Clinical Aspects of Blood Transfusion and Plasma Protein Therapies

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
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BERN UNIVERSITY HOSPITAL

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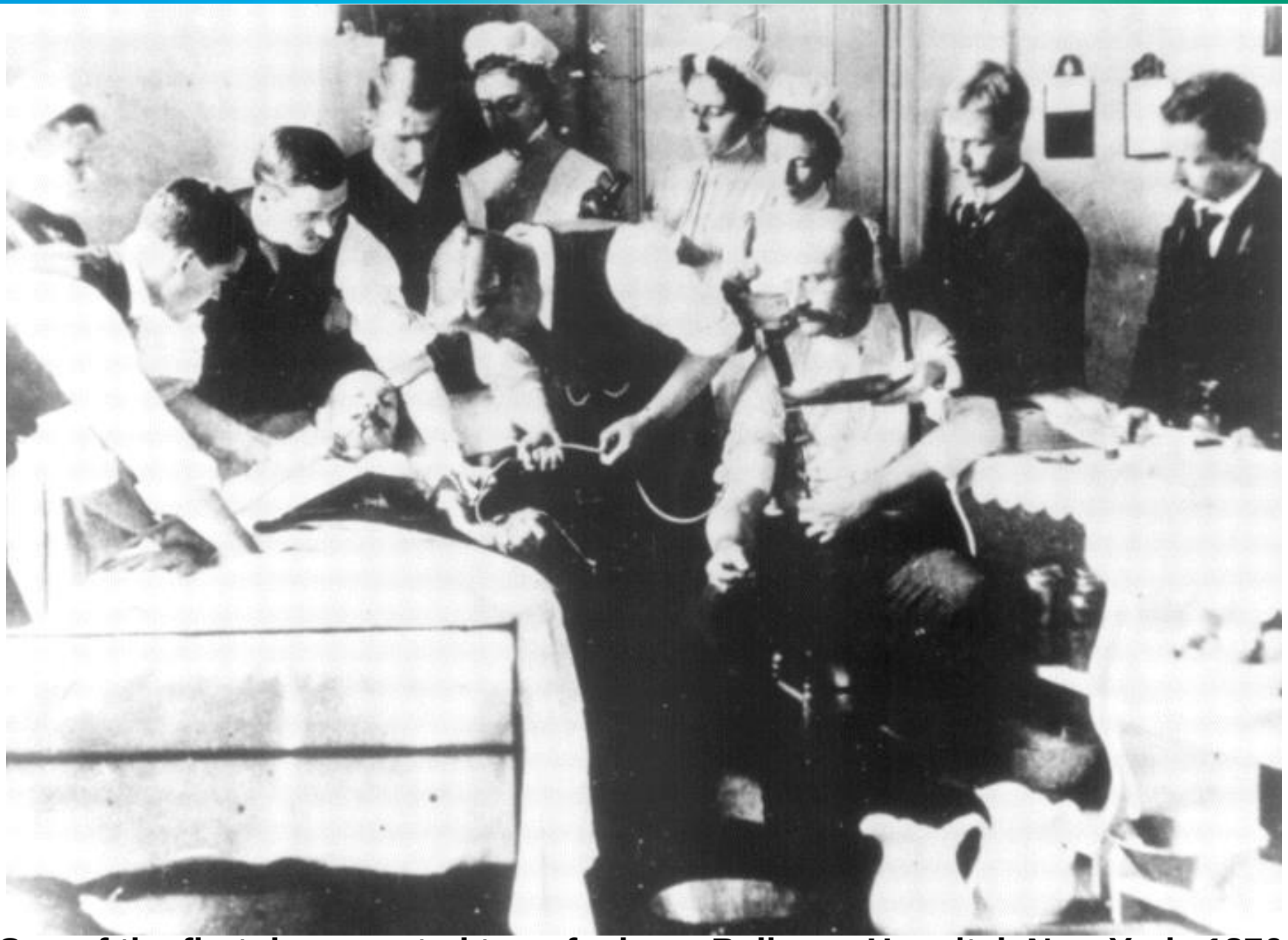
Agenda

- Introduction (Blood components and safety)
- Transfusion of Red Blood Cells and "Patient Blood Management" (PBM)
- Transfusion of platelet concentrates and some Swiss peculiarities
- Transfusion of plasma
- Treatment with plasma proteins – short overview and some examples
- Closing remarks



One of the first documented transfusions, Bellevue Hospital, New York, 1876

TRANS FUSION MEDICINE

Donor		Patient
Red Blood Cells		Anemia
Platelets		Low count / dysfuntion
Plasma / -factors	Safety Availability Compatibility Optimal Use	Coagulopathy, …
(Stem-) Cell products		SC-TX / Cell-therapy
Donor Apheresis		Therapeut. Apheresis

Some Definitions First…

- **BLOOD PRODUCT**

  Any therapeutic substance prepared from human blood

- **WHOLE BLOOD**

  Unseparated blood collected into an approved container containing an anticoagulant preservative solution

- **BLOOD COMPONENT**

  A constituent separated from whole blood, mainly

  - Red cell concentrate
  - Platelet concentrate
  - Plasma

Prerequisites of Blood Transfusion and Blood Component Therapies

- Availability of different blood components
- Components used separately or in combination

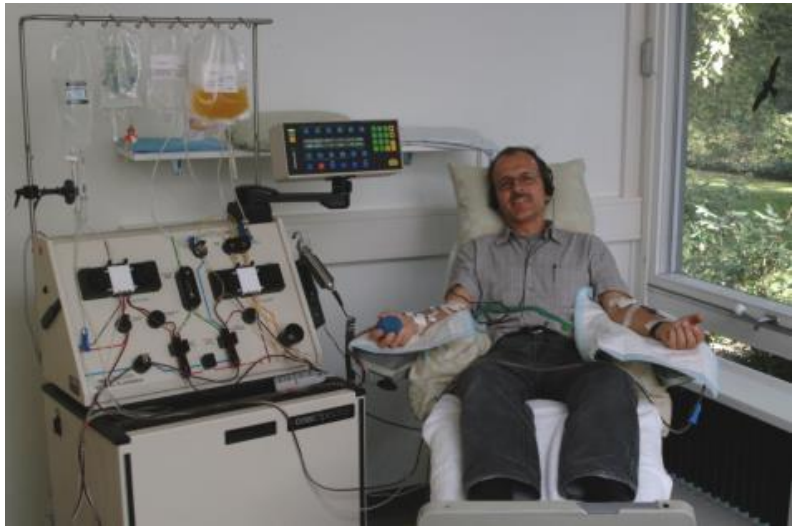
  can meet most patients specific needs and

  keep the risk of treatment to minimum

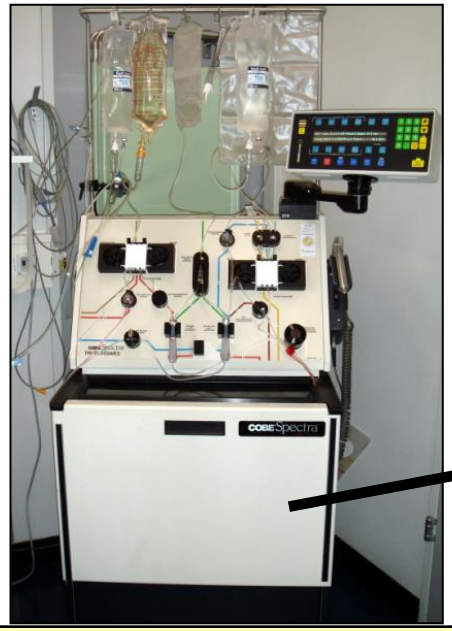
Separation of blood components are desirable because it allows …

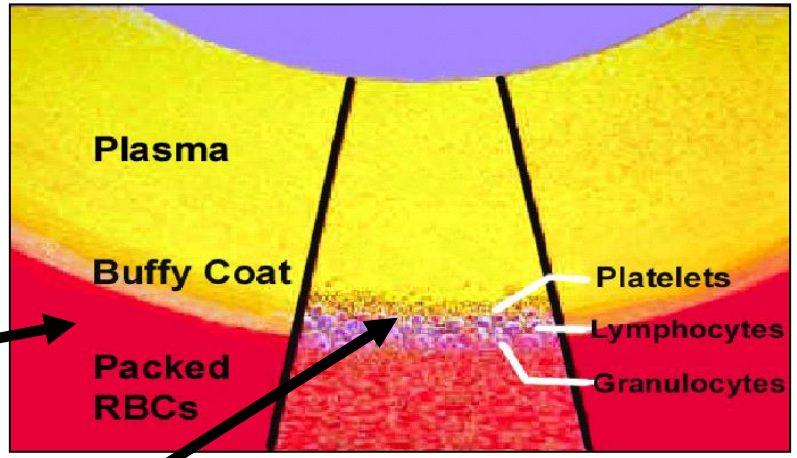
- Optimal survival for each component
- Transfusing specific blood components according to the need of the patient
- Avoiding unnecessary components, which may be contraindicated in a patient
- To treat several patients from one unit of donated blood
- To supplement blood supply and add to the blood inventory

Blood Donation and Component Preparation

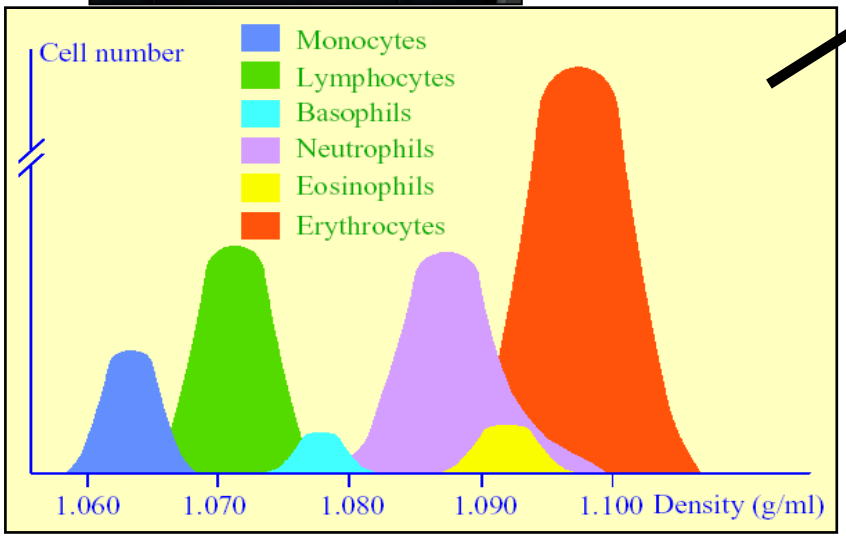


Apheresis Machines: „Cell Separators“





Principle mode of separation by centrifuge

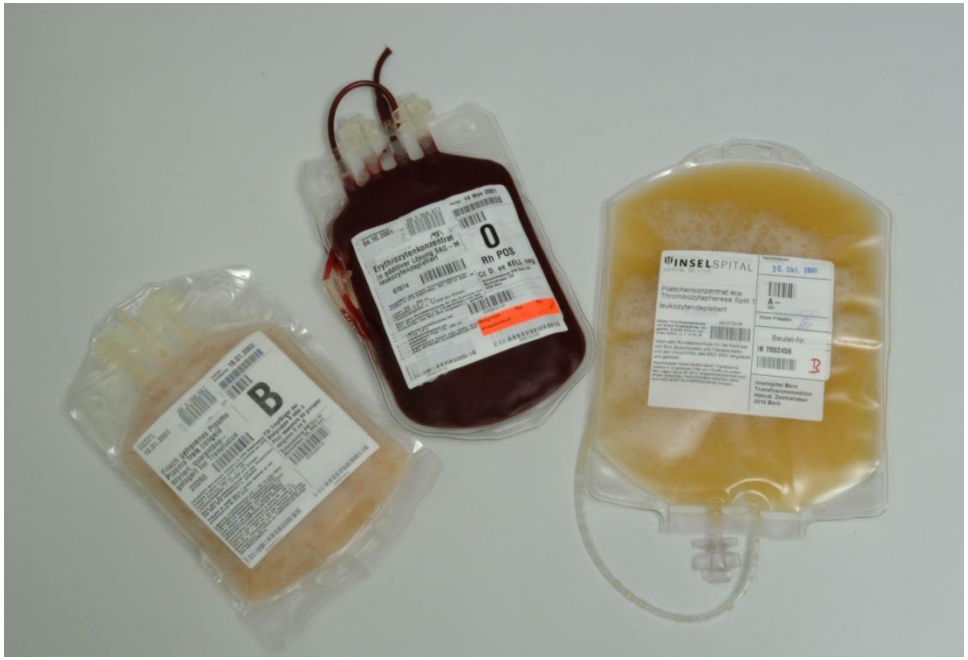


Blood constituents (plasma, cells) show differences in size and density

Principles of Transfusion Therapy

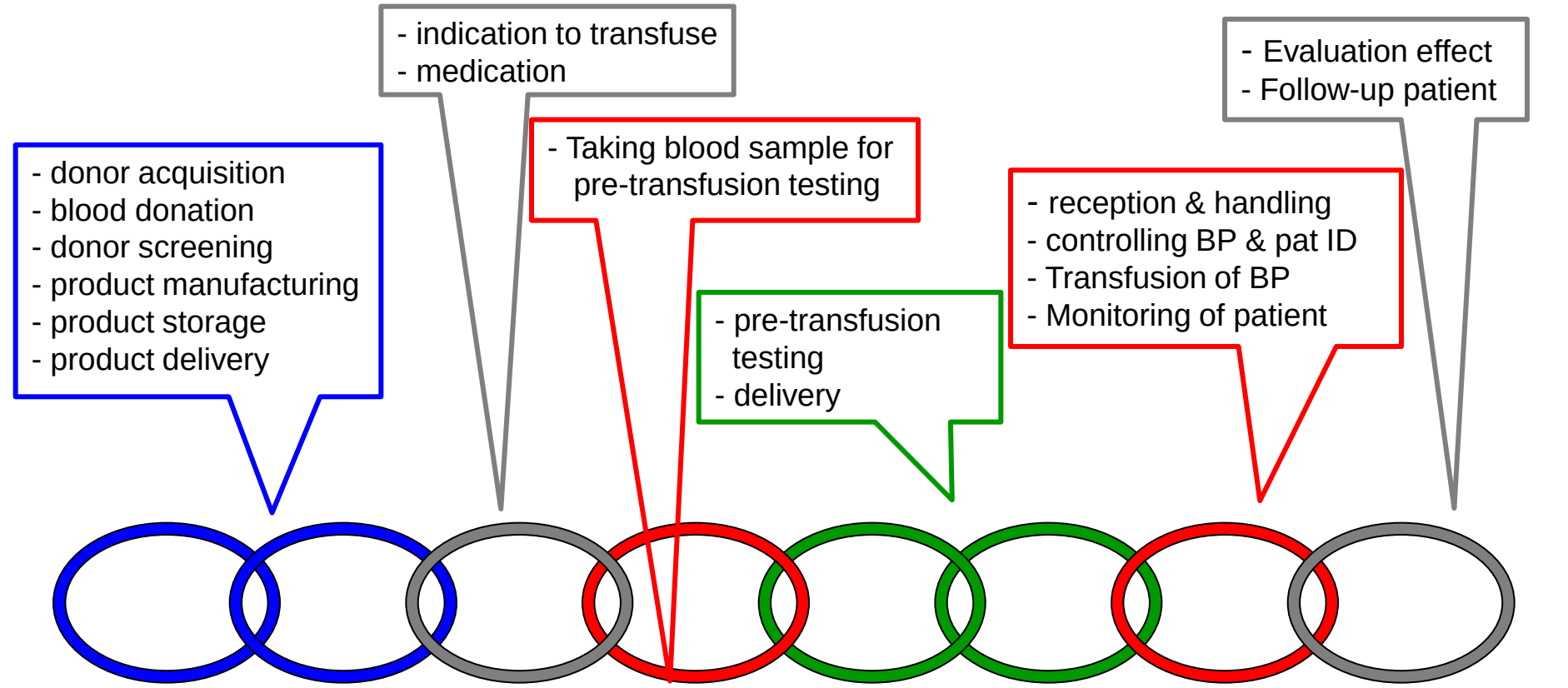
- Transfusion of individually needed blood components

- **Carefully weighing up benefits and risks**

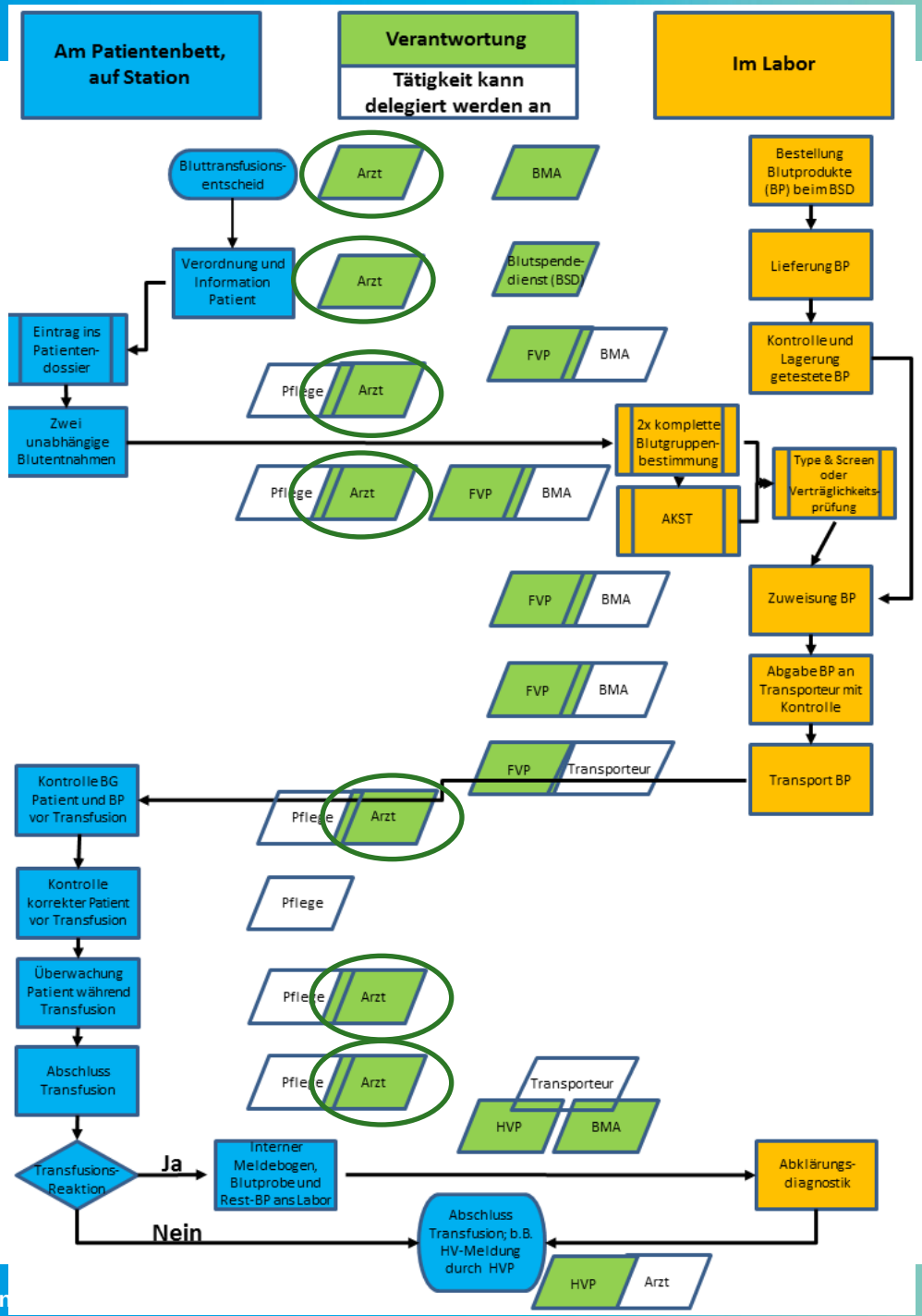


Blood Safety = Process safety, not only a product safety!

