



STRATEGIES TO REDUCE TRANSFUSION IN CARDIOVASCULAR SURGERY

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DISCLOSURE

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IN GRATIDUE

To Professor

Arisan Ergin

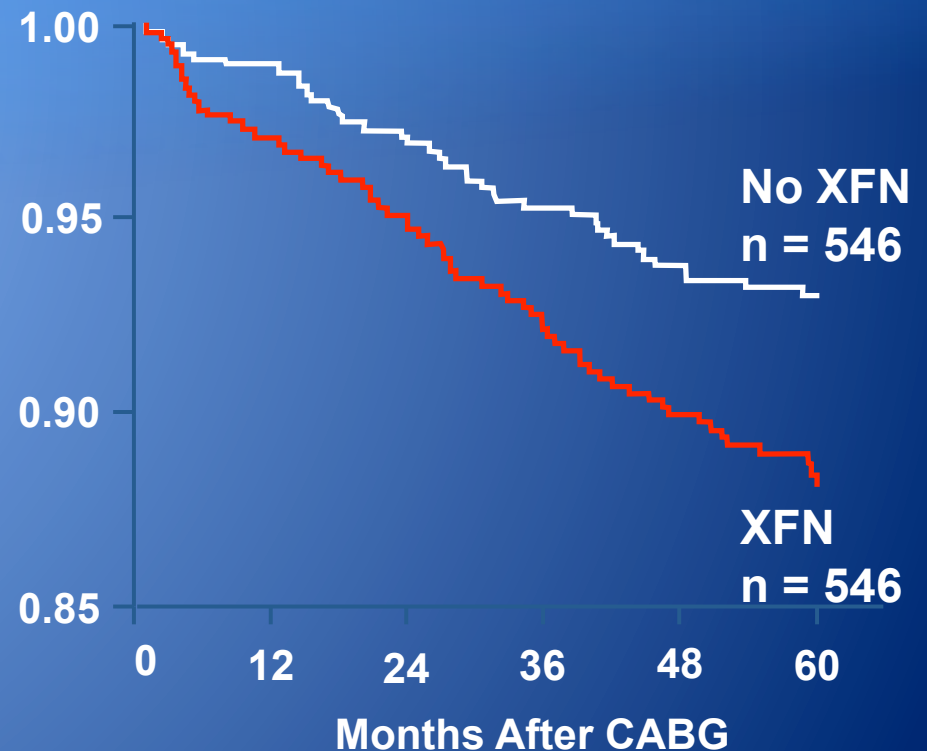
- ◆ A pillar in advancing medicine and surgery
- ◆ Humble
- ◆ Highest morals
- ◆ Inquisitive and outstanding investigator
- ◆ A mentor and a HERO

Objectives

- ◆ 1. Why reduce transfusions?
- ◆ 2. Variability of TX in CV surgery - a global problem
- ◆ 3. STS Guidelines for blood conservation - in the STS box and outside
 - ◆ a. Salient portion on a single summary slide
 - ◆ b. Preop Hgb. The #1 risk for transfusion, data
 - ◆ c. ESA, old and new data on treating anemia
- ◆ 4. Other techniques for blood conservation
 - ◆ a. ANH - benefits and cardiac protection/ Cell salvage
 - ◆ b. Drugs including routine antifibrinolytics
 - ◆ c. Post op anemia therapy. not to be afraid of low hgb after revascularization Use of Fe IV
 - ◆ d. EHMC outcome data and PBM def and matrix

Blood Transfusion and Long-term Survival After Cardiac Surgery

Patient s at Risk	1 y	2 y	3 y	4 y	5 y
XFN:	528	518	502	349	188
No XFN:	539	528	519	408	254

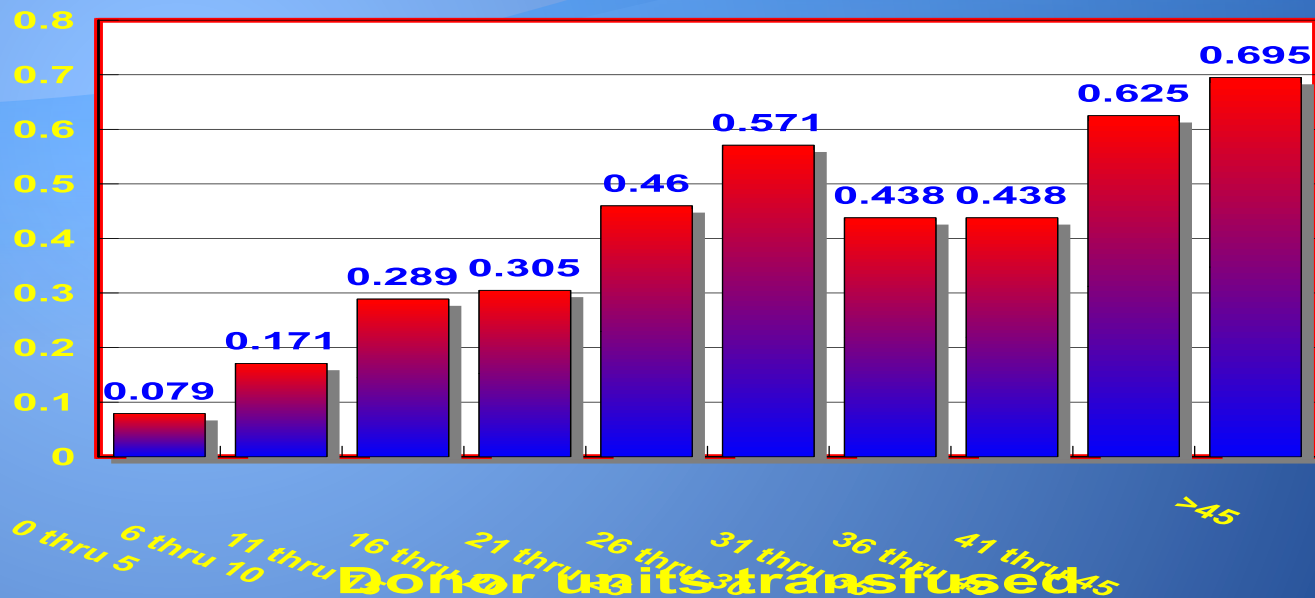


Kaplan-Meier estimates of survival based on equal propensity scores of any transfusion (XFN) versus no transfusion (No XFN).

CABG = coronary artery bypass grafting.

