Hildebrand, M.D., William MacCallister, M.D.,  
Donald Richard Cook, B.M.Sc., M.D., Gwendolyn Dobbin, C.C.R.P., Khwaun-Lee  
Rebecca A. Horney, B.A., and Jay Magaziner, Ph.D., M.S.Hyg.,



### CONCLUSIONS

A liberal transfusion strategy, as compared with a restrictive strategy, did not reduce rates of death or inability to walk independently on 60-day follow-up or reduce in-hospital morbidity in elderly patients at high cardiovascular risk. (Funded by the National Heart, Lung, and Blood Institute; FOCUS ClinicalTrials.gov number, NCT00071032.)

## Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock

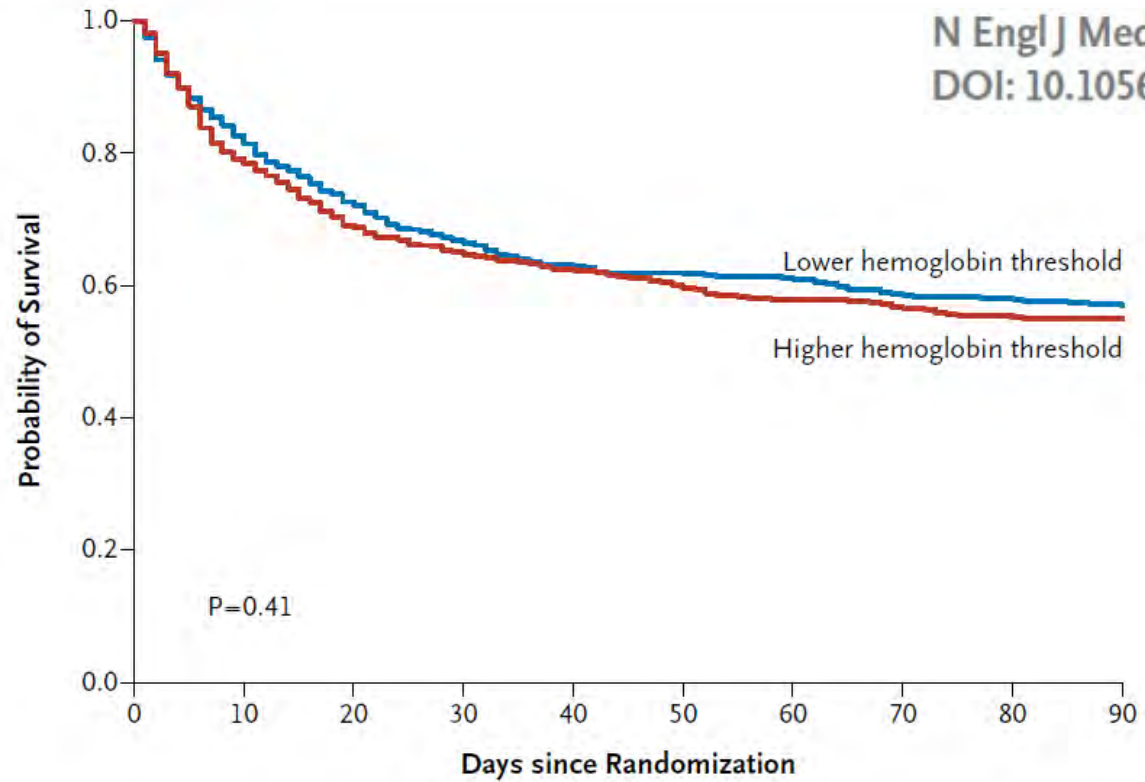
Lars B. Holst, M.D., Nicolai Haase, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Jan Wernerman, M.D., Ph.D.,  
Anne B. Guttormsen, M.D., Ph.D., Sari Karlsson, M.D., Ph.D., Pär I. Johansson, M.D., Ph.D.,  
Anders Åneman, M.D., Ph.D., Marianne L. Vang, M.D., Robert Winding, M.D., Lars Nebrich, M.D.,  
Helle L. Nibro, M.D., Ph.D., Bodil S. Rasmussen, M.D., Ph.D., Johnny R.M. Lauridsen, M.D., Jane S. Nielsen, M.D.,  
Anders Oldner, M.D., Ph.D., Ville Pettilä, M.D., Ph.D., Maria B. Cronhjort, M.D., Lasse H. Andersen, M.D.,  
Ulf G. Pedersen M.D., Nanna Reiter, M.D., Jørgen Wiis, M.D., Jonathan O. White, M.D., Lene Russell, M.D.,  
Klaus J. Thornberg, M.D., Peter B. Hjortrup, M.D., Rasmus G. Müller, M.D., Morten H. Møller, M.D., Ph.D.,  
Morten Steensen, M.D., Inga Tjäder, M.D., Ph.D., Kristina Kilsand, R.N., Suzanne Odeberg-Wernerman, M.D., Ph.D.,  
Brit Sjøbø, R.N., Helle Bundgaard, M.D., Ph.D., Maria A. Thyø, M.D., David Lodahl, M.D., Rikke Mærkedahl, M.D.,  
Carsten Albeck, M.D., Dorte Illum, M.D., Mary Kruse, M.D., Per Winkel, M.D., D.M.Sci.,  
and Anders Perner, M.D., Ph.D., for the TRISS Trial Group\* and the Scandinavian Critical Care Trials Group

### **CONCLUSIONS**

Among patients with septic shock, mortality at 90 days and rates of ischemic events and use of life support were similar among those assigned to blood transfusion at a higher hemoglobin threshold and those assigned to blood transfusion at a lower threshold; the latter group received fewer transfusions. (Funded by the Danish Strategic Research Council and others; TRISS ClinicalTrials.gov number, NCT01485315.)

# TRISS Results

## A Time to Death



### No. at Risk

Lower hemoglobin threshold	502	334	306	286
Higher hemoglobin threshold	496	321	287	273

## Liberal versus restrictive blood transfusion strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial

# FOCUS

Jeffrey L Carson, Frederick Sieber, Donald Richard Cook, Donald R Hoover, Helaine Noveck, Bernard R Chaitman, Lee Fleisher, Lauren Beaupre, William Macaulay, George G Rhoads, Barbara Paris, Aleksandra Zagorin, David W Sanders, Khwaja J Zakriya, Jay Magaziner

### Summary

Source: Lancet 2015;385:1183-9

**Background** Blood transfusion might affect long-term mortality by changing immune function and thus potentially increasing the risk of subsequent infections and cancer recurrence. Compared with a restrictive transfusion strategy, a more liberal strategy could reduce cardiac complications by lowering myocardial damage, thereby reducing future deaths from cardiovascular disease. We aimed to establish the effect of a liberal transfusion strategy on long-term survival compared with a restrictive transfusion strategy.

**Findings** Between July 19, 2004, and Feb 28, 2009, 2016 patients were enrolled and randomly assigned to the two treatment groups: 1007 to the liberal transfusion strategy and 1009 to the restrictive transfusion strategy. The median duration of follow-up was 3·1 years (IQR 2·4–4·1 years), during which 841 (42%) patients died. Long-term mortality did not differ significantly between the liberal transfusion strategy (432 deaths) and the restrictive transfusion strategy (409 deaths) (hazard ratio 1·09 [95% CI 0·95–1·25];  $p=0\cdot21$ ).

**Interpretation** Liberal blood transfusion did not affect mortality compared with a restrictive transfusion strategy in a high-risk group of elderly patients with underlying cardiovascular disease or risk factors. The underlying causes of death did not differ between the trial groups. These findings do not support hypotheses that blood transfusion leads to long-term immunosuppression that is severe enough to affect long-term mortality rate by more than 20–25% or cause of death.



# Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease

Jeffrey L. Carson, MD,<sup>a</sup> Maria Mori Brooks, PhD,<sup>b</sup> J. Dawn Abbott, MD,<sup>c</sup> Bernard Chaitman, MD,<sup>d</sup> Sheryl F. Kelsey, PhD,<sup>b</sup> Darrell J. Triulzi, MD,<sup>c</sup> Vankeepuram Srinivas, MD,<sup>f</sup> Mark A. Menegus, MD,<sup>f</sup> Oscar C. Marroquin, MD,<sup>g</sup> Sunil V. Rao, MD,<sup>h</sup> Helaine Noveck, MPH,<sup>a</sup> Elizabeth Passano, MS,<sup>b</sup> Regina M. Hardison, MS,<sup>b</sup> Thomas Smitherman, MD,<sup>g</sup> Tudor Vagaonescu, MD,<sup>i</sup> Neil J. Wimmer, MD,<sup>j</sup> and David O. Williams, MD<sup>j</sup> *New Brunswick, NJ; Pittsburgh, PA; Providence, RI; Saint Louis, MO; New York, NY; Durham, NC; and Boston, MA*

**Results** Baseline characteristics were similar between groups except age (liberal, 67.3; restrictive, 74.3). The mean number of units transfused was 1.6 in the liberal group and 0.6 in the restrictive group. The primary outcome occurred in 6 patients (10.9%) in the liberal group and 14 (25.5%) in the restrictive group (risk difference = 15.0%; 95% confidence interval of difference 0.7% to 29.3%;  $P = .054$  and adjusted for age  $P = .076$ ). Death at 30 days was less frequent in liberal group ( $n = 1$ , 1.8%) compared to restrictive group ( $n = 7$ , 13.0%;  $P = .032$ ).

**Conclusions** The liberal transfusion strategy was associated with a trend for fewer major cardiac events and deaths than a more restrictive strategy. These results support the feasibility of and the need for a definitive trial. (Am Heart J 2013;165:964-971.e1.)

Pilotstudie: n=110 Patienten mit ACS oder stabiler AP vor Herzkatheter



# The NEW ENGLAND JOURNAL of MEDICINE

TITRe2

ESTABLISHED IN 1812

MARCH 12, 2015

N Engl J Med 2015;372:997-1008.

DOI: 10.1056/NEJMoa1403612

## Liberal or Restrictive Transfusion after Cardiac Surgery

### RESULTS CONCLUSIONS

A restrictive transfusion threshold after cardiac surgery was not superior to a liberal threshold with respect to morbidity or health care costs. (Funded by the National Institute for Health Research Health Technology Assessment program; Current Controlled Trials number, ISRCTN70923932.)

There was no indication of heterogeneity according to subgroup. There were more deaths in the restrictive-threshold group than in the liberal-threshold group (4.2% vs. 2.6%; hazard ratio, 1.64; 95% CI, 1.00 to 2.67;  $P=0.045$ ). Serious postoperative complications, excluding primary-outcome events, occurred in 35.7% of participants in the restrictive-threshold group and 34.2% of participants in the liberal-threshold group. Total costs did not differ significantly between the groups.