Transfusion Chain



Blood Donation Service ↔ **IH-laboratory** ↔ **Nursing staff** ↔ **Doctor**

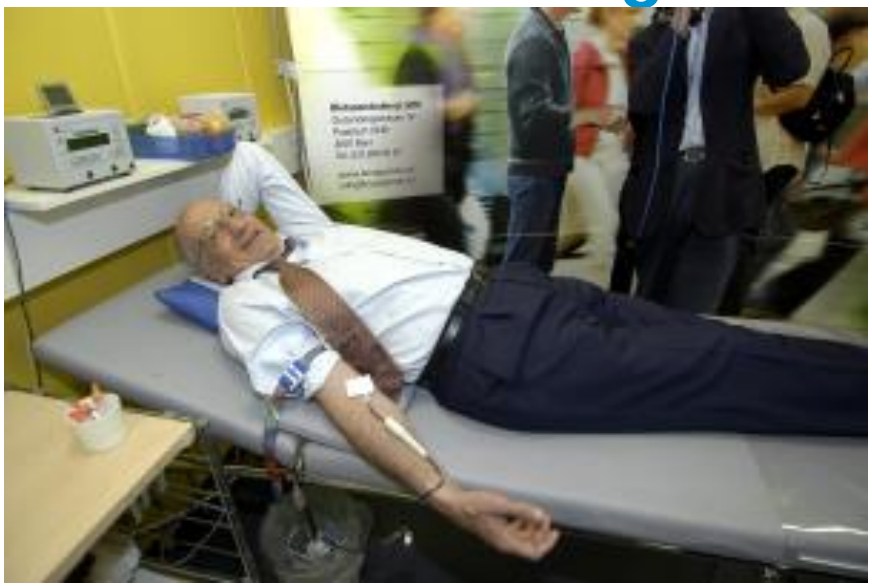


VERANT-WORTUNG?

→Arzt!

FVP: Fachtechnisch verantwortliche Person
HVP: Hämovigilanz-verantwortliche Person
BMA: Biomedizinische Analytiker/in
AKST: Antikörper-Suchtest

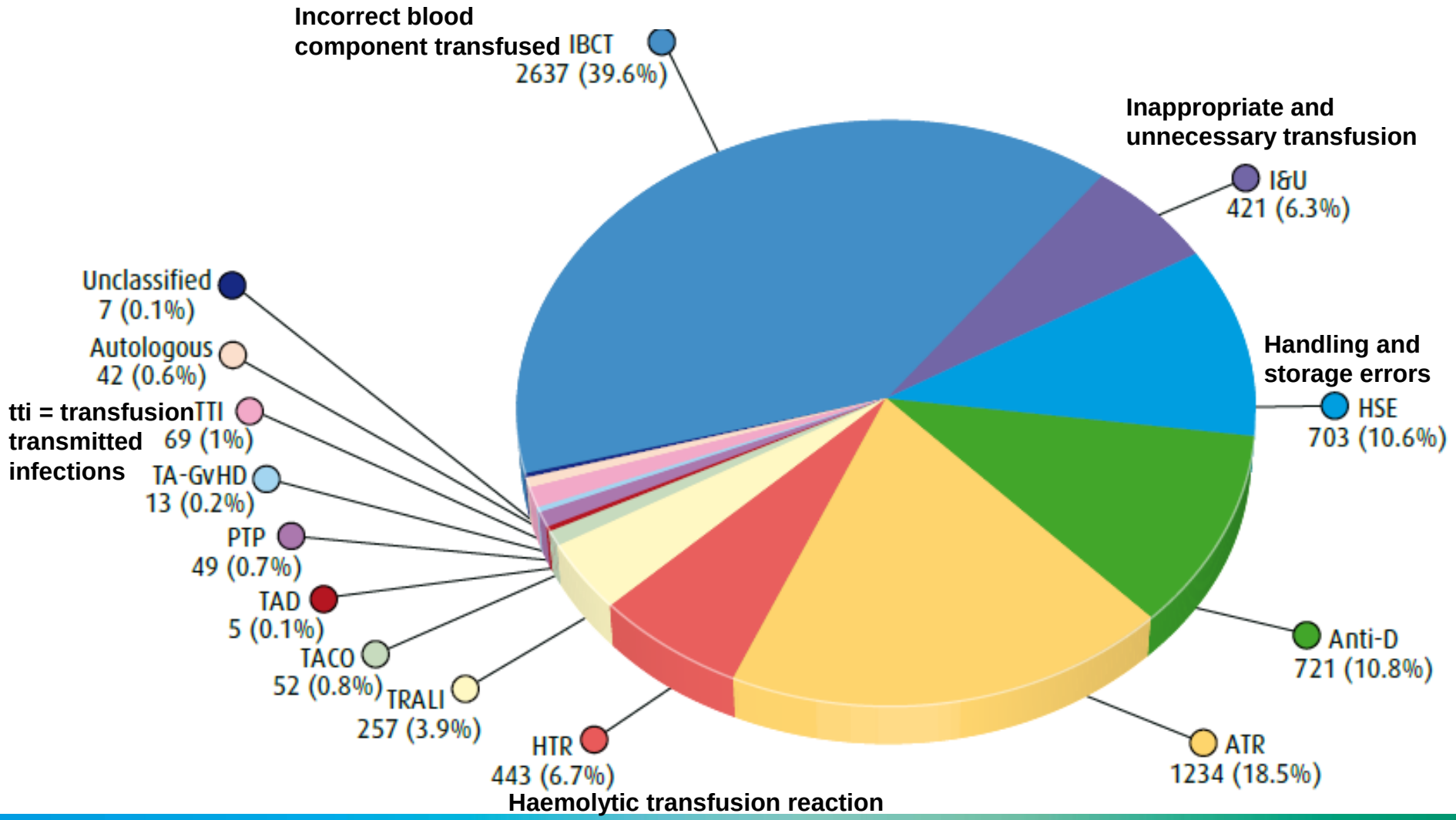
Transfusion Safety and Haemovigilance



- Establishment and monitoring of transfusion standards
- Reporting of adverse events (donation → transfusion)
  - Infections (TTI)
  - Immunological side effects
  - other adverse events
- Evaluation of results
- Implementation of corrective measures

~ 42 Mio Blood units issued in 1996 - 2009 with 6653 Severe Adverse Events

Serious Hazards of Transfusion (= SHOT, UK), Homepage: www.shot.demon.co.uk



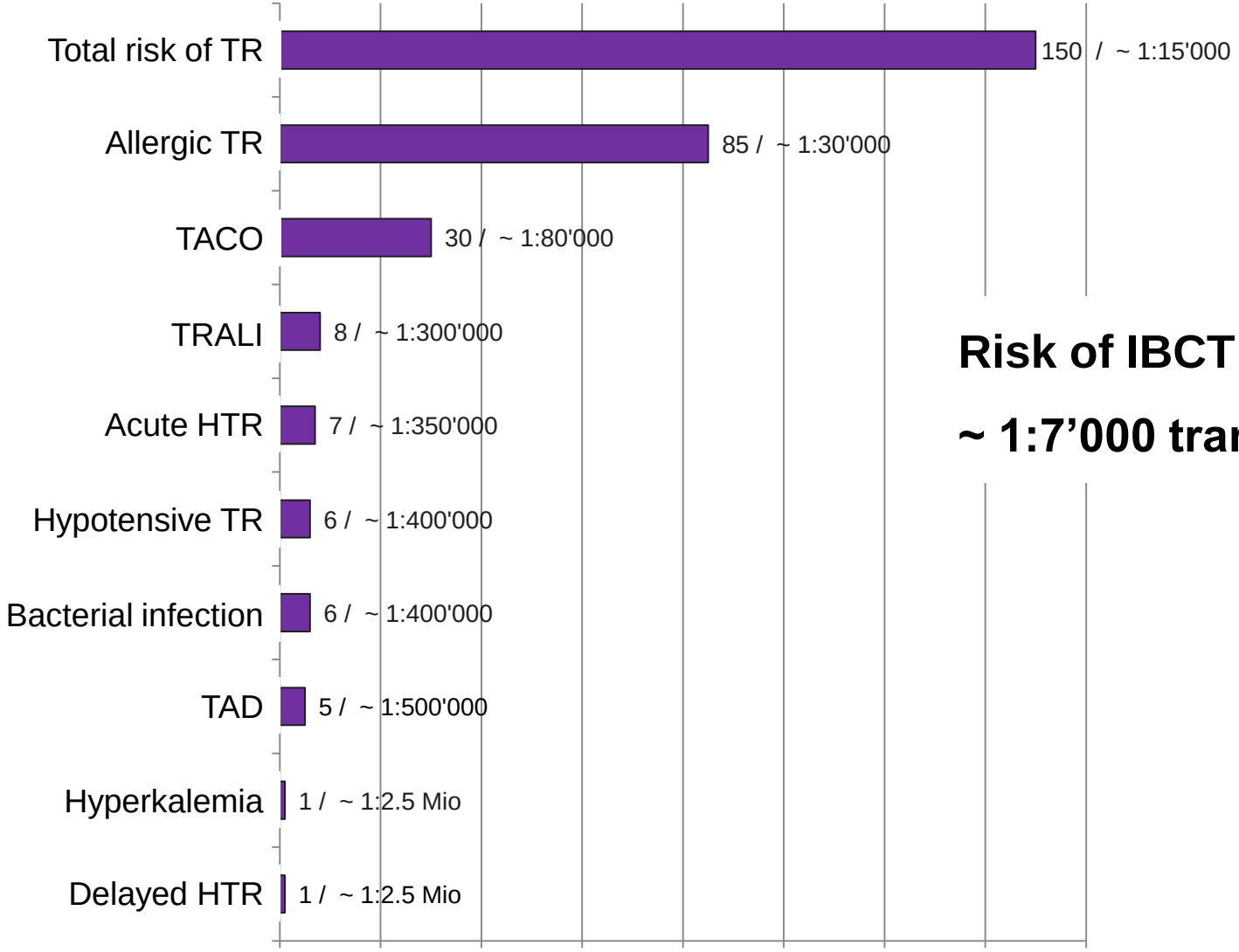
Current estimated residual risk (UK)*

Frequency for hospitals with ≈ 20.000 transfusions / year

Virus	Residual risk	Frequency
HBV	1 : 0.36 Mio	1 / 20 Y
HCV	1 : 10.8 Mio	1 / 500 Y
HIV	1 : 4.3 Mio	1 / 200 Y

*Niederhauser C; personal communication

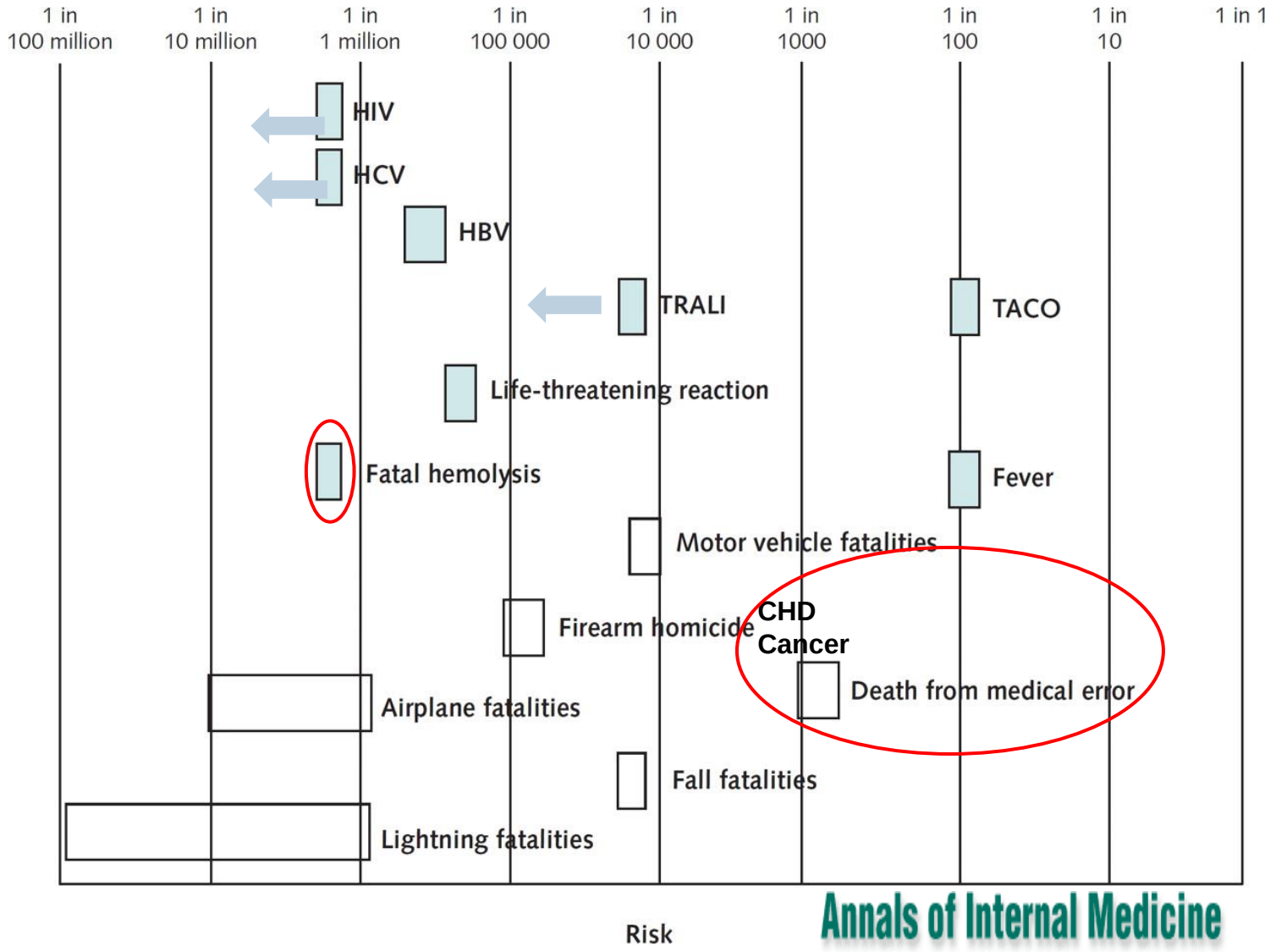
Risks of transfusions in CH (2008-13), all BP, grade 3&4



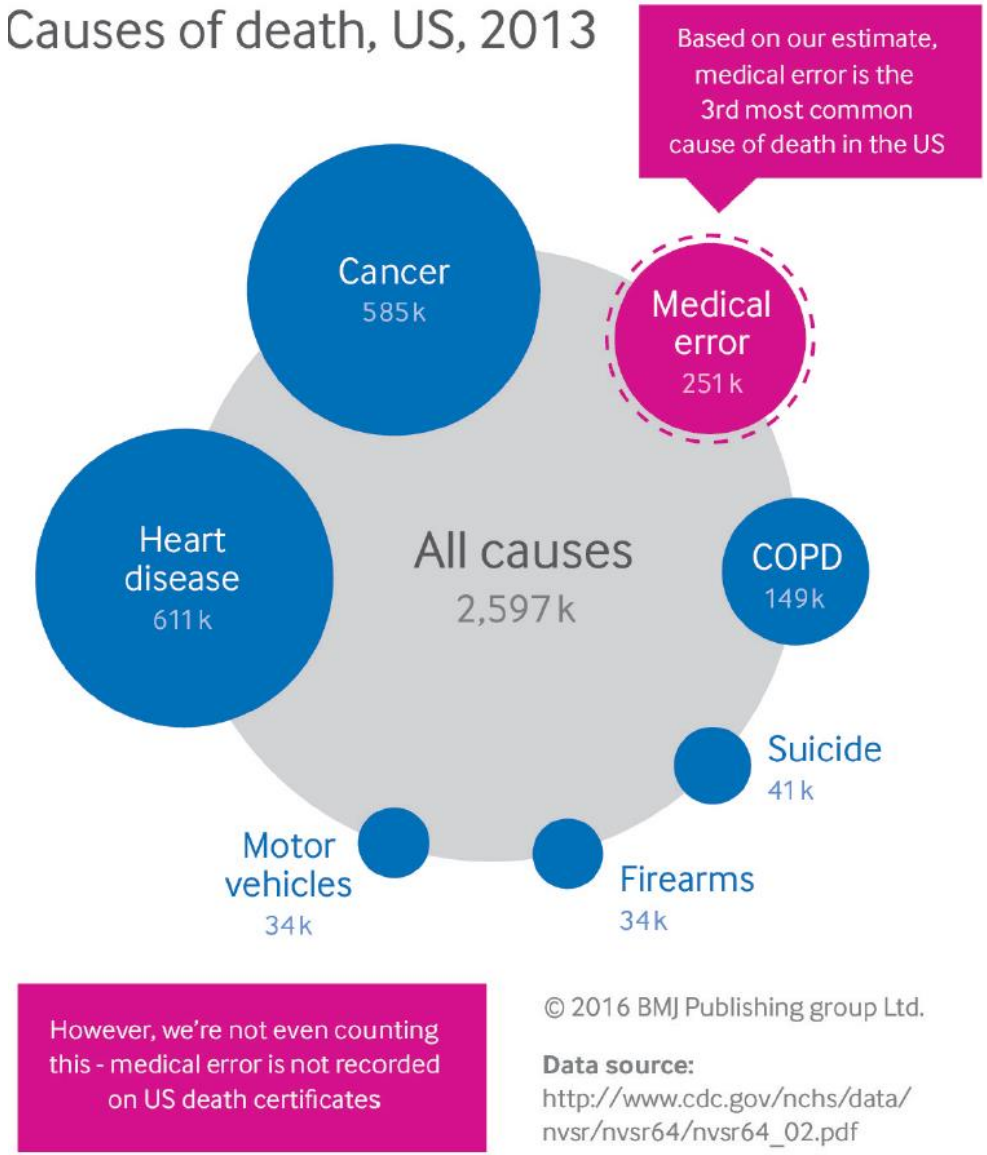
Risk of IBCT in 2014:

~ 1:7’000 transfusions

Adverse effects of RBC transfusion contrasted with other risks



Carson J L et al. Ann Intern Med 2012



USA population:

319.000.000 (2014)

Death from medical error:

251.000/Y:

➔1 in 1.271 residents/Y

Makary M, Daniel M: Medical error - the third leading cause of death in the US. BMJ 2016;353:1-5