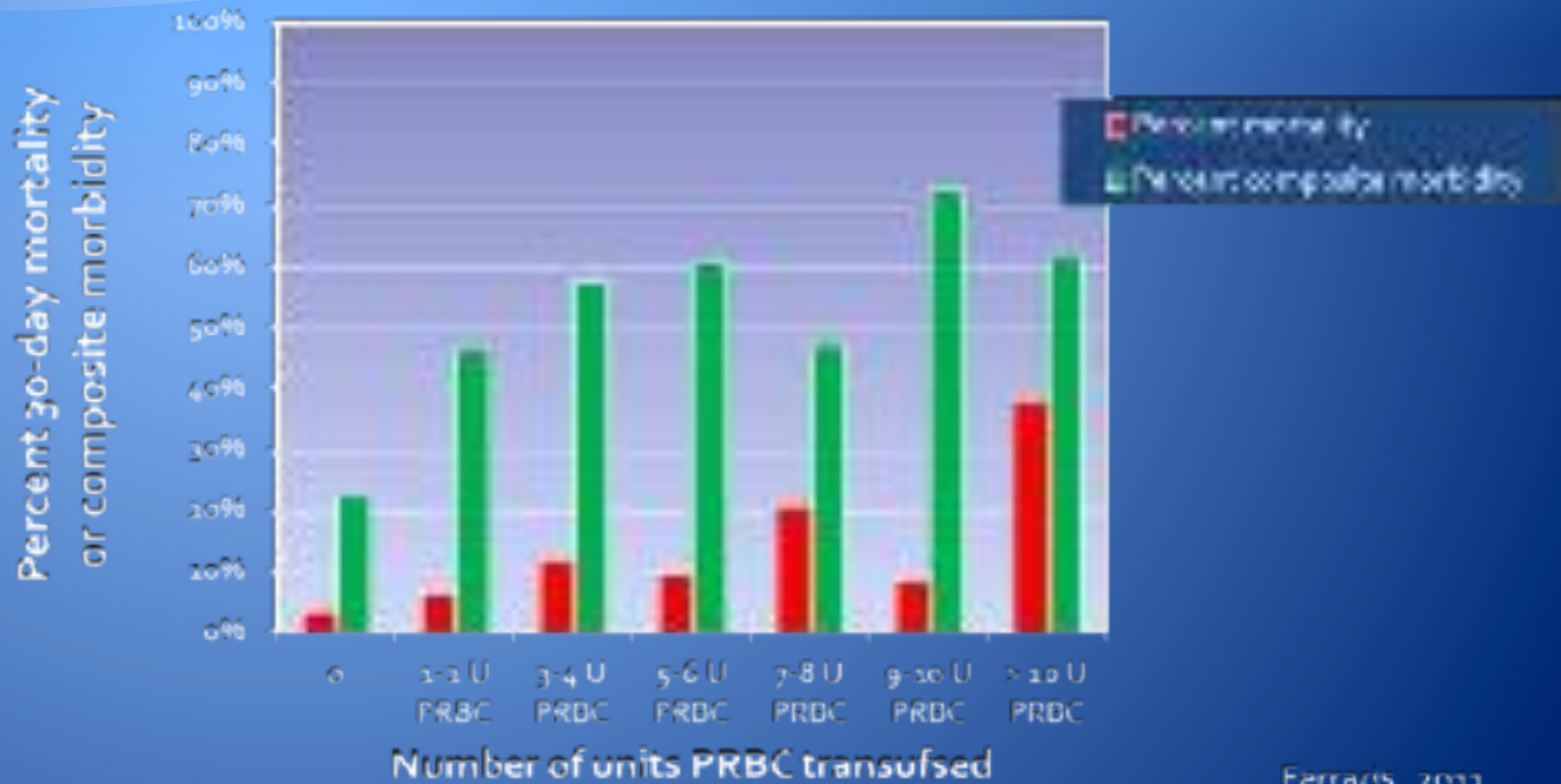
Figure reproduced with permission from Engoren MC et al. *Ann Thorac Surg.* 2002;74:1180-1186.

Transfusion & Serious Morbidity in 4,445 Cardiac Surgical Patients



Serious morbidity and mortality increase with the amount transfused.

Intraoperative Blood Transfusion & Lung Surgery



Association of Blood Transfusion With Increased Mortality in Myocardial Infarction

A Meta-analysis and Dose-response-Adjusted Study Sequential Analysis

Journal of the American Medical Association
Volume 308, Number 24, December 11, 2012
DOI: 10.1001/jama.2012.111111



- ◆ N = 729 (10 for analysis)
- ◆ A systematic search of publications (Jan 1966 – March 2012) utilizing
 - ◆ - MEDLINE, EMBASE, CINAHL, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials databases
- ◆ All cause mortality in MI (**Transfusion group 18.2% vs. non transfused group 10.2%**)
- ◆ Multivariate analysis - blood transfusion **associated with a higher risk for mortality**
 - ◆ -independent of baseline hgb, nadir hgb , and change in hgb during the hospital stay

Blood transfusion or a liberal blood transfusion strategy is **associated with higher all-cause mortality rates**

Association between Intra-operative Blood Transfusion and Mortality and Morbidity in Patients Undergoing Non-Cardiac Surgery

- ◆ N= 10,100 patients (general, vascular, or orthopedic surgery)
- ◆ Intraoperative blood transfusion associated with an increased risk of death (odds ratio [OR], 1.29; 95% CI, 1.03–1.62)
- ◆ Patients receiving one or two units of erythrocytes more likely to have:
 - ◆ Pulmonary complications (OR, 1.76; 95% CI, 1.48–2.09)
 - ◆ Sepsis (OR, 1.43; 95% CI, 1.21–1.68)
 - ◆ Thromboembolic complications (OR, 1.77; 95% CI, 1.32–2.38)
 - ◆ Wound complications (OR, 1.87; 95% CI, 1.47–2.37)
- ◆ Intraoperative blood transfusion is associated with a **higher risk** of mortality and morbidity in surgical patients with severe anemia

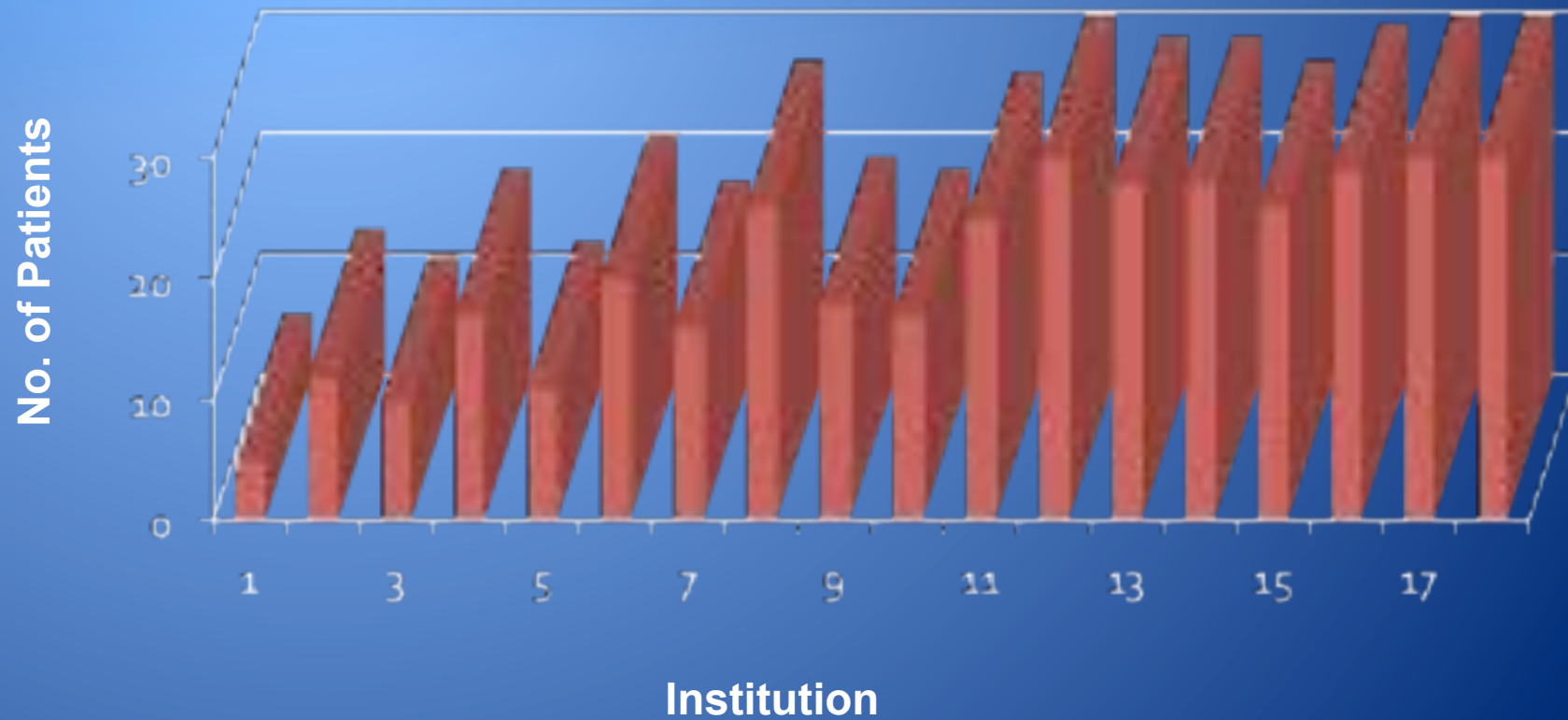
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Variability of Transfusion Practice

CABG (N=540)