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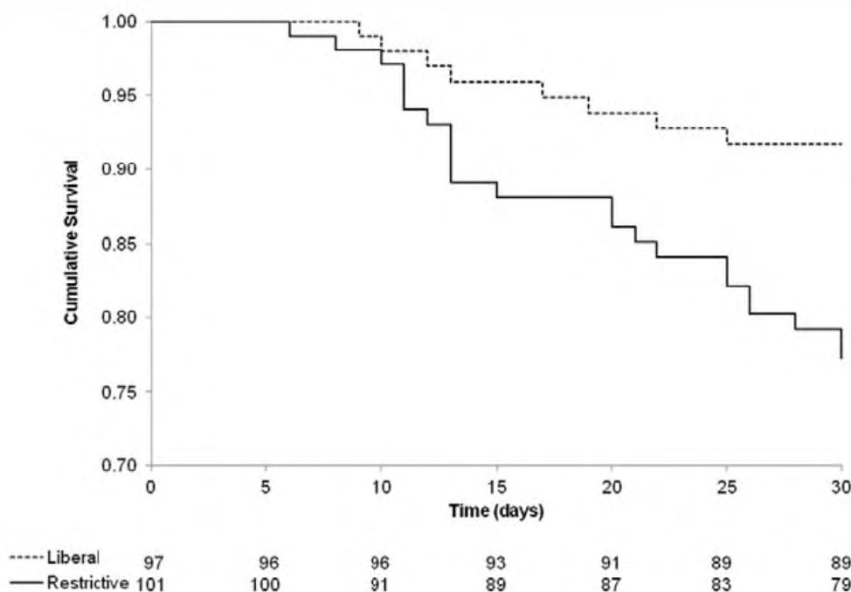


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und Schmerztherapie  
Direktor: Prof. Dr. Dr. Kai Zacharowski, FRCA

# Transfusion Requirements in Surgical Oncology Patients

## *A Prospective, Randomized Controlled Trial*

Juliano Pinheiro de Almeida, M.D., Jean-Louis Vincent, M.D., Ph.D.,  
Filomena Regina Barbosa Gomes Galas, M.D., Ph.D., Elisangela Pinto Marinho de Almeida, M.D.,  
Julia T. Fukushima, M.Sc., Eduardo A. Osawa, M.D., Fabricio Bergamin, M.D., Clarice Lee Park, M.D.,  
Rosana Ely Nakamura, M.D., Silvia M. R. Fonseca, M.D., Guilherme Cutait, M.D.,  
Joseane Inacio Alves, R.N., Mellik Bazan, P.T., Silvia Vieira, R.N., Ana C. Vieira Sandrini, L.D.N.,  
Henrique Palomba, M.D., Ph.D., Ulysses Ribeiro, Jr., M.D., Ph.D., Alexandre Crippa, M.D.,  
Marcos Dalloglio, M.D., Ph.D., Maria del Pilar Estevez Diz, M.D., Ph.D., Roberto Kalil Filho, M.D., Ph.D.,  
Jose Otavio Costa Auler, Jr., M.D., Ph.D., Andrew Rhodes, M.B., B.S.,



### What We Already Know about This Topic

- It remains unknown whether a liberal or restrictive transfusion strategy is superior in patients having major cancer surgery

### What This Article Tells Us That Is New

- In 198 patients randomly assigned to erythrocyte transfusions at a hemoglobin concentration of 7 or 9 g/dl
- Major complications were nearly twice as common in patients managed with the restrictive approach as in those managed with the liberal approach (36 vs. 20%)
- This study supports a more liberal transfusion strategy in major cancer surgery

**Conclusion:** A liberal erythrocyte transfusion strategy with a hemoglobin trigger of 9 g/dl was associated with fewer major postoperative complications in patients having major cancer surgery compared with a restrictive strategy. (**ANESTHESIOLOGY 2015; 122:29-38**)

# Restrictive *versus* Liberal Transfusion Strategy in the Perioperative and Acute Care Settings

## *A Context-specific Systematic Review and Meta-analysis of Randomized Controlled Trials*

Frédérique Hovaguimian, M.D., M.Clin.Res.Meth.,

Paul S. Myles, M.B.B.S., M.P.H., M.D., F.C.A.I., F.A.N.Z.C.A., F.R.C.A., F.A.H.M.S.

### ABSTRACT

---

**Background:** Blood transfusions are associated with morbidity and mortality. However, restrictive thresholds could harm patients less able to tolerate anemia. Using a *context-specific* approach (according to patient characteristics and clinical settings), the authors conducted a systematic review to quantify the effects of transfusion strategies.

**Methods:** The authors searched MEDLINE, EMBASE, CENTRAL, and grey literature sources to November 2015 for randomized controlled trials comparing restrictive *versus* liberal transfusion strategies applied more than 24 h in adult surgical or critically ill patients. Data were independently extracted. Risk ratios were calculated for 30-day complications, defined as inadequate oxygen supply (myocardial, cerebral, renal, mesenteric, and peripheral ischemic injury; arrhythmia; and unstable angina), mortality, composite of both, and infections. Statistical combination followed a *context-specific* approach. Additional analyses explored transfusion protocol heterogeneity and cointerventions effects.

**Results:** Thirty-one trials were regrouped into five *context-specific* risk strata. In patients undergoing cardiac/vascular procedures, restrictive strategies seemed to increase the risk of events reflecting inadequate oxygen supply (risk ratio [RR], 1.09; 95% CI, 0.97 to 1.22), mortality (RR, 1.39; 95% CI, 0.95 to 2.04), and composite events (RR, 1.12; 95% CI, 1.01 to 1.24—3322, 3245, and 3322 patients, respectively). Similar results were found in elderly orthopedic patients (inadequate oxygen supply: RR, 1.41; 95% CI, 1.03 to 1.92; mortality: RR, 1.09; 95% CI, 0.80 to 1.49; composite outcome: RR, 1.24; 95% CI, 1.00 to 1.54—3465, 3546, and 3749 patients, respectively), but not in critically ill patients. No difference was found for infections, although a protective effect may exist. Risk estimates varied with successful/unsuccessful transfusion protocol implementation.

**Conclusions:** Restrictive transfusion strategies should be applied with caution in high-risk patients undergoing major surgery. (ANESTHESIOLOGY 2016; 125:46-61)



**REVIEW**

**Open Access**

# Restrictive and liberal red cell transfusion strategies in adult patients: reconciling clinical data with best practice

Marek A Mirski<sup>1\*</sup>, Steven M Frank<sup>1</sup>, Daryl J Kor<sup>2</sup>, Jean-Louis Vincent<sup>3</sup> and David R Holmes Jr<sup>2</sup>

restrictive, Hb-based RBC transfusion practices in bleeding patients – or those at high risk for hemorrhage – may be hazardous. In patients with ischemic brain, spinal cord, or myocardium, or in debilitated patients requiring prolonged functional recovery, the optimal Hb transfusion trigger remains unknown, but may be higher than for a severe, restrictive algorithm. Until future studies further define the role of RBC transfusion in these specific clinical scenarios, a restrictive transfusion strategy should be recommended within the well-studied patient populations and clinical conditions, and the clinicians must continue to use their experience and bedside clinical judgment to advocate the best management for their patients.

# Methodologic quality assessment of red blood cell transfusion guidelines and the evidence base of more restrictive transfusion thresholds

*Hans Van Remoortel,<sup>1</sup> Emmy De Buck,<sup>1</sup> Tessa Dieltjens,<sup>1</sup> Nele S. Pauwels,<sup>1</sup> Veerle Compernelle,<sup>1,2</sup> and Philippe Vandekerckhove<sup>1,2,3</sup>*

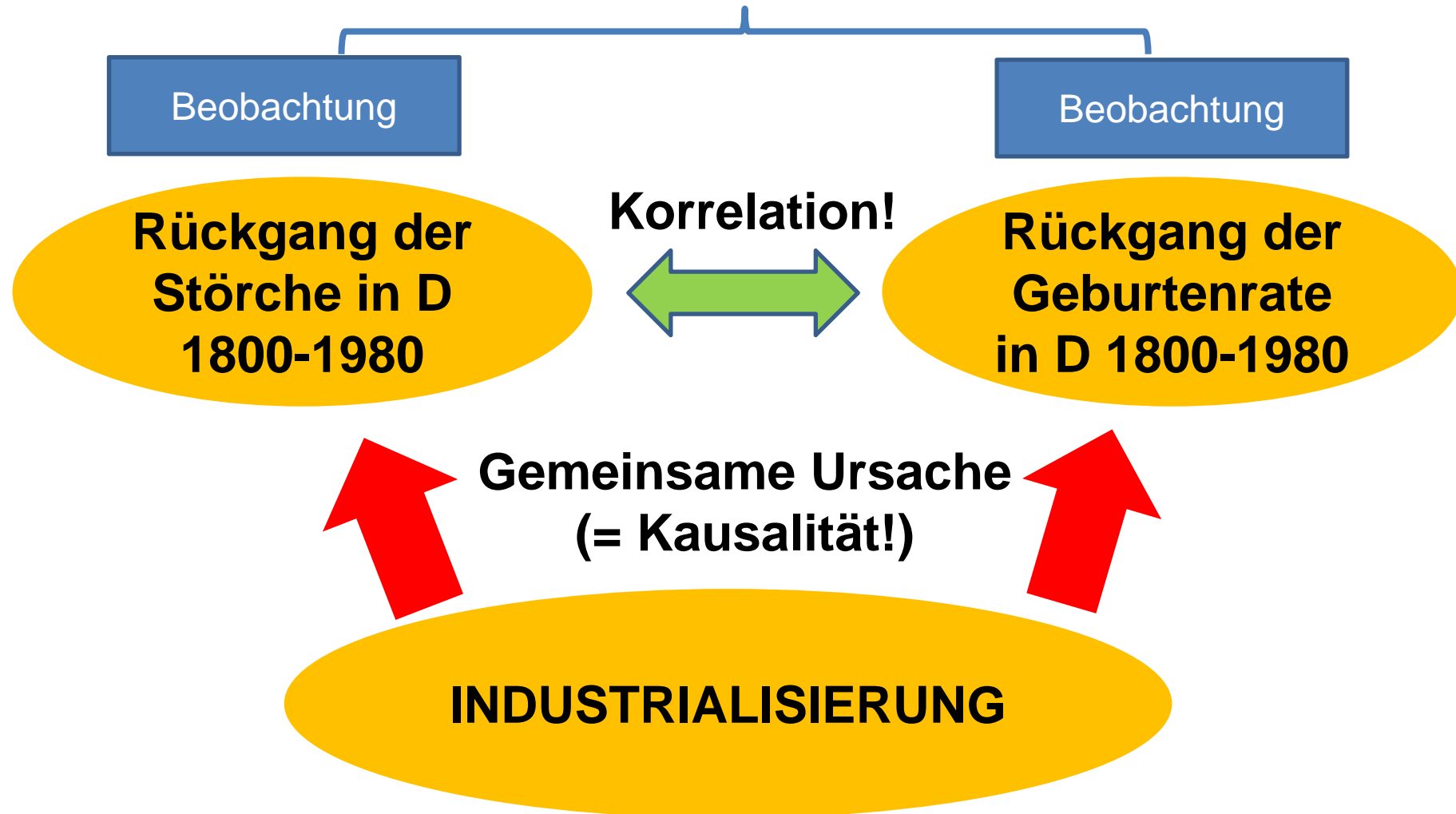
**TRANSFUSION** 2016;56;472–480

Therefore, we aimed to evaluate the quality of the development process of RBC transfusion guidelines and to investigate the underlying evidence of guidelines recommending a more restrictive hemoglobin (Hb) threshold.

**RESULTS:** The methodologic quality of 13 RBC transfusion guidelines was variable (18%-72%) but highest for those developed by Advancing Transfusion and Cellular Therapies Worldwide (72%), the Task Force of Advanced Bleeding Care in Trauma (70%), and the Dutch Institute for Healthcare Improvement (61%). A Hb level of less than 7 g/dL (intensive care unit patients) or less than 8 g/dL (postoperative patients) were the only thresholds based on high-quality evidence. Only four of 32 recommendations had a high-quality evidence base.



# Korrelation $\neq$ Kausalität



# Drei interessante Ergebnisse aus Voruntersuchungen

---

3.



