

Seuils transfusionnels en 2016



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Conflict of Interest Disclosure

In the past 5 years, I have received honoraria or travel support for consulting or lecturing from the following companies:

Fresenius-Kabi GmbH

CSL Behring GmbH

Janssen-Cilag SA

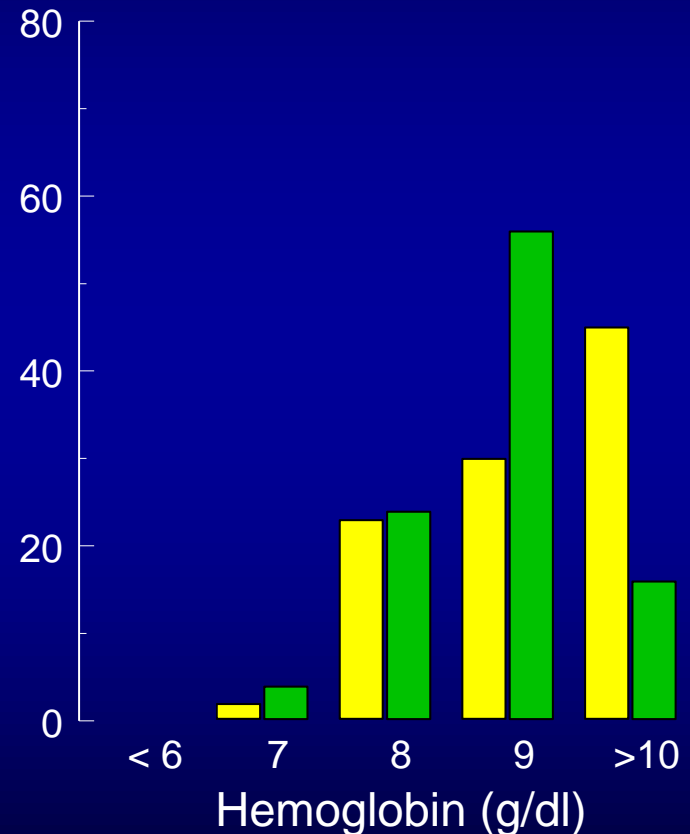


Transfusion Practices in Critically Ill Patients

Myocardial infarction

- ▶ 55-year-old man
- ▶ Major vascular surgery (AAA)
- ▶ POD4: retrosternal chest pain
- ▶ ECG: anterior wall myocardial infarction: ICU admission
- ▶ No other complication
- ▶ No evidence of a volume deficit

Frequency (%)

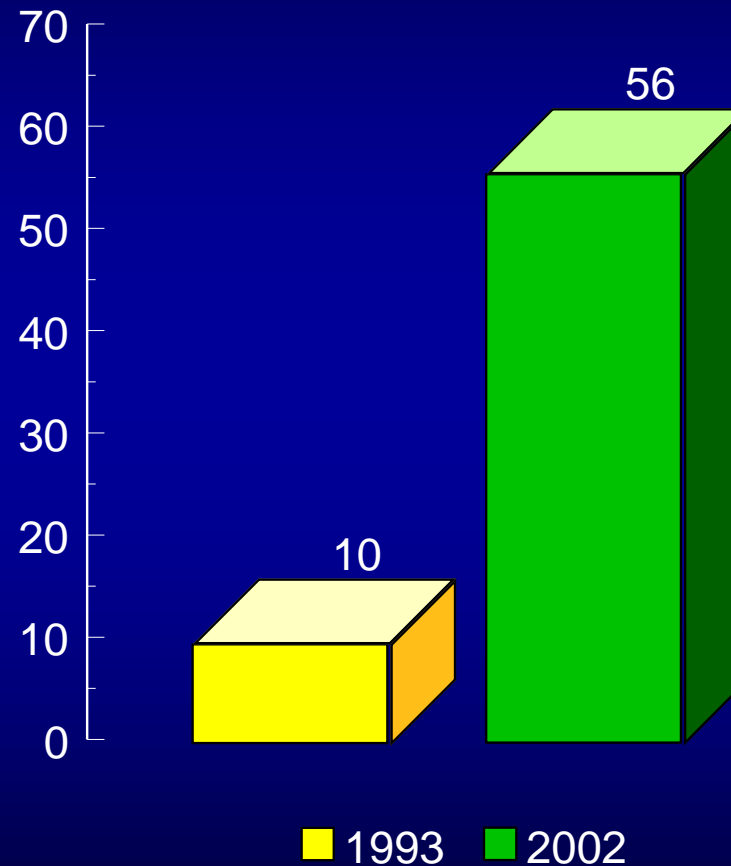


■ 1993 ■ 2002

From Hébert PC et al Crit Care Med 33:7-12, 2005.

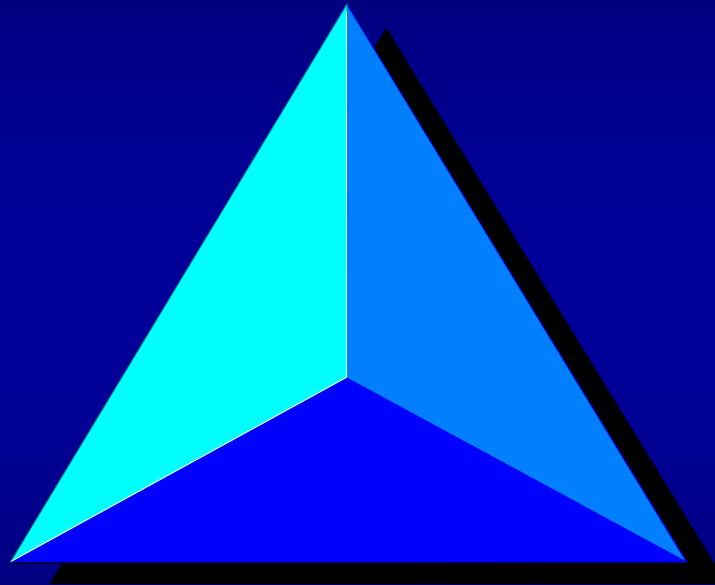
Transfusion Practices in Critically Ill Patients

Single unit transfusion (%)



