

Patient Blood Management

– zvýší bezpečnost a ušetří peníze

OA Dr. Stibor B.

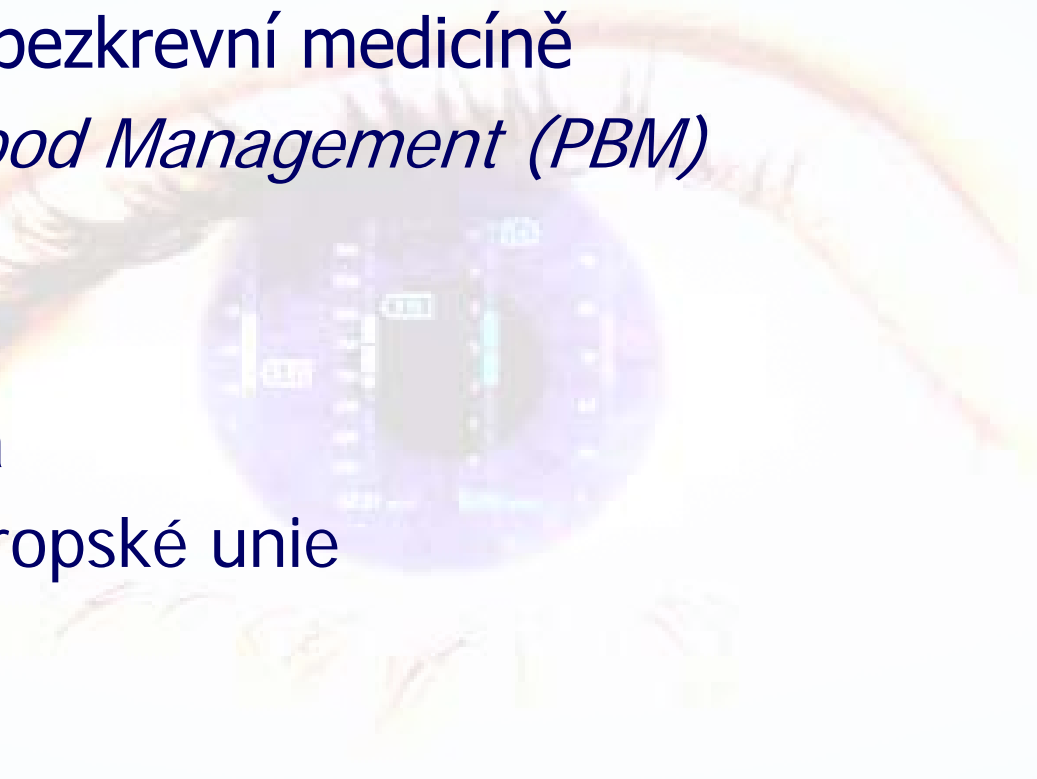
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no conflict of interest

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přehled

1. novinky v bezkrevní medicíně
 2. *Patient Blood Management (PBM)*
 3. proč PBM?
 4. výsledky
 5. ekonomika
 6. projekt Evropské unie
- 

*novinky
v bezkrevní
medicině*

hot news

- potvrzení restriktivní transfuzní strategie
- nová orální antikoagulancia (*NOACs*)
- (*NOACs*) – *reversal agents*
- BRIDGE study
- Patient blood management

Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomised trials with meta-analysis and trial sequential analysis