## 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

### Summary

Lancet 2011; 378: 1396-407

Published Online  
October 6, 2011  
DOI:10.1016/S0140-6736(11)61381-0

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

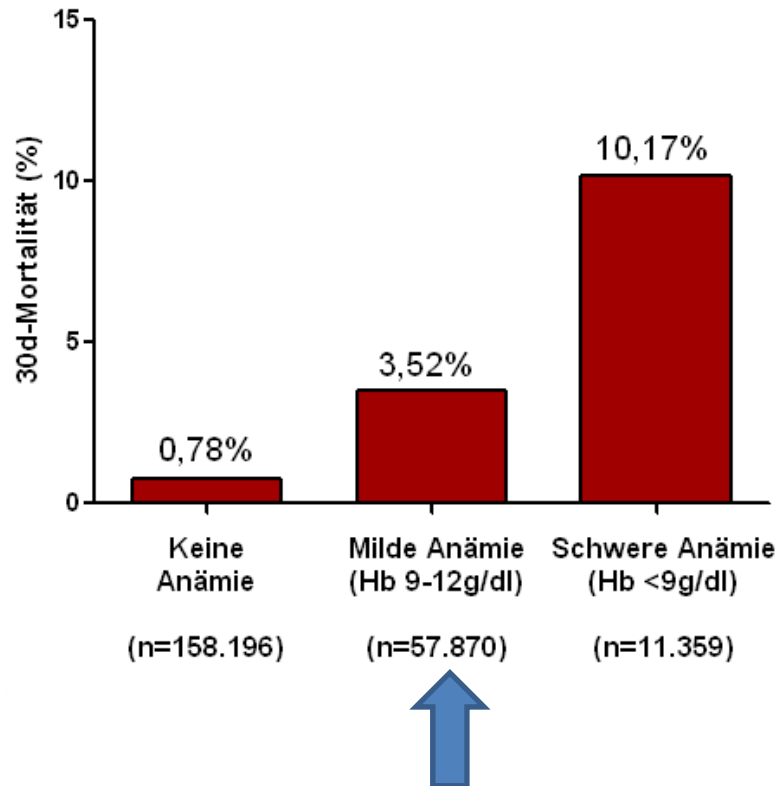
**Background** Preoperative anaemia is associated with adverse outcomes a non-cardiac surgery are not well established. We aimed to assess the el postoperative morbidity and mortality in patients undergoing major non-ca

**Methods** We analysed data for patients undergoing major non-cardiac surge Surgeons' National Surgical Quality Improvement Program database (a pro 211 hospitals worldwide in 2008). We obtained anonymised data for 3 respiratory, CNS, urinary tract, wound, sepsis, and venous thromboen preoperative and perioperative risk factors. We used multivariate logisti modified (nine predefined risk factor subgroups) effect of anaemia, w concentration >29-<39% in men and >29-<36% in women) or moderate- postoperative outcomes.

**Findings** We obtained data for 227 425 patients, of whom 69 229 (30·44%) ha postoperative mortality at 30 days was higher in patients with anaemia than i 1·42, 95% CI 1·31-1·54); this difference was consistent in mild anaemia ( anaemia (1·44, 1·29-1·60). Composite postoperative morbidity at 30 days than in those without anaemia (adjusted OR 1·35, 1·30-1·40), again consis 1·26-1·36) and moderate-to-severe anaemia (1·56, 1·47-1·66). When comj defined risk factor, patients with anaemia and most risk factors had a high morbidity than did patients with either anaemia or the risk factor alone.

**Interpretation** Preoperative anaemia, even to a mild degree, is independe 30-day morbidity and mortality in patients undergoing major non-cardiac s

**Funding** Vifor Pharma.



Retrospektive Datenanalyse (n=227.425 nicht-herzchirurgische Patienten)

➔ Musallam K et al. *Lancet* 2011;378:1396-407



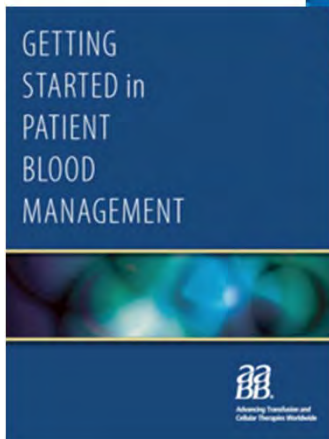
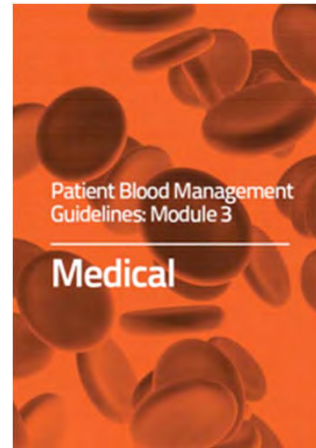
Institut für Transfusionsmedizin und Immunhämatologie  
DRK-Blutspendedienst Baden-Württemberg – Hessen  
Direktor: Prof. Dr. Dr. Erhard Seifried



Klinik für Anästhesiologie, Intensivmedizin  
und Schmerztherapie  
Direktor: Prof. Dr. Dr. Kai Zacharowski, FRCA



# PBM Konzepte weltweit



**Programme**  
Monday 18th June 2012  
A joint initiative with The Department of Health  
and The National Blood Transfusion Committee



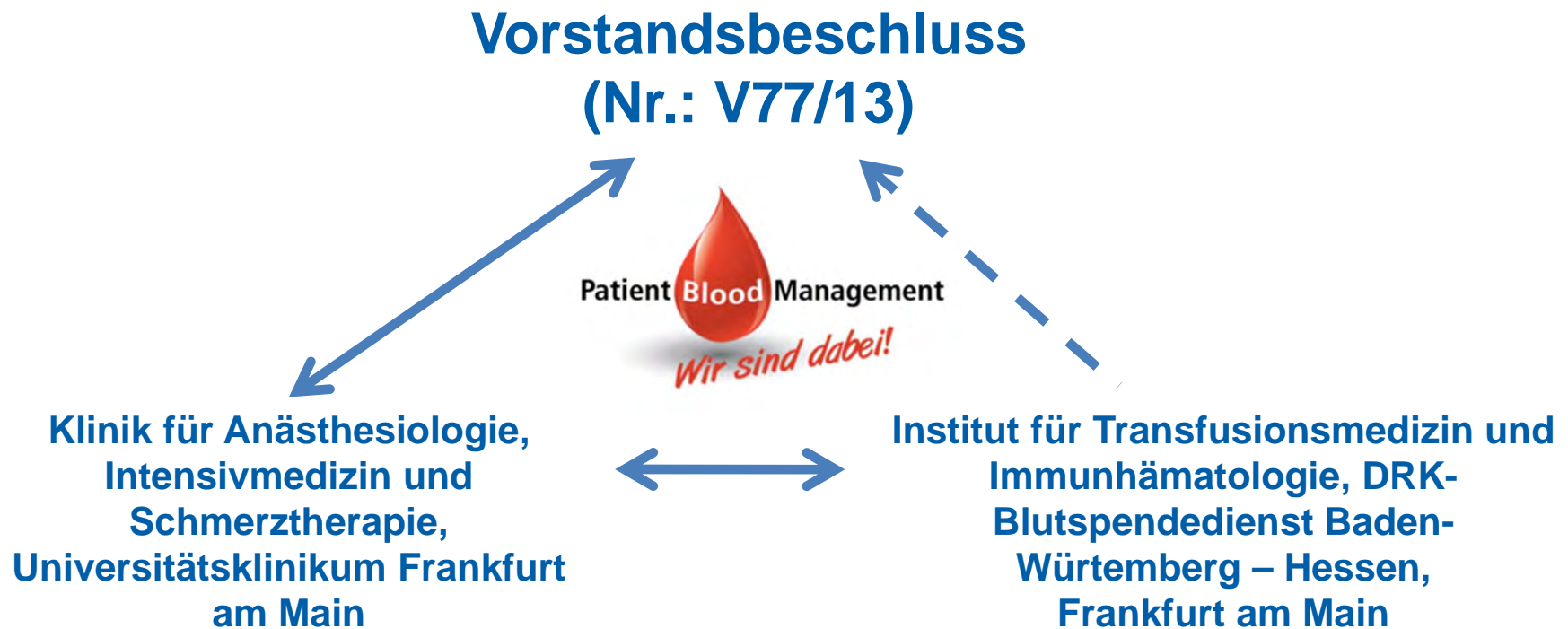
**Institut für Transfusionsmedizin und Immunhämatologie**  
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**Klinik für Anästhesiologie, Intensivmedizin  
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## Patient Blood Management

### - Klinisches Projekt zur Steigerung der Patientensicherheit



# Patient Blood Management

- **Klinisches Projekt zur Steigerung der Patientensicherheit in 9 Kliniken (THG, ACH, UCH, URO, GCH, NCH, HNO, MKPG, GYN)**

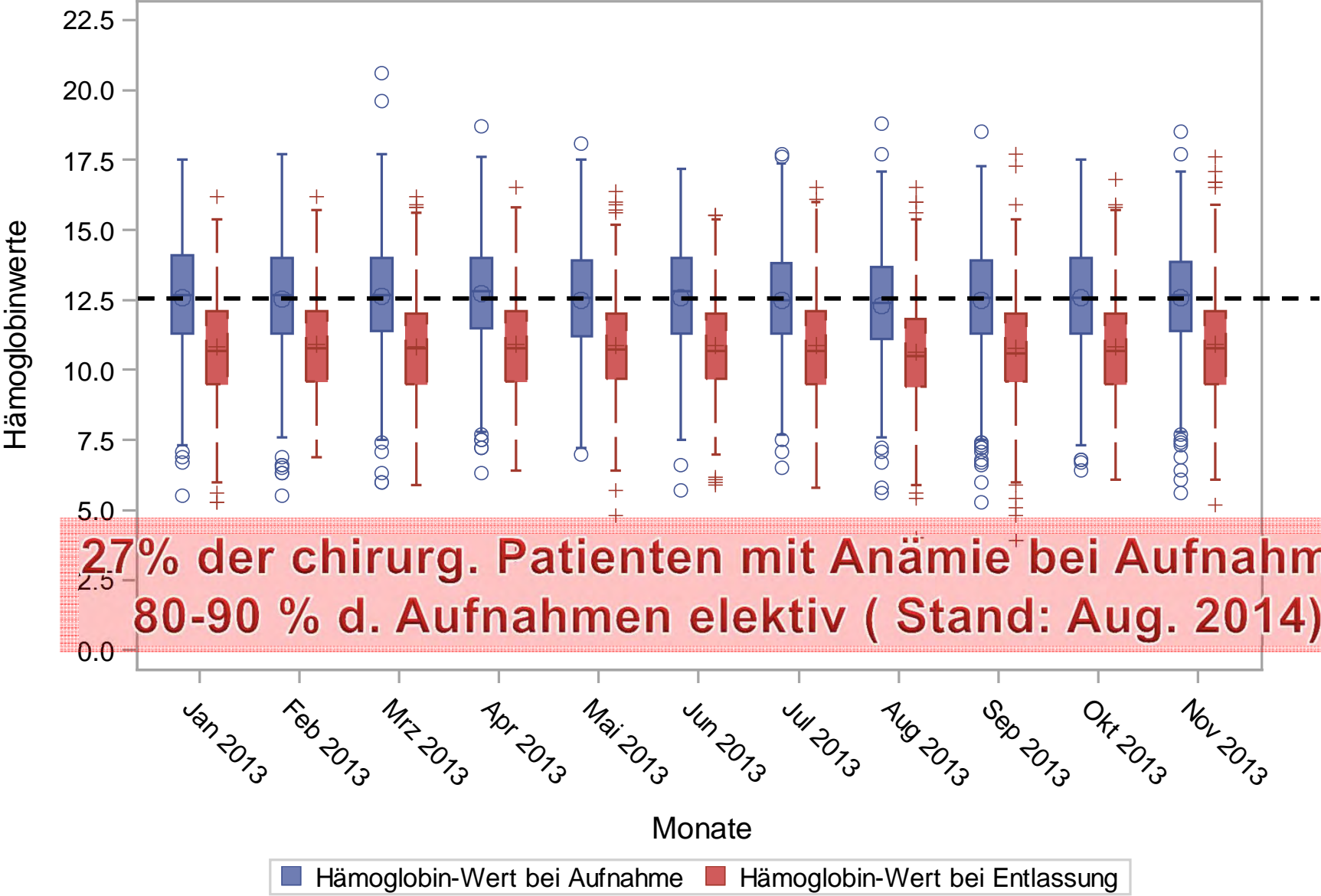
### 1. Optimierung der präoperativen Anämie

Optimierung der Anämie bei elektiven Eingriffen (Transfusionsrisiko >10%) über ein „PBM-/Anämiekonsil“, Nutzen der Wartezeit auf die OP, ggf. OP-Termin verschieben