The “Transfusion” Dilemma

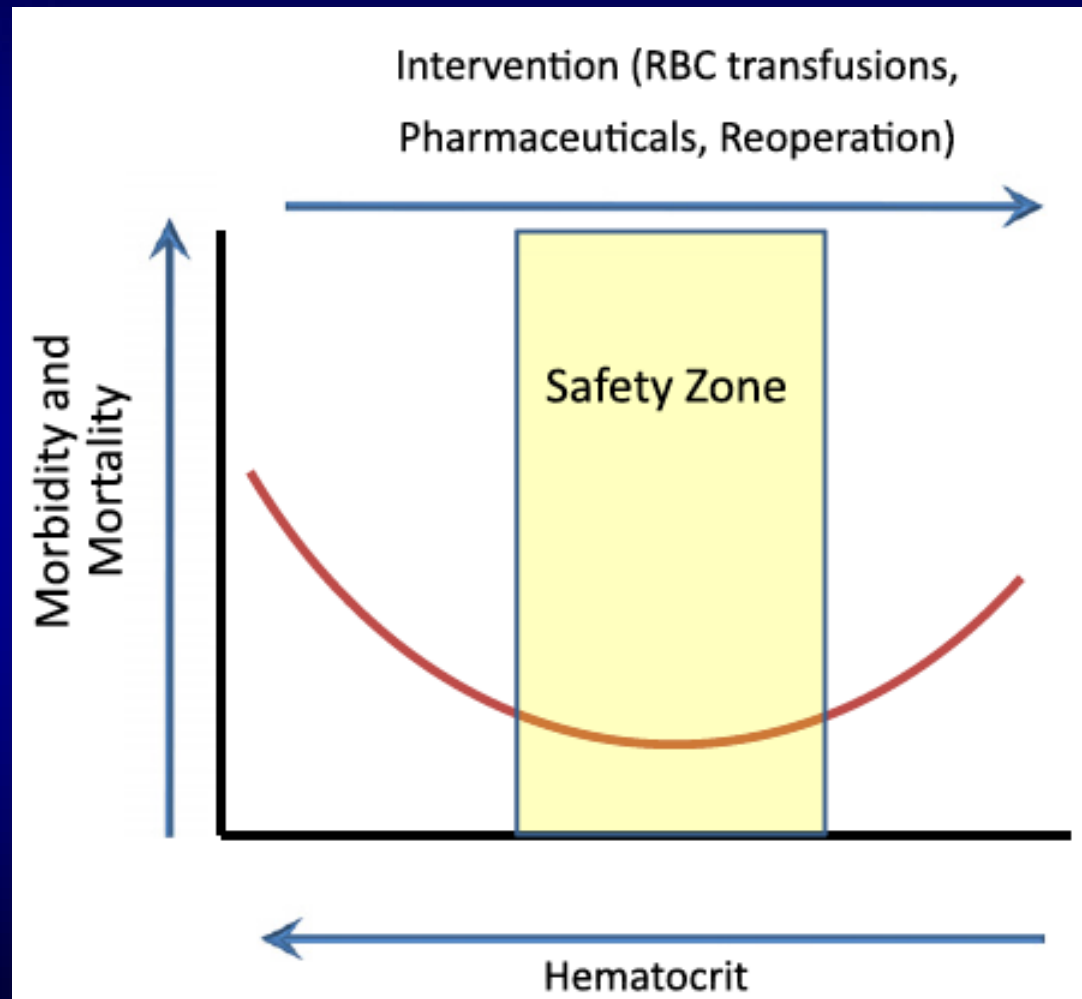
Risks associated with anemia



Effectiveness
of
blood transfusion

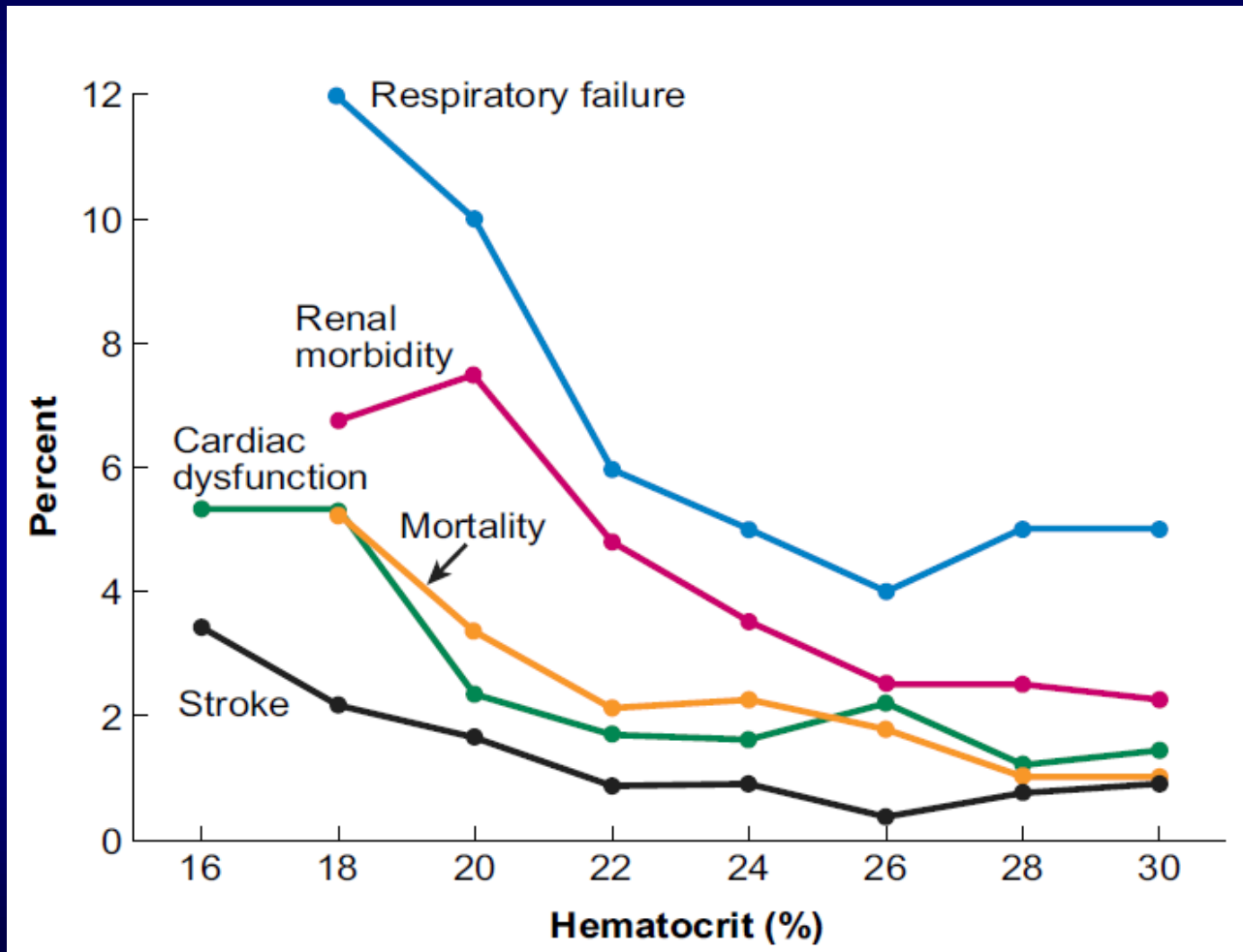
Risks associated
with
blood transfusion

Intraoperative Anemia & Postoperative Morbi-mortality After Cardiac Surgery

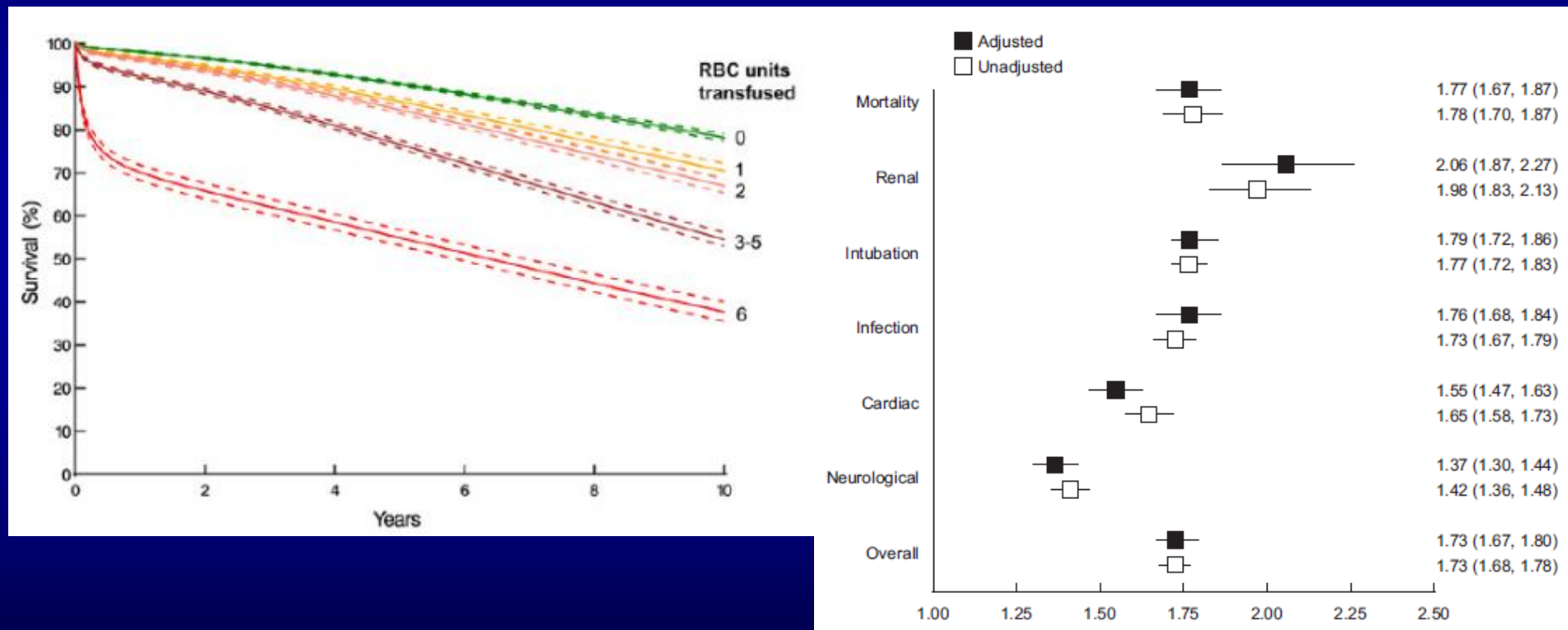


From Loor G et al. J Thorac Cardiovasc Surg 144:538-46, 2012.

Intraoperative Anemia & Postoperative Morbi-mortality After Cardiac Surgery



Blood Transfusion & Postoperative Morbi-Mortality After Cardiac Surgery



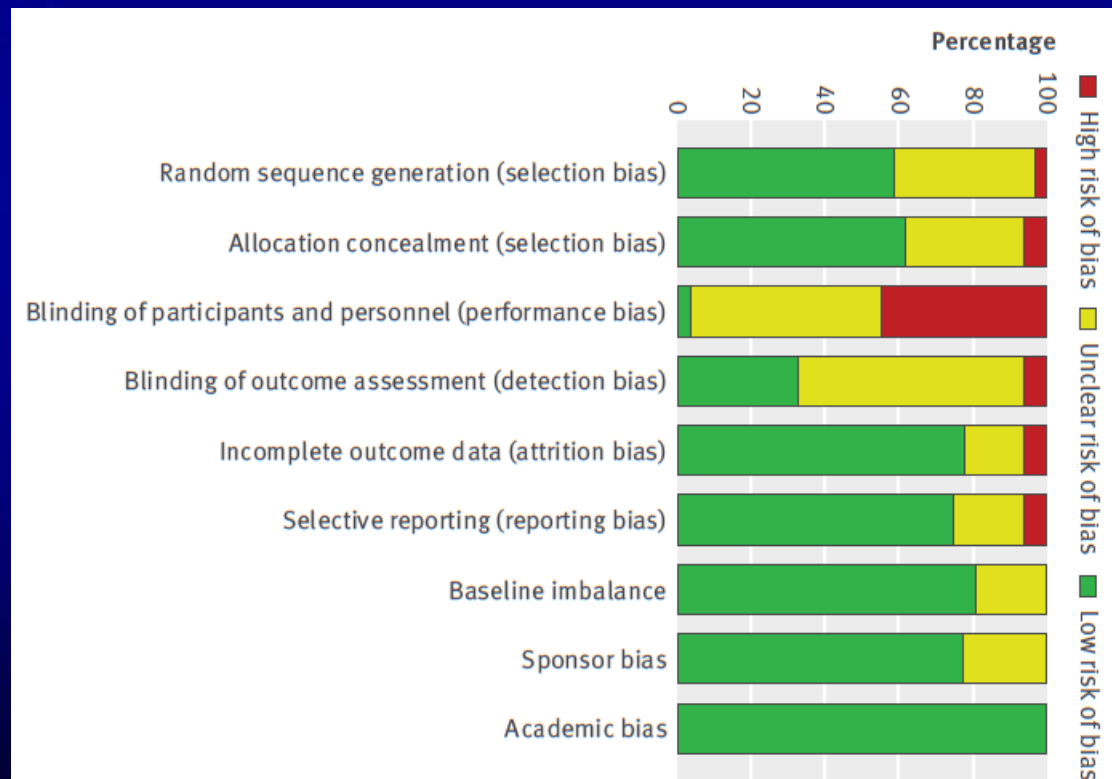
From Loor G et al. J Thorac Cardiovasc Surg 144:538-46, 2012.

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

31 trials – 9,813 patients

✓Objectives:

To compare the benefit and harm of restrictive versus liberal transfusion strategies to guide RBCs transfusions



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

31 trials – 9,813 patients

✓ Results: restrictive transfusion strategies

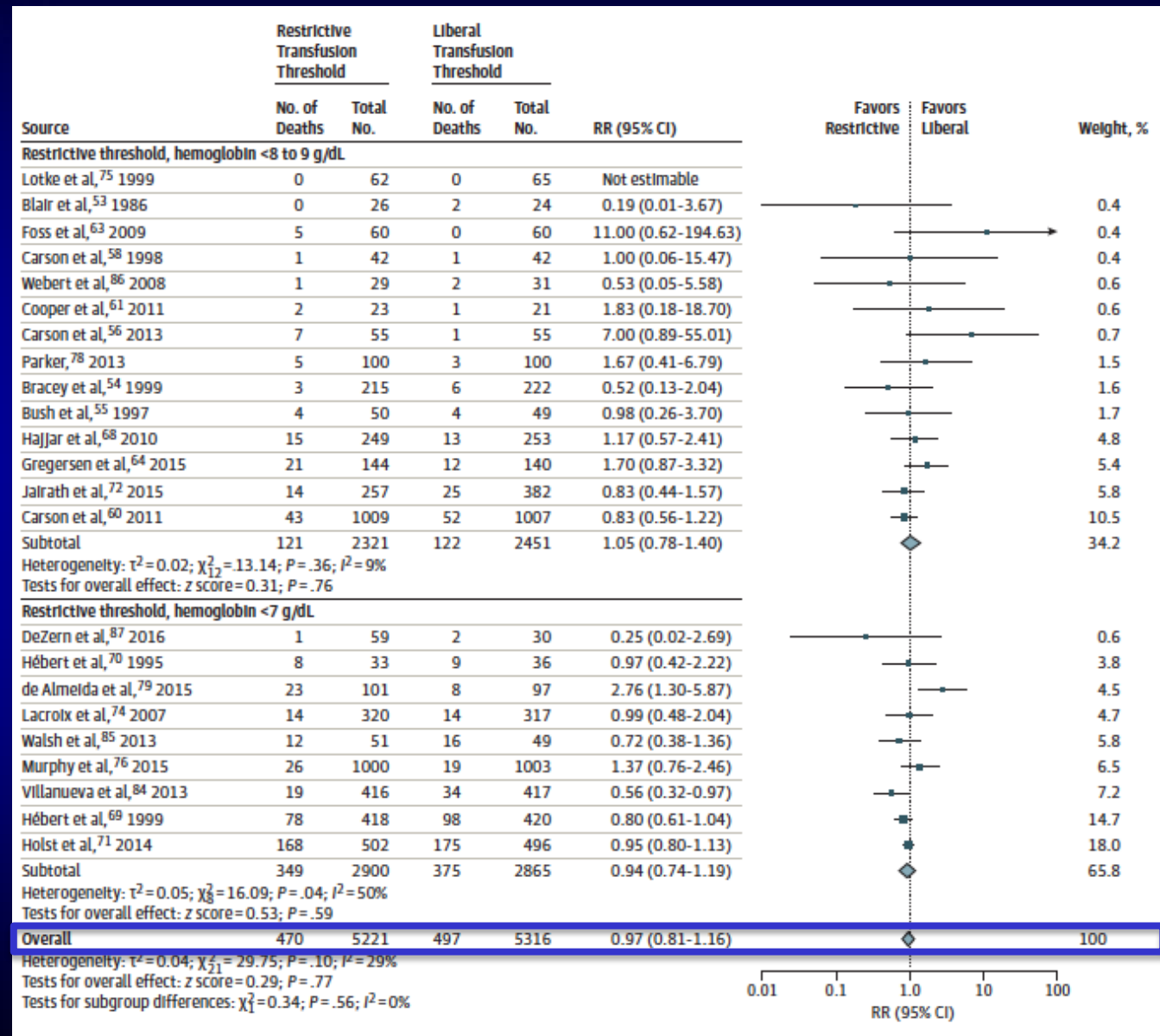
- ↓ risk of receiving RBC transfusion (RR: 0.54; 95% CI: 0.47 to 0.63)
- ↓ volume of transfused RBCs (MD: -1.43; 95% CI: -2.01 to -0.86)
- No impact on mortality (RR:0.86; 95% CI: 0.74 to 1.01)
- No impact on morbidity (RR:0.98; 95% CI: 0.85 to 1.12)
- No impact on fatal or non-fatal MI (RR: 1.28; 95% CI: 0.66 to 2.49)