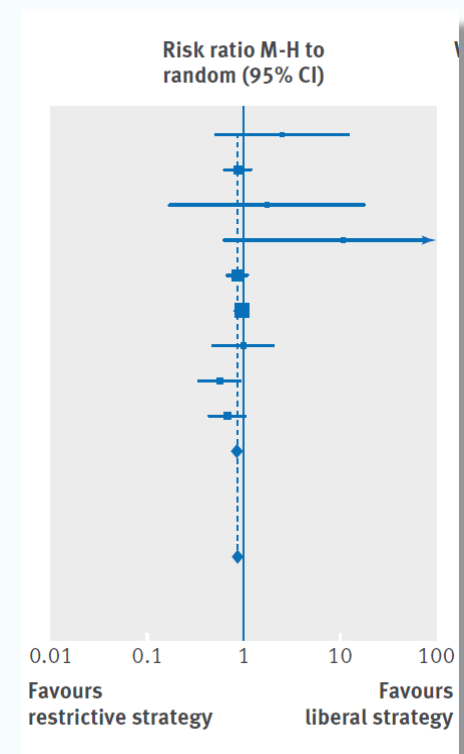
Lars B Holst,¹ Marie W Petersen,¹ Nicolai Haase,¹ Anders Perner,¹ Jørn Wetterslev²

CONCLUSIONS

Compared with liberal strategies, restrictive transfusion strategies were associated with a reduction in the number of red blood cell units transfused and number of patients being transfused, but mortality, overall morbidity, and myocardial infarction seemed to be unaltered. Restrictive transfusion strategies are safe in most clinical settings. Liberal transfusion strategies have not been shown to convey any benefit to patients.

TRIAL REGISTRATION

PROSPERO CRD42013004272.



WHAT IS ALREADY KNOWN ON THIS TOPIC

Red blood cells are commonly used in the treatment of haemorrhage and anaemia, but recent trials have shown potential harm with this intervention

Recent meta-analysis indicates no harm with the use of a restrictive transfusion strategy

WHAT THIS STUDY ADDS

This review includes new data from five recently published randomised trials of restrictive versus liberal transfusion strategies and includes data from more than 9000 patients

Pooled analyses did not show harm with restrictive transfusion strategies (no increased risk of mortality, overall morbidity, or acute myocardial infarction) but the number of units and number of patients transfused were reduced compared with liberal strategies

Liberal strategies have possible associations with harm (risk of infectious complications)

Further large trials with lower risk of bias are needed to establish firm evidence to guide transfusion in subgroups of patients

✓ Laborwerte Gesamt letzten 7 Tage
 15.09.2015 11:34 - 22.09.2015 11:34

Zeit	16.09.15	17.09.15	18.09.15	19.09.15	20.09.15	21.09.15
Variablen	06:04	05:40	06:06	06:07	06:00	05:54
	Blutbild					
Leukozyten 4-10[G/l]	12.0	12.4	11.7	13.2	14.1	13.3
Erythrozyten 4-5.2[T/l]	2.58	2.60	2.59	2.52	2.48	2.39
Hämoglobin 12-16[g/dl]	7.6	7.8	7.8	7.6	7.4	7.2
Hämatokrit 36-46[%]	24	24	24	23	23	22

✓ Laborwerte Gesamt letzten 7 Tage
 15.09.2015 11:52 - 22.09.2015 11:52

Zeit	16.09.15	17.09.15	19.09.15	20.09.15	21.09.15	22.09.15
Variablen	06:03	05:41	06:06	06:00	05:53	06:00
	Blutbild					
Leukozyten 4-10[G/l]	8.5	7.3	6.1	6.1	4.9	6.5
Erythrozyten 4-5.2[T/l]	2.95	2.81	2.77	2.72	2.80	2.79
Hämoglobin 12-16[g/dl]	9.2	8.6	8.5	8.2	8.6	8.6
Hämatokrit 36-46[%]	29	27	27	26	27	27

direct thrombin - inhibitors

dabigatran

Pradaxa[®]

argatroban*

Argartra[®]

bivaluridin*

Angiox[®]

Factor Xa - inhibitors

rivaroxaban

Xarelto[®]

apixaban

Eliquis[®]

edoxaban

Lixiana[®]

betrixaban

APEX study

eribaxaban

codename

ORIGINAL ARTICLE

Idarucizumab for Dabigatran Reversal

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhaar, M.D., Richard A. Dargatzis, M.D., Ph.D., Robert Dubielz, Pharm.D., Menno V. Huisman, M.D., Ph.D., Jeffrey J. Goldhaber, M.D., Jerrold F. Goldhaber, M.D., Mark W. Franks, M.D., Bushi Wang, M.D., and Frank W. Kellermann, M.D.,

Praxbind[®]
idarucizumab
INJECTION 5g

Moa150



Idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes. (Funded by Boehringer Ingelheim; REVERSE AD ClinicalTrials.gov number, [NCT02104947](https://clinicaltrials.gov/ct2/show/study/NCT02104947).)