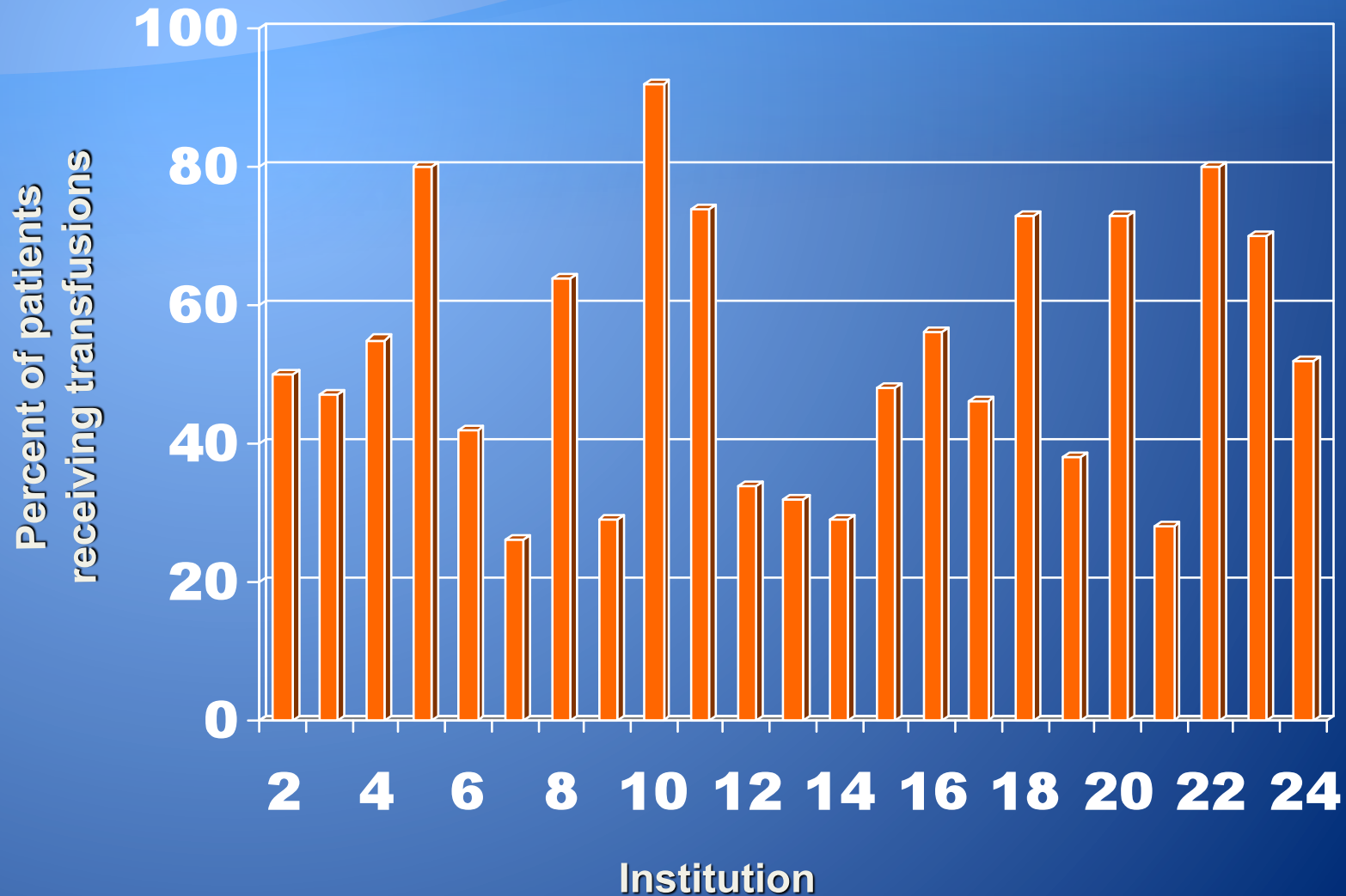
Goodnough LT et al. *J.A.M.A.* 1991



Variability of Transfusion Practice

CABG (N=713)