Specifications of Red Blood Cell (RBC) Units

RBC out of whole blood donations	RBC out of apheresis blood donations
Whole blood donations → Processing within 48 h	"Online" collection by cell separators
Variable Volume 275 ± 75 mL	Standardized: e.g. 275 mL
Hemoglobin > 40 g/Unit	
Hematocrit 0.6 ± 0.1	
Leukocytes < 1 x 10^6	
Storage: 42 - 49 days, 4 ± 2° C;	

Rational of RBC Transfusion…

Avoid anaemia induced hypoxemia, in order to

- **Reduce anaemia-associated mortality**
- **Reduce anaemia-associated morbidity**
  - **Cardiovascular complications**
  - **Cerebrovascular complications**
  - **Pulmonary complications**

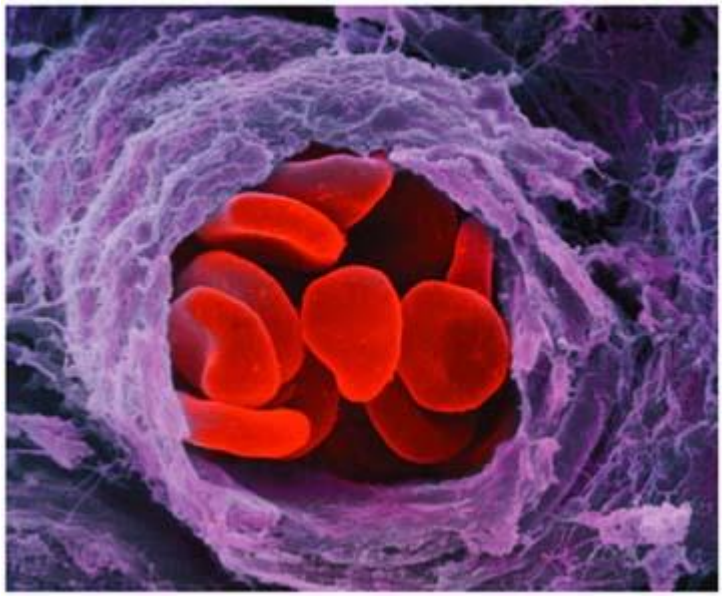
… Therefore the

Goal of Blood Transfusion is to

- **Improve Tissue Oxygen Delivery**
- **Avoid Critical Tissue Hypoxia**

Determinants of Oxygen Delivery (DO_2) to Tissues

- In Health:
  - DO_2 2 to 4-fold greater than requirements



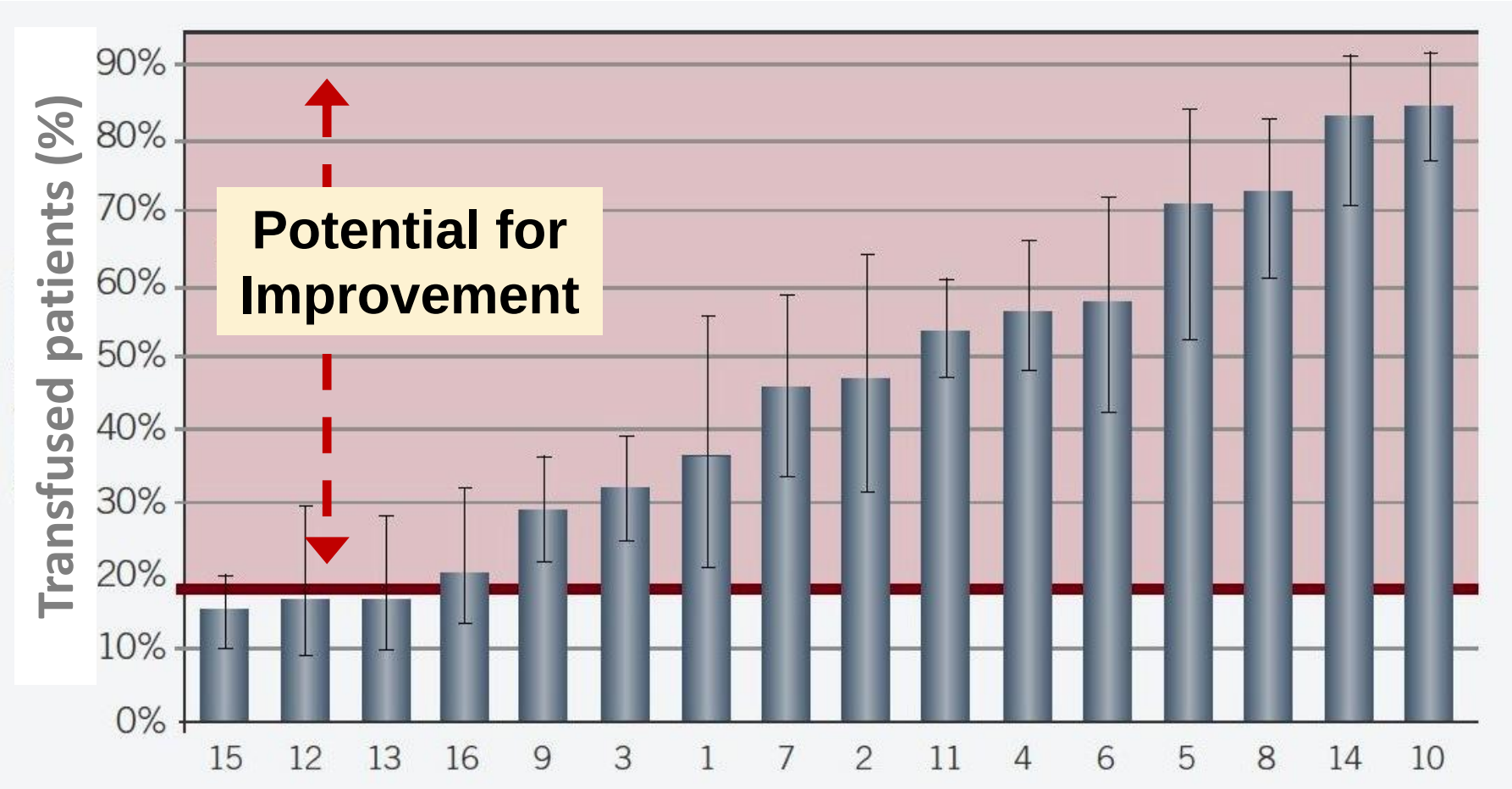
- Determinants of DO_2:
  - Hb level
  - Oxygen saturation
  - Cardiac output
  - Microcirculation
  - Hb O_2 release

black box in clinical practise

Hebert PC, CMAJ 1997; Tinmouth et al, Transfusion 2006

Blood use in elective surgery: the Austrian benchmark study

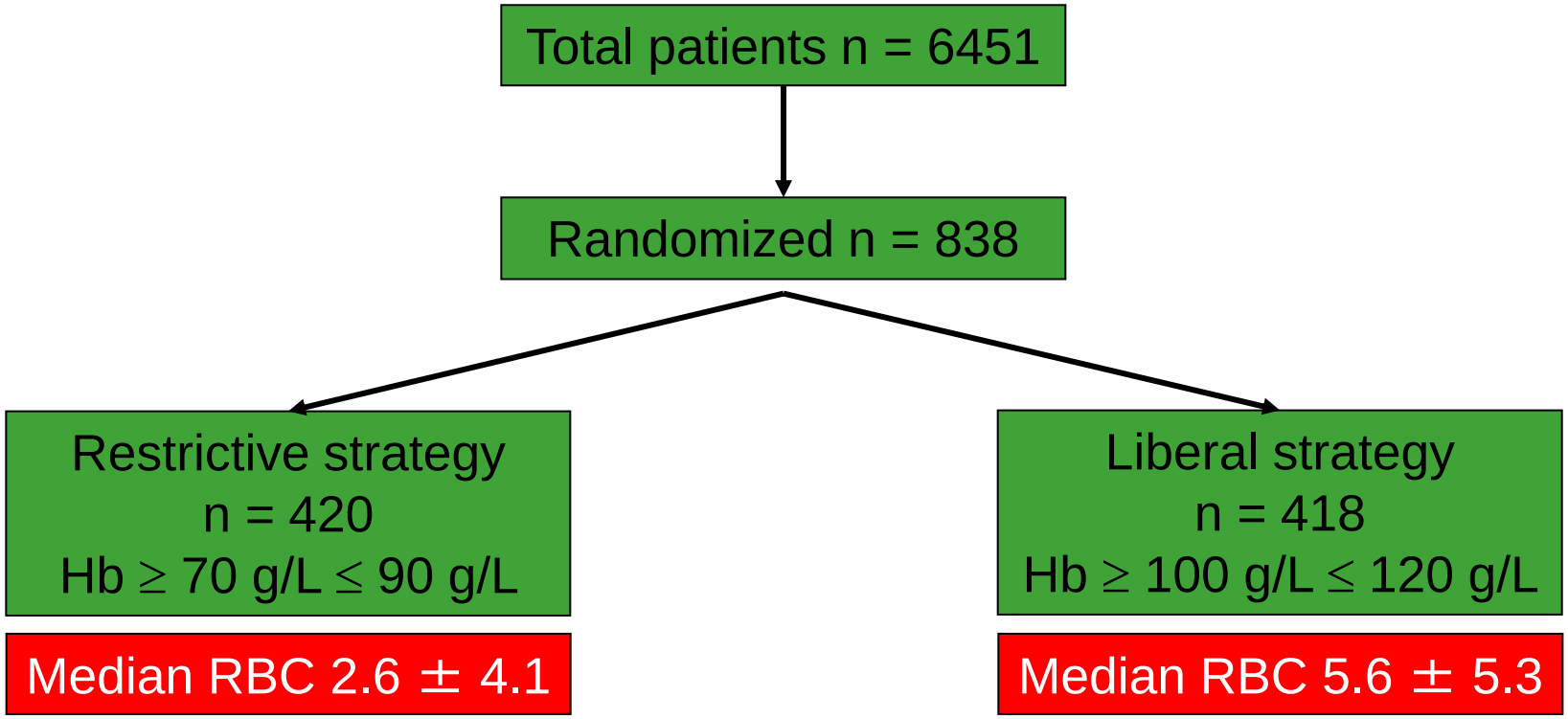
n=2600 TKP & THP; 04/2004 – 02/2005; Transfusion 2007;47:1468-80



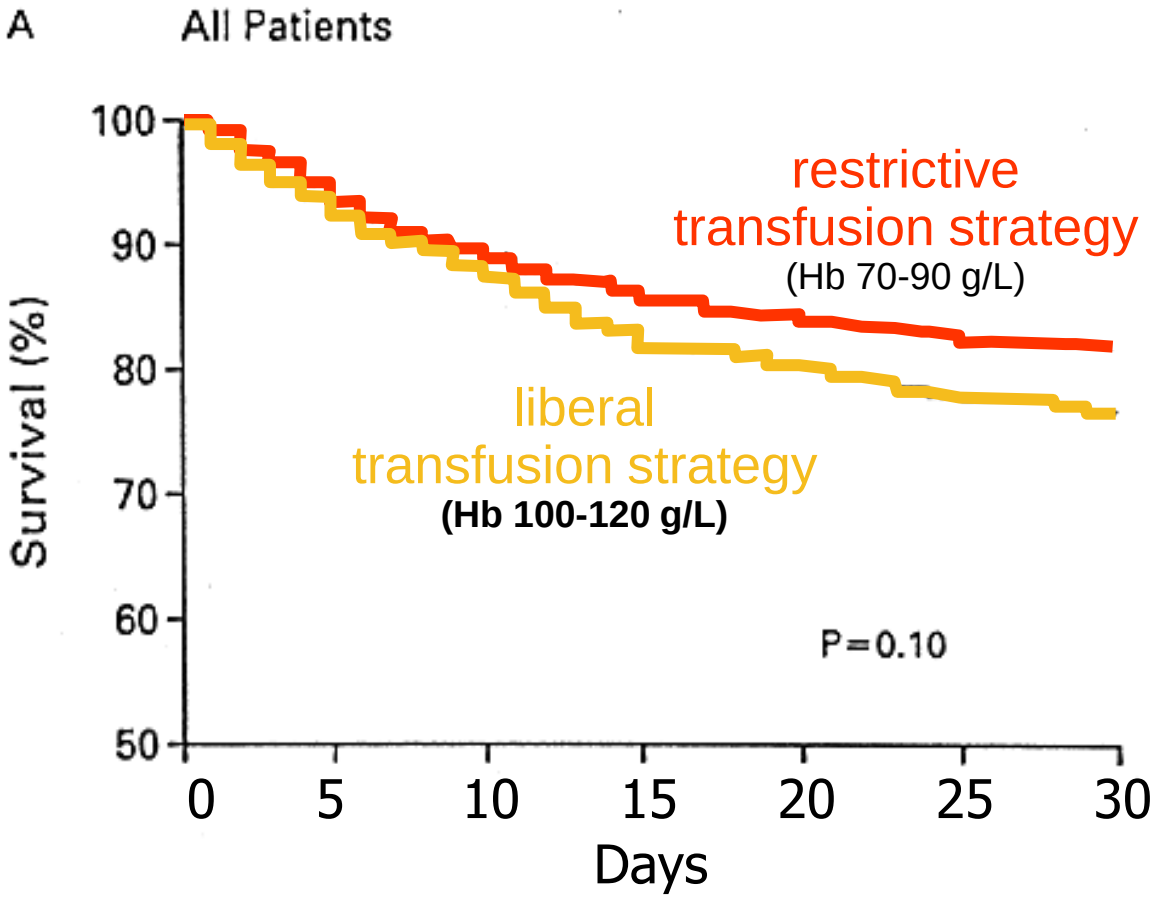
A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care (TRICC)

Hébert et al., N Engl J Med. 1999;340:409-417

- Intensive care patients of 25 Canadian hospitals, 11/94 – 11/97
- Inclusion criteria: - Hb ≤ 90 g/L within 72 h of hospitalization
  - Normovolemic