ORIGINAL ARTICLE

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

James D. Douketis, M.D., Alex C. Spyropoulos, M.D., Scott Kaatz, D.O.,
Richard C. Becker, M.D., Joseph A. Caprini, M.D., Andrew S. Dunn, M.D.,
David A. Garcia, M.D., Alan Jacobson, M.D., Amir K. Jaffer, M.D., M.B.A.,
David F. Kong, M.D., Sam Schulman, M.D., Ph.D., Alexander G.G. Turpie, M.B.,
Vic Hasselblad, Ph.D., and Thomas L. Ortel, M.D., Ph.D.,
for the BRIDGE Investigators*

RESULTS

In total, 1884 patients were enrolled, with 950 assigned to receive no bridging therapy and 934 assigned to receive bridging therapy. The incidence of arterial thromboembolism was 0.4% in the no-bridging group and 0.3% in the bridging group (risk difference, 0.1 percentage points; 95% confidence interval [CI], -0.6 to 0.8; $P=0.01$ for noninferiority). The incidence of major bleeding was 1.3% in the no-bridging group and 3.2% in the bridging group (relative risk, 0.41; 95% CI, 0.20 to 0.78; $P=0.005$ for superiority).

CONCLUSIONS

In patients with atrial fibrillation who had warfarin treatment interrupted for an elective operation or other elective invasive procedure, forgoing bridging anticoagulation was noninferior to perioperative bridging with low-molecular-weight heparin for the prevention of arterial thromboembolism and decreased the risk of major bleeding. (Funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health; BRIDGE ClinicalTrials.gov number, NCT00786474.)

*patient
blood
management*

Patient Blood Management

- multidisciplinární přístup na podkladě *evidence-based poznatků*

- cíle:

minimalizovat podání allogenní krve

zlepšit pacientův outcome

zajistit finanční úspory

- tři pilíře:

optimalizace krevního objemu a množství erytrocytů

minimalizace krevních ztrát

zvýšení tolerance anémie

1st Pillar

**Optimise
patient's own
red cell mass**

2nd Pillar

**Minimise
blood loss**

3rd Pillar

**Harness &
optimise
physiologic
reserve of
anemia**

Multidisciplinary team approach

Three Pillars of Patient Blood Management

1st Pillar
Optimise haemopoiesis

2nd Pillar
Minimise blood loss and bleeding

3rd Pillar
Harness and optimise tolerance of anaemia

Preoperative

- Screen for anaemia
- Identify underlying disorder(s) causing anaemia
- Manage underlying disorder(s)
- Refer for further evaluation if necessary
- Treat iron deficiency, anaemia of chronic disease, iron-restricted erythropoiesis
- Note: anaemia is a contraindication for elective surgery

- Identify and manage bleeding risk (past/family history, current medications, etc)
- Minimise iatrogenic blood loss
- Procedure planning and rehearsal
- Preoperative autologous blood donation (in selected cases or when patient choice)

- Assess/optimize patient's physiological reserve and risk factors
- Compare estimated blood loss with patient-specific tolerable blood loss
- Formulate patient-specific management plan using appropriate blood-conservation modalities to minimize blood loss, optimize red cell mass and manage anaemia
- Restrictive evidence-based transfusion strategies

Intraoperative

- Timing surgery with haematological optimisation

- Meticulous haemostasis and surgical techniques
- Blood-sparing surgical techniques
- Anaesthetic blood-conserving strategies
- Autologous blood options
- Pharmacological/haemostatic agents

- Optimize cardiac output
- Optimize ventilation and oxygenation
- Restrictive evidence-based transfusion strategies