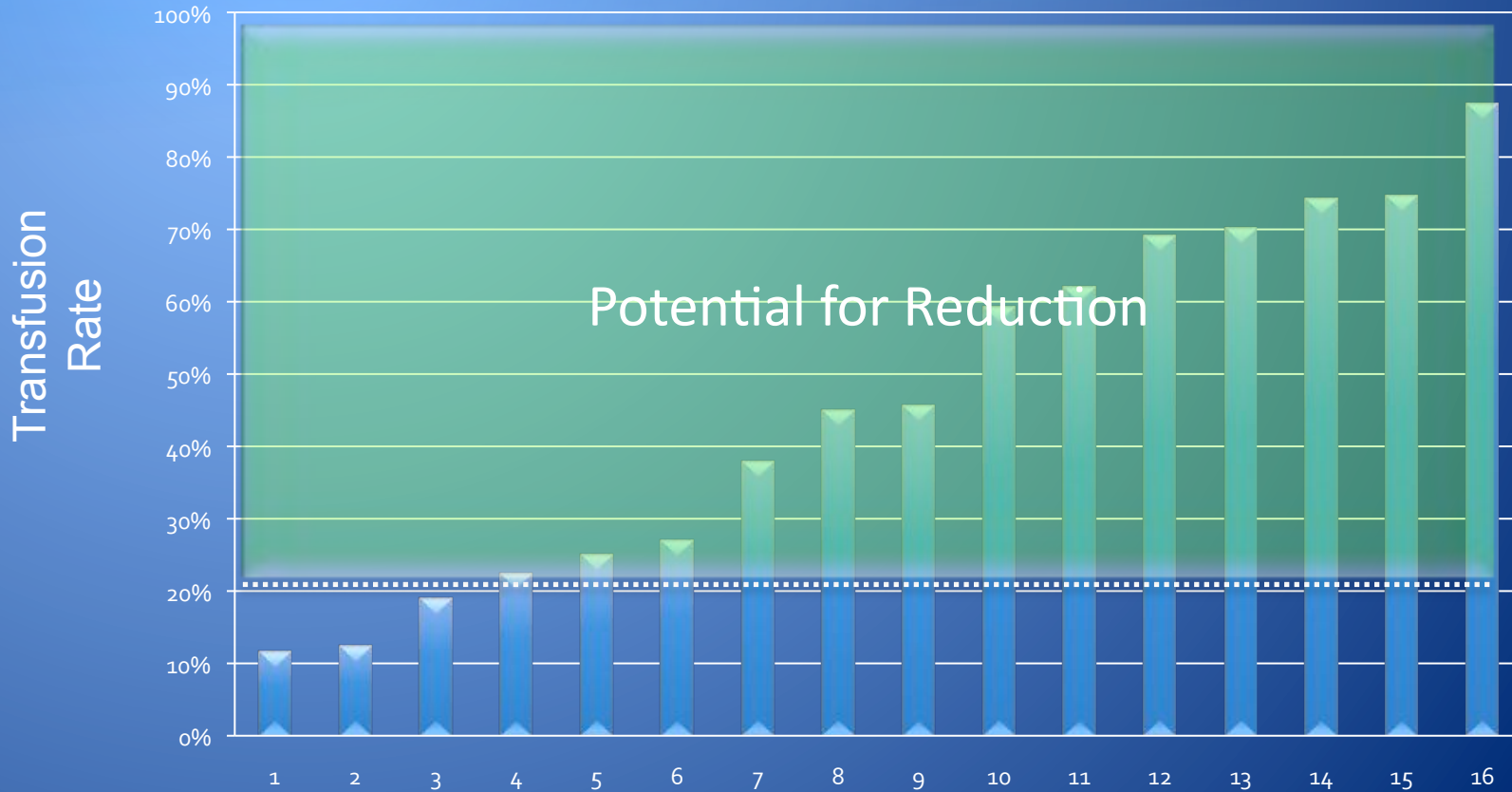
Stover PE *ANESTHESIOLOGY* 1998



Variability of Transfusion Rates For Matched Patients

*Gombotz H, Rehak P, Shander A, Hofmann A.
Transfusion 2007*

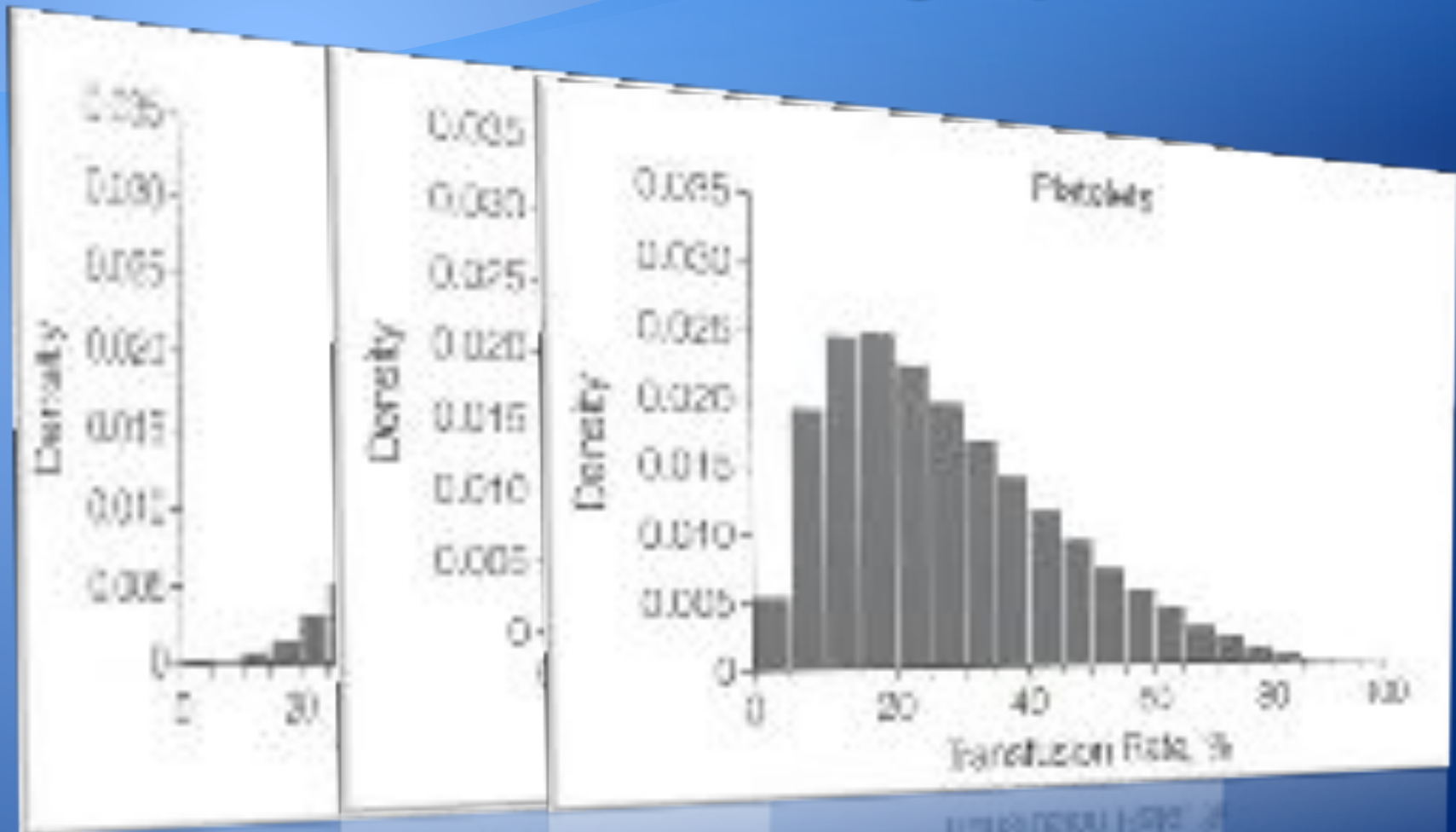
(n=1,401)



Variation In Use Of Blood Transfusion In CABG Surgery

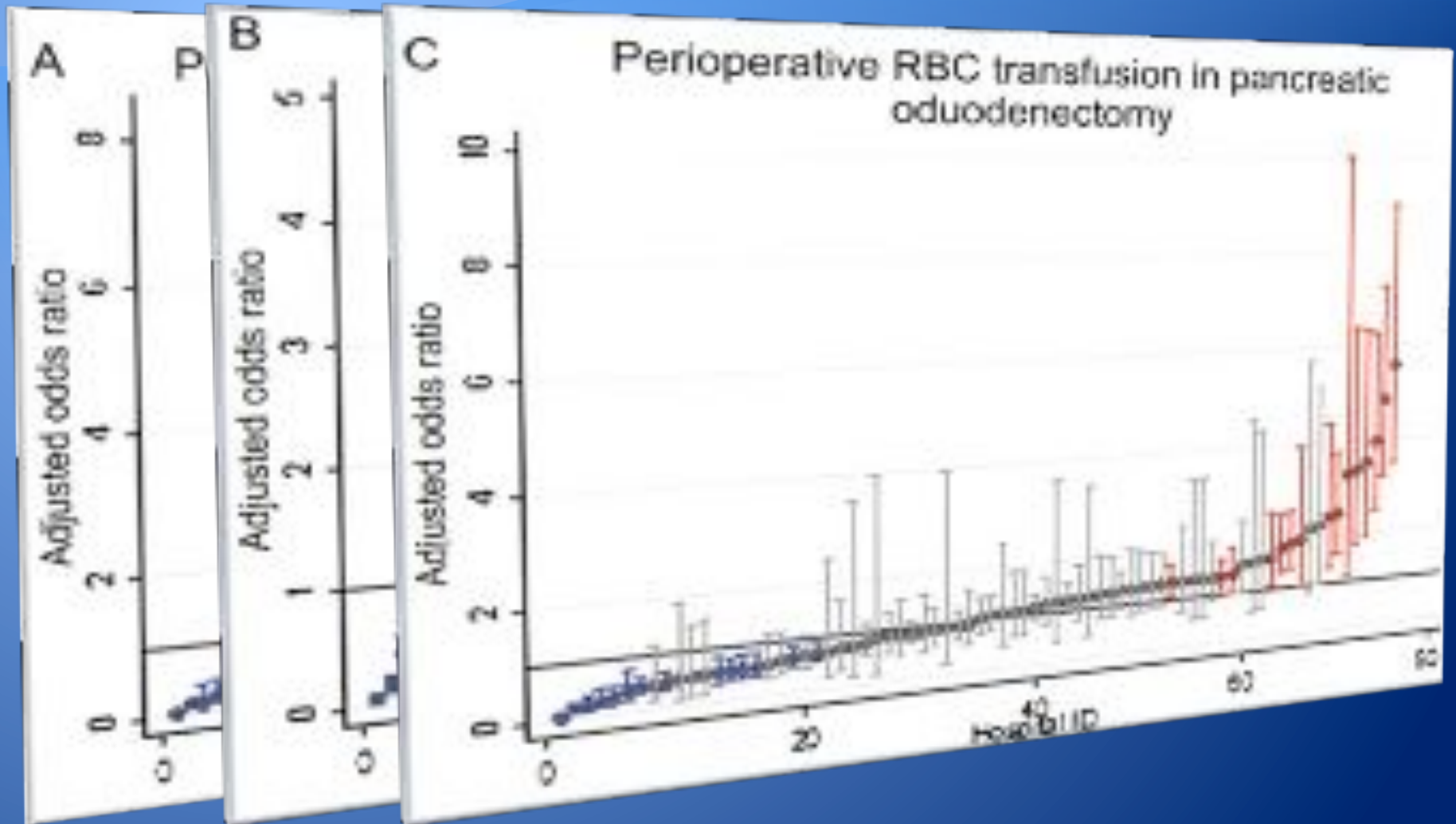
- ◆ To assess variation in use of allogeneic red blood cell (RBC), FFP, and platelet transfusions in patients undergoing (CABG) surgery.
- ◆ N = 102 470 CABG patients in 2008 at 798 sites in the US (STS Adult Cardiac Surgery Database)
- ◆ The rates of transfusions ranged from:
 - ◆ 7.8% to 92.8% for RBCs
 - ◆ 0% to 97.5% for fresh-frozen plasma
 - ◆ 0.4% to 90.4% for platelets.
- ◆ Multivariable analysis transfusion rates varied by:
 - ◆ *Geographic location (P=.007), Academic status (P=.03), and Hospital volume (P<.001)*
- ◆ Wide variability in rates of transfusion of all blood products in CABG operations in US hospitals

Variation in use of blood transfusion in CABG surgery



Variation of blood transfusion in patients undergoing major non-cardiac surgery

Qian F. Et al. Ann Surg. 2013 Feb;257(2):266-78



AMA convened

PCPI™

Physician Consortium for Performance Improvement®



NATIONAL SUMMIT ON OVERUSE *SEPTEMBER 24, 2012*

- *Elective PCI*
- *Myringotomy and Tubes*
- *Early C – section*
- *Antimicrobials in URI*
- *Blood transfusion*

TJC - National Patient Safety Goal (NPSG) overuse of treatments, procedures and tests for the hospital

- Consequences of overuse: tests, treatments and procedures
- Overuse may be defined as:
“The use of a health service in circumstances where the likelihood of benefit is negligible and, therefore, the patient faces only the risk of harm.”
- The focus is to identify and eliminate overuse
- NPSG provides for incremental **implementation** and an **evaluation of the effectiveness**

Costs of excessive postoperative hemorrhage in cardiac surgery

Malik H, Fradette P, Piloni A, et al. *Journal of Thoracic and Cardiovascular Surgery*. 2009;138(3):400-405.