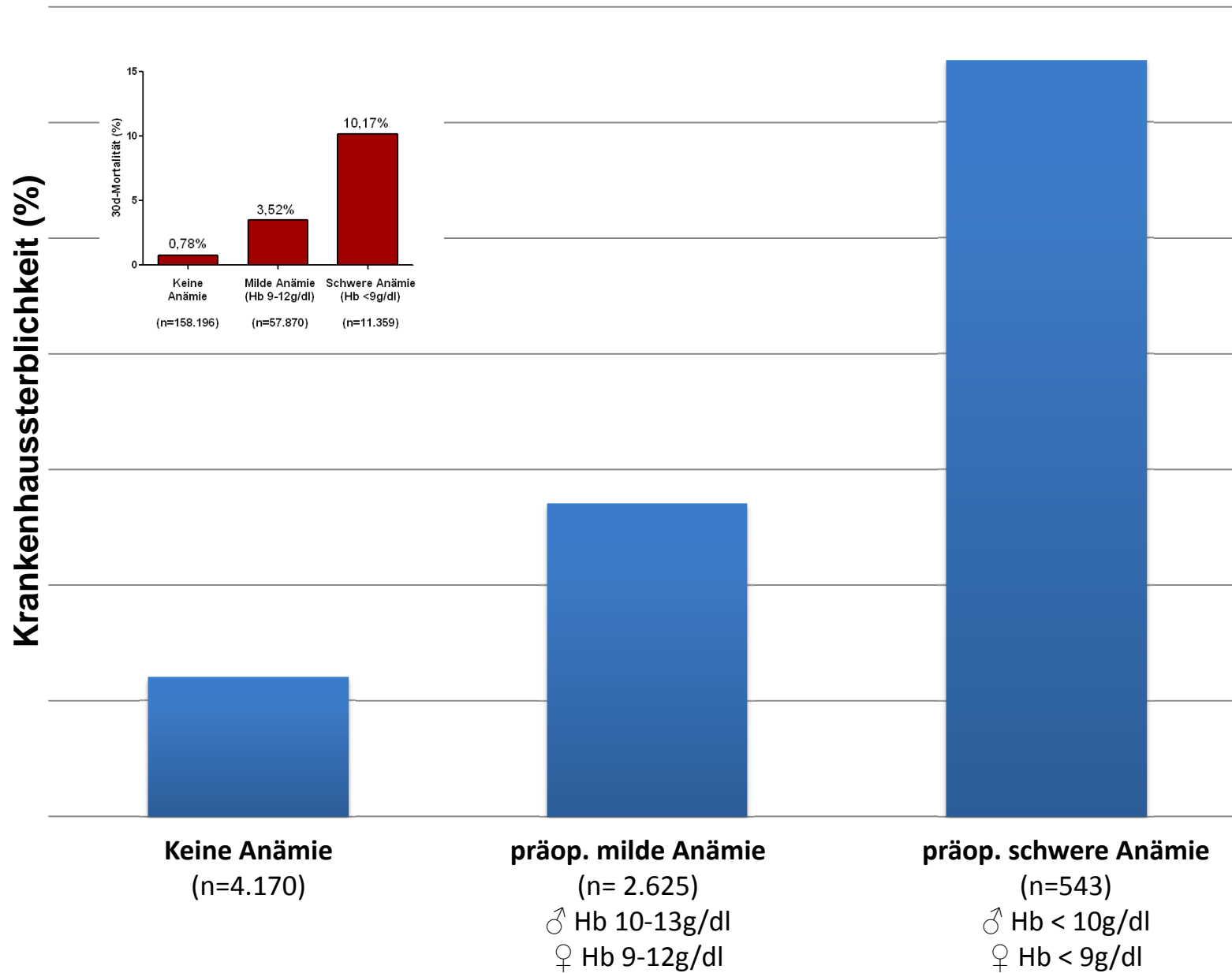




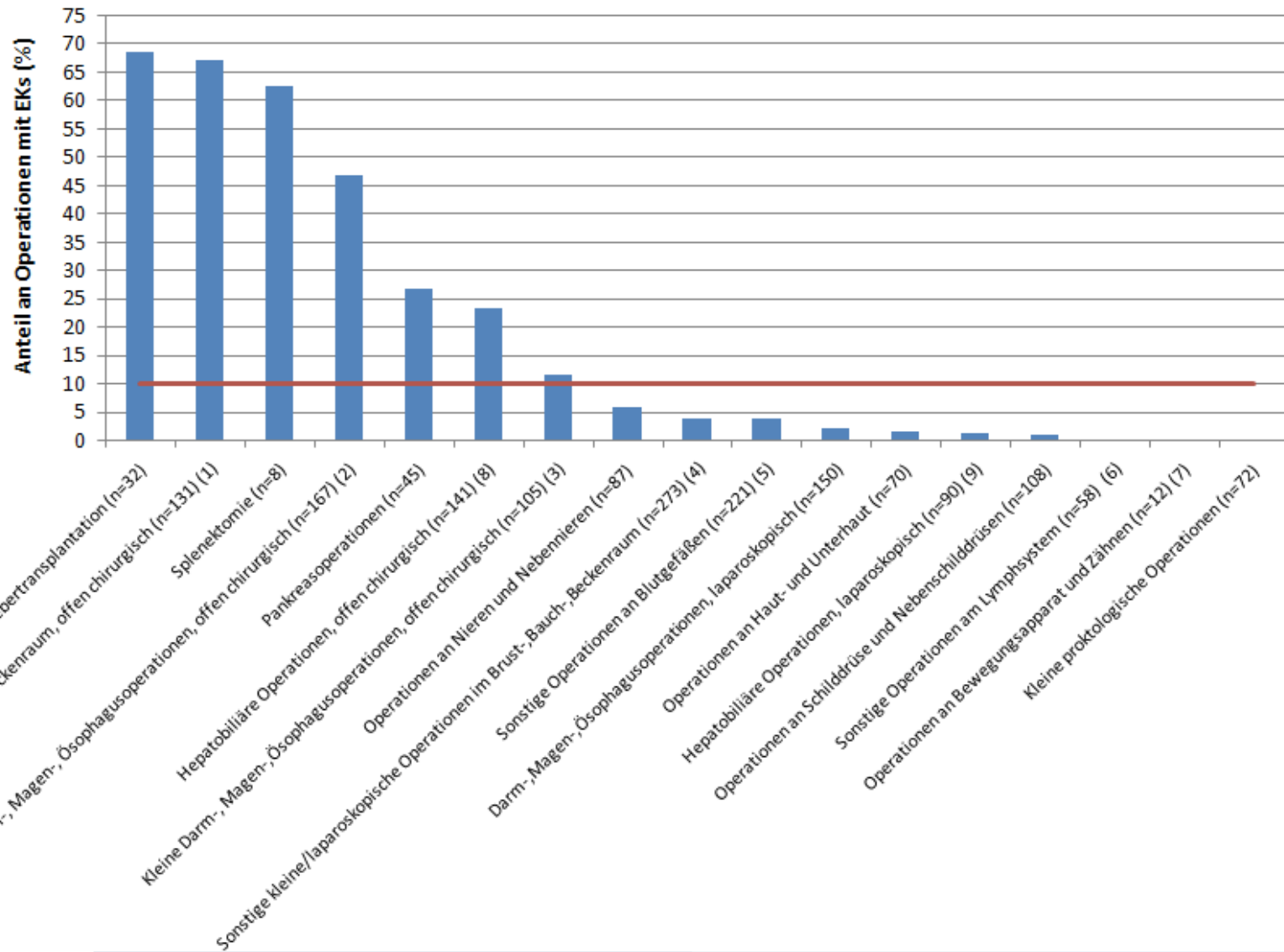
### Hämoglobinwerte insgesamt



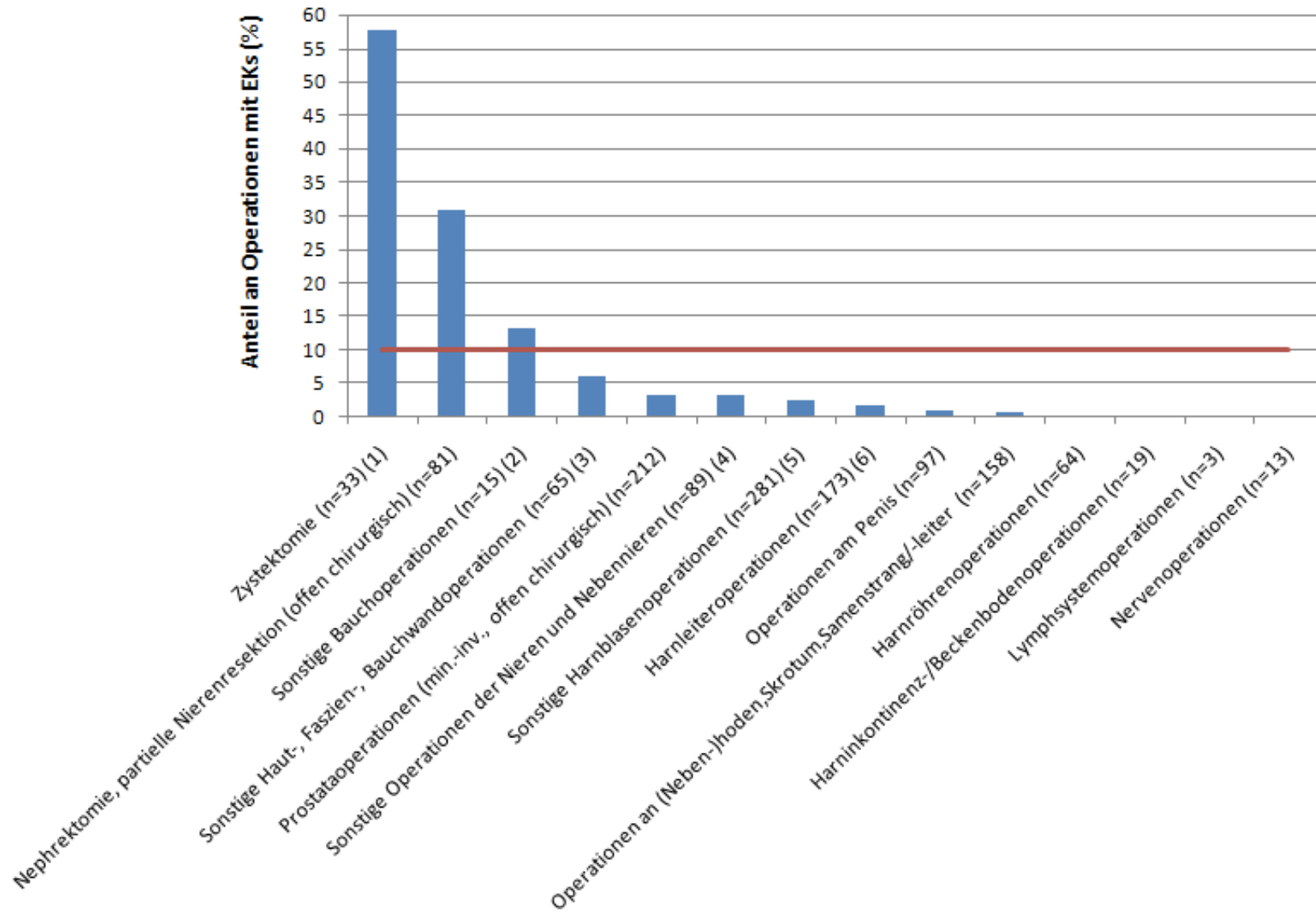
# Krankenhaussterblichkeit (UKF 2013)