The TRICC Trial

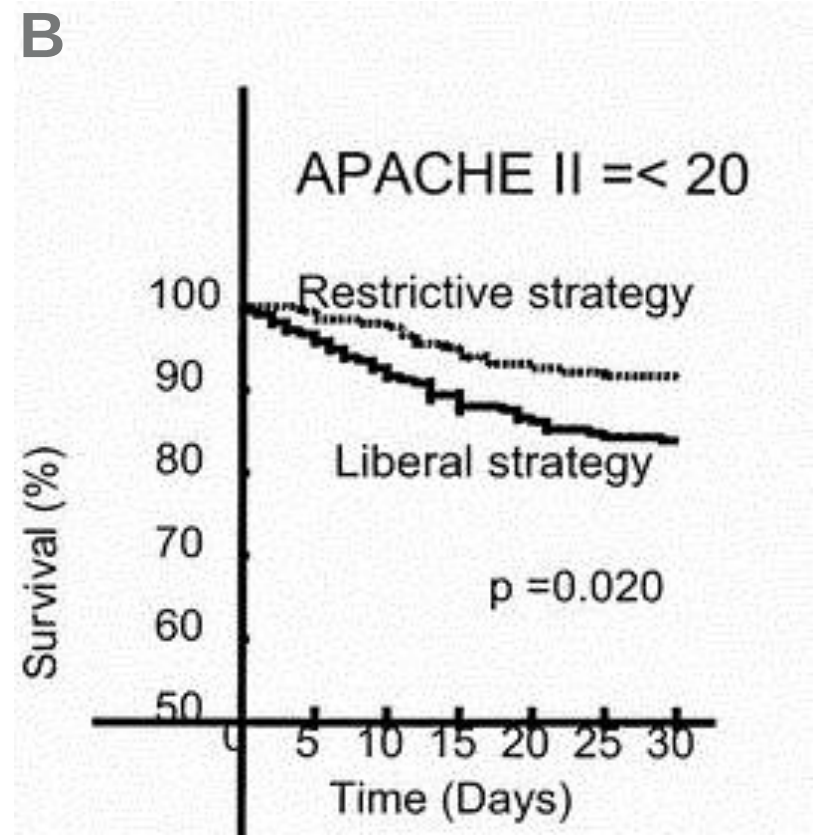


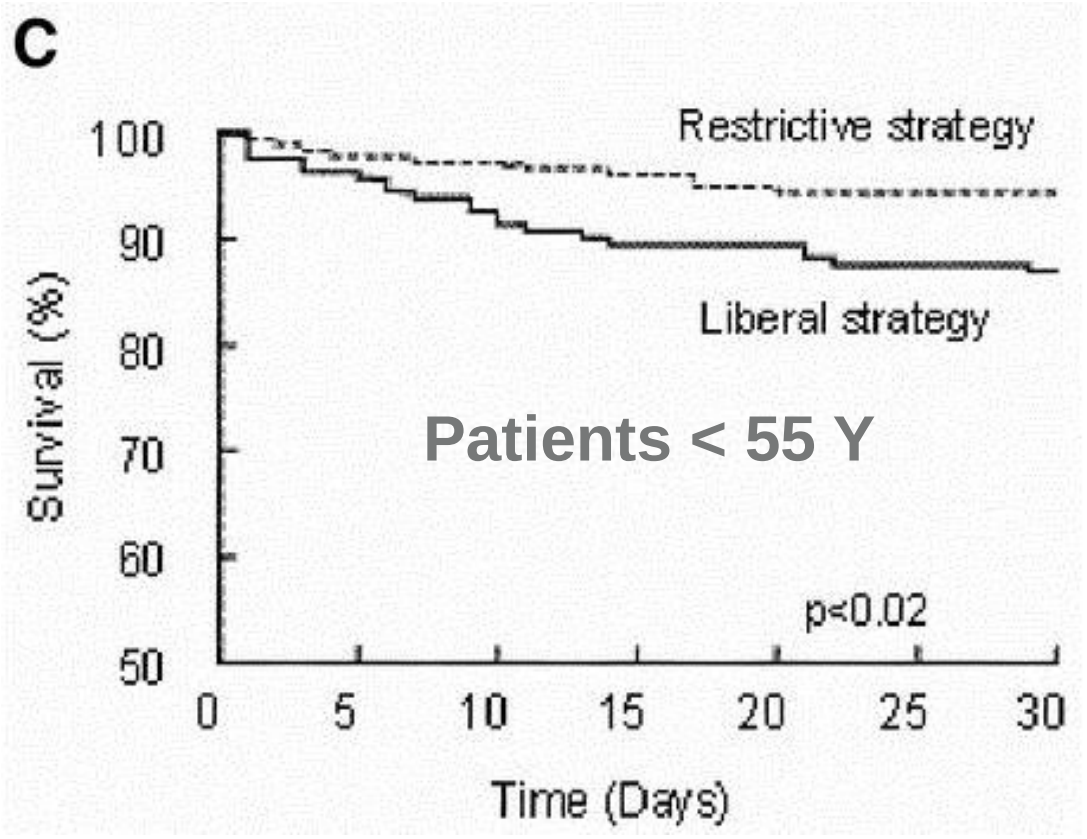
RBC 2.6 ± 4.1

RBC 5.6 ± 5.3

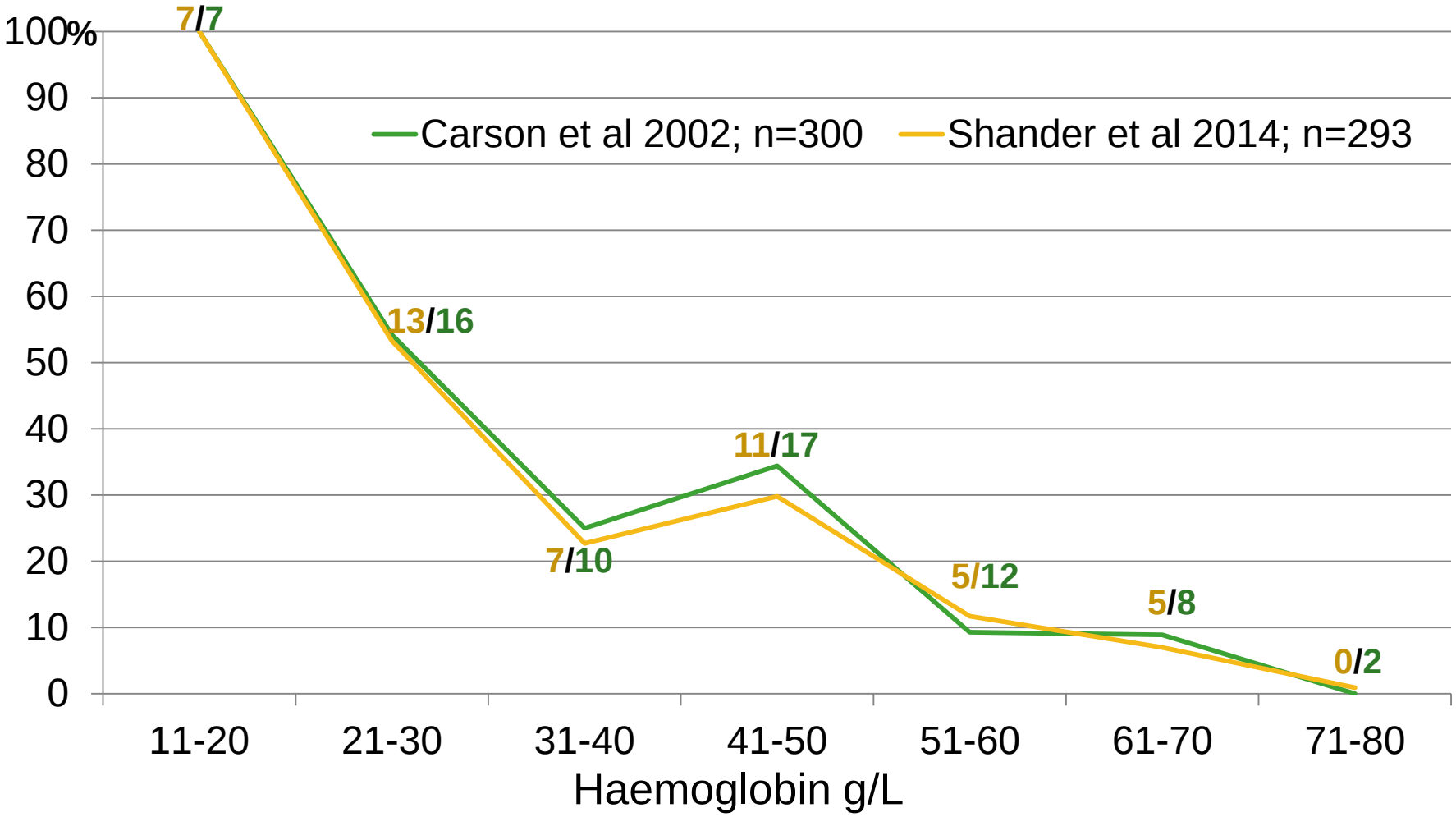
Hébert et al., N Engl J Med 1999;340:409-417

RBC Transfusion in Intensive Care





"How low can we go"
Mortality rate (% & #) and postop Hb-Nadir



Randomized Transfusion-Trigger-Studies for RBC (n>40)

TRICC

TRIPICU

FOCUS

Villanueva

FOCUS
3yr follow up

TRISS

MINT
(pilot)

TRACS

TITRe2

Almeida

etc., etc., …

Mirski MA et al: Restrictive and liberal red cell transfusion strategies in adult patients: reconciling clinical data with best practice. Anesthesiology. Critical Care 2015;19:202

- The conclusion is that **in the majority of clinical settings a restrictive RBC transfusion strategy is cost-effective, reduces the risk of adverse events specific to transfusion, and introduces no harm.**
- **In** anemic patients with **ongoing hemorrhage, with risk of significant bleeding,** or **concurrent ischemic brain, spinal cord, or myocardium, the optimal hemoglobin transfusion trigger remains unknown**.
- Broad-based **adherence to guideline** approaches of therapy **must respect** the **individual patient condition …**

Van Remoortel H et al: Methodologic quality assessment of red blood cell transfusion guidelines and the evidence base of more restrictive transfusion thresholds. Transfusion 2016;56:472-80

RESULTS:

… 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.

CONCLUSION:

…. More high-quality trials are needed to provide a stronger scientific basis for RBC transfusion guidelines that recommend more restrictive transfusion thresholds.

Carson JL, et al: Transfusion thresholds & other strategies for guiding RBC transfusion. Cochrane Database of Systematic Reviews 2016

Data analyzed

31 randomized trials testing “restrictive” (< 70 or 80g/L, sometimes <90) vs. “liberal” transfusion triggers between 1950-2016, involving 12,587 participants

Conclusions

- restrictive transfusion decreased exposure to RBC transfusion by 43%
- restrictive strategy without impact on 30-day mortality or morbidity
- Good evidence that transfusions with allogeneic RBCs can be avoided in most patients with haemoglobin thresholds above 70 g/L to 80 (to 90) g/L
- insufficient data in acute coronary syndrome, myocardial infarction, acute neurological disorders, neurological injury/traumatic brain injury, stroke, thrombocytopenia, solid/hematological malignancies, bone marrow failure

Hovaguimian F et al: Restrictive versus Liberal Transfusion Strategy in the Perioperative and Acute Care Settings: A Context-specific **Systematic Review and Meta-analysis of Randomized Controlled Trials**. Anesthesiology 2016;125:46-61

RESULTS: Thirty-one trials ...

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 …, but not in critically ill patients. …

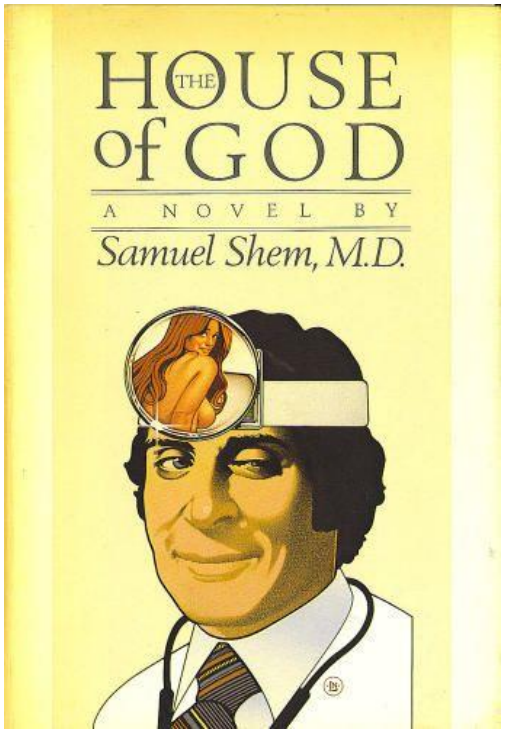
CONCLUSIONS:

Restrictive transfusion strategies should be applied with caution in high-risk patients undergoing major surgery.

LAWS OF THE HOUSE OF GOD: XIII

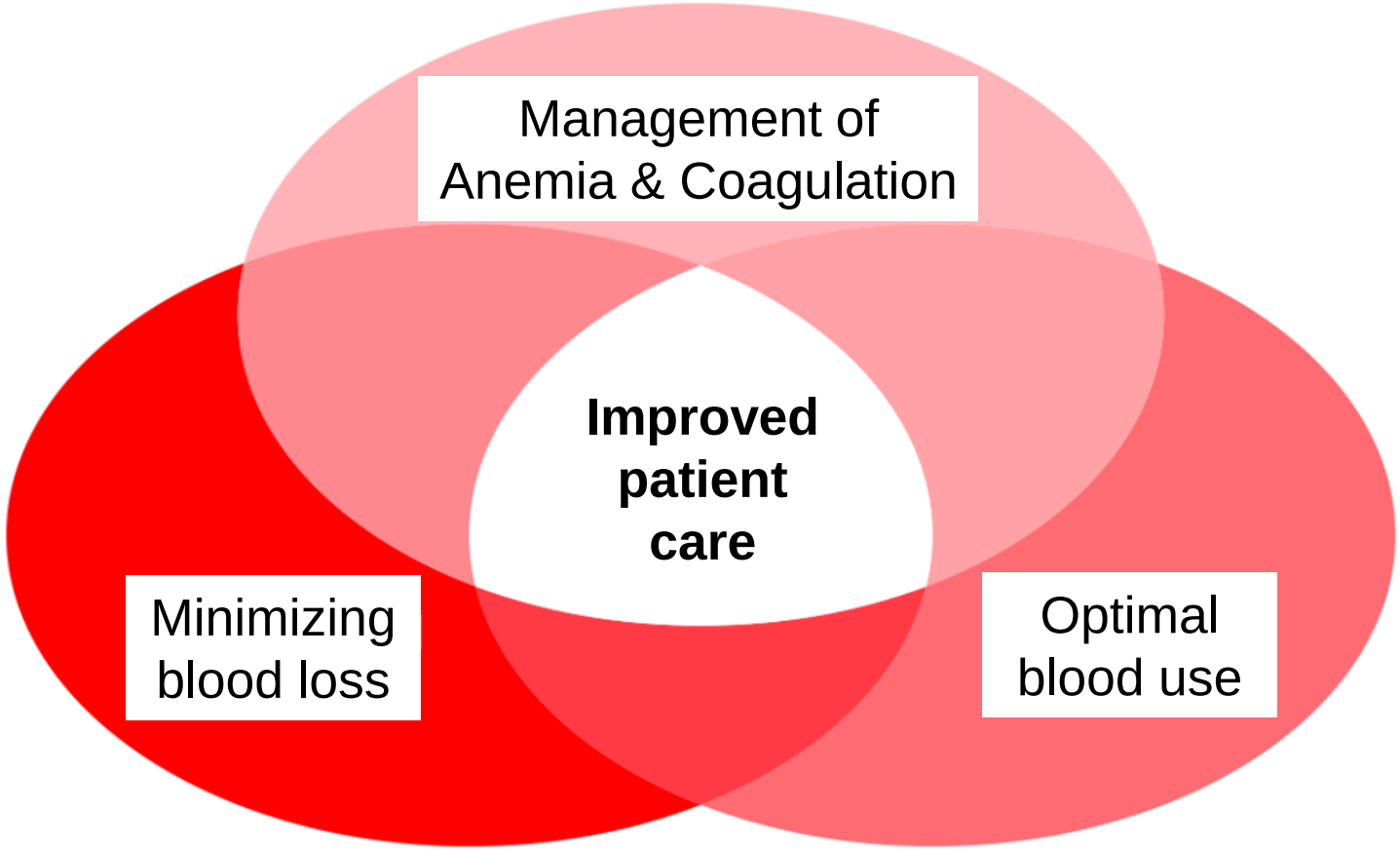
“The delivery of good medical care is to do as much nothing as possible”

Samuel Shem, M.D., 1978



“Hip”: Patient Blood Management

“The three pillars of PBM”



PBM – "old fashioned" synonym may be Optimal Hemotherapy & Blood Saving Measures*

- Optimal blood component use (as much as needed / as little as possible)
- If planning elective surgery
  - Treat iron-deficiency ± anemia in advance → iron ± Erythropoetin
  - Treat possible coagulopathies in advance
  - Consider autologous donation ± Erythropoetin
  - (Consider acute normovolemic Hemodilution)
- Optimize surgical techniques →„bloodless surgery"
- Intra-operative blood salvage
- Local and/or systemic measures for improving hemostasis
- Minimizing the volume of withdrawn blood samples (saving blood loss!)
- …

*e.g. Mansouri Taleghani B, Reith HB, Wiebecke D, Thiede A: Hämotherapie in der operativen Medizin (Teil 1+2). Zentralbl Chir 1999,124:W19-41

“Three Pillars of PBM”

1. Pre-operative Management of Anemia & Coagulation
PBM-ambulatory: Diagnosis and treatment of anemia and coagulopathy in elective surgery (risk of transfusion >10%). Utilization of waiting time until surgery.

2. Optimal Blood Use / Use of RBC
Adherence to implemented guidelines for transfusion

3. Further Blood Saving Measures
Restrictive taking of blood samples, blood-less surgery, Cell-Saver, management of body temperature, point-of-care diagnostic, management of coagulation

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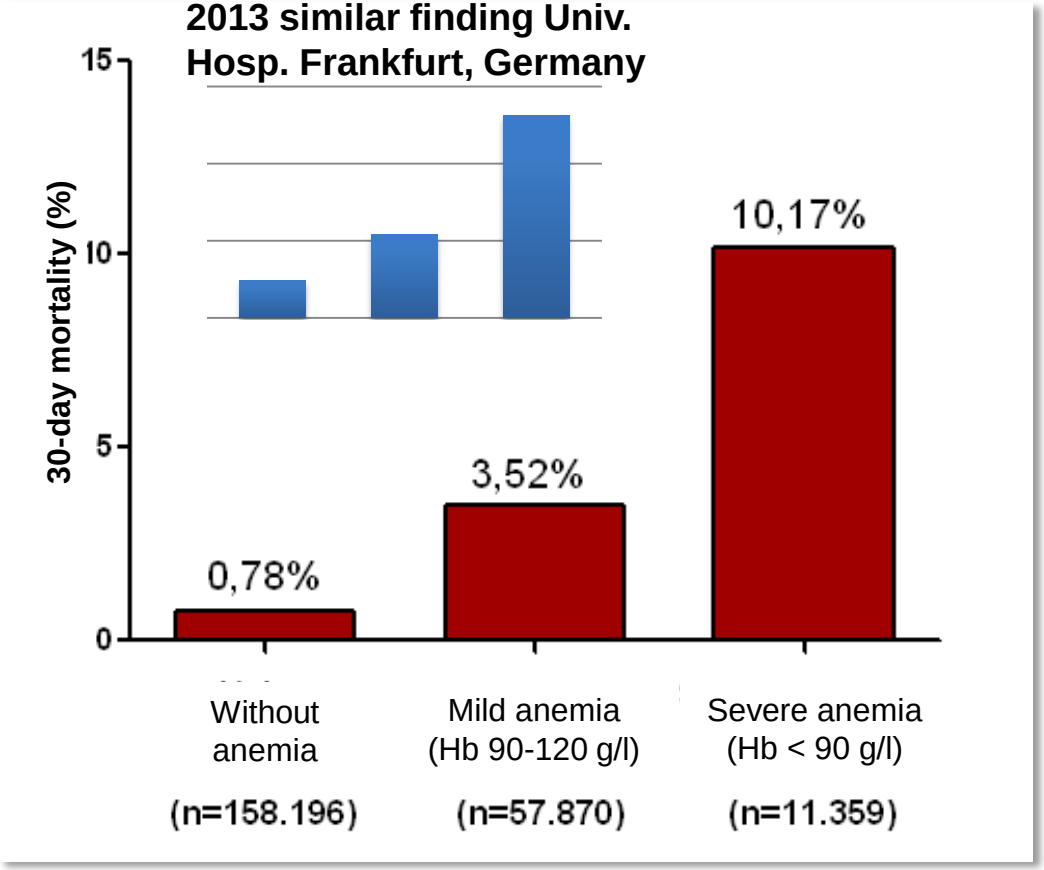
Musallam KM et al: Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet 2011;378(9800):1396-407

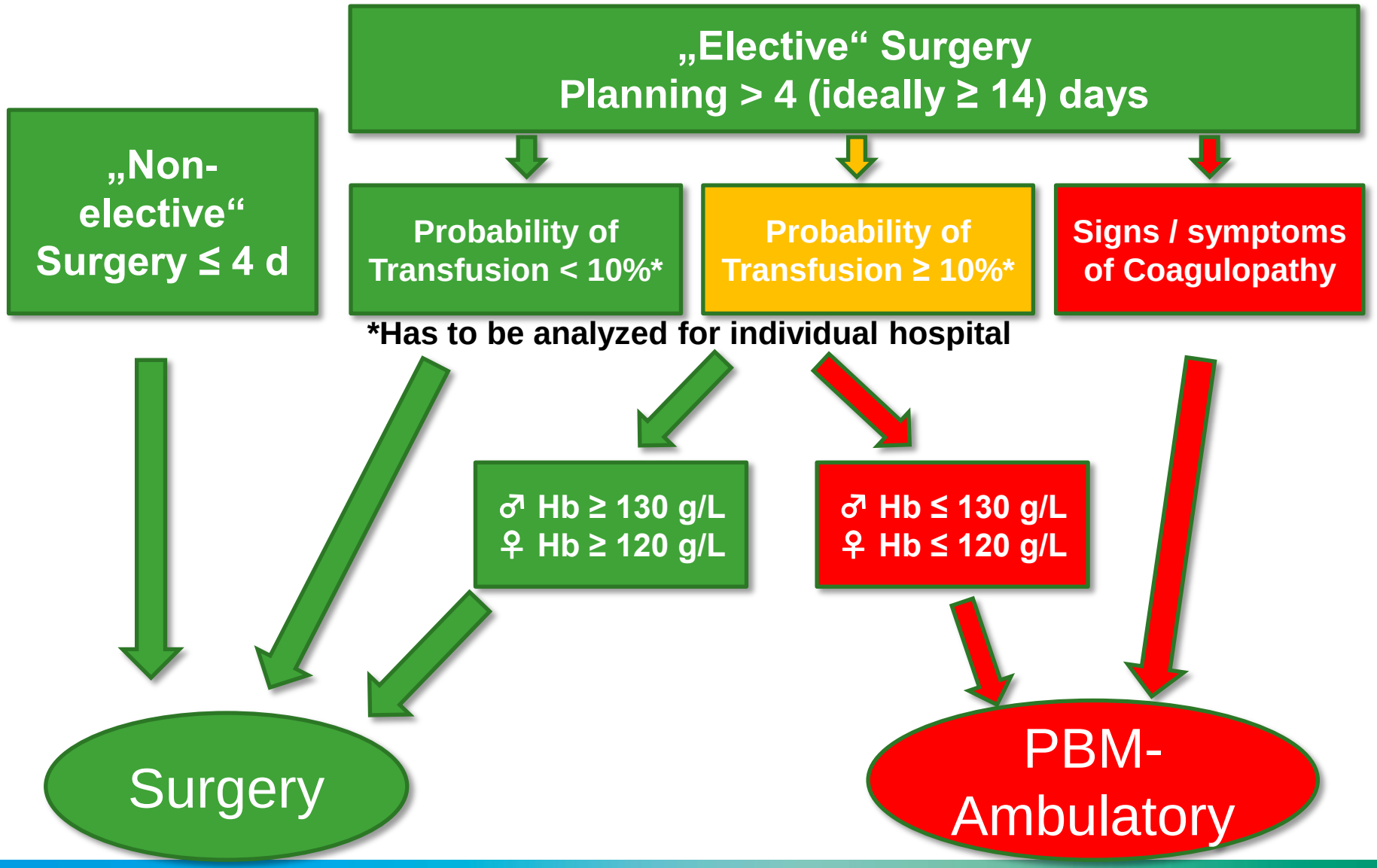
FINDINGS: … 227,425 patients, of whom 69,229 **(30·44%) had preoperative anaemia**….