Results not affected
by the inclusion of
studies with unclear
or high risk of bias

A 15% relative risk reduction or increase in overall morbidity with restrictive transfusion strategies could be excluded

Red Blood Cell Transfusion Threshold & Storage

Transfusion
threshold
31 RCTS
12,587 patients

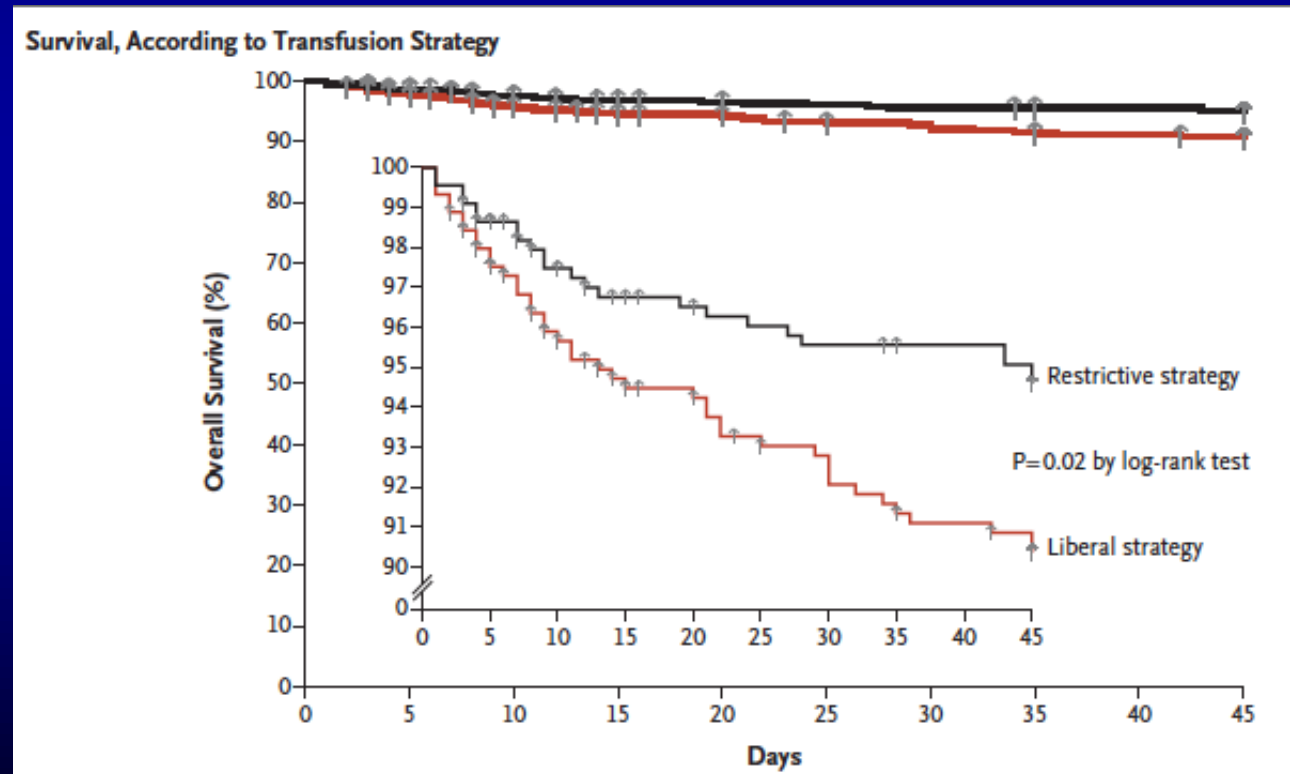


From Carson JL et al.
JAMA 316: 2025-35,
2016.

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

- ✓ Prospective randomized controlled trial:
 - Restrictive transfusion strategy: Hb < 7 g/dl (N=461)
 - Liberal transfusion strategy: Hb < 9 g/dl (N=460)

✓ 1 outcome:
45-day mortality



Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

✓ Prospective randomized controlled trial:

- Restrictive transfusion strategy: Hb < 7 g/dl (N=461)
- Liberal transfusion strategy: Hb < 9 g/dl (N=460)

Outcome	Restrictive Strategy (N = 444)	Liberal Strategy (N = 445)	Hazard Ratio with Restrictive Strategy (95% CI)	P Value
Death from any cause within 45 days — no. (%)	23 (5)	41 (9)	0.55 (0.33–0.92)	0.02
Further bleeding — no. of patients/total no. (%)				
Overall	45/444 (10)	71/445 (16)	0.62 (0.43–0.91)	0.01
Adverse events — no. (%) [†]				
Any [‡]	179 (40)	214 (48)	0.73 (0.56–0.95)	0.02
Transfusion reactions	14 (3)	38 (9)	0.35 (0.19–0.65)	0.001
Fever	12 (3)	16 (4)	0.74 (0.35–1.59)	0.56
Transfusion-associated circulatory overload	2 (<1)	16 (4)	0.06 (0.01–0.45)	0.001
Allergic reactions	1 (<1)	6 (1)	0.16 (0.02–1.37)	0.12
Cardiac complications [§]	49 (11)	70 (16)	0.64 (0.43–0.97)	0.04
Acute coronary syndrome [¶]	8 (2)	13 (3)	0.61 (0.25–0.49)	0.27
Pulmonary edema	12 (3)	21 (5)	0.56 (0.27–1.12)	0.07

From Villanueva C et al. N Engl J Med 368:1:11-21, 2013.

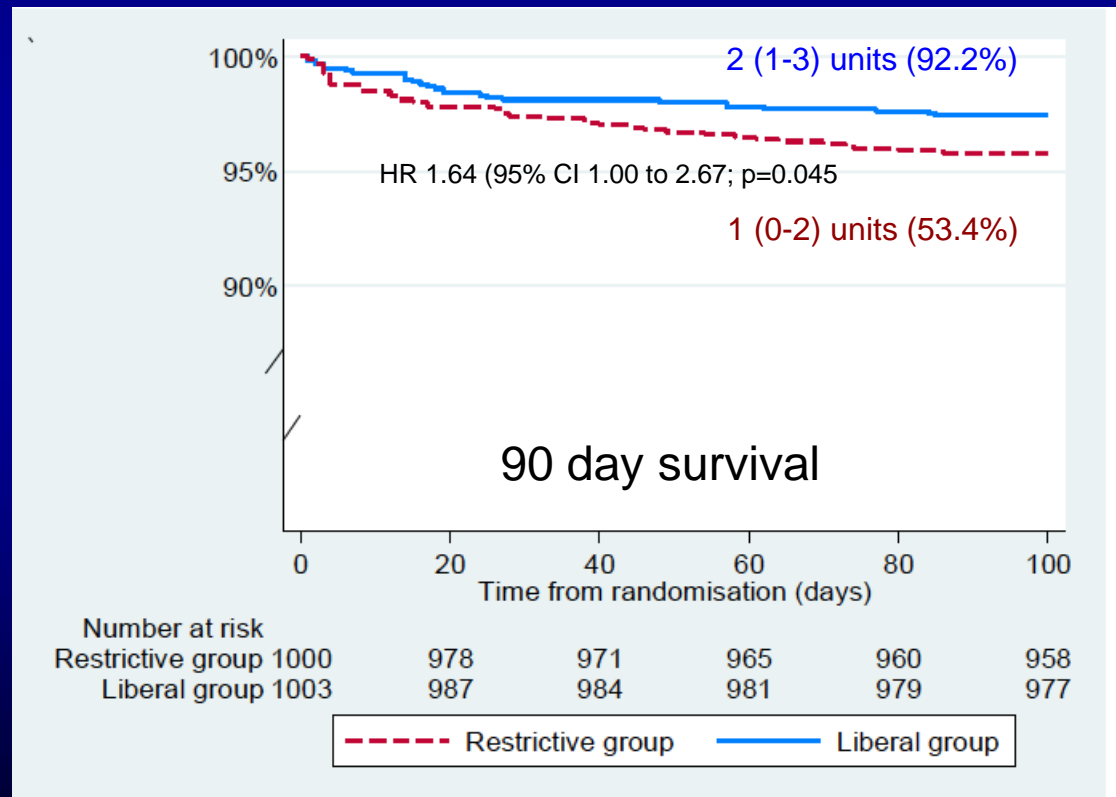
Liberal or Restrictive Transfusion after Cardiac Surgery

✓ Multicenter parallel-group trial (postoperative period):

- Restrictive transfusion strategy: Hb < 7.5 g/dl (N=1000)
- Liberal transfusion strategy: Hb < 9 g/dl (N=1003)

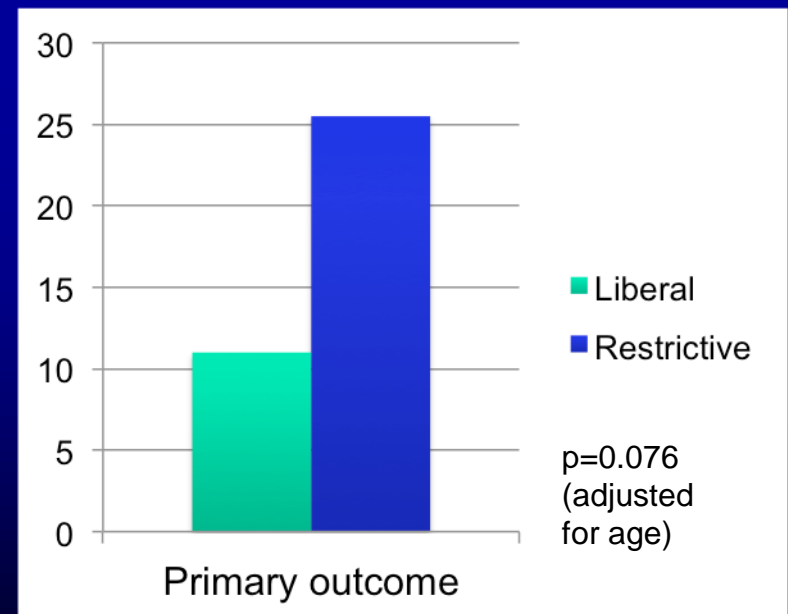
Pre storage leukoreduced
RBCs transfused unit by unit

✓ 1 outcome: 90-day mortality + morbidity



Blood Transfusion Strategy in Patients With Symptomatic Coronary Artery Disease

- ✓ Pilot trial: 110 ACS patients or stable angina undergoing cardiac catheterization and a Hb < 10 g/dl
 - Liberal strategy: Hb < 10 g/dl (N=55)
 - Restrictive strategy: symptoms of anemia or Hb < 8 g/dl (N=55)
- ✓ Primary outcome: composite of death, MI or unscheduled revascularization 30 days post randomization





Transfusion Medicine

Goodnough LT et al, NEJM 340:438-444,1999.