Postoperative

- Treat anaemia/iron deficiency
- Stimulate erythropoiesis
- Be aware of drug interactions that can cause/increase anaemia

- Vigilant monitoring and management of post-operative bleeding
- Avoid secondary haemorrhage
- Rapid warming – maintain normothermia (unless hypothermia specifically indicated)
- Autologous blood salvage
- Minimising iatrogenic blood loss
- Haemostasis/anticoagulation management
- Prophylaxis of upper gastrointestinal haemorrhage
- Avoid/treat infections promptly
- Be aware of adverse effects of medication

- Optimize tolerance of anaemia
- Treat anaemia
- Maximise oxygen delivery
- Minimise oxygen consumption
- Avoid/treat infections promptly
- Restrictive, evidence-based transfusion strategies

Fig 1 A multimodal approach to PBM (or blood conservation). Adapted from Hofmann and colleagues⁶² with permission. ESA, erythropoiesis-stimulating agents.

Transfusion trigger checklist

List has to be filled for each RBC!!!!
(Exception: massive bleeding)

Hb < 6 g/dl

- Independent of any compensation possibility

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:)

In case of Hb > 8 g/dl transfusion is related to an unclear risk-benefit balance

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

traumatic brain injury) and on the stability of the patient. PBM strategies are in place in a limited number of hospitals.

The Netherlands

Dutch hospitals began to implement PBM ~10 yr ago, especially for major orthopaedic surgery (Table 2). There is a legal requirement for a complete preoperative assessment 3–4 weeks before all elective surgery. Importantly, anaesthetists can cancel surgery until the outcome of treatment for anaemia is known. Preoperative PBM precautions include the use of cyclooxygenase-2-selective non-steroidal anti-inflammatory drugs to reduce the risk of bleeding after taking known risk factors into consideration.^{90–93} The introduction of ESA use for patients undergoing other surgery types is likely to occur in the future. National transfusion triggers were instituted in 2000 (e.g. Hb of 6.4 g dl⁻¹ for normal healthy patients).

All hospitals in the Netherlands report transfusion rates in knee and hip surgery, and these can be compared on the central website of the Dutch Health Authority.⁹⁴ The results of national surveys of Dutch orthopaedic surgery departments performed in 2002 and 2007 have documented the increasing use of PBM measures to avoid transfusion.⁹⁵ The use of preoperative autologous blood donation was similar in 2002 and 2007 for both hip and knee arthroplasty (Fig. 2). However, the preoperative use of ESA approximately doubled between 2002 and 2007, while the use of postoperative autologous cell salvage increased by 4- to 5-fold. Smaller increases were observed in the use of intraoperative autologous cell salvage.

Annual reports from the Dutch blood bank Sanquin⁹⁶ showed a decline in the total number of allogeneic transfusions by 12% in the period from the year 2000 to 2009 (Fig. 3). This decrease was concurrent with an increase in healthcare usage. Hospital admissions increased from 1600

zákonný požadavek na
kompletní předoperační
zhodnocení a úpravu anémie
anesteziolog může *cancel*
surgery dokud není anémie
vyřešená

ustanoven národní transfúzní
trigger u zdravých pacientů:

Hb 6,4 g.l⁻¹

všechny nemocnice hlásí
četnost transfúzí u TEP

vše dostupné na *Dutch Health*
Authority

.....

proč
PBM?