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**.



Pre-operative Patient Pathway in PBM



Surgical Procedures with Transfusion Probability ≥ 10%

Inselspital 2014

Herz- und Gefässeingriffe
- Eingriffe an Herz, Perikard, Aorta ± ECC
- Re-Sternotomie, Rethorakotomie
- Transkatheter-Klappenimplantationen
- Aorteneingriffe (offen, endovaskulär)
- Iliaco-femoro-politeale Eingriffe

Thoraxchirurgie
- Erweiterte Pleuropneumonektomie

HNO, Schädel-, Gesichts- und Kieferchirurgie
- Free-Flap-Chirurgie grosser Tumoren

Säuglings- und Kinderchirurgie
- Skoliose Aufrichtung
- Kraniosynostosen

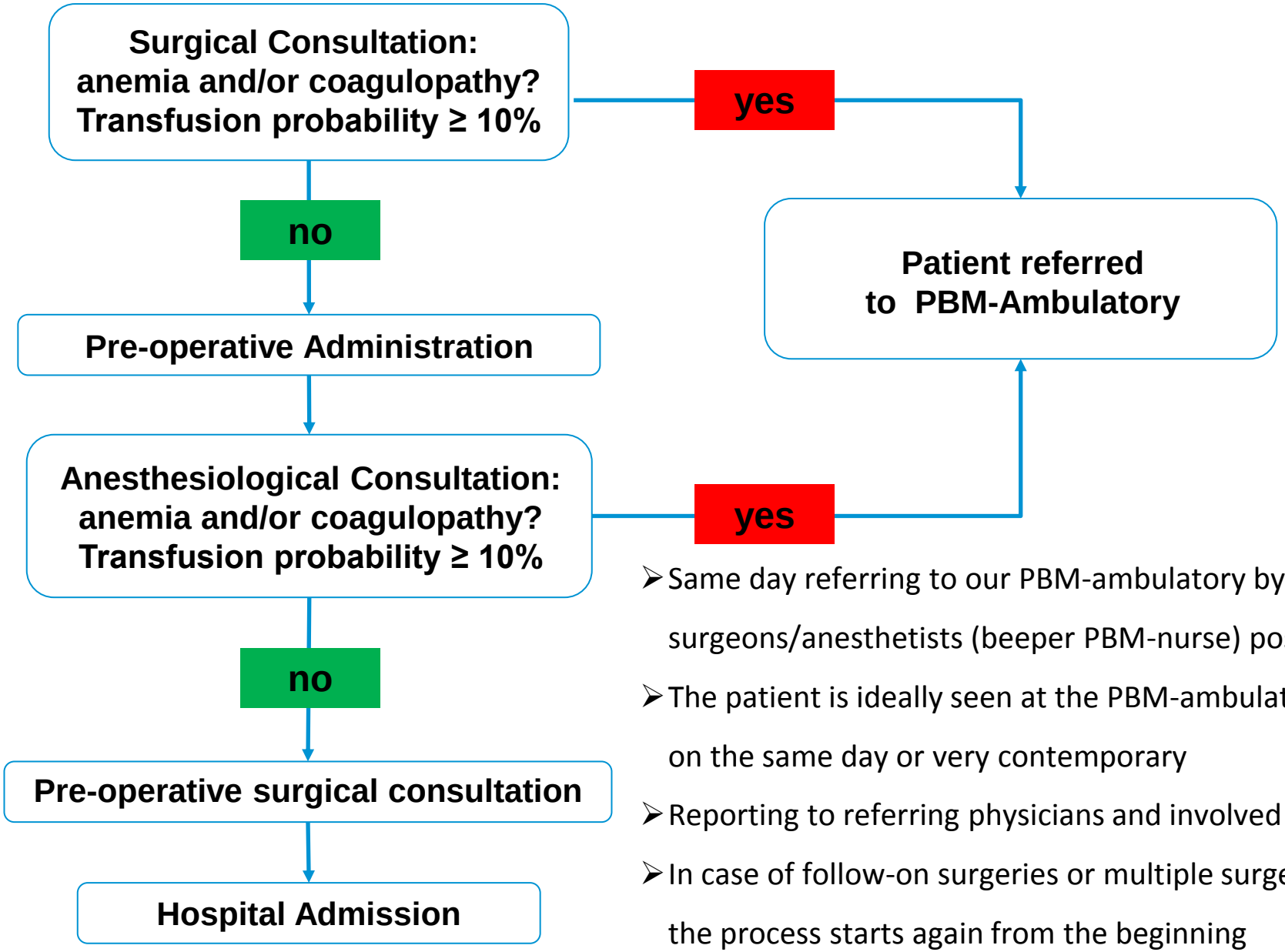
Neurochirurgie
- Tumoren
- Tumoren nähe eloquente Zentren
- Aneurysmen

Orthopädie
- Wirbelsäulen-OP (offen)
- Becken-OP (Prothetik, Osteosynthese, Re-OP)
- Hüft-OP (Prothetik, Osteosynthese, Re-OP)
- Femur- oder Knie-OP (Prothetik, Osteosynthese, Re-OP, Amputation)

Urologie
- Offene Tumorchirurgie der Nieren, Nebennieren
- Radikale Zystektomie
- Blasenersatzplastik
- Suprapubische Prostatektomie

Viszeralchirurgie
- Lebertransplantation
- Offene Leberteilresektion grosser Tumoren
- Resektion grosser retroperitonealer Tumoren
- Resektion grosser intraperitonealer Tumoren ± intraoperativer Chemotherapie-Perfusion
- Ösophagusresektion

H.U. Rieder, 15.01.2015; ergänzt / modifiziert B. Eberle 20.9.16



- Same day referring to our PBM-ambulatory by the surgeons/anesthetists (beeper PBM-nurse) possible
- The patient is ideally seen at the PBM-ambulatory on the same day or very contemporary
- Reporting to referring physicians and involved units
- In case of follow-on surgeries or multiple surgeries the process starts again from the beginning

“Three Pillars of PBM”

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Utilization of waiting time until surgery.

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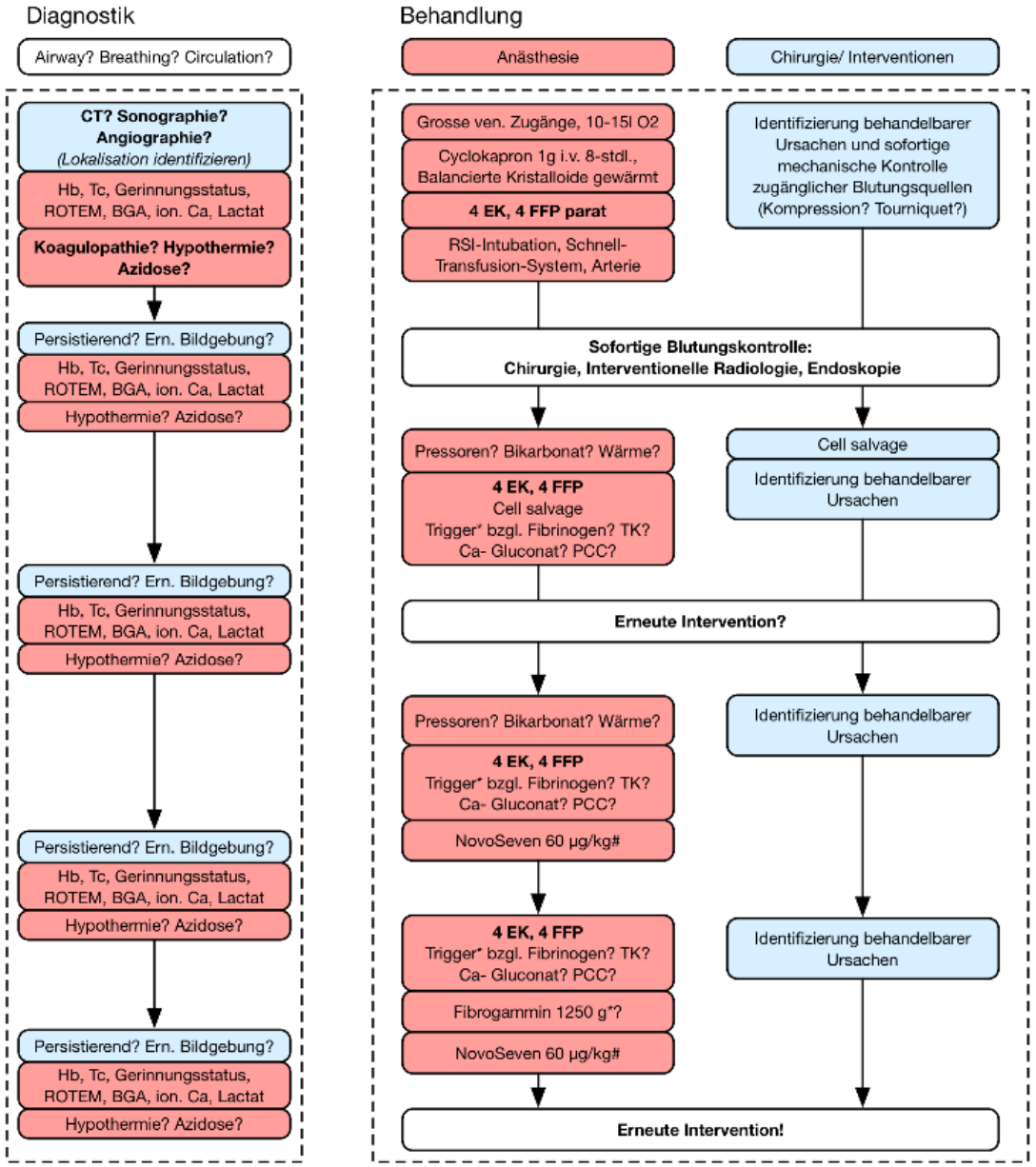
Adopted* Recommendations of RBC Transfusions in Normovolemic Surgical Patients

Hemoglobin	Compensation capacity risk factors	Transfusion: YES/NO	Evidence
≤ 60 g/L (≤ 3,7 mmol/L)	–	YES (exceptions possible)	1 C+
> 60 – 80 g/L (> 3,7 – 5,0 mmol/L)	Adequate compensation and no risk factors	**NO**	1 C+
	Reduced compensation risk factors present	YES	1 C+
	Signs and symptoms of anemic hypoxemia	YES	1 C+
> 80 – 100 g/L (> 5,0 – 6,2 mmol/L)	Signs and symptoms of anemic hypoxemia	YES	2 C
> 100 g/L (> 6,2 mmol/L)	–	**NO** (exceptions possible)	1 A

***„Querschnitts-Leitlinien zur Therapie mit Blutkomponenten und Plasmaderivaten; Herausgeber: BÄK; 2017“ (under review)**

MANAGEMENT MASSIVER BLUTUNGEN



Zielwerte

KREISLAUF MAP ≥ 50 mmHg SAP 80-90 mmHg Kerntemp. > 35°C ScvO2 > 70%	**AZIDOSE** pH ≥ 7.3 BE > -5 mmol/l Laktat < 2.2 mmol/l	*Spezielle Situationen:* **SHT, KHK, SO2↓:** Hb > 80 g/l **SHT/Polytrauma:** Tc > 100 G/l **Schweres SHT:** MAP ≥ 80 mmHg
HÄMATOLOGIE Hb 70 - 90 g/l Tc > 50 g/l	**GERINNUNG** Fibrinogen ≥ 2 g/l Fibtem A10 ≥10 mm Ca ≥ 1.0 mmol/l Q > 50%, CT ↔	

*Behandlungstrigger

EK (ggf. mit FFP≈1:1)	Hb ≤ 70 g/l *(SHT, KHK etc ≤ 80 g/l)*
TK	Tc ≤ 50 G/l *(anhaltende Blutung oder SHT ≤100 G/l)*
Fibrinogen 2 g	Fibrinogen < 2 g/l, Fibtem A10 < 10 mm
Ca-Gluconat 1g	Ca ≤ 1.1 mmol/l
PCC	Q < 50%, CT > Norm *(trotz FFP)* bzw. Q < 70-80% *(Vitamin K-Antagonisten)*
Fibrogammin 1250 g	MCF↓ trotz adäquatem Fibrinogen, PCC, FFP und persist. diffuse Blutung

Behandlung spezifischer Ursachen

Postpartale Blutung	siehe separate Guideline
Obere GI-Blutung	Frühzeitig Endoskopie & Vasopressoren
Antikoagulantien	siehe separate Guideline
Antiaggregantien	TK, evtl. Desmopressin 0.3 µg/kg
DIC	FFP, Dienstarzt Hämatologie
Hämophilie	Dienstarzt Hämatologie
Andere hereditäre Störungen	Dienstarzt Hämatologie
#VAD-/ECMO-/Koronarstent	Extreme Zurückhaltung mit NovoSeven und Zurückhaltung mit PCC

Standorte der Gerinnungsfaktoren

INO-D OP-Zentrum Einleitungsraum OP 7
Frauenklinik FKL Geschoss A (Gyn. OP)
Frauenklinik FKL Geschoss B (Geburtshilfe)
Dezentrale Notfalllager: *UNZ, Klinik für Intensivmedizin, Intensivstation der Kinderklinik*

Blutprodukte

Transfusionsmedizin („Massive Blutung"): 2 3307

Hämostaseologischer Support

Hämostaselabor:	2 3307
Dienstarzt Hämatologie:	181 6220
Dr. Nagler (Bereichsleitung):	181 8265

M. Nagler 08.06.2016

Aktuell in Bearbeitung

Postpartale Hämorrhagie bei vaginaler Geburt[1]

1 Def n.WHO: FortdauerndeBlutung
EBV > 500 ml n. vag. Geburt,
EBV > 1000ml n. Sectio

Geburtshelfer	Anästhesie

G E B S

Geburtshilfliche Beurteilung
- Tonus (**Uterotonika**)
- Trauma (**Inspektion Geburtswege, Uterusruptur ausschliessen**)
- Restgewebe (**Ultraschall**)

Basislabor, T/S, Hb, Tc, Quick/INR, aPTT, Fibrinogen, TZ, FXIII, Röhrli für Rotem,

Bestelle 4 EK, 4 FFP, 1PKT,2g, Hämocompletan, Novo Seven
Code PPH Tel 2 3307

Massnahmen

Cyclocapron 1 g in 100 ml NaCl iv (10')

Syntocinon 5IU i.v.10-20 IU /2 H per Infusion und /oder

Cytotec 1000 µg rektal

Methergin 0,2mg im oder iv (nicht bei Hypertonie / Präeklampsie!)

Nalador 100-500µg/h i.v.am Infusomat

181 5912 → **Anästhesie**

Venöse Zugänge in genügender Anzahl und Grösse, O_2 10-15l/min. Reservoir-Maske

Volumen/Blutprodukte

- Voluven (gewärmt) max. 20ml/kg
- Cyclocapron 1g i.v. über 10min. falls noch nicht erhalten
- 2 EK O neg. n. Bedarf

Evt. **Interventionelle Radiologie** im frühen **stabilen** Stadium **Embolisation Aa. uterinae**

Entscheidungshilfe, wann in Op fahren
Puls>100 Cave Bradycardie b. Sportlern
oder Pat mit /bei Betablocker, PM, congenitaler Herzblock

O P S

Curettage
Geburtsverletzung / Trauma versorgen
Uterustamponade Bakriballon oder Gazekompressen

Persistierende Blutung

RSI – Intubation, Level 1 , Arterie

Syntocinon 10-20 IU /2 h per infusion

Nalador 100-500µg/h i.v.am Perfusor

Ziel:
- MAP 50mmHg, pH>7,2
- Hb>85g/l Kerntemp.>35°C
- Tc> 50 10^9

1. 4 EK, 4 FFP, 1 PKT
2. Ca Gluconat 1 g erwägen.
3. Hämocompletan 2g i.v. bei Fbg<1g/L
4. 1. Dosis Novo Seven 60 µg/kg i.v.bei anhaltender Blutung nach 4 EK 4 FFP

Evt. **Interventionelle Radiologie** wenn stabil **Embolisation** Aa. uterinae

Persistierende Blutung nach 4-6 EK, 4FFP, 1PKT& Tamponade. Zielwert erfüllt

Basislabor ohne T/S: Gerinnungsstatus plus Röhrli für Rotem, ABGA oder VBGA, ion. Ca^{++}.
2. Serie **Code PPH** Tel 2 3307

1. 2. Dosis Novo Seven
2. 4 EK, 4FFP, 1PKT
3. Ca gluconat gem. ion. Ca.
4. Hämocompletan 2g iv bei Fbg<1g/L

Laparatomie
- Kompressionsnähte
- Evt. Gefässligaturen

Abnahme Gerinnungsstatus und Röhrli für Rotem
3. Serie **Code PPH und Fibrogammin** Tel 2 3307

1. 2g Hämocompletan i.v.(unabh. V. Fbg-Wert)
2. Fibrogammin 1250 E i.v. (unabh. v. FXIII-Wert, n. Rückspr. 181 6220)
3. Evtl. 3.. Dosis Novo Seven 60 µg/kg i.v.(n. Rückspr. 181 6220)

Persistierende Blutung unter Transfusion

Ziel
1. Tc>50, Fbg>1g/L, FXIIb>20

Hysterektomie

Aktuell in Bearbeitung

„Erwartete" Peripartale Blutung bei Sectio[1]

Bei Placenta praevia, uterus myomatosus und/oder bei V.a. Plazenta accreta, increta oder percreta.

Es muss zusätzlich ein individuelles operatives Vorgehen gemeinsam mit der Patientin geplant und dokumentiert sein.
Es handelt sich um ein präop interdisziplinär abgesprochenes OP und Anästhesieprozedere

G E B S

Geburtshelfer	Anästhesie

1 Def. n.WHO: Fortdauernde Blutung
EBV > 500 ml n. vag. Geburt,
EBV > 1000ml n. Sectio

Basislabor: T/S, Hb, Tc, Quick/INR, aPTT, Fibrinogen, TZ, FXIII, Röhrli für Rotem abnehmen

Statt SSS evt Wechsel auf RSI

Venöse Zugänge in genügender Anzahl und Grösse, Arterie LEVEL1, **Autolog,** O_2 10-15l/min. Reservoir-Maske

Autolog Sauge!!

Sectio

Pabal 100 µg iv (nicht bei Präeklampsie/Eklampsie)

Syntocinon 10-20 IU per infusion

Evtl. Cytotec 1000 mcg rectal

Nalador 100-500µg/h i.v.am Perfusor

Methergin 0.2 mg iv (nicht bei Hypertonie / Präeklampsie!)