« It is unlikely that any level of hemoglobin can be used as a universal threshold for transfusion ».

Transfusion Thresholds

Barr PJ, Bailie KEM NEJM 365; 26: 2532-3, 2011.

« The decision to transfuse should be guided by an assessment of individual patient on the basis of a combination of symptoms, signs, lab measures and not by a single hemoglobin level ».

Blood Transfusion Strategy in High-Risk Patients after Hip Fracture Surgery

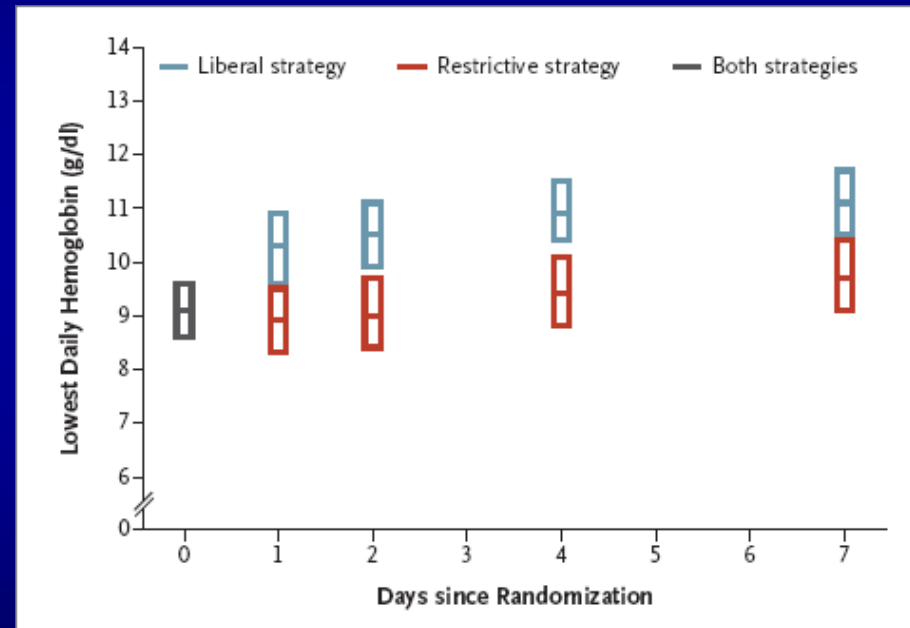
✓ Prospective randomized trial: patients ≥ 50 years of age with a history or risk factors for CVD with Hb < 10 g/dl after surgery

✓ Transfusion strategy:

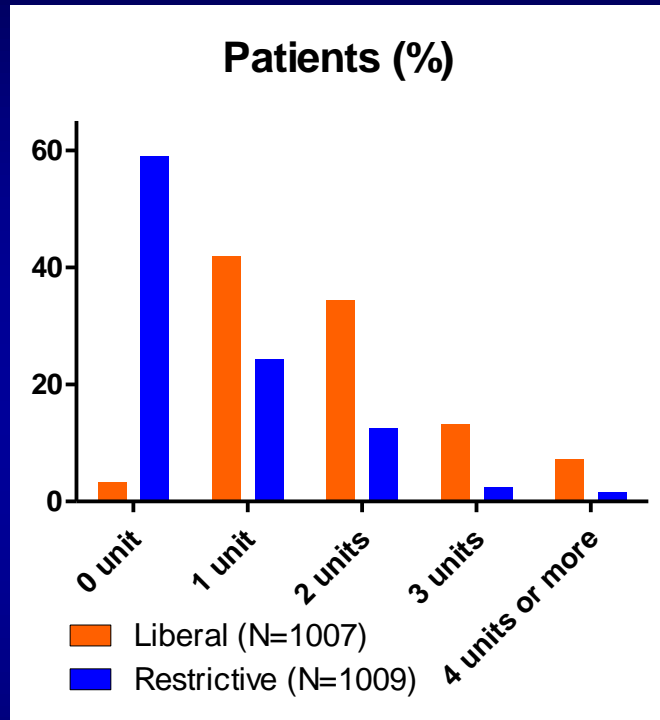
- Liberal Hb threshold of 10 g/dl
- Restrictive: symptoms of anemia or for Hb < 8 g/dl

✓ RBC transfused unit by unit

✓ Primary outcome: death or inability to walk across room without human assistance on 60-day follow-up



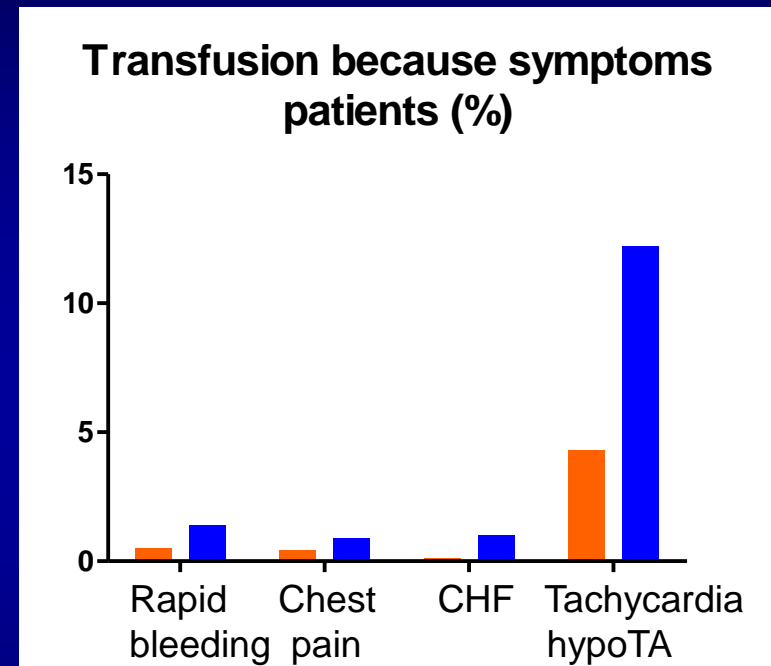
Blood Transfusion Strategy in High-Risk Patients after Hip Fracture Surgery



Age of the patients 82 ± 10 y

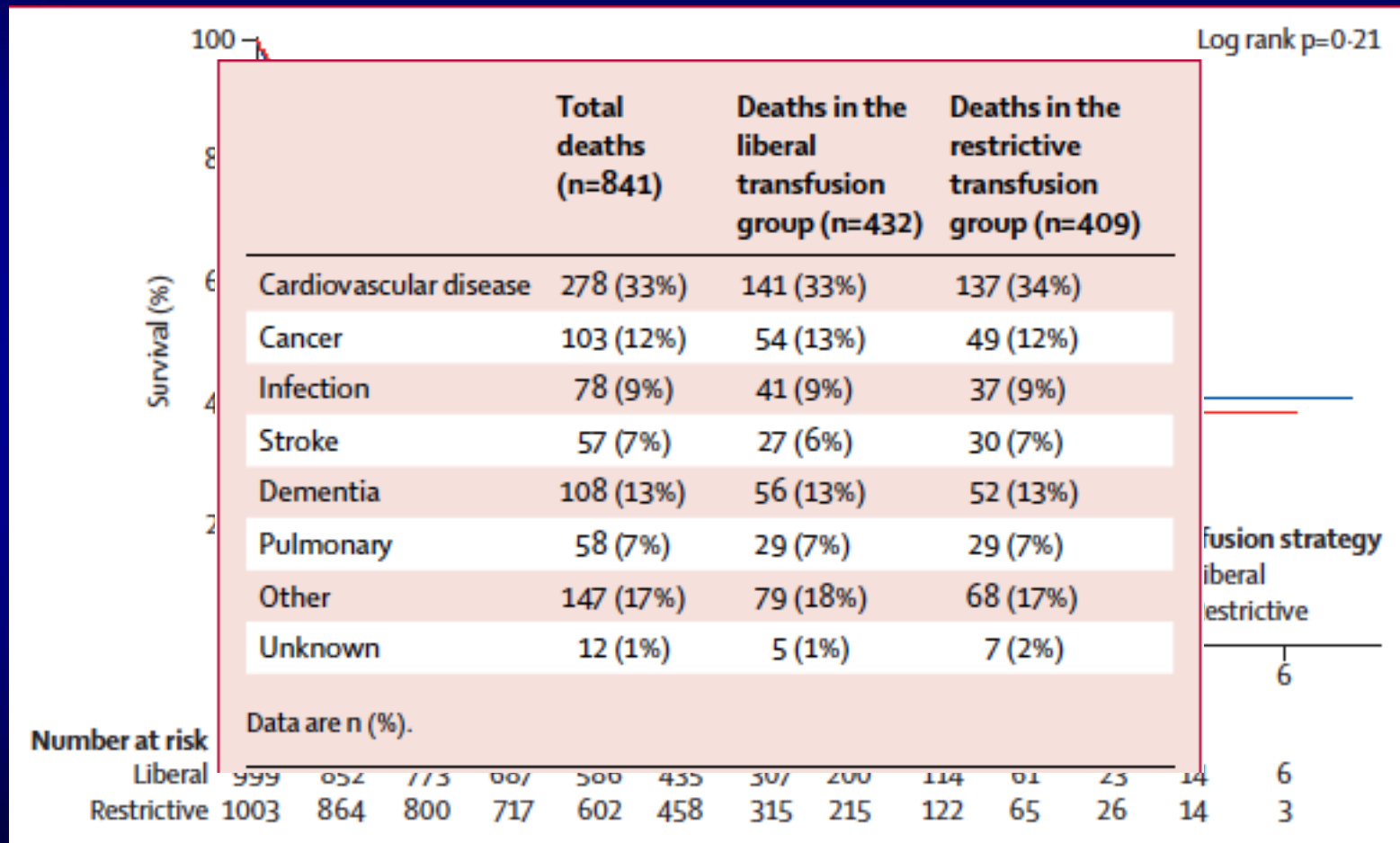
Age of de blood: 22 ± 10 days

Leukoreduction: 90%



Primary outcome: death or inability to walk across room without human assistance on 60-day follow-up: **35,2 %** vs **34,7%**