The Oncologist®

Five Drivers Shifting the Paradigm from Product-Focused Transfusion Practice to Patient Blood Management

AXEL HOFMANN,^{a,b} SHANNON FARMER,^{b,c,d} ARYEH SHANDER^e

The Oncologist 2011;16(suppl 3):3–11

5 důvodů pro PBM

1. rostoucí **nepoměr** mezi nabídkou a potřebou alogenní krve
2. rostoucí **náklady** na transfúze
3. problematika **bezpečnosti** transfúzí
4. **nežádoucí** účinky transfúzí
5. problematická **efektivita** transfúzí

Patient blood management in Europe

A. Shander^{1*}, H. Van Aken², M. J. Colomina³, H. Gombotz⁴, A. Hofmann⁵, R. Krauspe⁶, S. Lasocki⁷, T. Richards⁸, R. Slappendel⁹ and D. R. Spahn¹⁰

‘patient blood management’ (PBM). PBM involves the use of multidisciplinary, multimodal, individualized strategies to minimize RBC transfusion with the ultimate goal of improving patient outcomes. PBM relies on approaches (pillars) that detect and treat perioperative anaemia and reduce surgical blood loss and perioperative coagulopathy to harness and optimize physiological tolerance of anaemia. After the recent resolution 63.12 of the World Health Assembly, the implementation of PBM is encouraged in all WHO member states. This new standard of care is now established in some centres in the USA and Austria, in Western Australia, and nationally in the Netherlands. However, there is a

- Patient blood management aims to minimize the need for transfusion.
- Early detection and treatment of anaemia and minimizing blood loss are key strategies.

anaemia and reduce surgical blood loss and perioperative coagulopathy to harness and optimize physiological tolerance of anaemia. After the recent resolution 63.12 of the World Health Assembly, the implementation of PBM is encouraged in all WHO member states. This new standard of care is now established in some centres in the USA and Austria, in Western Australia, and nationally in the Netherlands. However, there is a pressing need for European healthcare providers to integrate PBM strategies into routine care for patients undergoing orthopaedic and other types of surgery in order to reduce the use of unnecessary transfusions and improve the quality of care. After reviewing current PBM practices in Europe, this article offers recommendations supporting its wider implementation, focusing on anaemia management, the first of the three pillars of PBM.

Keywords: anaemia; outcome; patient blood management; transfusion

výsledky?

traumatic brain injury) and on the stability of the patient. PBM strategies are in place in a limited number of hospitals.

The Netherlands

Dutch hospitals began to implement PBM ~10 yr ago, especially for major orthopaedic surgery (Table 2). There is a legal requirement for a complete preoperative assessment 3–4 weeks before all elective surgery. Importantly, anaesthetists can cancel surgery until the outcome of treatment for anaemia is known. Preoperative PBM precautions include the use of cyclooxygenase-2-selective non-steroidal anti-inflammatory drugs to reduce the risk of bleeding after taking known risk factors into consideration.^{90–93} The introduction of ESA use for patients undergoing other surgery types is likely to occur in the future. National transfusion trig-