Volumen/Blutprodukte

Voluven gewärmt max. 20ml/kg
Cyclocapron 1g i.v. über 10min.
4 EK (wurden durch Geburtshelfer bestellt und sind im Blutkühlschrank neben Sectio OP.)

O P S

Blutung +++

Kompressionsnähte, evtl. Gefässligaturen

LABOR: Gerinnungsstatus
Blutprodukte bestellen: 4 EK, 4 FFP, 1PKT, 2g Hämocompletan, Novo Seven mit **Code"PPH"**
Tel: **2 3307**

Persistierende Blutung

Ziel:
- MAP 50mmHg, pH>7,2
- Hb>85g/l, Kerntemp.>35°C
- Tc> 50 10^9

1. 4 EK, 4 FFP, 1 PKT
2. 1g Ca Gluconat erwägen
3. Hämocompletan 2g i.v. bei Fibrinogen<1g/L
4. Novo Seven 60 µg/kg i.v. bei anhaltender Blutung nach 4 EK und 4 FFP

Evt Embolisation Aa. Uterinae in der intervent. Radiologie bei stabilem KL !

Persistierende Blutung nach 4-6 EK / 4 FFP / 1 TK

LABOR: Basislabor ohne T/S, Gerinnungsstatus, ABGA oder VBGA, ion. Ca^{++} plus Röhrli für Rotem neu abnehmen.
Blutprodukte: 2.Serie **Code PPH**

1. 2. Dosis Novo Seven 60 µg/kg i.v.
2. 4 EK, 4 FFP, 1 PKT
3. Ca gluconat gem. ion. Ca substituieren
4. Hämocompletan 2g i.v. bei Fibrinogen<1g/L

Persistierende Blutung unter fortlaufender TRANSFUSION

Abnahme Gerinnungsstatus und Röhrli für Rotem
3. Serie **Code PPH und Fibrogammin** Tel 2 3307

1. 2g Hämocompletan i.v.(unabh. V. Fbg-Wert)
2. Fibrogammin 1250 E i.v. (unabh. v. FXIII-Wert, n. Rückspr. 181 6220)
3. Evtl. 3.. Dosis Novo Seven 60 µg/kg i.v.(n. Rückspr. 181 6220)

Persistierende Blutung

Ziel
1. Tc>50 10^9,Fbg>1g/L, FXIIb>20

Hysterektomie

REGEL:Nach hämostasiologischen Interventionen IMMER 15 -30 min später einen Gerinnungsstatus abnehmen zur hämostasiologischen Effektkontrolle. Regelmässig ion. Ca kontrollieren

Katrin Flückiger, Martin Luginbühl, Luigi Raio, Lorenzo Alberio, Behrouz Mansouri, Balthasar Eberle, Daniel Surbek. Version vom 15.9.2010. Seite

“Three Pillars of PBM”

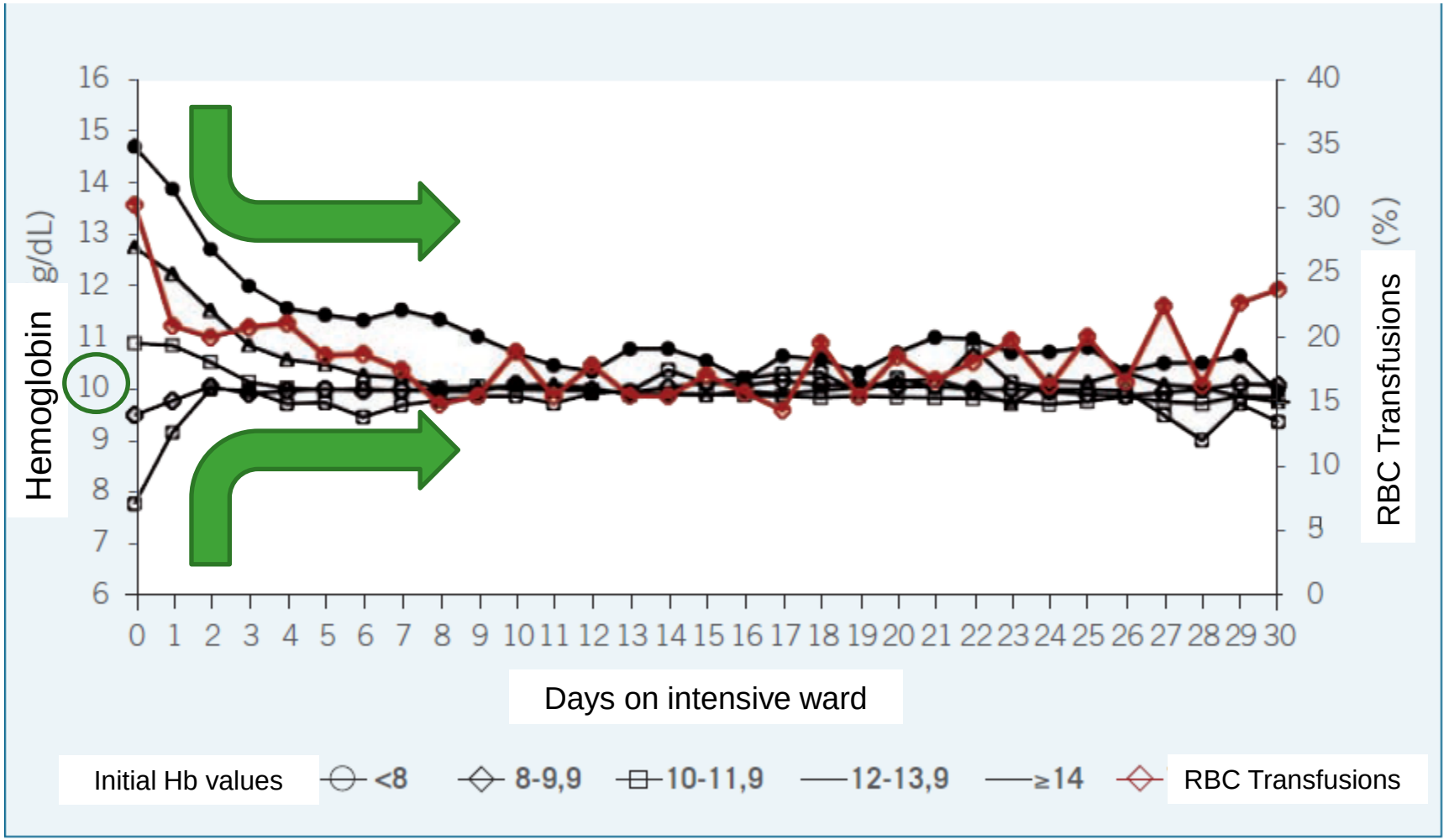
1. Pre-operative Management of Anemia & Coagulation
PBM-ambulatory: Diagnosis and treatment of anemia in elective surgery (risk of transfusion >10%).
Utilization of waiting time until surgery.

2. Optimal Blood Use / Use of RBC
Adherence to implemented guidelines for transfusion

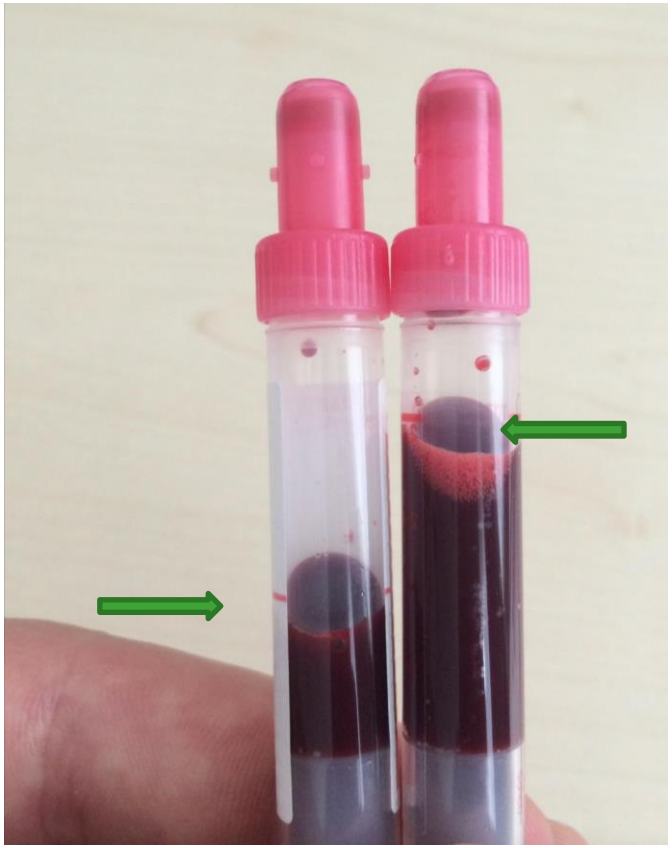
3. Further Blood Saving Measures
Restrictive taking of blood samples, blood-less surgery, Cell-Saver, management of body temperature, point-of-care diagnostic, management of coagulation

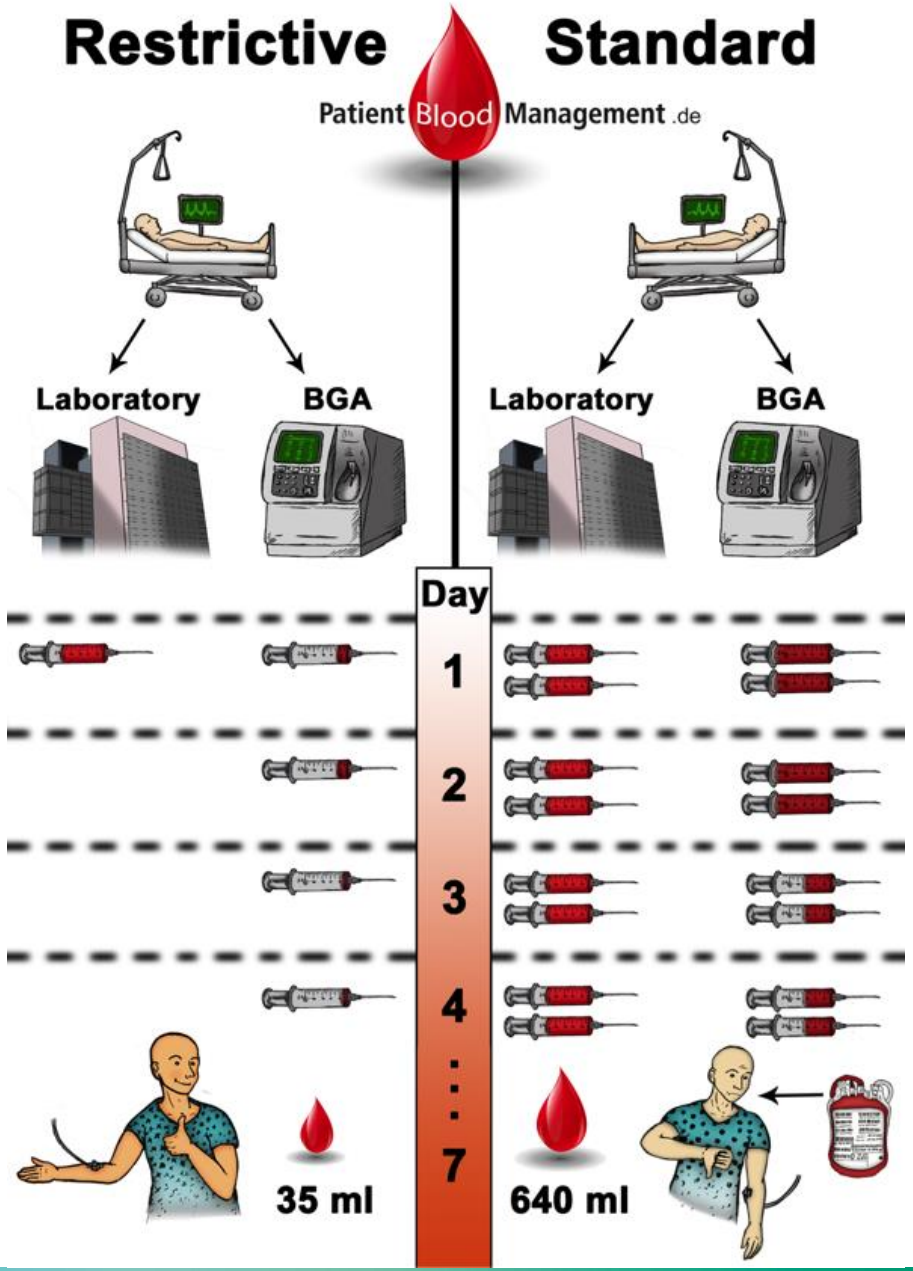
Univ.-Prof. Dr. Michael Hiesmayr, Dr. Arno Schiferer, Klinische Abteilung für Herz-Thorax-Gefäßchirurgische Anästhesie und Intensivmedizin,
Universitätsklinik für Anästhesie, Allgemeine Intensivmedizin und Schmerztherapie, Medizinische Universität Wien **3/2011 Klinik**

Hemoglobin of patients in an intensive care unit after cardio-thoracic surgery



Restrictive taking of blood samples





First multi-center, prospective study of PBM

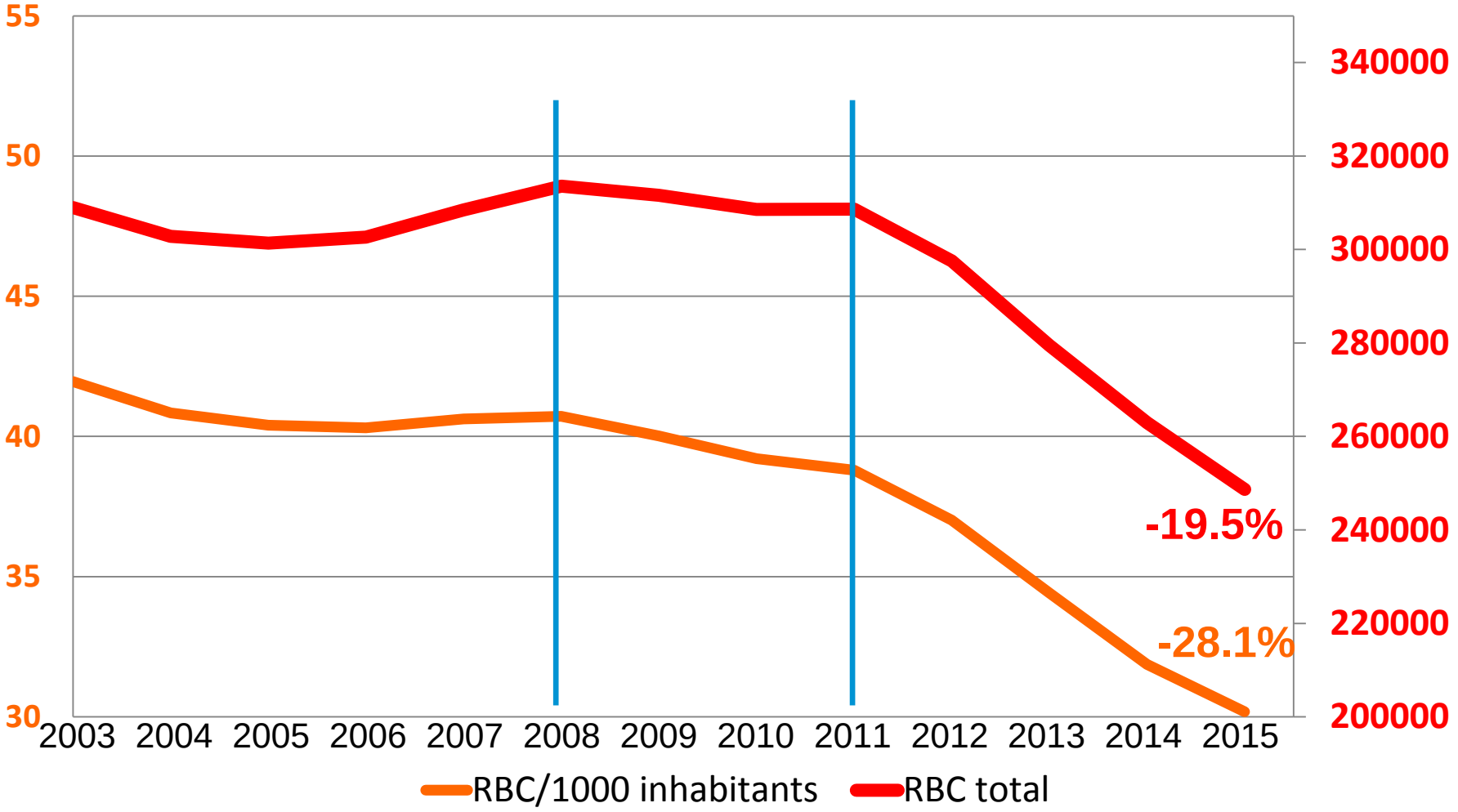
Meybohm P et al: Patient Blood Management is Associated With a Substantial Reduction of RBC Utilization and Safe for Patient's Outcome: A Prospective, Multicenter Cohort Study With a Non-inferiority Design. Ann Surg 2016;264:203–211

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 non-inferiority 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 1.210.05 to 1.000.05 (relative change by 17%, $P < 0.001$). *(But cave at: On average a comparable reduction was also observed in all other regions of Germany)*

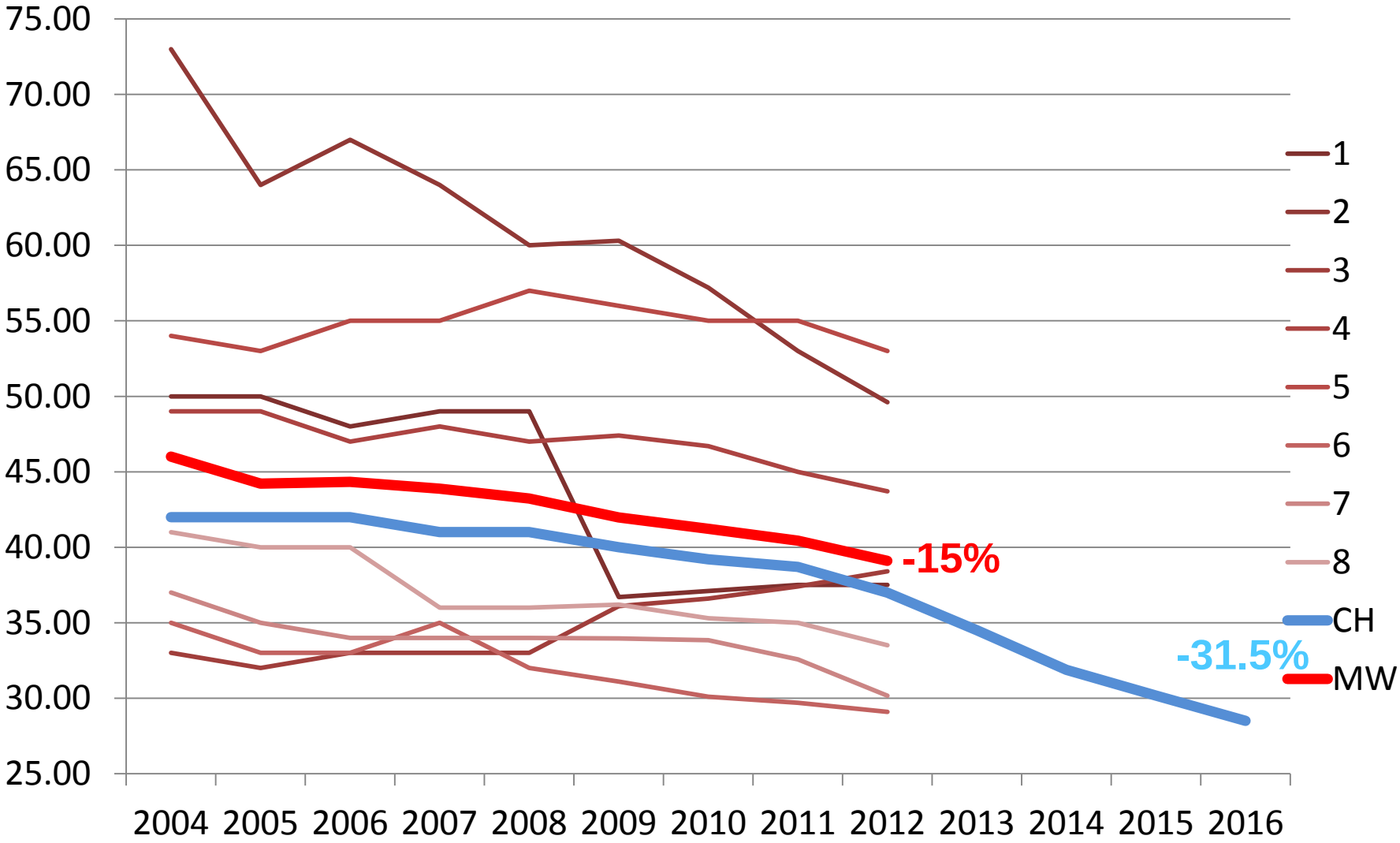
CONCLUSIONS: The data presented show that implementation of PBM with a more conscious handling of transfusion practice can be achieved even in large hospitals without impairment of patient's safety. Further studies should elucidate which PBM measures are most clinically and cost effective.