- ◆ N = 1118 patients had cardiac surgery (January - December 2006)
- ◆ Patients with excessive postoperative hemorrhage had **HIGHER**:
 - ◆ Risk of **experiencing a postoperative complication** (including death) (P < .0001)
 - ◆ Rate of **re-exploratory surgery** (P < .0001)
 - ◆ Stay in ICU- > 72 hours (P < .0001)
 - ◆ Rate of receiving ventilation > 24 hours (P < .0001)
 - ◆ Rate of postoperative blood transfusion (P < .0001)
- ◆ Mortality - **22% (excessive postop hemorrhage)** vs. 6% (w/o excessive postop hemorrhage) (P < .0001)
- ◆ Incremental costs of excessive postoperative hemorrhage was €6251

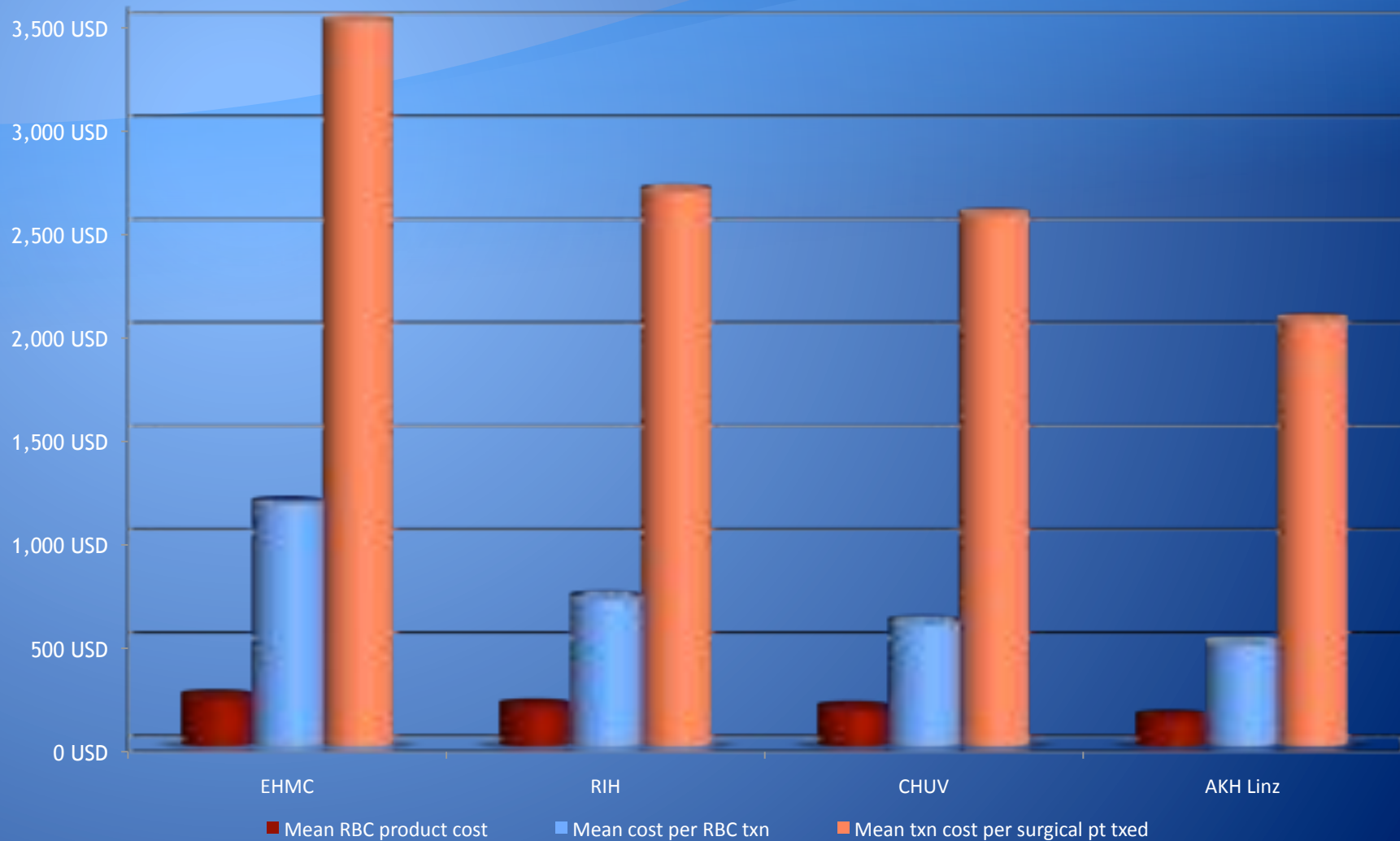
Cost escalation

(2008 NBCUS Data)

	2008	2006
RBC	\$223.09/ unit	\$211.50
Plasma	\$53.85/unit	\$52.65/unit
Apheresis platelets	\$538.56/unit	\$525.05/unit
	RBC and platelets statistically higher than 2006	

Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Transfusion. 2010 Apr;50(4):753-65.

Activity Based Cost of Transfusion from a Provider's Perspective



*Shander A, Hofmann A, Ozawa S, Theusinger O, Gombotz H, Spahn D.
Activity-Based Costs of Blood Transfusions in Surgical Patients at Four Hospitals. Transfusion Vol. 50, April 2010*

Costs per 2 units of transfused blood In Europe according to the studies

Authors	Cost provided by the study	Converted EUR	2011 EUR	Population in 2011	Coefficient	Weighted cost
Agrawal et al. (2006)	£546.12	€804.86	€969.73	62,435,709	0.0275	€26.55
Glennard et al. (2005)	€702.00	€702.00	€784.00	8,404,252	0.0293	€25.77
Shander et al. (2010)	\$1,222.88	€893.68	€972.56	62,435,709	0.0275	€24.84
	\$1,044.90	€752.00	€842.00	62,435,709	0.0293	€23.97
Van Bellinghen et al. (2003)	€702.00	€702.00	€784.00	65,075,310	0.2272	€208.07
Varney and Guest (2003)	€858.39	€858.39	€972.56	8,404,252	0.0293	€25.18
Hadjianastassiou et al. (2002)	€351.04	€517.52	€672.38	62,435,709	0.2179	€146.54
Total				286,473,011	1.0000	€877.69