Blood Transfusion Strategy in High-Risk Patients after Hip Fracture Surgery: 3 Years Survival



Transfusion Triggers

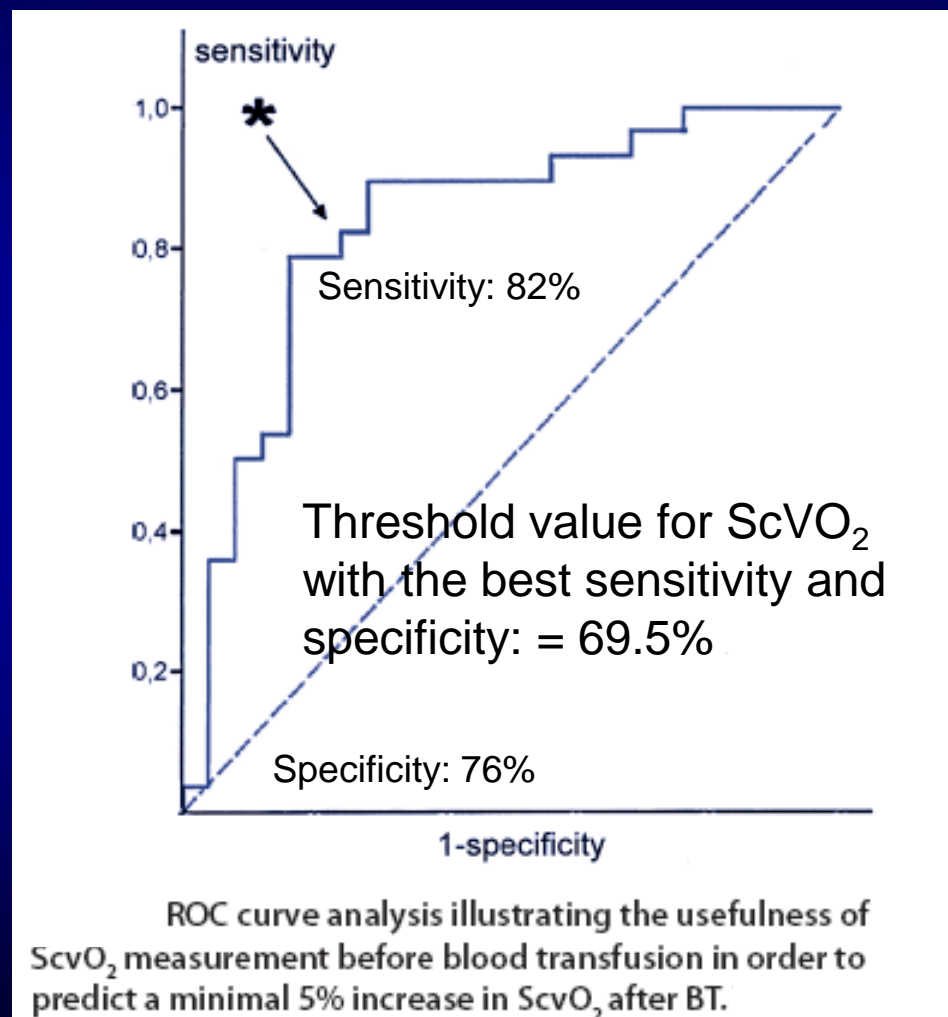
- Dyspnea
- Tachycardia
- Hypotension
- ST-T Abnormalities
- PvO₂, SvO₂, O₂ER
- Central venous O₂ saturation ?
 - Others (lactate) ?

Central Venous O₂ Saturation as a Physiologic Transfusion Trigger

$$\begin{aligned} \text{O}_2\text{ER} &= \text{VO}_2 / \text{DO}_2 \\ &\approx (\text{SaO}_2 - \text{SvO}_2) / \text{SaO}_2 \\ &\approx 1 - \text{SvO}_2 \end{aligned}$$

SvO₂ normal range: 68-77%
Central venous O₂ saturation
(ScVO₂): 5% above

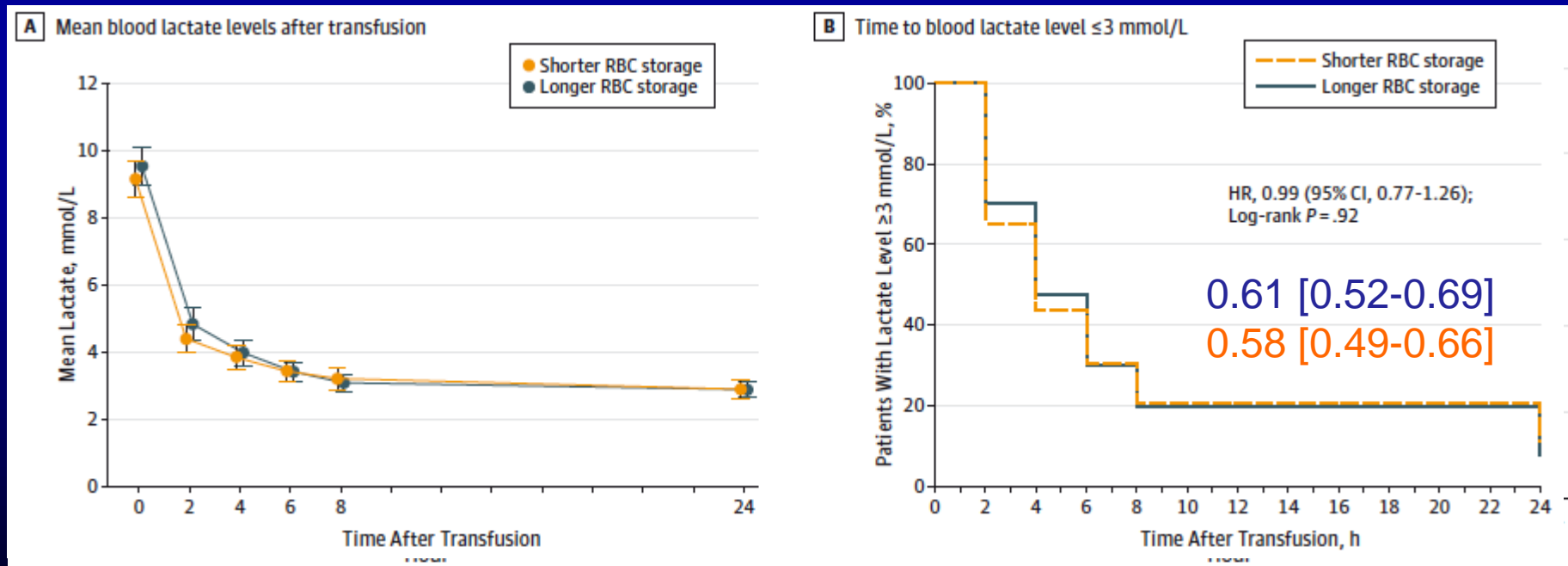
Reinhart K et al. Intensive Care Med 30:1572-8, 2004.



From Vallet B et al. Critical Care 14:213, 2010.

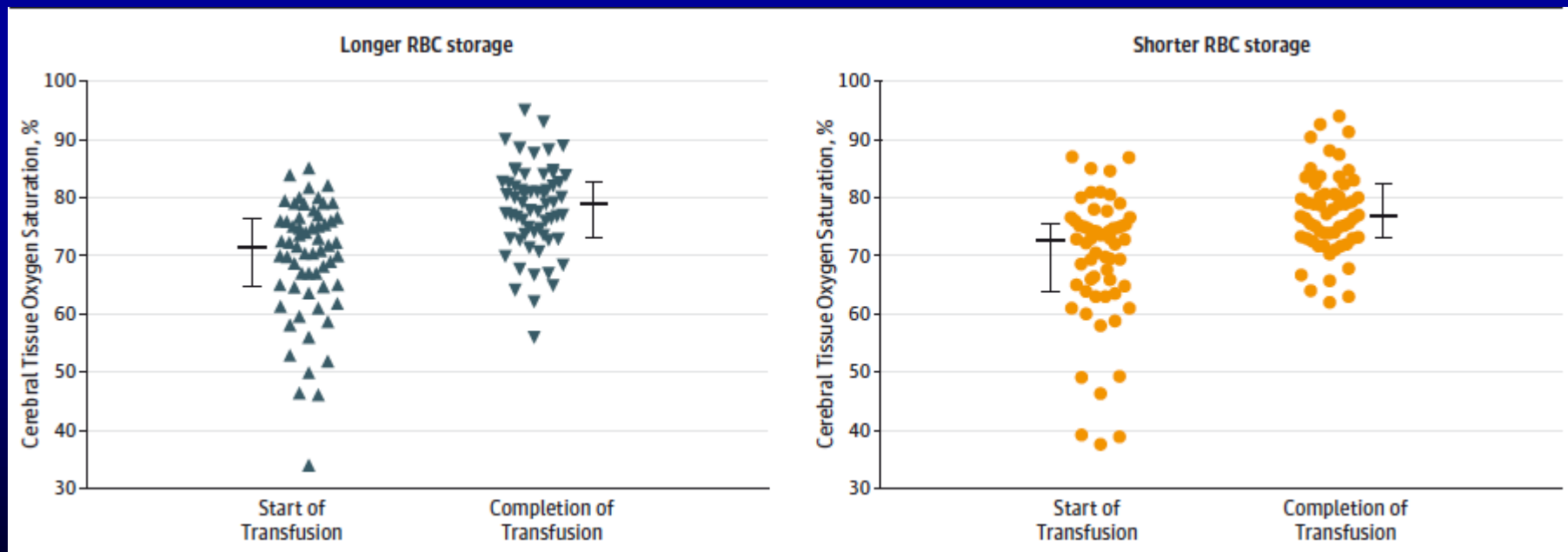
Effect of Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration on Elevated Blood Lactate Levels in Children With Severe Anemia

- ✓ Randomized noninferiority trial: children with a Hb concentration ≤ 5 g/dL and a lactate level ≥ 5 mmol/L
- ✓ Pre-storage leukoreduced RBC transfusion (10-20 ml/kg)
 - Long storage RBC units (32 [30-34] days; N=145)
 - Short storage units (8 [7-9] days; N=145)