Development of RBC-Transfusion in Switzerland

(Delivered! units to hospitals)



Development of RBC-Transfusion per 1000 inhabitants in 9 European Countries



“Platelets on tour”

Circulation of the donor

↓

Donation: extracorporeal circulation / centrifugation

↓

Pathogen reduction, storage, ...

↓

Transportation

↓

Transfusion

↓

Foreign / harmful (?!) circulation of the recipient

(Antibodies, drugs, toxins, …)

Platelet products in Switzerland

- Apheresis platelet concentrates (APC):

  Collection using blood cell separators

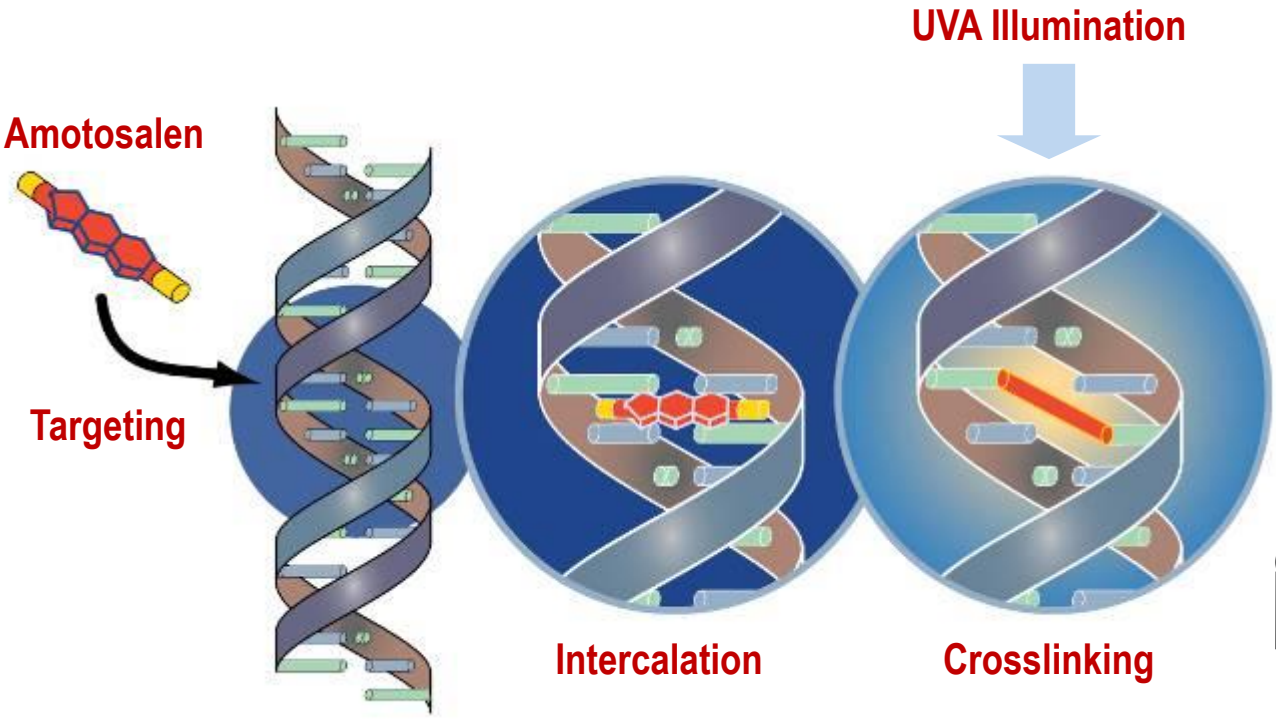
  → single-donor platelets

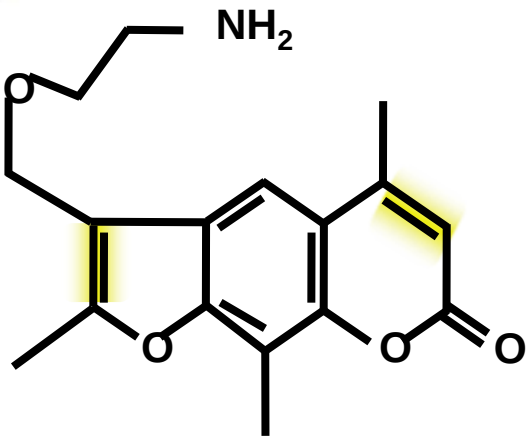
- Buffy coat / PRP platelet concentrates:

  Preparation of buffy coat or PRP from pooled ABO/Rh-identical whole blood donations (4 – 6)

  → multi-donor platelets

Pathogen Reduction by INTERCEPT: Mechanism of Action





Amotosalen

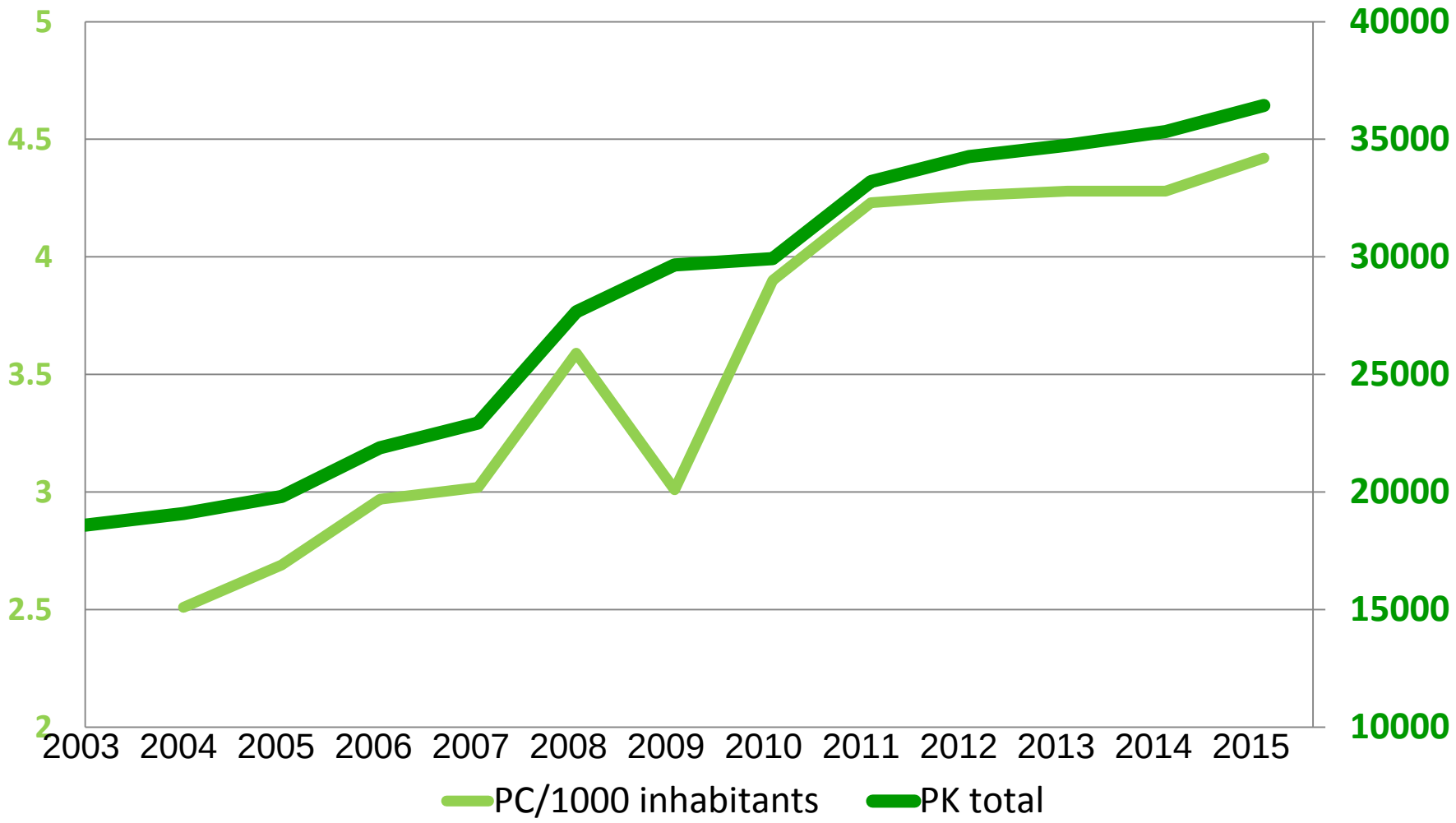
The "new" Swiss PLT Unit*

*Starting in 2011 - reaching 80% in 2011 and 100% since 11/2011

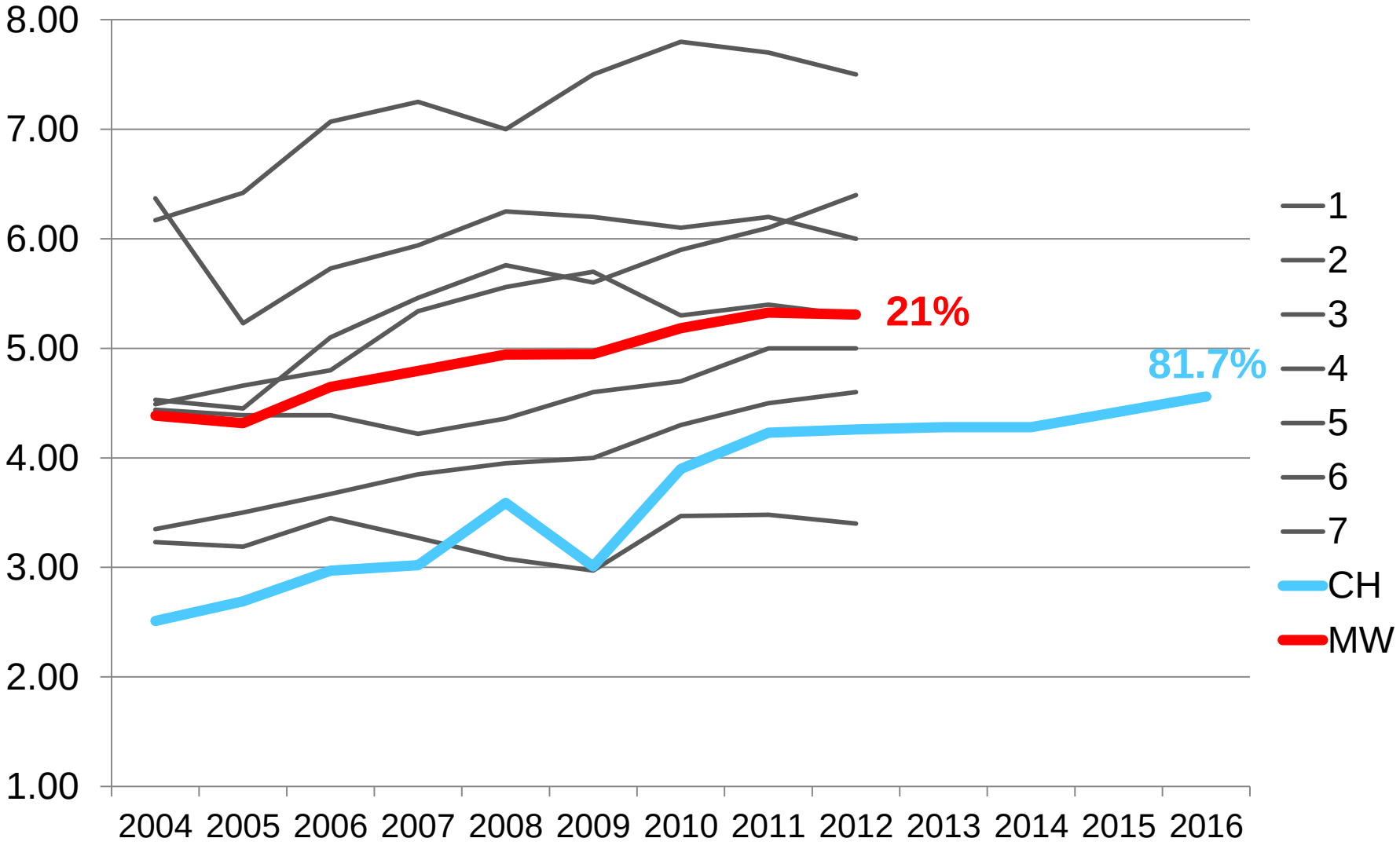
- **> 2.4x10^{11} / unit**
- **Pathogen reduced**
- **Intersol or SSP+**
- **7 day storage**
- **Apheresis or pooled BC**

Development of PC-Transfusion in Switzerland

(Delivered! units to hospitals)



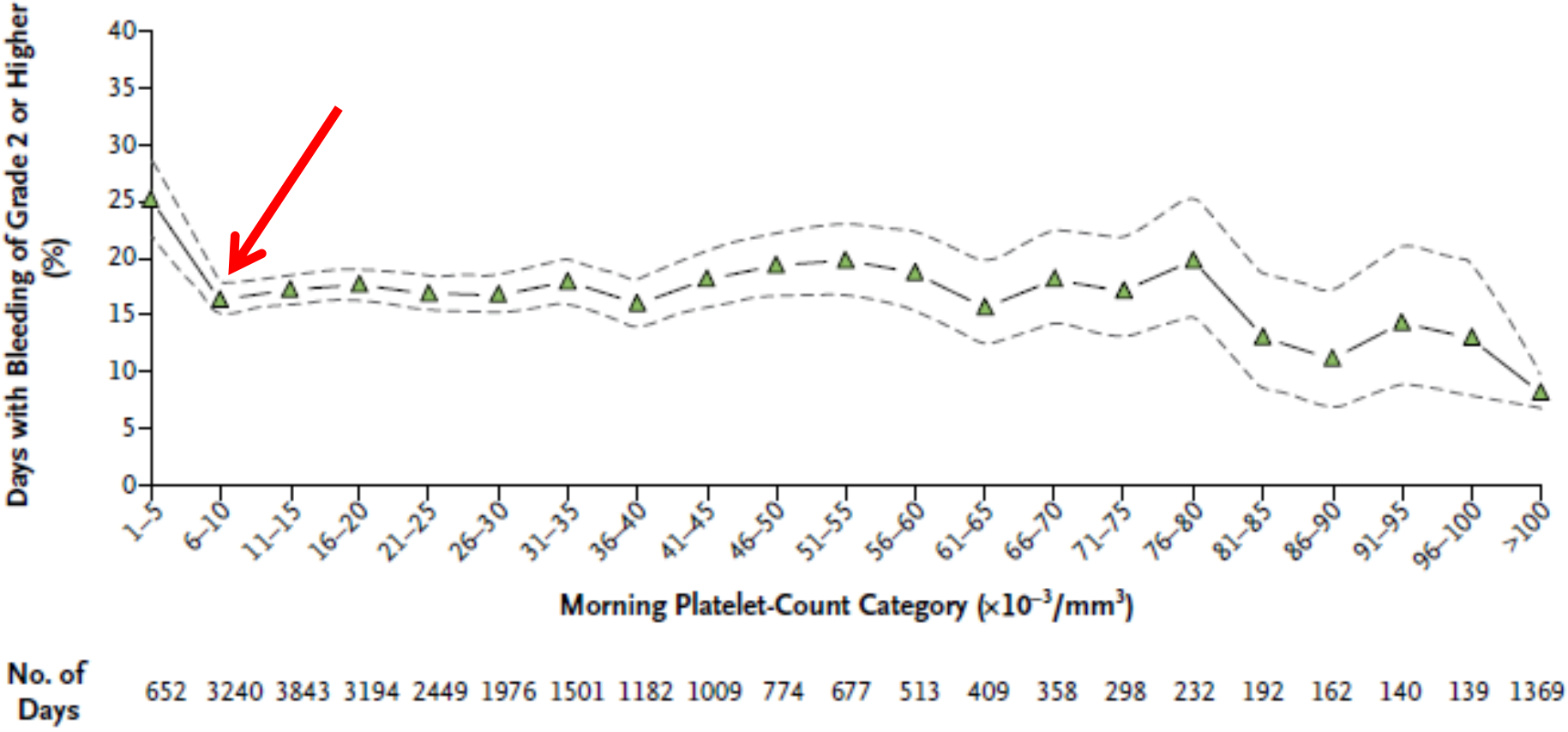
Development of PLT-Transfusion per 1000 inhabitants in 8 European Countries



Platelet transfusion: aims

Treat active bleeding	Prevent bleeding
Therapeutic	**Prophylactic**
Prove of effectiveness:	**Prove of effectiveness:**
Stop of bleeding	**(?)**

Why we transfuse PLT



Slichter S, N Engl J Med, 2010 362:600-613

Platelet transfusion: a systematic review of the clinical evidence

Kumar A et al: Platelet transfusion: a systematic review of the clinical evidence. Transfusion 2015;55:1116–1127

Key results

- …**RCTs** (n=17) showed a **beneficial effect of prophylactic compared with therapeutic transfusion** for the prevention of significant bleeding in … hematologic disorders undergoing chemotherapy or stem cell Tx.
- …**no difference in significant bleeding events related to the PLT count threshold for transfusion or the dose of PLTs transfused**.
- Overall **methodologic quality of RCTs was moderate.**

- … **observational studies** (n=55) … no evidence that PLT transfusion prevented significant bleeding in patients undergoing central venous catheter insertions, lumbar puncture, or other surgical procedures.
- The methodologic **quality of observational studies was very low**.