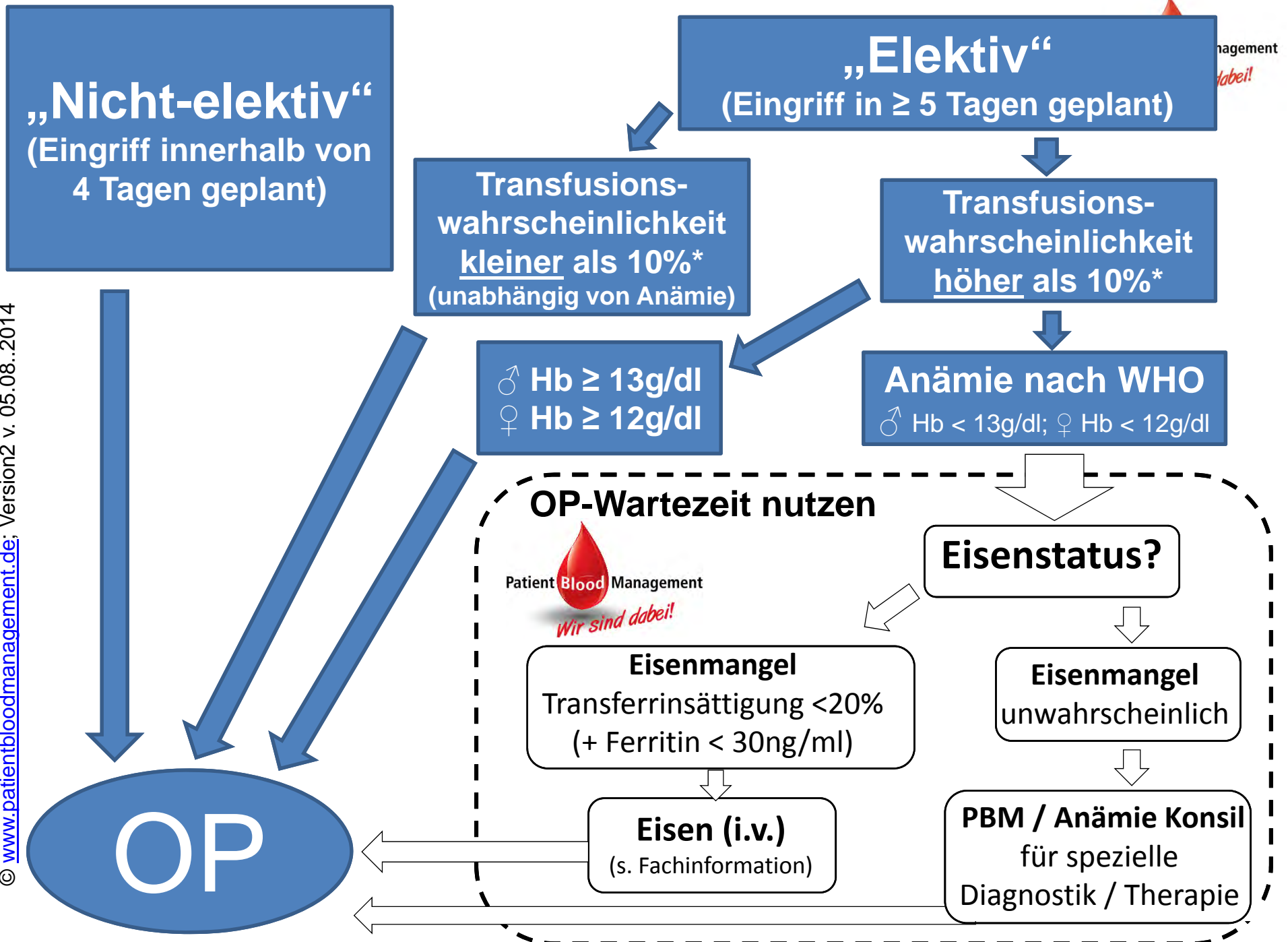


## Allgemeinchirurgie



## Urologie





# Anämiediagnostik in Frankfurt



ORBIS(3) 16.07.2013 13:50:59 KGU@KHVUX 08.04.19.05.0001600

File Bearbeiten Extra Administration 2 vom Test, Dipl.-Math. Manfred 6170179 \*02.02.1940

**Anforderung Funktionsstellen (PBM-Konsil Anämie)**

Anforderung  
 Auftragsdatum: 16.07.2013 13:50  
 Leistungserbringer: PBM-Konsil Anämieabklärung  
 Orgaeinheit 2: Hals-Nasen-Ohrenheilkunde  
 Orgaeinheit 1: 8-6 HNO/Kinder  
 Anforderer: [ ]  
 Externer Arzt: [ ]  
 Kostenstelle: wird automatisch berechnet  
 Berechnung: Aus dem Fall

Terminwunsch: am 16.07.2013 um [ ]  
 Kommentar: ehemals MRSA (Kontrollabstriche)  
 Cave: gehfähig

Geplante Operation mit Blutungsrisiko > 10% :  
 Blutabnahme Anämie/PBM (Lauris Profil) erfolgt  Wartezeit > 2 Wochen

Größe: [ ] cm  
 Hb-Wert: [ ]  
 BMI: [ ] kg/m<sup>2</sup>

**Anamnestiche Informationen**

- Gynäkologisch
- Gastroenterologisch

**blutiger Urin**

**Hämoptysen**

**sonstige Blutungszeichen:**

**Hämoccult-Test:**

Kurzhilfe  
 Ausschneiden STRG+X  
 Kopieren STRG+C  
 Einfügen STRG+V  
 Rückgängig STRG+Z  
 Wiederherstellen STRG+Y  
 Textbausteine  
 Sonderzeichen  
 Klinik für Allgemein- und Viszeralchirurgie  
 Klinik für Frauenheilkunde und Geburtshilfe  
 Klinik für Gefäß- und Endovascularchirurgie  
 Klinik für Hals-, Nasen-, Ohrenheilkunde  
 Klinik für Mund-, Kiefer- und Plastische Gesichtschirurgie  
 Klinik für Neurochirurgie  
 Klinik für Thorax-, Herz- und Thorakale Gefäßchirurgie  
 Klinik für Unfall-, Hand-, und Wiederherstellungschirurgie  
 Klinik für Urologie und Kinderurologie

Bestimmungen

**Auftrag**

ZL Routine Anforderung

- Dringlichkeit: Routine**
- Abnahmezeitpunkt**
- Klinische Chemie**
  - Kreatinin i.S.
  - Harnstoff i.S.
  - Bilirubin dir. i. S. (neu)
  - Bilirubin ges. i.S.
  - GOT i.S.
  - GPT i.S.
  - Alk. Phosphatase i.S.
  - GGT i.S.
  - LDH i.S.
  - Eisen i.S.
  - Haptoglobin i.S.
- Hämatologie**
  - Blutbild
  - Differentialblutbild BB
  - Manuelles Diff
  - Retikulozyten ( maschinell )
- Eisenstoffwechsel**
  - Transferrin i.S.
  - Ferritin i.S.
  - Folsäure im Serum
  - Vitamin B12 im Serum
  - Totale Eisenbindungskapazität
  - Transferrin-Sättigung

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### 1. Optimierung der präoperativen Anämie

Optimierung der Anämie bei elektiven Eingriffen (Transfusionsrisiko >10%) über ein „PBM-/Anämiekonsil“, Nutzen der Wartezeit auf die OP, ggf. OP-Termin verschieben

### 2. Rationaler Einsatz von Erythrozytenkonzentraten

Strenges Einhalten der Querschnitts-Leitlinien der Bundesärztekammer mittels 'Checkliste' der Transfusionstrigger



# Empfehlungen zur Transfusion von EK bei akuter Anämie (normovolämischer Patient!)



Hämoglobin-Bereich	Kompensation/ Risikofaktoren	Transfusion: JA/NEIN	Be- wertung
≤ 6 g/dL (≤ 3,7 mmol/L)	–	<b>JA</b> (in Einzelfällen niedrigere Hb-Werte tolerabel)	<b>1 C+</b>
> 6 g/dL – 8 g/dL (> 3,7 – 5,0 mmol/L)	Gute Kompensation/ keine Risiken	<b>NEIN</b>	<b>1 C+</b>
	Eingeschr. Kompens. / Risikofaktoren vorh.	<b>JA</b>	<b>1 C+</b>
	Zeichen anämischer Hypoxie	<b>JA</b>	<b>1 C+</b>
> 8 g/dL – 10 g/dL (> 5,0 – 6,2 mmol/L)	Zeichen anämischer Hypoxie	<b>JA</b>	<b>2 C</b>
> 10 g/dL (> 6,2 mmol/L)	–	<b>NEIN</b> (in Einzelfällen auch Transfusion bei Hb-Werten > 10 g/dL)	<b>1 A</b>





## Querschnitts-Leitlinien (BÄK) zur Therapie mit Blutkomponenten und Plasmaderivaten

### 4. Auflage 2008

Herausgegeben vom Vorstand der Bundesärztekammer auf  
Empfehlung des Wissenschaftlichen Beirats



Querschnitts-Leitlinien (BÄK) zur Therapie mit  
Blutkomponenten 2008; 1-171

## Transfusionstrigger-Checkliste

Bei jeder EK erneut Angabe des Transfusionstriggers!!!!!!

(Ausnahme: Massivtransfusion)

### Hb < 6 g/dl

Unabhängig von Kompensationsfähigkeit

### Hb 6 - 8 g/dl

Hinweise auf anämische Hypoxie (Tachykardie, Hypotension, EKG-Ischämie, Laktatazidose)

Kompensation eingeschränkt, Risikofaktoren vorhanden (KHK, Herzinsuff, zerebro-vaskuläre Erkrankungen)

(Sonstige Indikation: .....)

-----  
*Die Transfusion bei einem Hb > 8g/dl ist mit einem  
unklaren Nutzen-Risiko Verhältnis verbunden.*

Hb > 8 g/dl (Indikation nur in Einzelfällen;  
sehr schwacher Empfehlungsgrad (2 C))



ORBIS(2) 06.12.2013 10:01:48 KGU@SPIEL1 08.04.19.06.0000800

File Bearbeiten Extra Administration ? KG ACH ANÄSTHESIE/C1 HMAPPES

Mustermann, Herbert 6024273 \*09.08.1946

Bereiche/Übersichten - Anforderungen BSD - im Test [KG ACH] > Anforderung BSD\*

Anforderung Absenden an BSD Vorbereiten Freigabe Blutentnahme Freigabe Arzt

Bestrahlungsindikation Alle Etiketten drucken Etiketten nachdrucken Hilfe

	unbekannt	Nein	Ja
ABO-Blutgruppe !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rh !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Anti-erythrozytäre Alloantikörper !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<b>Frühere Transfusionen</b>	<b>unbekannt</b>	<b>Nein</b>	<b>Ja</b>
länger als 3 Monate zurückliegend !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
in den letzten 3 Monaten:			
außerhalb der Uniklinik FFM !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
in der Uniklinik FFM !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Frühere Knochenmark- oder Butstammzelltransplantation !	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<b>Hämatologischer Patient</b>			<input type="radio"/>
<b>CMV negativ</b>			<input type="radio"/>

**Transfusionstrigger-Checkliste**

**Hb < 6 g/dl**

- Unabhängig von Kompensationsfähigkeit

**Hb 6 - 8 g/dl**

- Hinweise auf anämische Hypoxie (Tachykardie, Hypotension, EKG-Ischämie, Laktatazidose)
- Kompensation eingeschränkt, Risikofaktoren vorhanden (KHK, Herzinsuff, zerebro-vaskuläre Erkrankungen)
- Sonstige Indikation:

**Hb 8 - 10 g/dl**

- Hinweise auf anämische Hypoxie (Tachykardie, Hypotension, EKG-Ischämie, Laktatazidose)
- Sonstige Indikation:

**Hb > 10 g/dl**

- 

**Zusatzinfos:**

**Nachrichten:**

Meldungen

HB

Bitte geben Sie in der Transfusionstrigger-Checkliste einen Hb-Wert an!