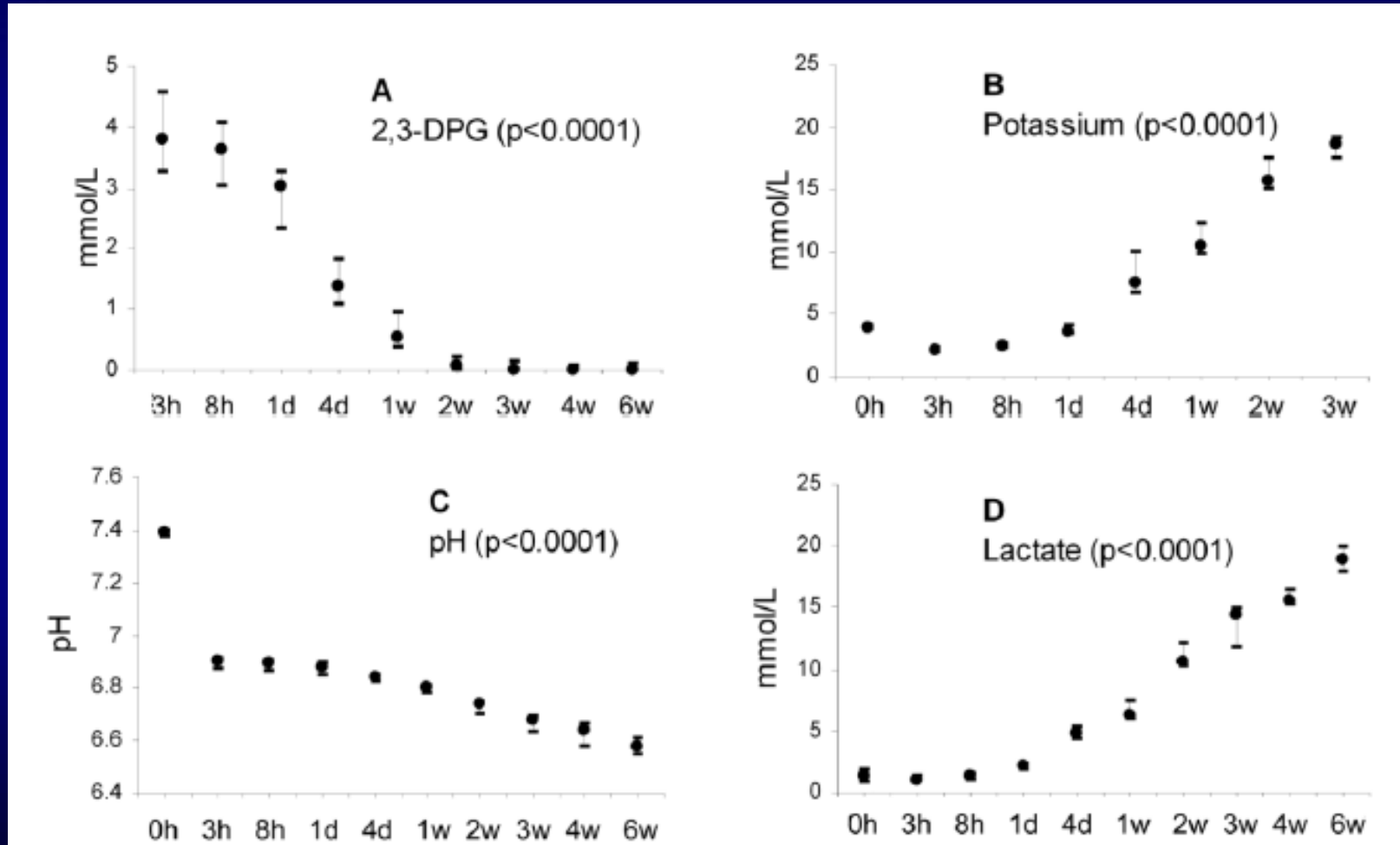


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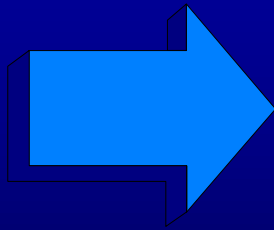


Change in Stored Red Blood Cell Characteristics Over Time



Blood Transfusion: "Storage Effects"

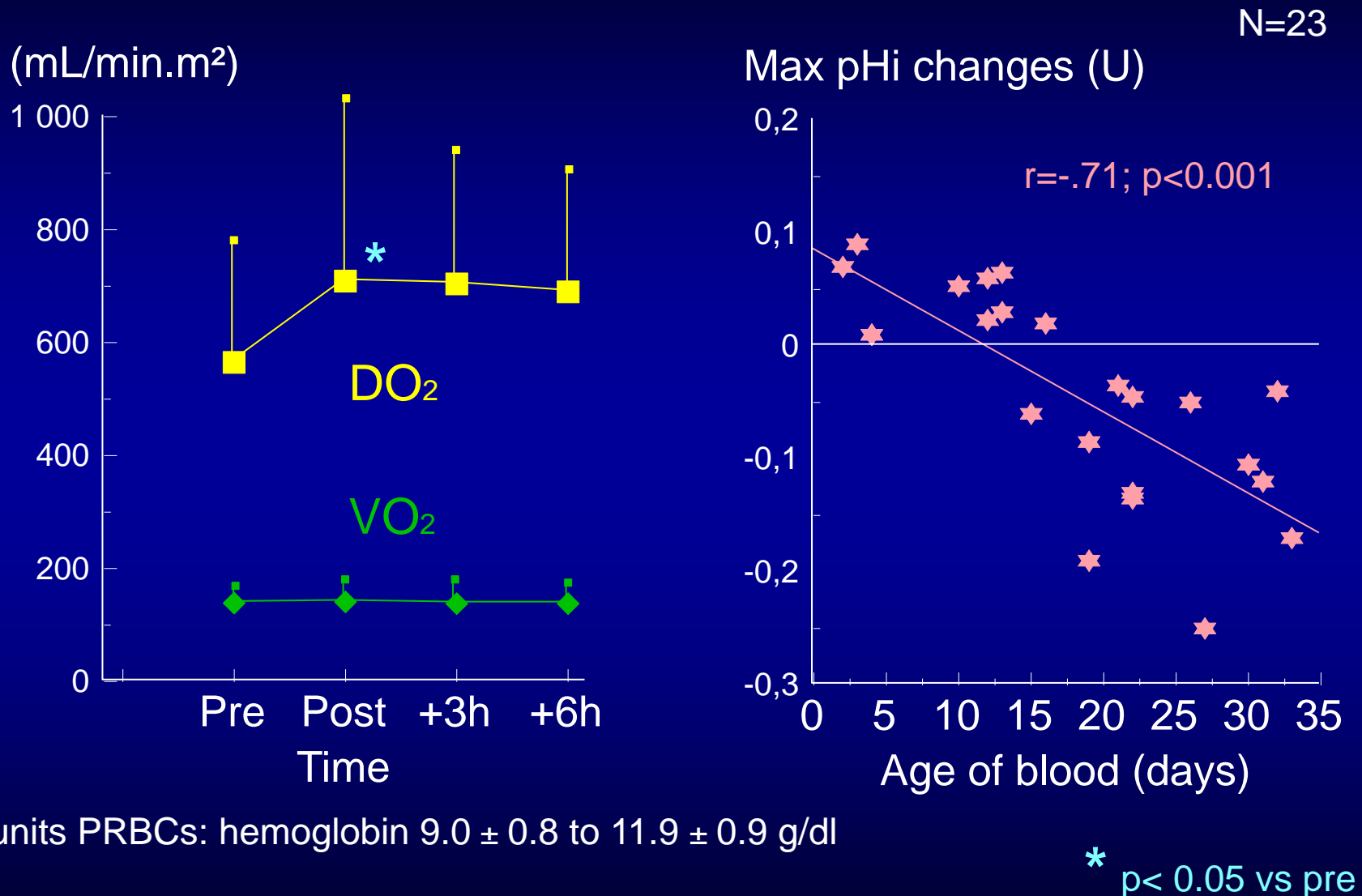
- ✓ Decreased 2, 3 - diphosphoglycerate (~ 0 after 15 days)
 - ▶ Increased affinity of hemoglobin for oxygen
- ✓ Decreased in red blood cell ATP
 - ▶ Change in RBC shape (discoid to spherocytic)
 - ▶ Reduced cellular deformability



Decreased tissue oxygen availability

Endothelial swelling and tissue edema in sepsis
reduce capillary luminal diameter

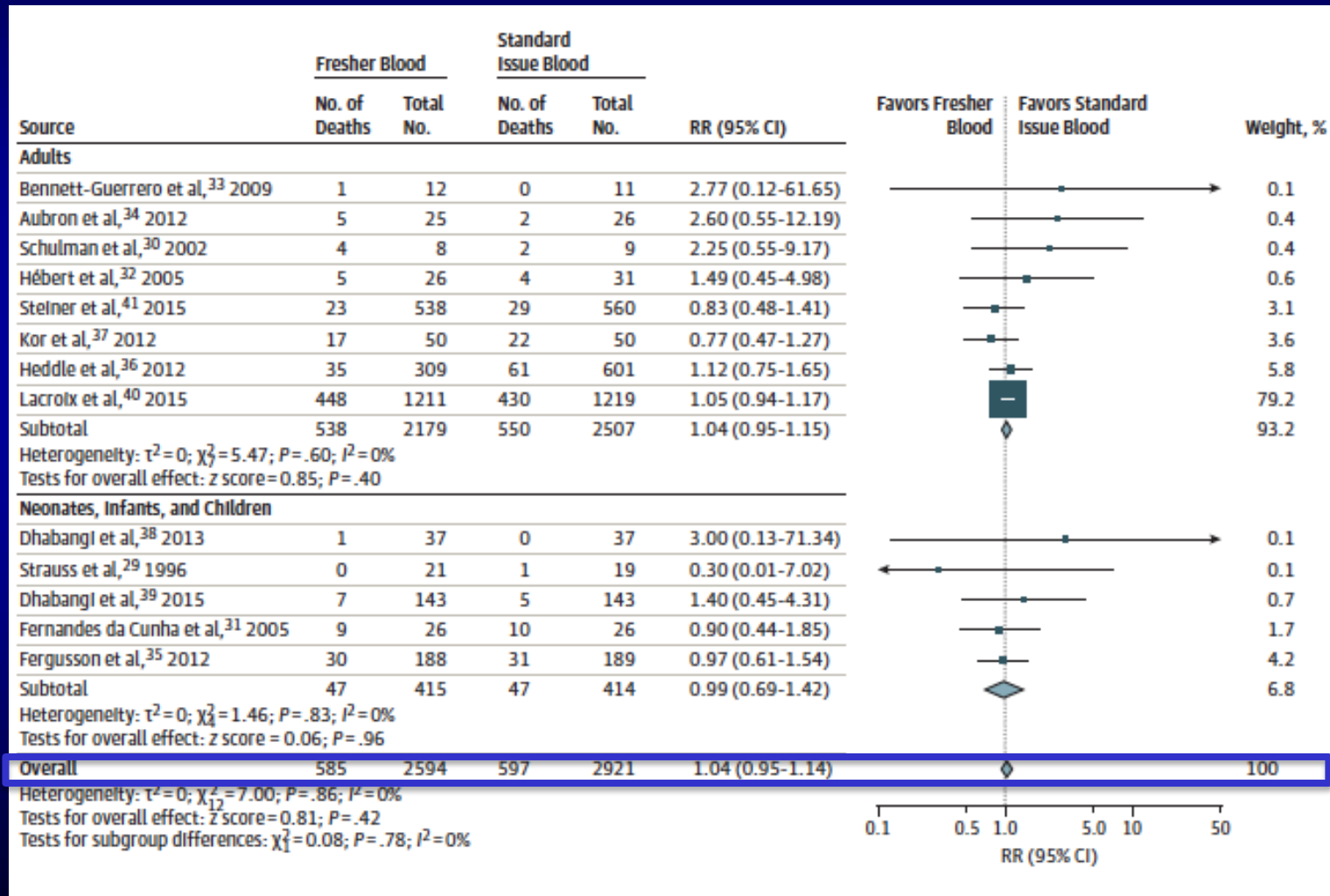
Effects of Allogeneic Blood Transfusion on $\dot{V}O_2$