Therapeutic vs prophylactic platelet transfusion

Crighton GL et al: A therapeutic-only versus prophylactic platelet transfusion strategy for preventing bleeding in patients with haematological disorders after myelosuppressive chemotherapy or stem cell transplantation. Cochrane Database Syst Rev. 2015 Sep 30;(9):CD010981

Key results

- Giving platelet transfusions to prevent **and** treat bleeding in patients with low platelet counts due to blood cancers or their treatments may result in a reduction in bleeding when compared with giving platelet transfusions only to treat bleeding.
- There may not be an increased risk of death or adverse events if platelet transfusions are only given to treat bleeding versus giving platelet transfusions to prevent and treat bleeding, but there was not enough evidence to be certain about this.
- Giving platelet transfusions only when bleeding occurs probably reduces the number of platelets given.
- None of the six studies reported any quality-of-life outcomes.

Kaufman RM et al: Platelet Transfusion: A Clinical Practice Guideline From the AABB. Ann Intern Med 2015;162:205-213

Recommendation 1: (Grade: strong recommendation; moderate-quality evidence)

- … PLT should be transfused prophylactically to reduce the risk for spontaneous bleeding in hospitalized adult patients with therapy induced hypo-proliferative thrombocytopenia with a platelet count of ≤ 10 G/L
- …transfusing up to a single apheresis unit or equivalent per episode … greater doses are not more effective

Recommendation 2: (Grade: weak recommendation; low-quality evidence)

- … prophylactic PLT transfusion for patients having elective central venous catheter placement with a platelet count less than 20 G/L.

Recommendation 3: (Grade: weak recommendation; very-low-quality evidence)

- … prophylactic PLT transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than 50 G/L.

Kaufman RM et al: Platelet Transfusion: A Clinical Practice Guideline From the AABB. Ann Intern Med 2015;162:205-213

Recommendation 4: (Grade: weak recommendation; very-low-quality evidence) … prophylactic PLT transfusion for patients having major elective non-neuraxial surgery with a platelet count less than 50 G/L.

Recommendation 5: (Grade: weak recommendation; very-low-quality evidence) … against routine prophylactic platelet transfusion for patients who are non-thrombocytopenic and have cardiac surgery with cardiopulmonary bypass. The AABB suggests PLT transfusion for patients having bypass who exhibit perioperative bleeding with thrombocytopenia and/or evidence of PLT dysfunction

Recommendation 6: (Grade: uncertain recommendation; very-low-quality evidence) … cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous).

“The art of platelet transfusion”

"He who feels confident that he has a thorough understanding of platelet transfusion is confused.“

Petz LD. Platelet transfusions. Swisher SN, Spence RK, Strauss RG, editors. *Clinical practice of transfusion medicine*. 3rd ed. New York: Churchill Livingstone; 1995. p. 359

“PLT transfusion practices are being questioned more than ever before. As we develop better therapies & guidelines, the practice of PLT therapy can be expected to change in the near future..“

Kyle Annena, and Jordan E. Olson; Curr Opinion Hematology 2015;22:559-564

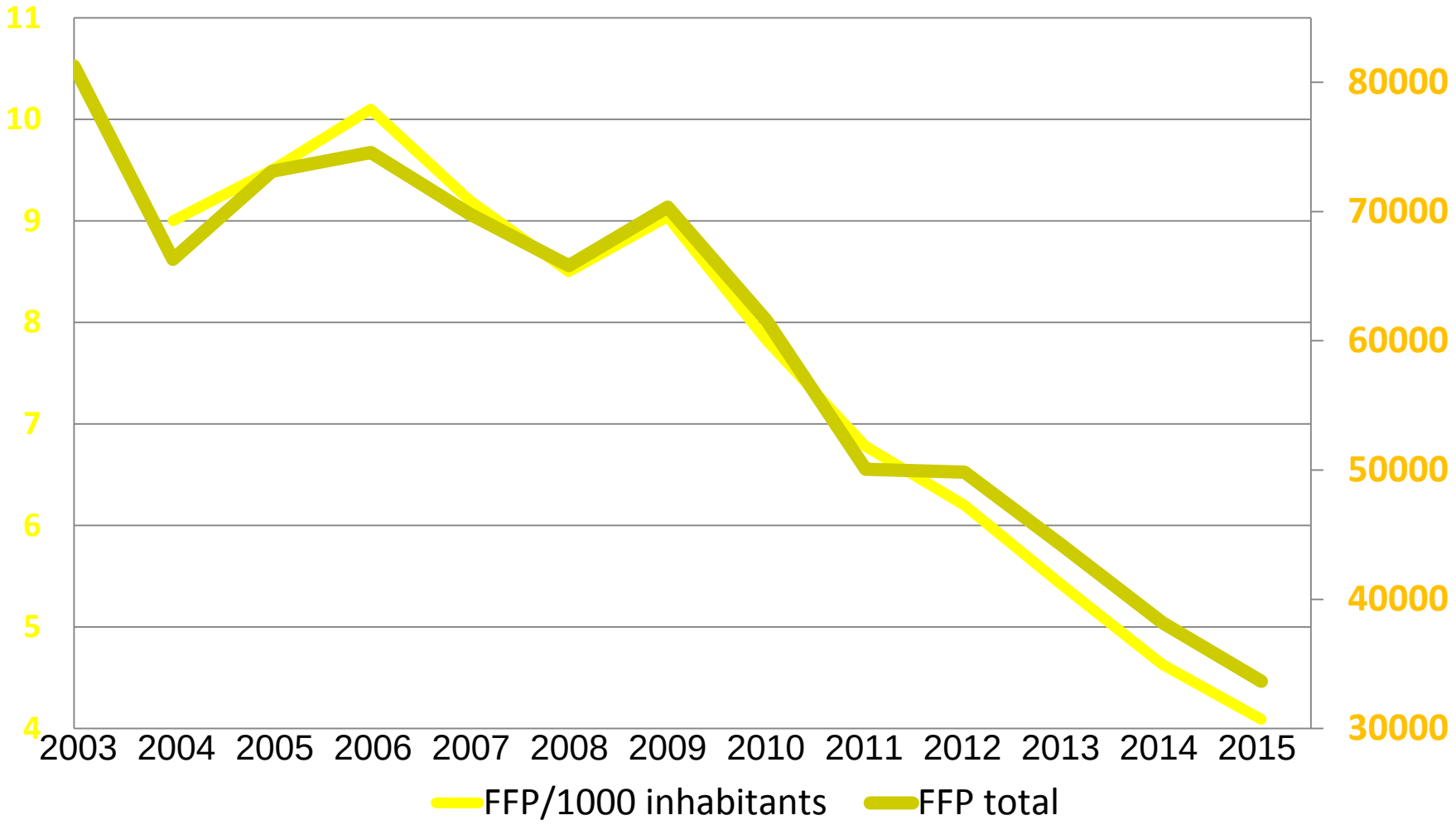
Plasma Products for Transfusion

- Quarantine storage, second testing after ≥ 4 months (q-FFP)
- Solvent/Detergent treated (out of plasma-pools, e.g. Octaplas®)
- Amotosalen treated (single donor / small pools, 2014 CH-approval)

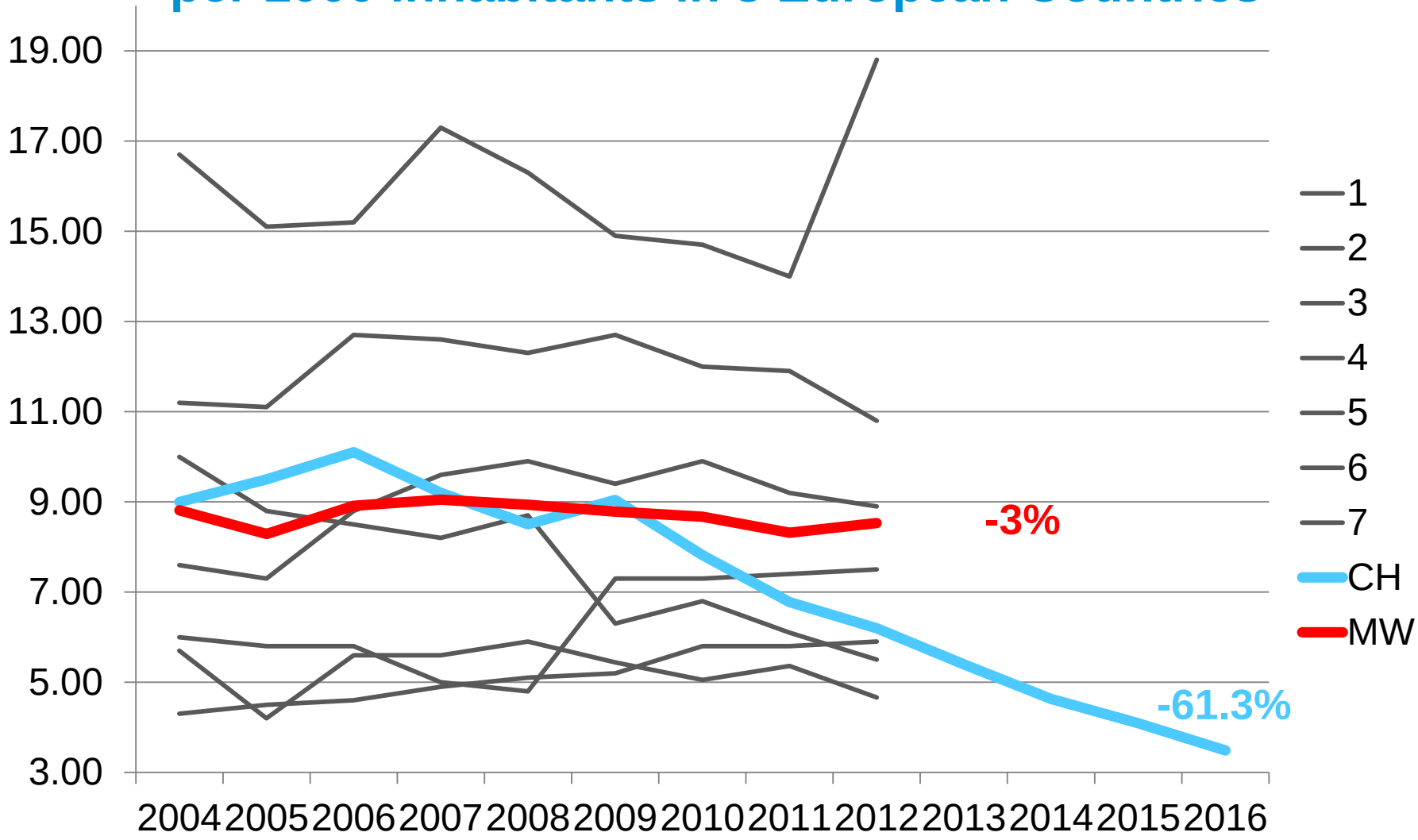
- Untreated and not quarantine stored (not available in CH)
- Methylen-blue treated (single donor plasma, not available in CH)

Development of Plasma-Transfusion in Switzerland

(Delivered! units to hospitals)



Development of Plasma-Transfusion per 1000 inhabitants in 8 European Countries



When to Transfuse FFP

In case of an insufficient coagulation potential

Plasma and Plasma Protein Product Transfusion: A Canadian Blood Services Centre for Innovation Symposium

Zeller MP et al: Plasma and Plasma Protein Product Transfusion: A Canadian Blood Services Centre for Innovation Symposium. Transf Med Rev 2015;29:181–194

Highlights

- Plasma is usually transfused to prevent or reduce bleeding, but evidence of benefit of plasma transfusion is scant
- The use of plasma before invasive procedures, the clinical benefit of prothrombin complex concentrates & the optimal ratio of plasma to red blood cells during massive transfusion remain areas of controversy
- In Canada, plasma use has declined more than 30% since 2004, whereas prothrombin complex concentrate utilization has climbed
- Next-generation factor VIII or factor IX products may revolutionize care in hemophilia
- Optimal plasma utilization remains a challenge in the interconnected worlds of transfusable plasma, plasma protein products & recombinants

“The art of plasma transfusion”

"He who feels confident that he has a thorough understanding of platelet transfusion is confused.“

Petz LD. Platelet transfusions. Swisher SN, Spence RK, Strauss RG, editors. *Clinical practice of transfusion medicine*. 3rd ed. New York: Churchill Livingstone; 1995. p. 359

"The sentiment could be equally applied to plasma transfusion therapy with a disturbing degree of accuracy.“

Triulzi DJ. The art of plasma transfusion therapy. Transfusion 2006;46:1268-1270

"Optimal plasma utilization remains a challenge in the interconnected worlds of transfusable plasma, plasma protein products & recombinants.“

Zeller MP et al: Plasma and Plasma Protein Product Transfusion… Transf Med Rev 2015;29:181–194

Plasma Protein Products I

Therapy	Conditions Treated	Treatment Outcomes
Coagulation factors: Essential for blood clotting, used to treat genetic bleeding disorders and surgical bleeding.	➢ ***Bleeding from trauma*** ➢ ***Over dosage of anticoagulants*** ➢ ***Liver disease*** ➢ ***Bleeding Disorders*** ➢ ***Hemophilia A and B –*** Disorders that prohibit a person's blood from clotting. ➢ ***Von Willebrand disease –*** The most common inherited bleeding disorder.	Improved quality of life and life expectancy

http://www.pptaglobal.org/plasma-protein-therapies/therapies

Plasma Protein Products II

Therapy	Conditions Treated	Treatment Outcomes
Immunoglobulins: Proteins used to neutralize foreign objects such as bacteria and viruses. In primary and secondary immunodeficiencies and autoimmune disorders.	***Immunodeficiencies:*** ***Primary -*** Life threatening genetic defect of immune system. ***Secondary*** - Caused by outside factors such as viruses, chemotherapy, etc. ***Autoimmune disorders: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)*** – (***Auto-***)immune disorder of the peripheral nerves. ***Idiopathic Thrombocytopenic Purpura (ITP) -*** (Auto-)immune bleeding disorder in which the immune system destroys platelets,	Improved quality of life and life expectancy Infection prevention

http://www.pptaglobal.org/plasma-protein-therapies/therapies

Plasma Protein Products III

Therapy	Conditions Treated	Treatment Outcomes
Hyperimmune Globulins: Prevention and treatment of specific infections and other foreign bodies.	**Rabies, tetanus and hepatitis** **Rh negative pregnancy** **Liver transplant and surgery**	Prevention Treatment Protection of fetus
Alpha-1 Proteinase Inhibitors: Protects tissues from enzymes of inflammatory cells.	***Alpha-1 Antitrypsin Deficiency*** - Genetic deficiency which may result in life-threatening lung disease in adults and/or liver disease in people of any age.	Improved quality of life Halts progression

http://www.pptaglobal.org/plasma-protein-therapies/therapies

Plasma Protein Products IV

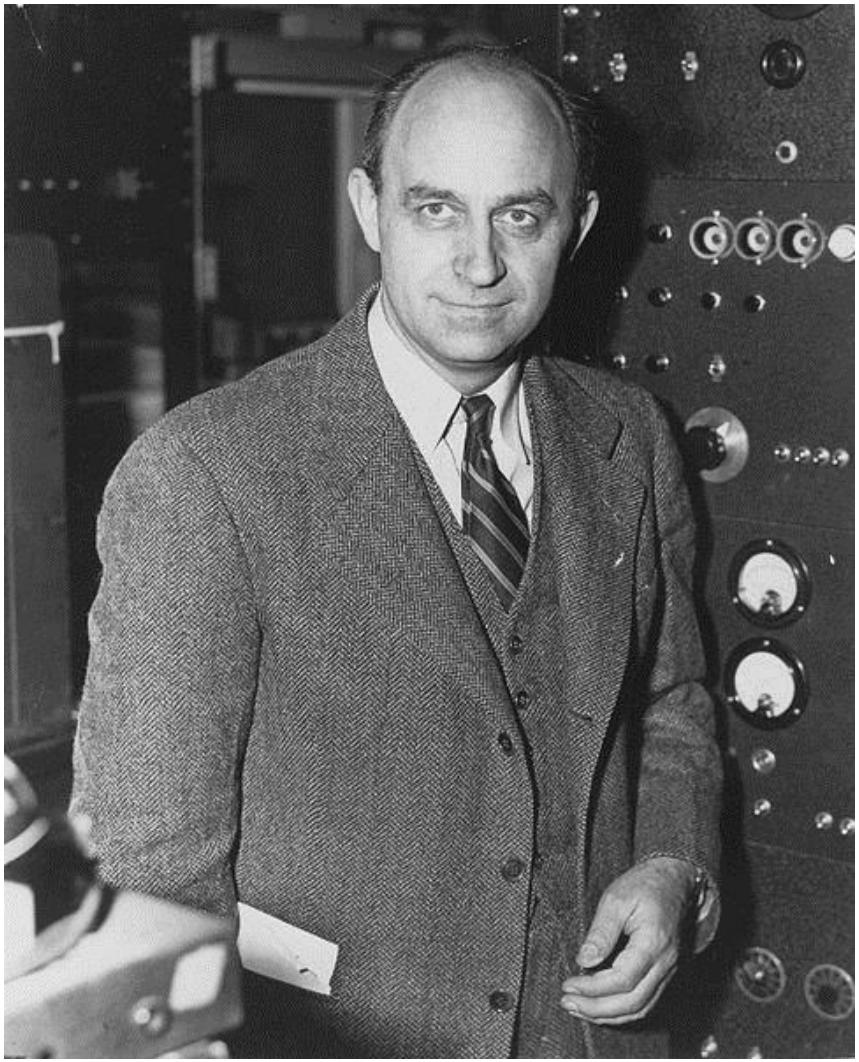
Therapy	Conditions Treated	Treatment Outcomes
Albumin: The major plasma protein, regulating blood volume and providing many essential functions.	***Cardiac surgery*** ***Liver disease*** ***Severe infections*** ***Emergency and Surgical Medicine*** - Used to treat shock, severe burns and during surgery	Life-saving in severe situations Decreased morbidity and mortality
C1-esterase inhibitor (C1-INH): A blood protein controlling a protein called C1, which is part of the complement system.	***Hereditary angioedema*** – Rare but potentially life-threatening condition characterized by acute attacks of usually non-itching edema (swelling) of the face, larynx (airway), abdomen and extremities.	Improved quality of life Increased life expectancy

http://www.pptaglobal.org/plasma-protein-therapies/therapies

Many thanks to…

- **Markus Müller, Frankfurt**
- **Markus Jutzi, Bern**
- **Balthasar Eberle, Bern**
- **Transfusion Committee, Insel Gruppe**
- **…**

And to all of you for your attention



‘We’re still confused, but on a higher level.’

Enrico Fermi
* 29.09.1901 Rom, † 28.11.1954 Chicago, einer der bedeutendsten Kernphysiker des 20. Jahrhunderts.
1938 Nobelpreis für Physik

5 Key Questions

- What are the common kinds of blood donation and products?
- When do you transfuse RBC?
- When do you transfuse PLT?
- When do you transfuse plasma?
- What do you know about adverse events, safety and haemovigilance in blood transfusion?