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### 2. Rationaler Einsatz von Erythrozytenkonzentraten

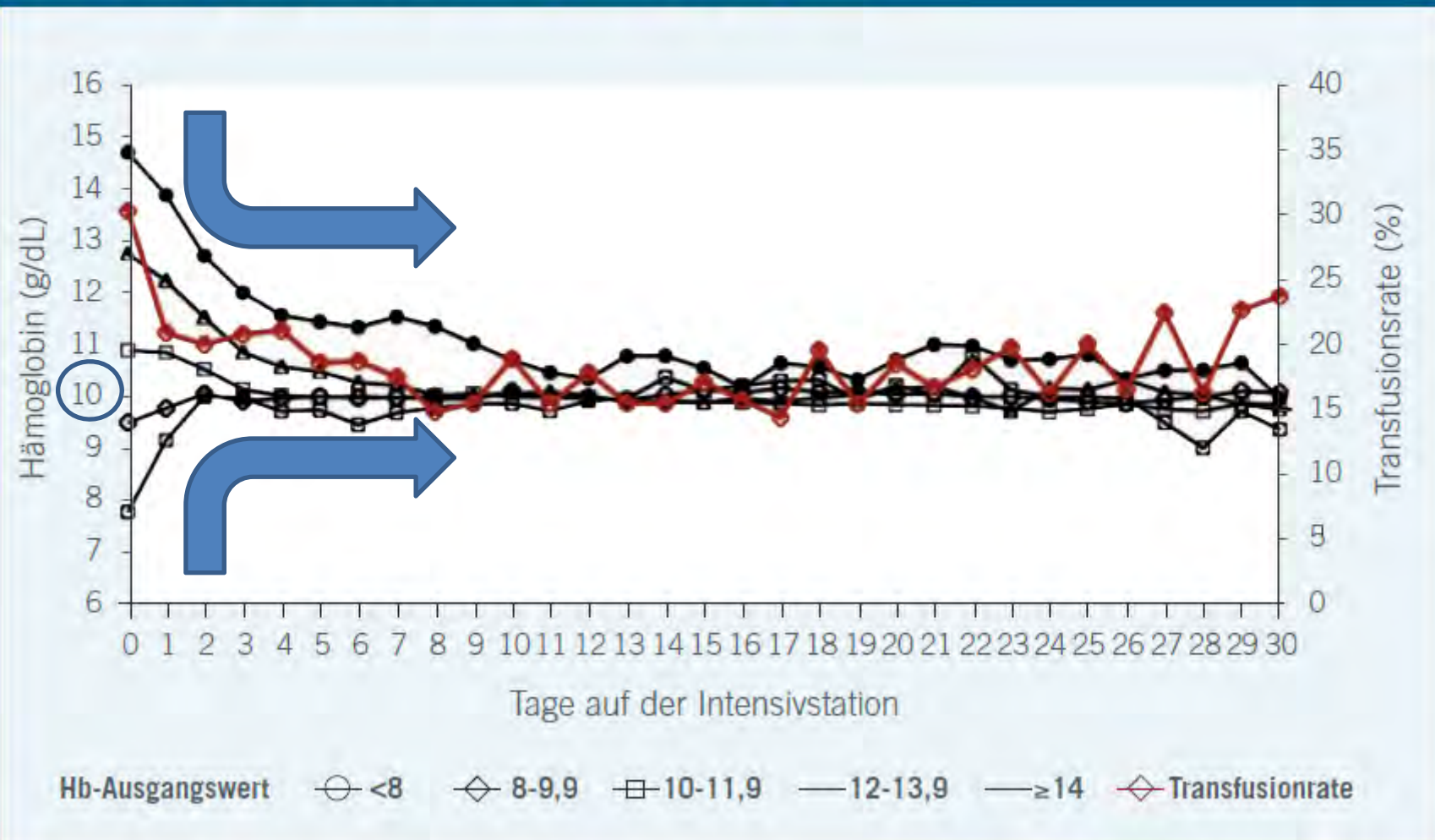
Strenges Einhalten der Querschnitts-Leitlinien der Bundesärztekammer mittels 'Checkliste' der Transfusionstrigger

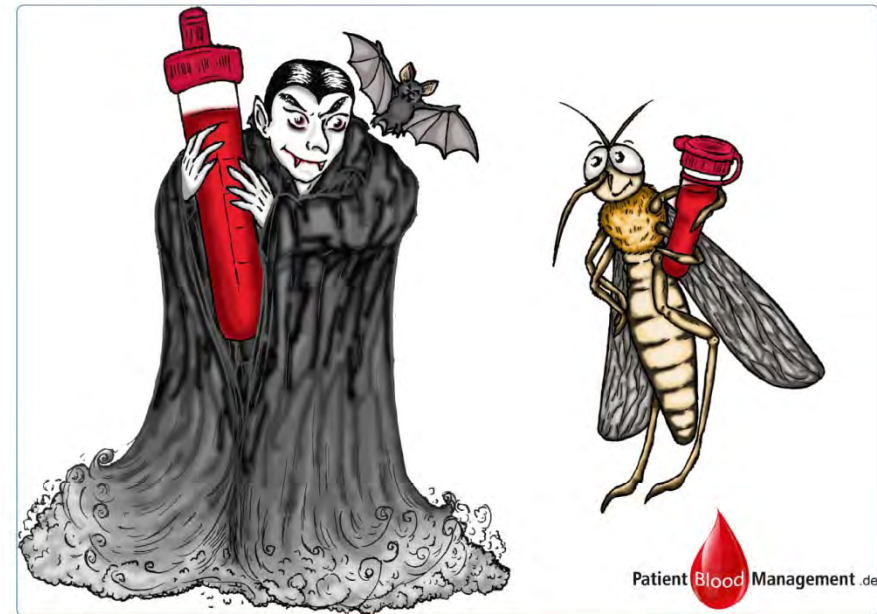
### 3. Weitere Fremdblutsparende Maßnahmen

Restriktive Blutentnahmen, Reduktion Blutverlust, Cell-Saver Einsatz, Wärmemanagement, Point-of-Care Diagnostik, Gerinnungsmanagement



## Abb. 2: Hämoglobinverlauf auf einer Intensivstation nach herz- und thoraxchirurgischen Eingriffen





Fischer et al. *Critical Care* 2014, 18:306  
<http://ccforum.com/content/18/3/306>



## VIEWPOINT

# Savoring every drop

Dania Patricia Fischer, Kai D Zacharowski\* and P

# Savoring every drop – Vampire or Mosquito?

Fischer et al.

 **BioMed Central**

Fischer et al. *Critical Care* 2014, 18:306  
<http://ccforum.com/content/18/3/306>

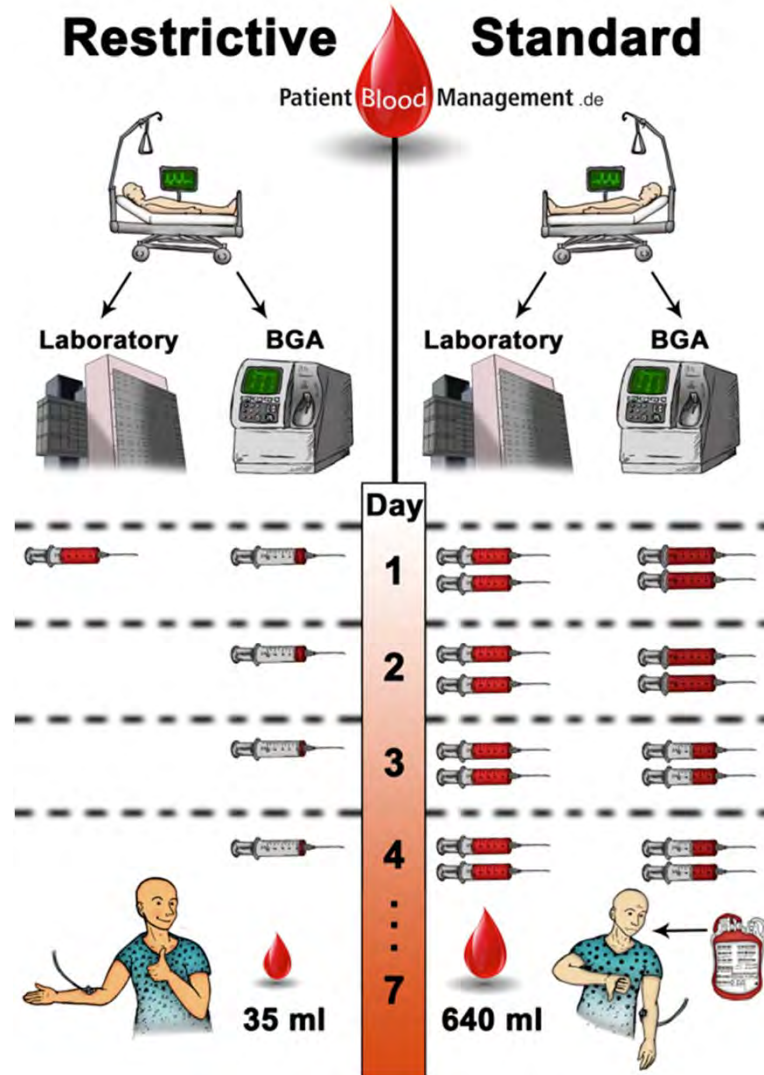


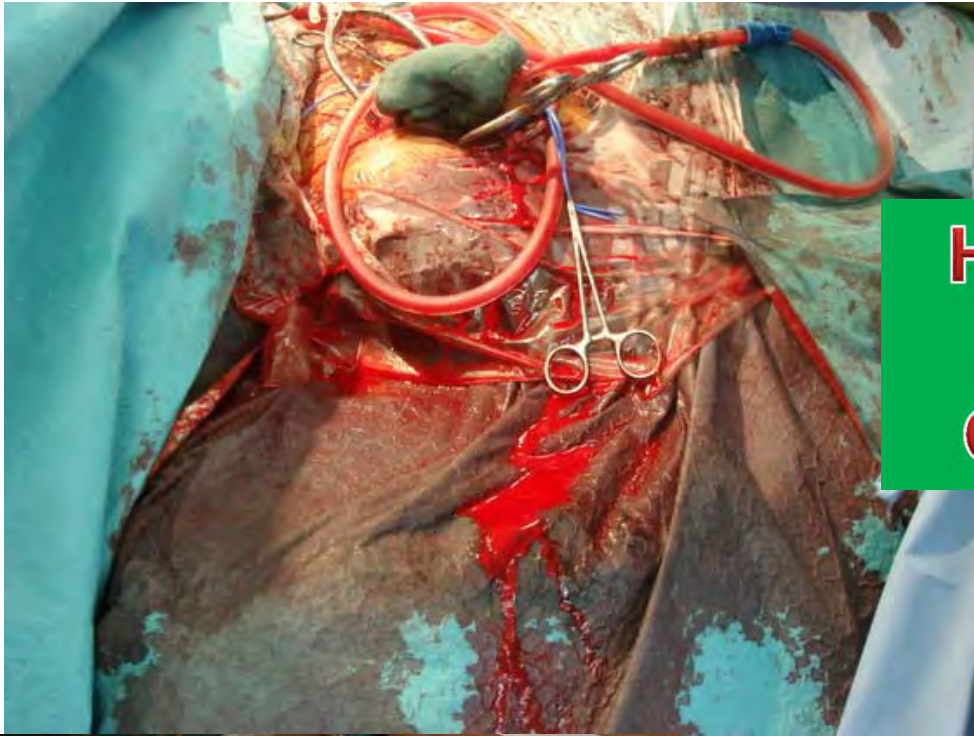
**Institut für Transfusionsmedizin und Immunhämatologie**  
DRK-Blutspendedienst Baden-Württemberg – Hessen  
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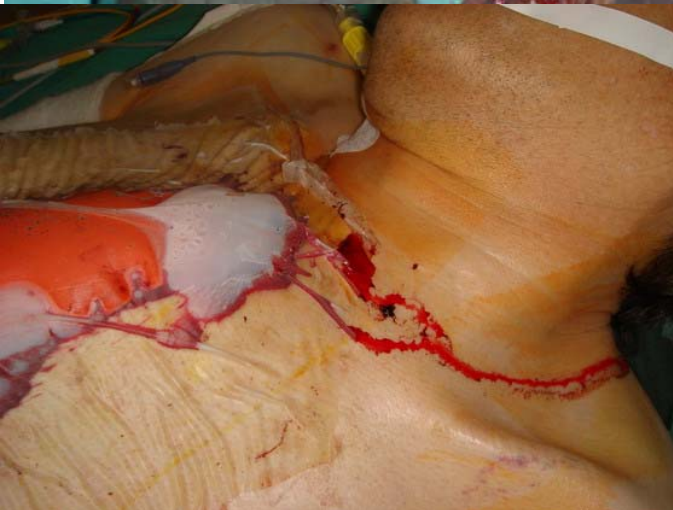
**Klinik für Anästhesiologie, Intensivmedizin  
und Schmerztherapie**  
Direktor: Prof. Dr. Dr. Kai Zacharowski, FRCA