3 units PRBCs: hemoglobin 9.0 ± 0.8 to 11.9 ± 0.9 g/dl

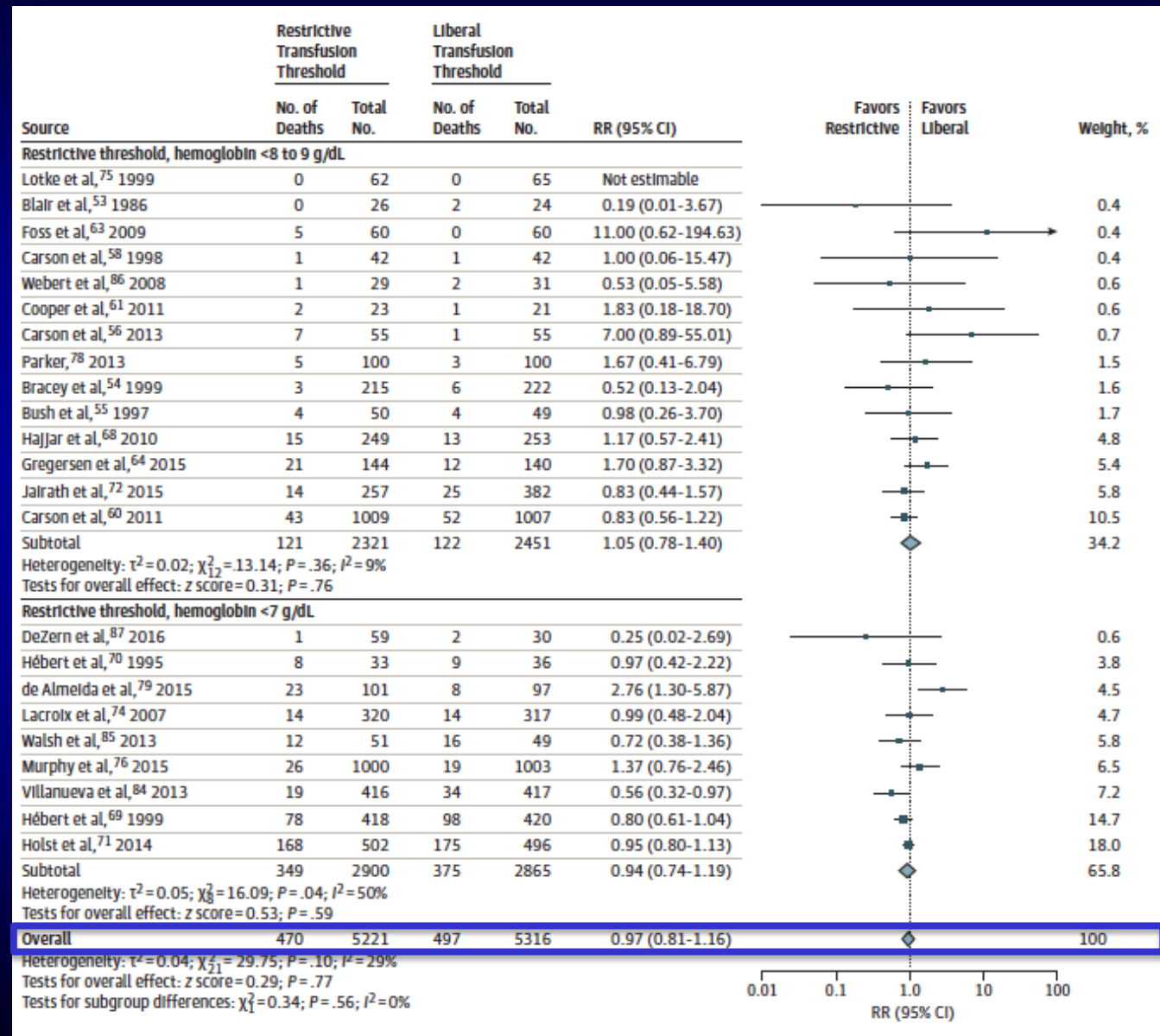
Red Blood Cell Transfusion Threshold & Storage

- ✓ RBC storage duration: 13 RCTS; 5,515 patients



Red Blood Cell Transfusion Threshold & Storage

Transfusion
threshold
31 RCTS
12,587 patients



From Carson JL et al.
JAMA 316: 2025-35,
2016.

Relationship of Erythrocyte Transfusion With Short & Long-term Mortality

✓ Population-based cohort study through analysis of administrative databases. Patients undergoing elective hip or knee surgery from 1999 to 2008 in Ontario (N=162,190 patients)

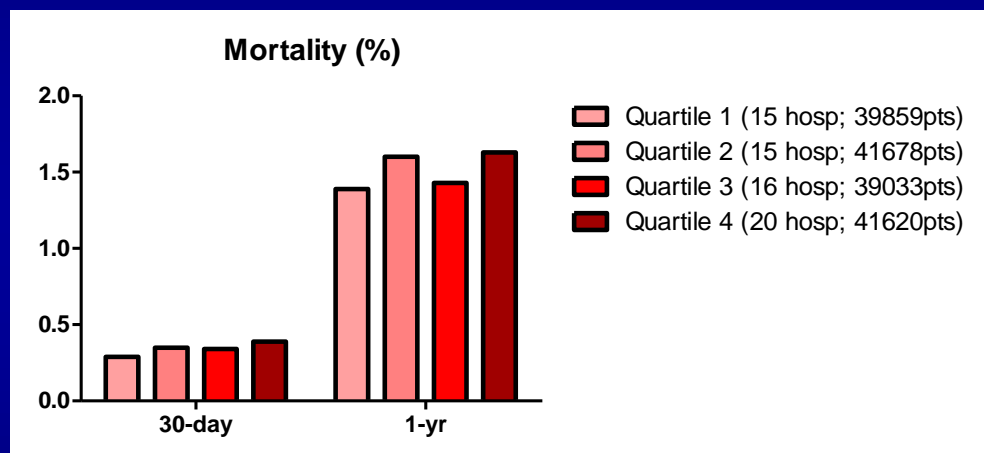
Transfusion rate:

Quartile 1: 12.7%

Quartile 2: 17.5%

Quartile 3: 23.7%

Quartile 4: 37.0%



Hospital-specific Transfusion Quartile

30-day Mortality

1-yr Mortality

Quartile 1 (lowest)

Reference

Reference

Quartile 2

HR 1.06 (95% CI, 0.83–1.35; $P = 0.66$)

HR 1.05 (95% CI, 0.91–1.22; $P = 0.50$)

Quartile 3

HR 1.07 (95% CI, 0.81–1.40; $P = 0.65$)

HR 0.99 (95% CI, 0.87–1.13; $P = 0.88$)

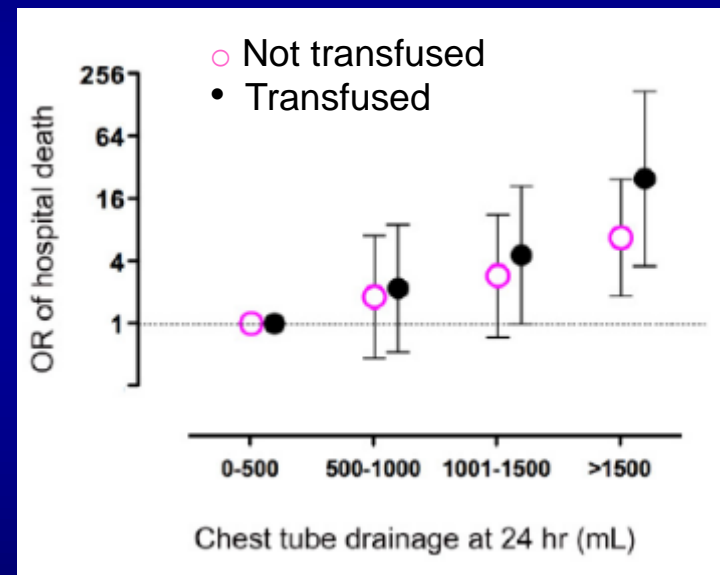
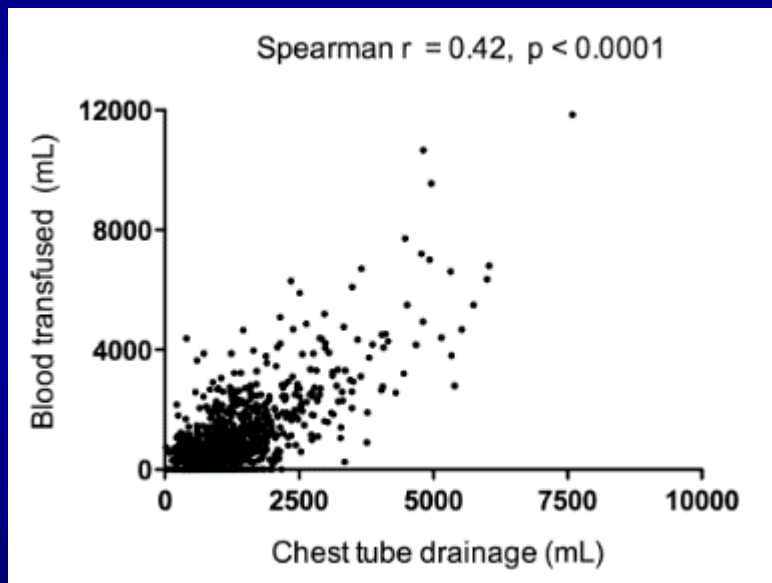
Quartile 4 (highest)

HR 1.11 (95% CI, 0.82–1.50; $P = 0.50$)

HR 1.02 (95% CI, 0.82–1.26; $P = 0.88$)

Association of Blood Transfusion With Mortality: Cause or Confounding?

- ✓ Retrospective study of patient data (2002-8; N=2599 patients)
- ✓ Risk factors associated with in-hospital mortality



- ✓ Chest tube drainage was the strongest independent predictor of mortality while blood transfusion was not

Association Between Blood Transfusion & Morbidity After Major Surgery



Is transfusion the causal event leading to worse outcome or rather a marker for a sicker patient population that is more likely to undergo transfusion for many reasons?