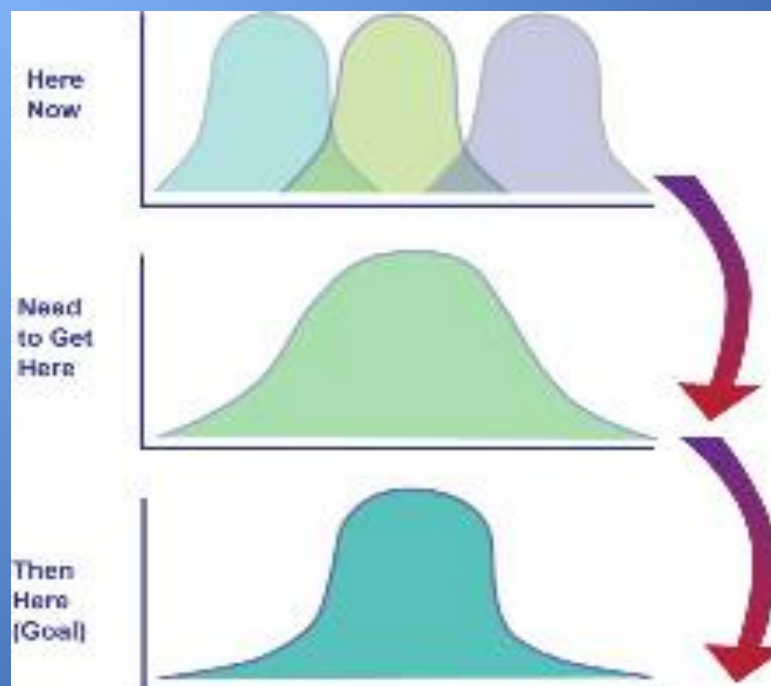
RANGE €517.52 - €804.86

TURKEY

- ◆ 394 blood centers/collection 3 national regions
 - ◆ TRC
 - ◆ Ministry of Health
 - ◆ University Hospital
- ◆ 1.5 Million units/yr 80% TRC, 60% family replace
- ◆ Blood Banking and Transfusion Services (BBTM)
Under the Ministry of health
- ◆ Governed by Blood laws
- ◆ Not all are VNRBD
- ◆ Blood Budget in Turkey – complex - IT IS NOT FREE!
- ◆ No national guideline - ~ 50% variability

Transfusion Confusion

- ◆ Articles demonstrating significant variability in practice
- ◆ Goal is to reduce variability practice



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2007 Society of Thoracic Surgeons Blood Conservation Guidelines

- ◆ 61 recommendations regarding blood conservation.
 - ◆ 6 Class I recommendations
 - ◆ 39 Class II recommendations
 - ◆ 20 Class IIa
 - ◆ 19 Class IIb
 - ◆ 16 Class III recommendations

Ferraris, et al. Ann Thorac Surg, 2007.

Blood Conservation Interventions 2007

Class I Recommendations

- ◆ Identify high risk preoperatively.
- ◆ Blood transfusion algorithm w/ point-of-care testing.
- ◆ Multimodality approach.
- ◆ Anti-fibrinolytic drugs (esp. for high risk)
- ◆ Cell recovery
- ◆ Preop platelet count and HCT for risk prediction.

Ferraris VA, et al. STS Guidelines on blood conservation. Ann Thorac Surg, 2007.

Evidence-Based Blood Conservation Strategies

◆ 2007

- ◆ Preoperative risk assessment – drugs & blood volume.
- ◆ Limit blood loss during operation – antifibrinolytics.
- ◆ Salvage & sequester blood
- ◆ Manage blood resources (process of care variables)

◆ 2011

- ◆ Preoperative risk assessment – drugs & blood volume.
- ◆ Blood derivatives.
- ◆ Blood recovery
- ◆ Minimally invasive techniques.
- ◆ Topical hemostats.

Predictors of Postoperative Bleeding

2007*

- 1) Advanced age
- 2) Small body size or preoperative anemia (low RBC volume)
- 3) Anti-platelet & anti-thrombotic drugs.
- 4) Prolonged operation (CPB time) – high correlation with OR type.
- 5) Emergency operation
- 6) Other co-morbidities (CHF, COPD, HTN, PVD, renal failure, etc.)

2011

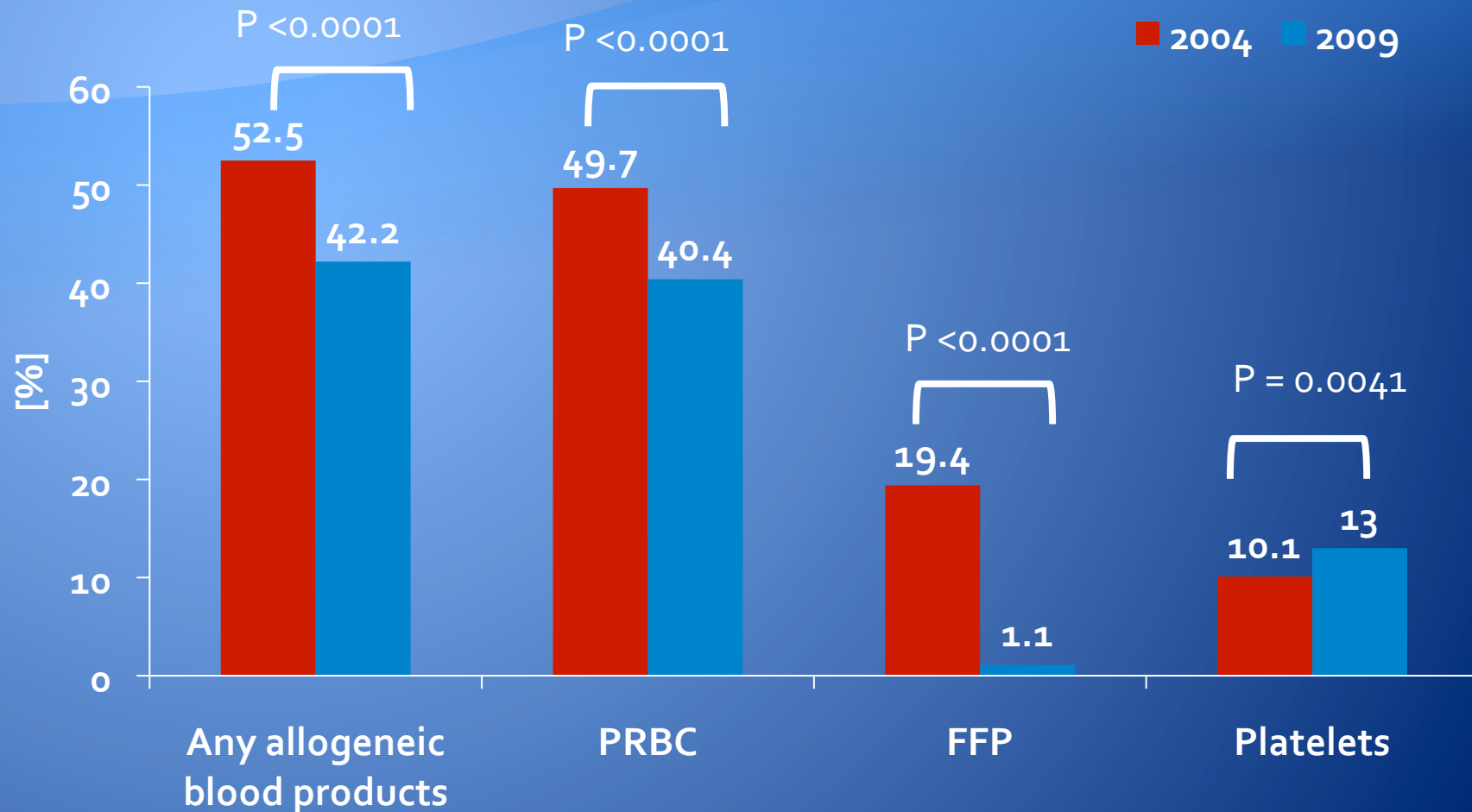
1. Advanced age
2. RBC volume
 - a) Small body size
 - b) **Preoperative anemia**
3. Drugs
 - a) **Anti-platelet drugs**
4. Co-morbidities
5. **Emergent or complex operations.**

* Ferraris, et al. STS Guidelines. Ann Thorac Surg. 2007

Transfusion guidelines at a glance

	100% platelets	40% platelets	40% platelets	40% platelets	40% platelets	40% platelets
Transfusion	None	Platelets platelets	Platelets platelets	Platelets platelets	Platelets platelets	Platelets platelets
100% platelets	10-20 g/dL	10-20 g/dL	10-20 g/dL 10-20 g/dL platelets platelets platelets	10-20 g/dL platelets platelets platelets platelets	10-20 g/dL platelets platelets platelets	10-20 g/dL platelets platelets platelets platelets
100% platelets	10-20 g/dL	10-20 g/dL	10-20 g/dL	10-20 g/dL	10-20 g/dL	
100% platelets	10-20 g/dL	10-20 g/dL				
Transfusion criteria criteria	100% platelets platelets platelets	100% platelets platelets platelets	100% platelets platelets platelets	100% platelets platelets platelets	100% platelets platelets platelets	100% platelets platelets platelets