# Restriktive Blutentnahmen





# Homöostasemanagement Wärmemanagement Gerinnungsmanagement



# Blutsparende Maßnahmen

- **Gerinnungsanamnese & Medikamentenanamnese**
- **ggf. frühzeitige (!) Voruntersuchung (BB!)**
- **Bei Mangel: Substitution von Fe, Vitamin B12, etc.**
- Autologe Hämotherapieverfahren:
  - Präoperative autologe Erythrozytenspende: sehr wenige Indikationen!
  - Akute normovolämische Hämodilution: Effekt???
  - **Maschinelle Autotransfusion (MAT): Wundblut** und Drainageblut
- **Lagerung und Op-Verfahren (minimal invasiv, intensive Blutstillung, etc.)**
- **Wärmemanagement (Gerinnung → Enzymkaskade optimal bei +37°C)**
- Perioperativer **pH-Wert** und **ionisiertes Ca<sup>++</sup>** im physiologischen Normbereich
- **Fibrinolysehemmung:** Tranexamsäure lokal, oral, per infusionem, ...
- Thrombozytopathie/vWF-Dysfunktion: **DDAVP** (Minirin®)
- Frühzeitige Gabe von Blutprodukten und Gerinnungsfaktoren (vor Eintritt einer Dilutions-Koagulopathie!)



## Patient Blood Management Checkliste für Transfusionen bei Erwachsenen

### Präoperativ

- bei ausgewählten Risikoeingriffen, Wartezeit >14 Tage und Transfusionsrisiko >10%:  
- > präoperative Anämiediagnostik (PBM-Konsil Anämie in Agfa ORBIS) erwägen
- Blutgruppenbestimmung & Antikörpersuchtest
- Stopp Plättchenaggregationsinhib. ?
- Stopp Antikoagulation ?

### Intraoperativ

- Restriktiver Transfusionstrigger (BÄK)
- Wärmemanagement (Normothermie)
- Gerinnungsmanagement (pH>7,2, Ca<sup>2+</sup>>1,2)
- Blut sammeln (Cellsaver)
- Point-of-Care Diagnostik (ROTEM, Multiplate) bei diffuser Blutungsneigung
- Einsatz von Tranexamsäure/ Desmopressin ?
- optimales Herzzeitvolumen ?
- Normovolämie/ Normoxie ?
- THG: Hämokonzentration? Postfiltration ?

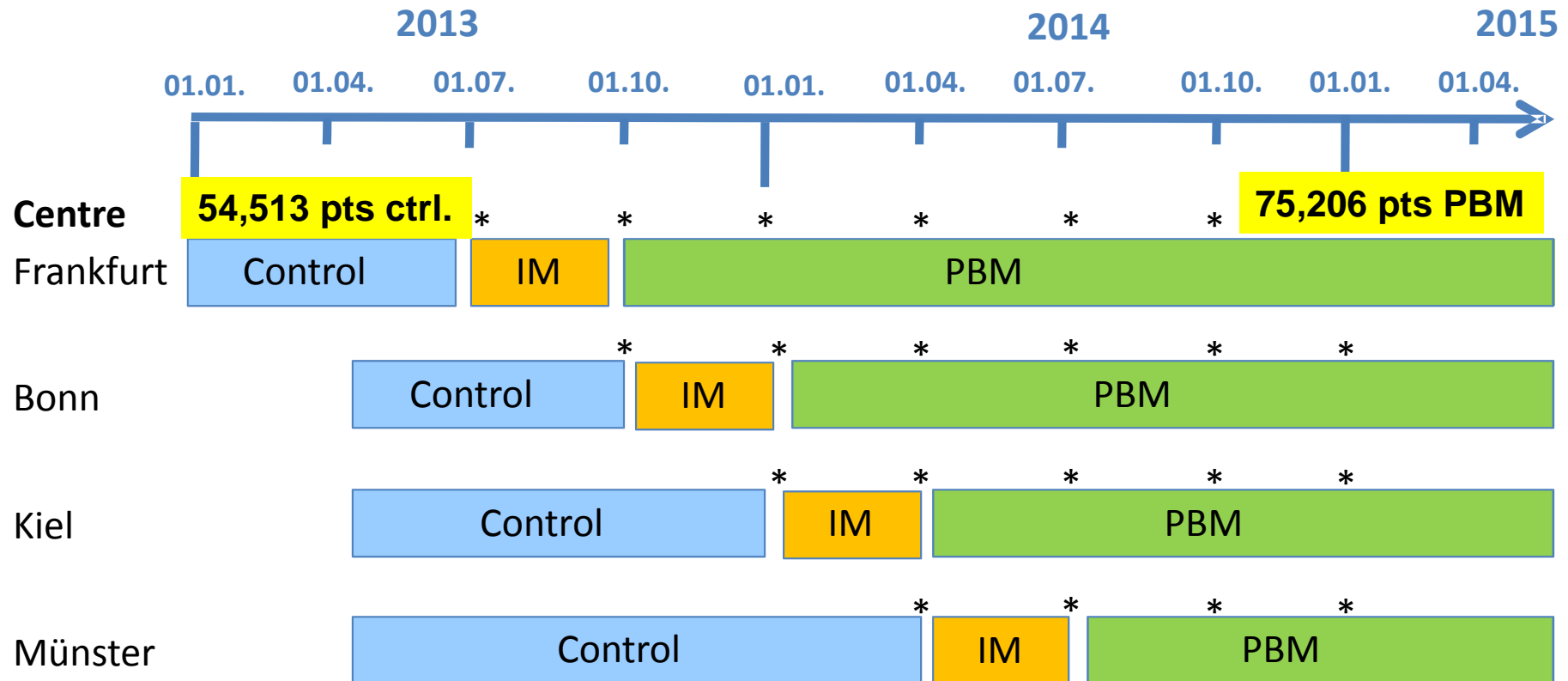
### Postoperativ

- Restriktive Blutentnahmen
- Restriktiver Transfusionstrigger (BÄK)
- Wärmemanagement (Normothermie)
- Gerinnungsmanagement (pH>7,2, Ca<sup>2+</sup>>1,2)
- Blut sammeln (Cellsaver)
- Einsatz von Tranexamsäure/ Desmopressin ?
- Optimales Herzzeitvolumen ?
- Normovolämie/ Normoxie ?



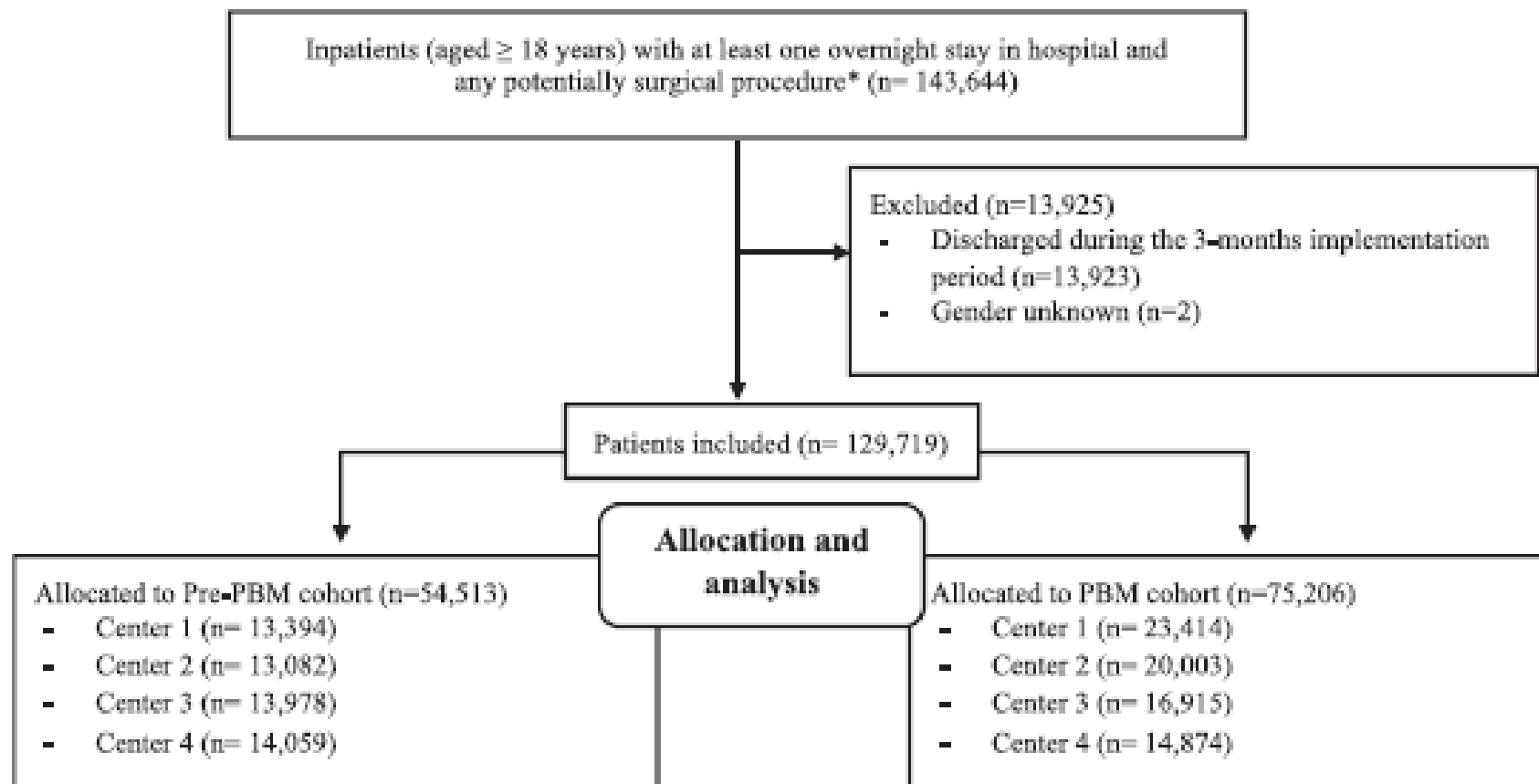
# „Safety of the Implementation of Patient Blood Management“

(ClinicalTrials.gov: NCT01820949; 129 719 pts.)