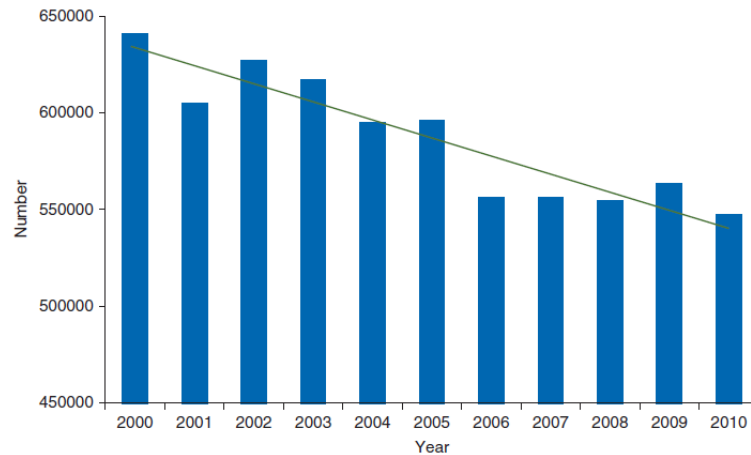
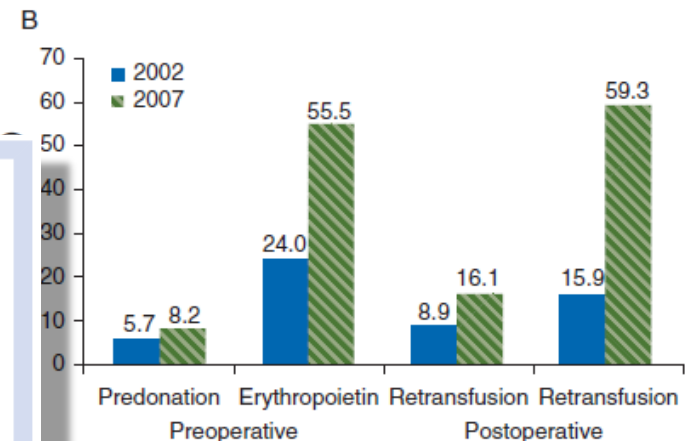
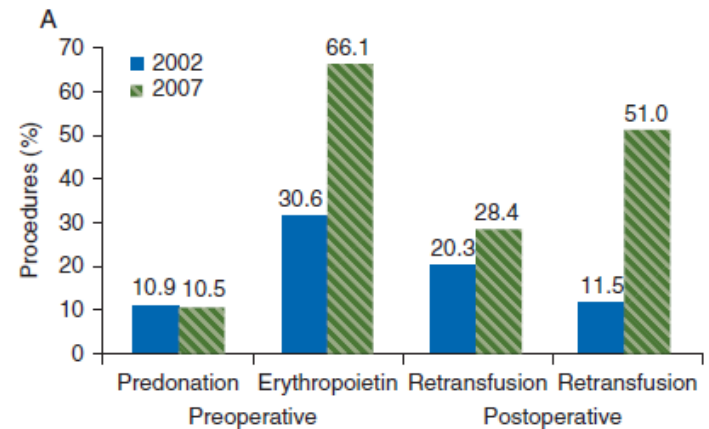


Fig 3 Number of allogeneic transfusions in the Netherlands from 2000 to 2010.⁹⁶

Annual reports from the Dutch blood bank Sanquin⁹⁶ showed a decline in the total number of allogeneic transfusions by 12% in the period from the year 2000 to 2009 (Fig. 3). This decrease was concurrent with an increase in healthcare usage. Hospital admissions increased from 1600



Results of a national survey of rates of autologous pre-
 vious blood donation, erythropoietin use, and autologous
 fusion in patients undergoing (A) hip or (B) knee arthro-
 in 2002 and 2007 in the Netherlands.⁹¹

to 2300 per year per 10 000 inhabitants from 2000 to 2009. Based on the current price of an allogeneic transfusion of RBCs at €204, PBM is estimated to have saved a net cost of €100 million nationwide every year.

ORIGINAL RESEARCH

Implementation of a patient blood management monitoring and feedback program significantly reduces transfusions and costs

Tarun Mehra,¹ Burkhardt Seifert,² Silvina Bravo-Reiter,¹ Guido Wanner,³ Philipp Dutkowski,⁴ Tomas Holubec,⁵ Rudolf M. Moos,¹ Jörk Volbracht,¹ Markus G. Manz,⁶ and Donat R. Spahn⁷

STUDY DESIGN AND METHODS: We designed a prospective, interventional cohort study with a 3-year time frame (January 1, 2012 to December 31, 2014). In total, 101,794 patients aged 18 years or older were included. The PBM monitoring and feedback program was introduced on January 1, 2014, with the subsequent issuance of quarterly reporting.

Transfusion, 11 August 2015

RESULTS: Within the first year of introduction, transfusion of all allogeneic blood products per 1000 patients was reduced by 27% (red blood cell units, –24%; platelet units, –25%; and fresh-frozen plasma units, –37%; all $p < 0.001$) leading to direct allogeneic blood product related savings of more than 2 million USD. The number of blood products transfused per case was significantly reduced from 9 ± 19 to 7 ± 14 ($p < 0.001$). With an odds ratio of 0.86 (95% confidence interval, 0.82-0.91), the introduction of our PBM monitoring and feedback program was a significant independent factor in the reduction of transfusion probability ($p < 0.001$).