Incidence of intra-operative transfusion of allogeneic blood products



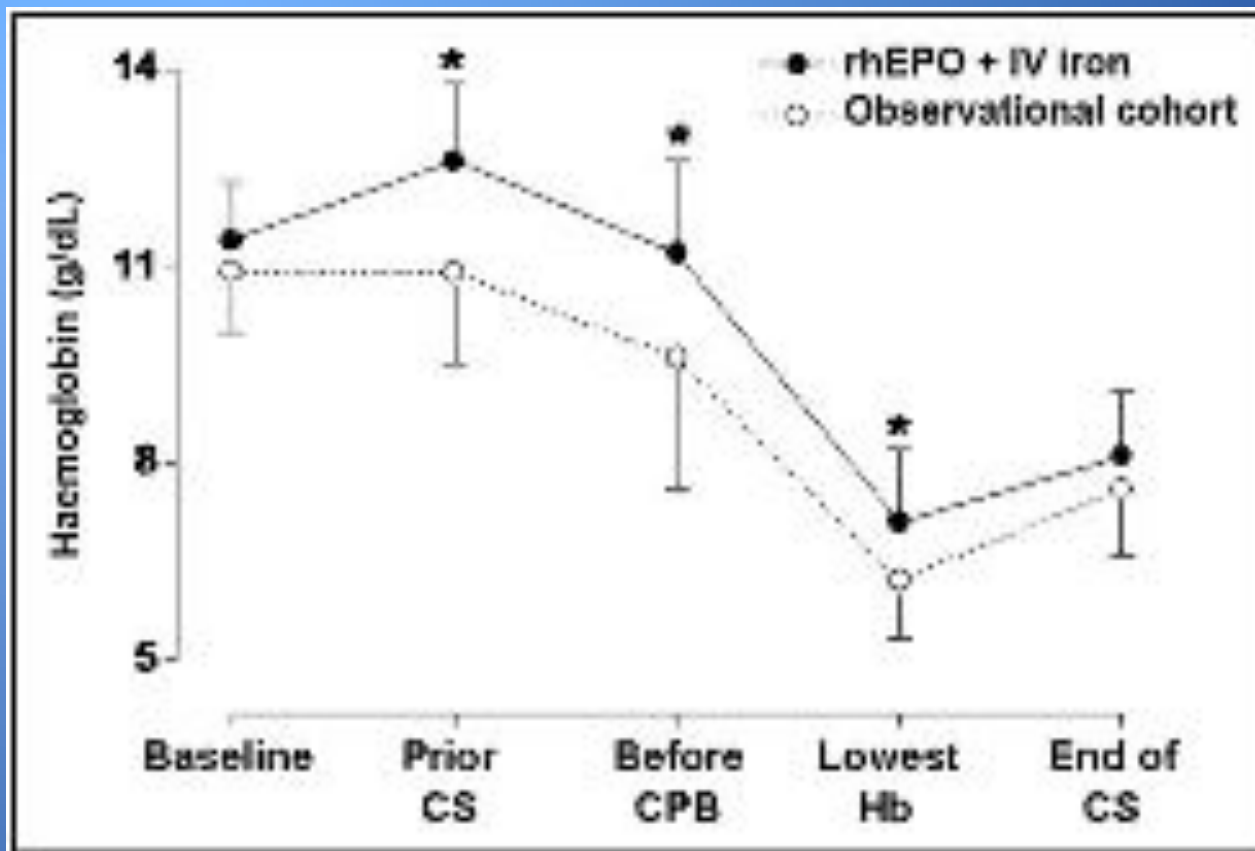
Total intra-operative transfusion requirements per year

FFP, fresh frozen plasma; concentrate;
PRBCs, packed red blood cells

Görlinger K. *et al. Anesthesiology* 2011;115:1179-91

Effects of Preoperative Intravenous Erythropoietin Plus Iron on Outcome in Anemic Patients After Cardiac Valve Replacement

Mercè Cladellas, MD, PhD^{a,c}, Nuria Farré, MD^a, Josep Comin-Colet, MD, PhD^a, Miquel Gómez, MD^a, Onna Meroño, MD^a, M. Alba Bosch, MD^a, Joan Vila, MSc^d, Rosa Molera, BS^d, Anna Segovia, BS^d, and Jordi Bruguera, MD^a



N=134



Single High Dose of Erythropoietin Two Days Before Surgery: A Simplified Short Term Approach To Blood Spare

Welfort, Luca¹, Falco, Marco, Martella, Severo, Ricci, Alessandra, Mosca, Daniele¹, Balsani, Alessandro¹, Rondelli, Sandro¹, Fiori, Luca², De Paulis, Ruggiero¹

400 patients randomized to EPO or control
Primary end point – Transfusion
Secondary – Safety M&M

	<u>EPO</u>	<u>CONTROL</u>	<u>P value</u>
Transfusion	0.39	1,12	<0.01
Death	2.92%	3.42%	NS
SAE	4.10%	4.87%	NS

The effect of a preoperative erythropoietin protocol as part of a multifaceted blood management program in daily clinical practice

Hirshowitz J, Davidson J, Aguilera M, et al. *Transfusion*. 2012;52(12):2100-2106.



- ◆ N = 4568 - EPO protocol in THA patients in 2003 [2 Groups - EPO group (pre-op hgb 10 to 13 g/dL) vs. Non EPO group (> than 13 g/dL)]
- ◆ Absolute reductions in ABTs after the intervention:
- ◆ Total study population was 17%
- ◆ 25% for Hb groups 10 to 13 and 8% for > 13 g/dL
- ◆ The transfusion rate in the EPO group was lower vs. non-EPO group: 14 and 50%, respectively ($p < 0.01$).
- ◆ Introduction of a preoperative EPO protocol reduced the transfusion rate in THA patients in daily clinical practice