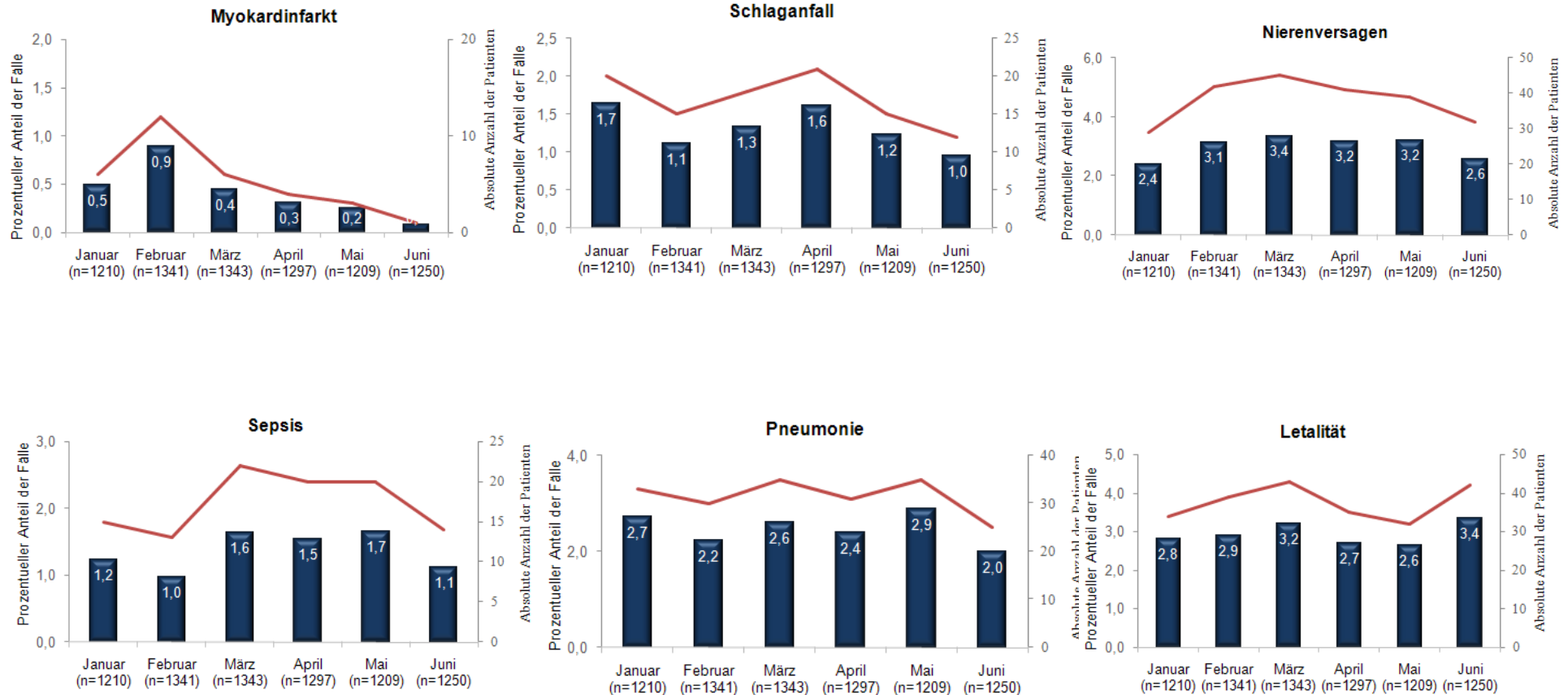
IM = Implementation 3 months each; \* = teaching sessions (3 month interv.)





**Ann Surg 2016;264:203-211**

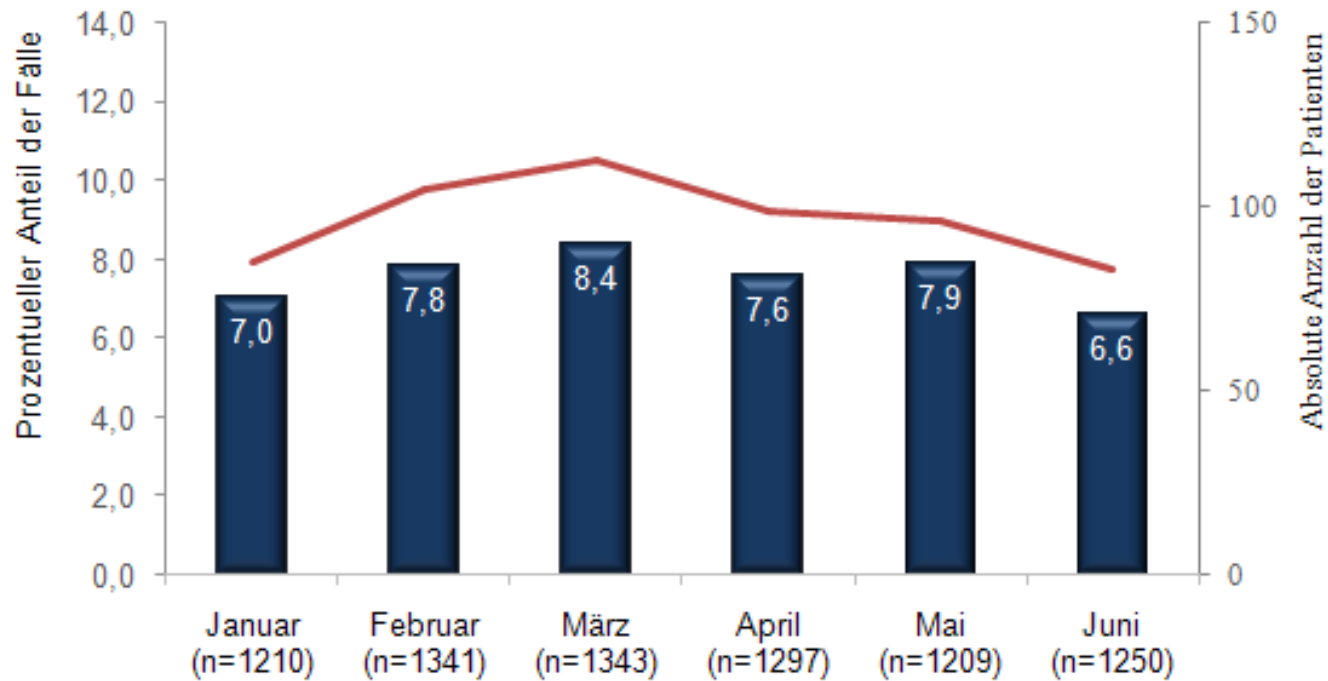
# Primärer Sicherheitsendpunkt (Auswertung Agfa ORBIS)



Daten von allen stationär operierten Patienten  
Testauswertung von Januar – Juni 2012  
Universitätsklinikum Frankfurt

# Primärer Sicherheitsendpunkt (Auswertung Agfa ORBIS)

## Composite Endpoint (Myokardinfarkt, Schlaganfall, Nierenversagen, Sepsis, Pneumonie, und/oder Letalität)



**Prä-PBM:**  
**(54.513 Pat.)**  
**6,53 %**  
**PBM Kohorte**  
**(75.206 Pat.)**  
**6,34%**  
**Nichtunter-**  
**legenheit**  
**erreicht**  
**(p<0.001)**

## **Sekundäre Endpunkte:**

**Rückgang der Inzidenz akuten Nierenversagens  
von 2,39% (Kontrolle) auf 1,67% (PBM)**

**Reduktion der durchschnittlichen Anzahl an EK-Transfusionen/Patient  
und Aufenthalt von 1,2 auf 1,0 (minus 17%)**

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	Center 1		Center 2		Center 3		Center 4	
	Pre-PBM	PBM	Pre-PBM	PBM	Pre-PBM	PBM	Pre-PBM	PBM
<b>Project management and education sessions</b>								
Support by medical director with official directive	⊙	↑	⊙	⊙	⊙	↗	↑	↑
Support by transfusion committee	⊙	↑	⊙	↑	⊙	↗	⊙	↑
Multidisciplinary PBM core team	⊙	↑	⊙	↑	⊙	↑	⊙	↑
Education of physicians	⊙	↑	⊙	↑	⊙	↑	↗	↑
Presentation of PBM at surgical wards	⊙	↑	⊙	↑	⊙	↑	⊙	↑
Use of handouts, laminated cards, posters, checklists; Marketing with PBM logo (pens, buttons, shirts, etc.)	⊙	↑	⊙	↑	⊙	↑	⊙	↑
Use of Patient Blood Management checklist	⊙	↑	⊙	↑	⊙	↑	⊙	↑
Standard Operating Procedures for PBM	⊙	↑	⊙	↑	⊙	↗	⊙	↑
<b>Preoperative optimization of hemoglobin levels</b>								
Identification of anemic patients (screening)	⊙	↑	⊙	↗	⊙	↗	⊙	↑
Diagnosis of type of anemia (iron-deficiency, vitamin B <sub>12</sub> or folic acid deficiency)	⊙	↑	⊙	↗	⊙	⊙	⊙	↑
Extended diagnostic of anemia (e.g. consultant for gastroenterology, hematology)	⊙	⊙	⊙	↗	⊙	⊙	⊙	↑
Administration of intravenous iron	⊙	↗	⊙	↗	⊙	⊙	↗	↑
Administration of vitamin B <sub>12</sub> and/or folic acid	⊙	↗	⊙	↗	⊙	⊙	↗	↑
Therapy of non-iron deficiency anemia (e.g. erythropoietin)	⊙	⊙	⊙	↗	⊙	⊙	↗	↑
Referral to general practitioner	⊙	⊙	⊙	↗	⊙	⊙	⊙	↑
<b>Alternatives to transfusion and blood-sparing techniques</b>								
Physiological conditions of hemostasis (body temperature > 36°C, pH > 7.2; Ca <sup>2+</sup> > 1.1 mmol/l)	↗	↑	↗	↗	↗	↑	↑	↑
Autologous red cell recovery and retransfusion	↗	↑	↗	↗	↗	↑	↗	↑
Emphasis on surgical hemostasis	↗	↑	⊙	↗	↗	↑	↑	↑
Reducing blood collection tubes with smaller draw volumes	⊙	↑	⊙	⊙	⊙	⊙	⊙	↑
Reduced blood waste with a closed in-line flushing device	⊙	↑	⊙	⊙	⊙	⊙	⊙	↑
Point-of-Care diagnostic in coagulopathy	↗	↑	⊙	↗	↗	↑	↑	↑
Use of a hemotherapy algorithm	↗	↑	⊙	↗	⊙	↗	↗	↑
Cardiac surgery (decreasing extracorporeal volumes, retrograde autologous priming)	⊙	↑	↗	↑	⊙	⊙	⊙	⊙
Empiric treatment of hyperfibrinolysis/ platelet dysfunction	↗	↑	↗	↗	↗	↑	↗	↑
<b>Standardization of transfusion practice for RBC</b>								
Checklist when RBC are requested	⊙	↑	⊙	⊙	⊙	↑	⊙	↑
Documentation of the indication for RBC transfusion	⊙	↑	⊙	⊙	⊙	↗	↑	↑

FIGURE 2. Measures of PBM. Details on the degree of implemented PBM measures are provided before (pre-PBM) and after implementation of PBM: not implemented (⊙), partly pre-existing/ not fully implemented (↗), and fully implemented (↑).

# 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

**Results:** A total of 129,719 patients discharged between July 2012 and June 2015 with different inclusion periods for pre-PBM (54,513 patients) and PBM (75,206 patients) were analyzed. The primary endpoint was 6.53% in the pre-PBM versus 6.34% in the PBM cohort. The noninferiority aim was achieved ( $P < 0.001$ ). Incidence of acute renal failure decreased in the PBM cohort (2.39% vs 1.67%;  $P < 0.001$ , regression model). The mean number of red blood cell transfused per patient was reduced from  $1.21 \pm 0.05$  to  $1.00 \pm 0.05$  (relative change by 17%,  $P < 0.001$ ).

**Conclusions:** The data presented show that implementation of PBM with a more conscious handling of transfusion practice can be achieved even in large hospitals without impairment of patient's safety. Further studies should elucidate which PBM measures are most clinically and cost effective.



# Offene Fragen

- **Präoperative Anämie**
  - Korrelation oder Kausalität bzgl. schlechtem perioperativem Outcome?
  - Methode zur Korrektur einer perioperativen Anämie?
- **EK**
  - Transfusionstrigger bei klinisch instabilen Patienten?
  - Transfusionstrigger bei blutenden Patienten?
  - Transfusionstrigger bei (traumatischen) ZNS-Schäden?
  - Transfusionstrigger bei internistischen Patienten?
  - Transfusionstrigger bei neurologischen Patienten?
- **TK**
  - Transfusionstrigger?
  - Therapeutische versus prophylaktische Gabe?
- **Therapeutisches Plasma und Gerinnungsfaktoren**
  - Transfusionstrigger?
- **Prospektiv randomisierte Studien mit harten Endpunkten (z.B. Mortalität)**
  - Finanzierung?
  - Patientenversicherung?