CONCLUSION: Our PBM monitoring and feedback program was highly efficacious in reducing the transfusion of allogeneic blood products and transfusion-related costs.

BLOOD MANAGEMENT

Patient blood management in cardiac surgery results in fewer transfusions and better outcome

Irwin Gross,¹ Burkhardt Seifert,² Axel Hofmann,² and Donat R. Spahn²

CONCLUSIONS: Implementing meticulous surgical technique, a goal-directed coagulation algorithm, and a more restrictive transfusion threshold in combination resulted in a substantial decrease in RBC, FFP, and PLT transfusions; less kidney injury; a shorter length of hospital stay; and lower total direct costs.

TABLE 2. Blood loss and transfusion outcome*

	Pre-PBM epoch	PBM epoch	p value
RBC loss (mL)	810 ± 426	605 ± 369	<0.001
	721 [538-993]	552 [370-756]	
Hb (g/dL)			
Before transfusion	7.2 ± 1.4	6.6 ± 1.2	<0.001
After transfusion	8.3 ± 1.3	7.7 ± 1.1	<0.001
% of patients transfused			
RBCs	39.3	20.8	<0.001
FFP	18.3	6.5	<0.001
PLTs	17.8	9.8	<0.001
RBCs (units/patient)	1.28 ± 2.34	0.61 ± 1.57	<0.001
	0 [0-2]	0 [0-0]	
FFP (units/patient)	0.78 ± 1.98	0.23 ± 1.05	<0.001
	0 [0-0]	0 [0-0]	
PLTs (units/patient)	0.39 ± 1.03	0.17 ± 0.65	<0.001
	0 [0-0]	0 [0-0]	
Discharge Hb (g/dL)	9.1 ± 1.2	9.4 ± 1.5	<0.001

* Data are mean ± SD and median [interquartile range] for nonnormally distributed data.

TABLE 3. Clinical and economic outcomes

	Pre-PBM epoch	PBM epoch	p value
Mortality (%)	3.9	4.4	0.642
CVA (%)	3.40	2.10	0.130
Kidney injury (%)	7.60	5.00	0.039
ICU LOS (days)	5.0 ± 7.1	5.0 ± 7.1	0.970
	3 [1-6]	3 [1-6]	
Hospital LOS (days)	12.2 ± 9.6	10.4 ± 8.0	<0.001
	10 [7-15]	8 [6-12]	
30-day readmission rate (%)	0.3	0.1	0.467
Total direct costs (\$)	48,375 ± 28,053	44,300 ± 25,915	<0.001
	39,709 [32,470-54,994]	36,906 [29,510-49,967]	

* Data are mean ± SD and median [interquartile range] for nonnormally distributed data.
LOS = length of stay.

> 4.000\$ per patient



Německo



Safety and effectiveness of a Patient Blood Management Programme in surgical patients – the study design for a multicentre epidemiological non-inferiority trial by the German PBM network

P. Meybohm,¹ D. P. Fischer,¹ E. Herrmann,² C. Geisen,³ M. M. Müller,³ E. Seifried,³ A. U. Steinbicker,⁴ C. F. Weber,¹ K. D. Zacharowski¹ & the German PBM Network

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Preoperative

- Transfusion probability > 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, Ca²⁺ > 1.2)
- Point-of-Care diagnostics: ROTEM, Multiplate
- Tranexamic acid, desmopressin
- Cell saver
- Normovolaemia
- Optimise cardiac output
- Minimise blood samples
- Cardiac surgery:
Haemoconcentration? Postfiltration?

Postoperative

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



Patient Blood Management

End point

Primary efficacy end-point = safety

Composite outcome comprising in-hospital myocardial infarction, stroke, acute renal failure, death of any cause, pneumonia and sepsis until discharge from hospital in patients before and after implementation of PBM programme.