Blood Conservation Intraoperatively

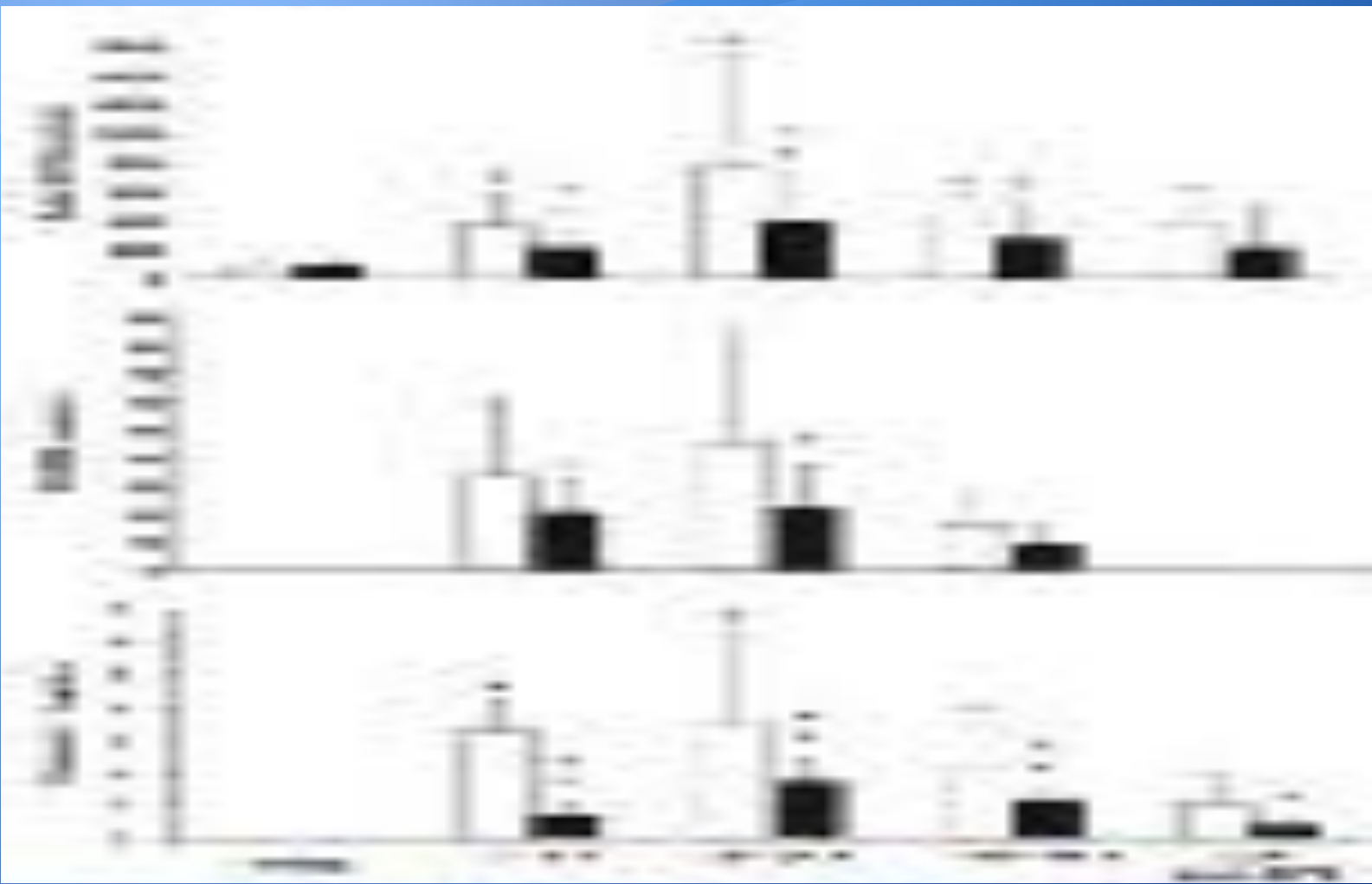
- ◆ Acute normovolemic hemodilution
 - ◆ remove whole blood prior to incision, return at end of case
 - ◆ protects whole blood (RBC's, plasma and platelets) from negative effects of the CPB circuitry
 - ◆ safe, proven effective, cost effective
- ◆ Tolerance of anemia
 - ◆ must be euvolemic
 - ◆ Aline, PAC, TEE, urine output
 - ◆ pre-CPB Hgb 9-10 gm/dl
 - ◆ on CPB Hgb 7-8 gm/dl (hypothermic)
 - ◆ post-CPB Hgb 8 gm/dl
- ◆ Pharmacological agents
 - ◆ antifibrinolytics
 - ◆ Amicar
 - ◆ Aprotinin
 - ◆ DDAVP



Cardioprotective effects of acute normovolemic hemodilution in patients with severe aortic stenosis undergoing valve replacement

- ◆ N = 40 patients scheduled for elective AVR - randomly assigned to a control group (standard care) or an ANH group (target hematocrit level of 28%)
- ◆ In the ANH group:
 - ◆ Postoperative release of troponin I (1.7 ng/mL) and myocardial fraction of creatine kinase (22 U/L) was significantly lower than in the control group (3.6 ng/mL and 45 [U/L, respectively)
 - ◆ Circulating levels of erythropoietin (EPO) were higher than in control patients (13.6 +/- 4.2 mUI/mL vs. 7.3 +/- 2.4 mUI/mL; $p < 0.05$).
- ◆ Fewer hemodiluted patients presented adverse cardiac events
- ◆ Preoperative ANH further attenuates myocardial injuries
- ◆ ANH-induced cardioprotection:
 - ◆ Optimization of preischemic myocardial oxygen delivery and/or consumption
 - ◆ Postconditioning effects of endogenous EPO

Perioperative time course of serum concentrations of total CPK (A), CK-MB (B), and cTnI (C) in the control (■) and ANH (■) groups. *p < 0.05, between the two groups; #p < 0.05, compared with baseline



Blood Conservation Intraoperatively

- ◆ Intraoperative retransfusion of shed mediastinal blood
 - ◆ cell saver
 - ◆ only saves shed RBC' s!!!!!!
 - ◆ coronary suckers
 - ◆ when pt heparinized
 - ◆ squeeze lap pads of salvageable



Blood Conservation Intraoperatively

- ◆ Surgical techniques
 - ◆ Meticulous technique
 - ◆ Careful dissection
 - ◆ LIMA, reops, etc.
 - ◆ Attention to minimize bleeding
 - ◆ progress safely, vigilant
 - ◆ Endoscopic vein harvesting
 - ◆ CPB
 - ◆ smaller prime volume
 - ◆ hemofiltration
 - ◆ retransfuse as much of the blood in the circuit prior to termination of CPB
 - ◆ Maintenance of normothermia after CPB and postoperatively



INTRA-OPERATIVE

◆ PUMP PRIME VOLUME

- ◆ ELIMINATE UNECESSARY VOLUME
- ◆ 2,100 cc...1,350 cc...1,250 cc
 - ◆ SHORTER LINES
 - ◆ MOVE PUMP CLOSER TO FIELD
 - ◆ SMALLER LINES
 - ◆ VACUUM ASSISTED VENOUS RETURN
 - ◆ RETROGRADE AUTOLOGOUS PRIMING
 - ◆ EVACUATE LAST AMOUNT OF PRIME VOLUME

Blood Conservation CPB



Blood Conservation CPB



Blood Conservation CPB



Blood Conservation Intraoperatively

- ◆ Point-of-care (on-site) coagulation monitoring
 - ◆ Activated clotting time (ACT)
 - ◆ global anticoagulation monitor
 - ◆ avoid microvascular coagulation on CPB
 - ◆ Hepcon[®]
 - ◆ monitor heparin blood levels
 - ◆ more precise Protamine dosing
 - ◆ TEG[®] (thromboelastogram)
 - ◆ graphical display of the formation of a clot
 - ◆ ⇒ see where coagulopathy exist
 - ◆ results faster than standard lab tests
 - ◆ prevented many transfusions
 - ◆ Non- invasive Hgb (SpHB) monitor
(Masimo Rainbow monitor)



The Institute for Patient Blood Management Englewood Hospital & Medical Center

TRANSFUSION RATES

Moskowitz DM Klein J. Shander A.. *Ann Thorac Surg* 2010

	PRBC	FRESH FROZEN PLASMA	PLATELETS	CRYOPRECIPITATE
ALL CASES	16.78%	4.19%	5.49%	1.70%
CABG	10.79%	1.44%	1.98%	0.72%
VALVE	12.99%	2.60%	6.49%	1.29%
ANEURYSM	38.67%	21.33%	21.33%	9.33%

The Institute for Patient Blood Management Englewood Hospital & Medical Center

Moskowitz DM Klein J. Shander A.. *Ann Thorac Surg* 2010

	ALL COMERS	ELECTIVE	EMERGENT
ALL CASES	2.70%	1.82%	3.48%
CABG	0.56%	0.26%	0.72%
VALVE	3.68%	2.18%	5.77%
ANEURYSM	8.64%	3.70%	15.58%

Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery

Grimaldi JA, Pagan ML, Mihalik EA, et al. *Ann Surg*. 2013;257(3):485-492. doi:10.1097/SLA.0b013e3182911111



- ◆ N = 14,259 patients (2006-2010) - nonemergency, primary, isolated CABG operations [2 Groups -pre-guideline (n = 7059) vs. post-guideline (n = 7200,)]
- ◆ Overall intraop (24% vs 18%) and postop (39% vs 33%) (P < .001) **blood product transfusion were significantly reduced** in the post-guideline era
- ◆ Post-guideline era - **reduced morbidity with decreased pneumonia, prolonged ventilation, renal failure, new-onset hemodialysis and major complications**
- ◆ Operative mortality (P < .001) and postop ventilation time (P < .001) were **reduced** in the post-guideline era
- ◆ Post-guideline era were associated with **a 47% reduction** in the odds of death
- ◆ Intra & post-op transfusions - associated with **increased costs** (\$4408 and \$10,479, respectively)

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Summary

**PBM (Blood Conservation)
in CV Surgery is SAFE and
EFFECTIVE**

2013 ANNUAL MEETING

September 19-21, 2013

Shrine Auditorium, Los Angeles, California

www.ubm.com/annualmeeting/2013

Patient Blood Management
—from Research to Bedside



ANNUAL MEETING OF THE SOCIETY OF
CRITICAL CARE MEDICINE

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