Secondary end-points = effectiveness

- Length of stay on the intensive care unit
- Total hospital stay
- Quantitative utilization of iron and erythropoietin in the pre- and perioperative phase
- Quantitative utilization of allogeneic RBC units, platelet concentrates, other blood products (e.g. fresh frozen (therapeutic) plasma), coagulations factors and cell saver systems during hospital stay

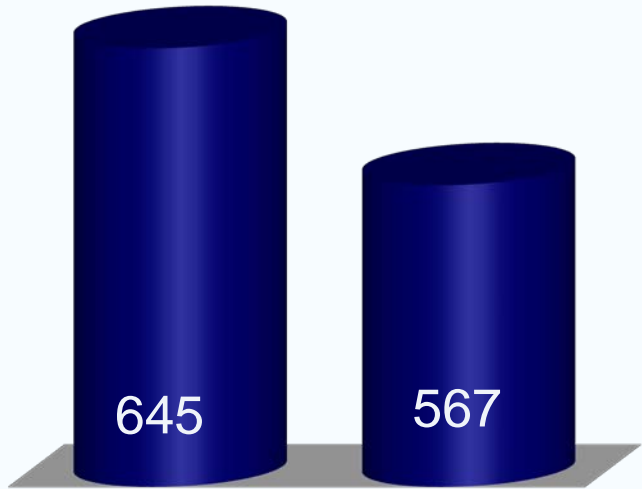


Fig. 1 Map of Germany displaying hospitals that will take part in the German PBM network or are participating already.

ekonomika

2000

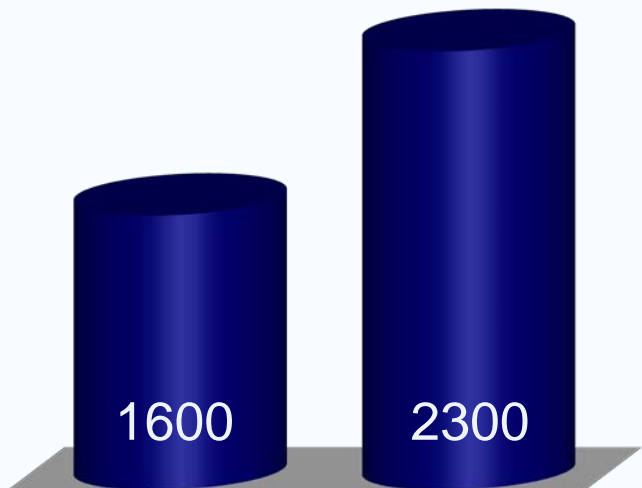
2009



počet alogenních transfuzí klesl

o **12%**

(v tisících)



počet hospitalizací vzrostl

o **44% (!)**

(hospitalizovaných na 10 tis. obyv.)



to save a net cost of
€100 million
nationwide every year

BJA,2012;109(1):55-68



possible to save a net cost of
€200 million
nationwide every year

Prof. Gombotz, persönlich X/2015

projekt
Evropské unie



EU-PBM

*European Guide on
Good Practices for
Patient Blood Management*

www.europe-pbm.eu

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- Axel Hofmann, Zurich
- Kai Zacharowski, Frankfurt
- Günter Schreier, Graz
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Klaus Markstaller
- Universitätsklinikum Frankfurt
Kai Zacharowski

Hans Gombotz

Professor Hans Gombotz was the former head of the Department of Anesthesia, Intensive Care Medicine and Pain Therapy at the General Hospital Linz, Austria where he has successfully introduced PBM as new standard of care.



Kai Zacharowski

Medical University of Frankfurt

Professor Kai Zacharowski holds the position of the Ordinarius and is the Director of the Department of Anesthesia, Intensive Care Medicine and Pain Therapy at the University Hospital Frankfurt.






Patient Blood Management
Wir sind dabei!



Patient Blood
Management

Patient Blood Management

Individuelles Behandlungskonzept zur Reduktion und Vermeidung von Anämie und Blutverlust sowie zum rationalen Einsatz von Blutprodukten

Herausgegeben von
Hans Gombotz
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Patient Blood Management

 Thieme



...děkuji Vám za pozornost