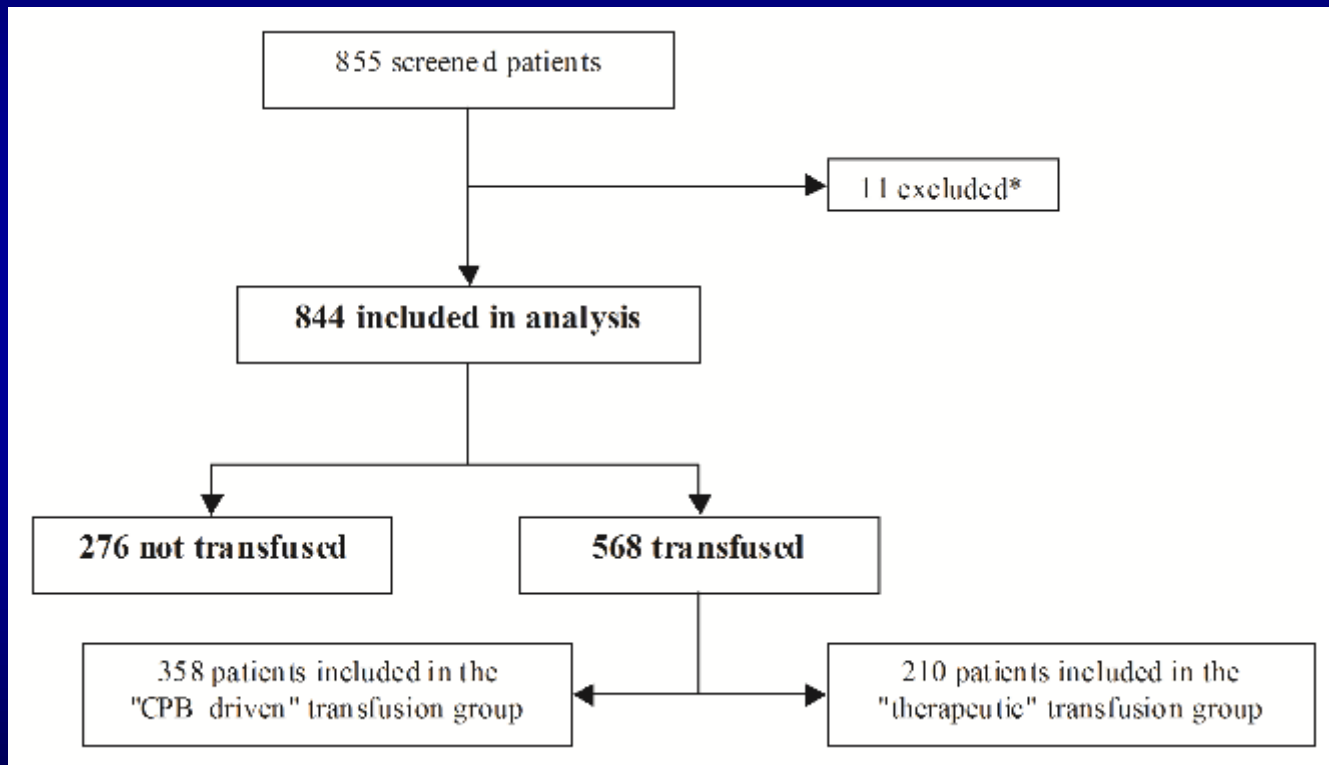
Indications For Red Blood Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Indications for RBC transfusion:
 - To maintain a predefined hematocrit on bypass
 - To treat perioperative blood loss and/or inadequate oxygen delivery

- ✓ Hypothesis: indication for RBC transfusion may impact the effects of transfusion on postoperative morbi-mortality in pediatric cardiac surgery

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Retrospective cohort study (2006-2009; N=855)



* Excluded patients were moribund (ASA5) or Jehovah's witness patients

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Retrospective cohort study (2006-2009; N=855)
- ✓ Transfused children (N=568)
 - Maintenance on-bypass hct of 24% (CPB driven: N=358)
 - Hemorrhage or O₂ delivery increase (therapeutic: N= 210)
- ✓ Standardized anesthetic, CPB and surgical techniques

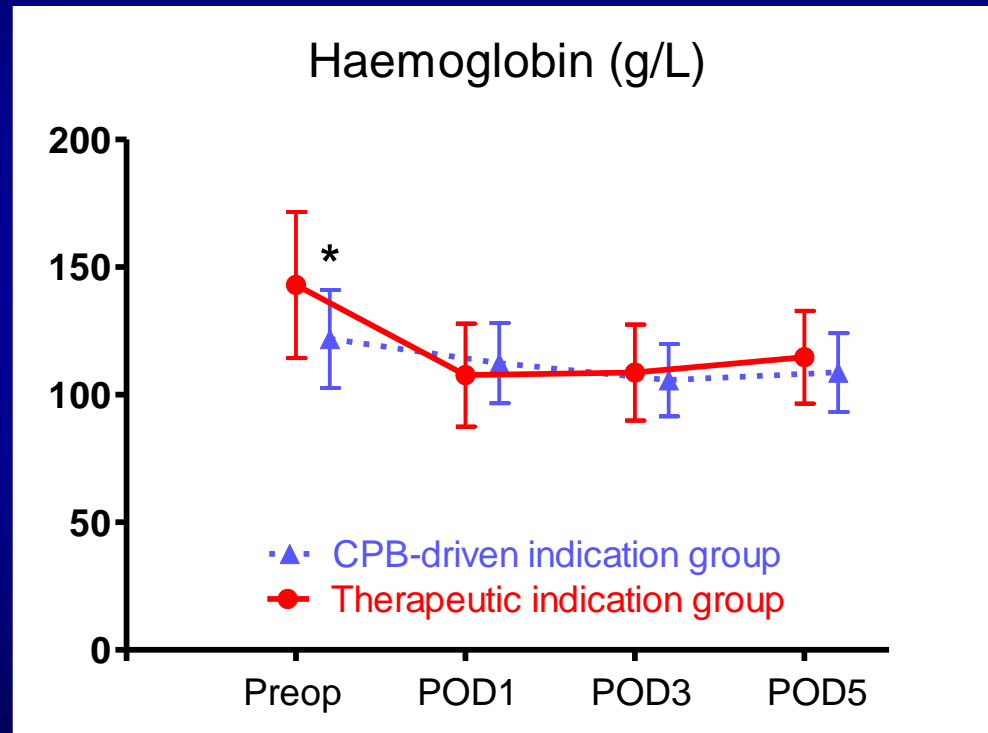
Hematocrit $\geq 24\%$, depending on clinical conditions: degree of hemorrhage, arterial hypoxemia, low cardiac output syndrome...

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Retrospective cohort study (2006-2009; N=855)
- ✓ Transfused children (N=568)
 - Maintenance on-bypass hct of 24% (CPB driven: N=358)
 - Hemorrhage or O₂ delivery increase (therapeutic: N= 210)
- ✓ Primary outcome: composite measure including either hospital death and/or the presence of at least 2 of the following events:
 - Pulmonary failure (mechanical ventilation duration > 75th percentile)
 - Prolonged inotropic support (inotropes > 5 µg/kg.min for more than 48h)
 - Renal failure (reduction of postop creat clearance ≥ 75% from baseline)

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Retrospective cohort study (2006-2009; N=855)

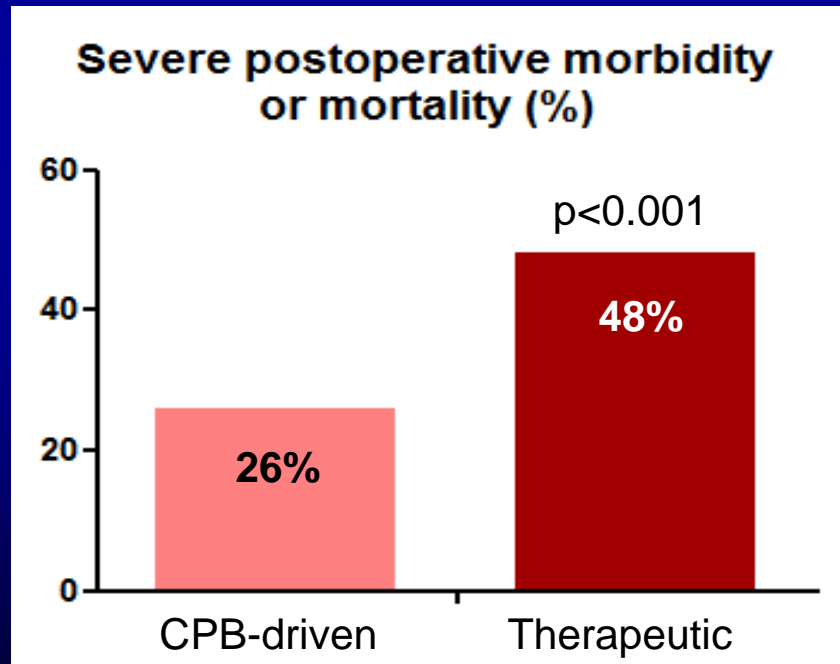


* $p < 0.05$ CPB versus therapeutic transfusion group

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

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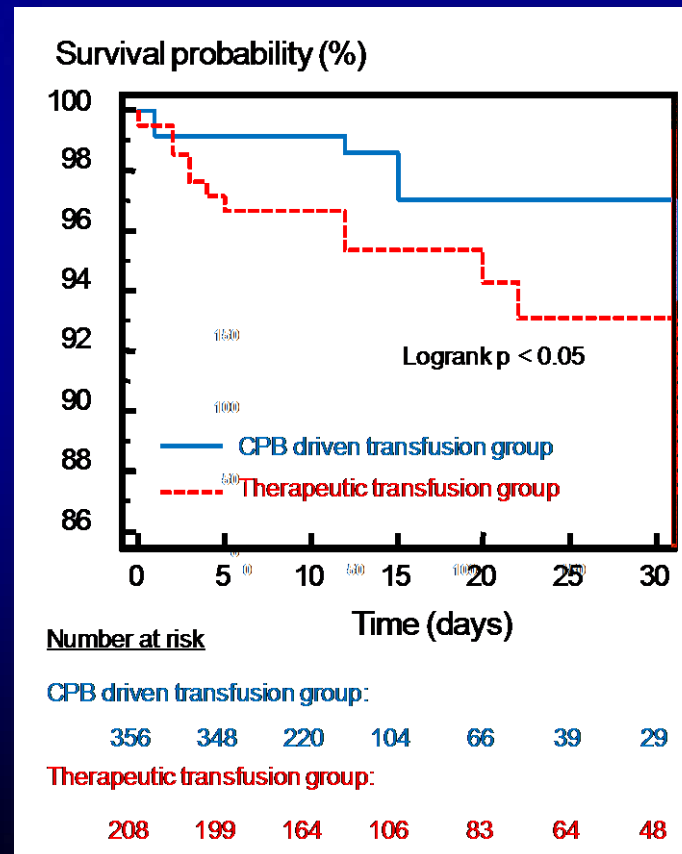
Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Transfused children (N=568)
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- ✓ Adjusted multivariate analysis (age, gender, preop weight, redo-surgery, RACHS-1 score, and RBC transfusion volume)

Variable	OR (95% CI)	p value
ASA score	3.06 [1.50-6.23]	0.002
Indication for transfusion	1.90 [1.13-3.19]	0.016
PRISM II score	1.09 [1.04-1.13]	<0.001
Preoperative SaO ₂ (%)	1.03 [1.01-1.05]	0.006
Total intraoperative blood loss (ml/lkg)	1.01 [1.00-1.02]	0.002
CPB time (min)	1.01 [1.00-1.02]	0.014
Total blood loss (ml/kg)	1.01 [1.00-1.01]	0.021

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

- ✓ Transfused children (N=568)
 - Maintenance on-bypass hct of 20% (CPB driven: N=358)
 - Hemorrhage or O₂ delivery increase (therapeutic: N= 210)



From Willems A et al.
Eur J Cardiothorac Surg
45:1050-7, 2014.

Indications For Red Cell Transfusion In Pediatric Cardiac Surgery: Effects on Outcome

The indication for transfusion per se influences the effect of RBC transfusion on postoperative morbi-mortality. This parameter should be considered in further research on the effects of blood transfusion on outcome

Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

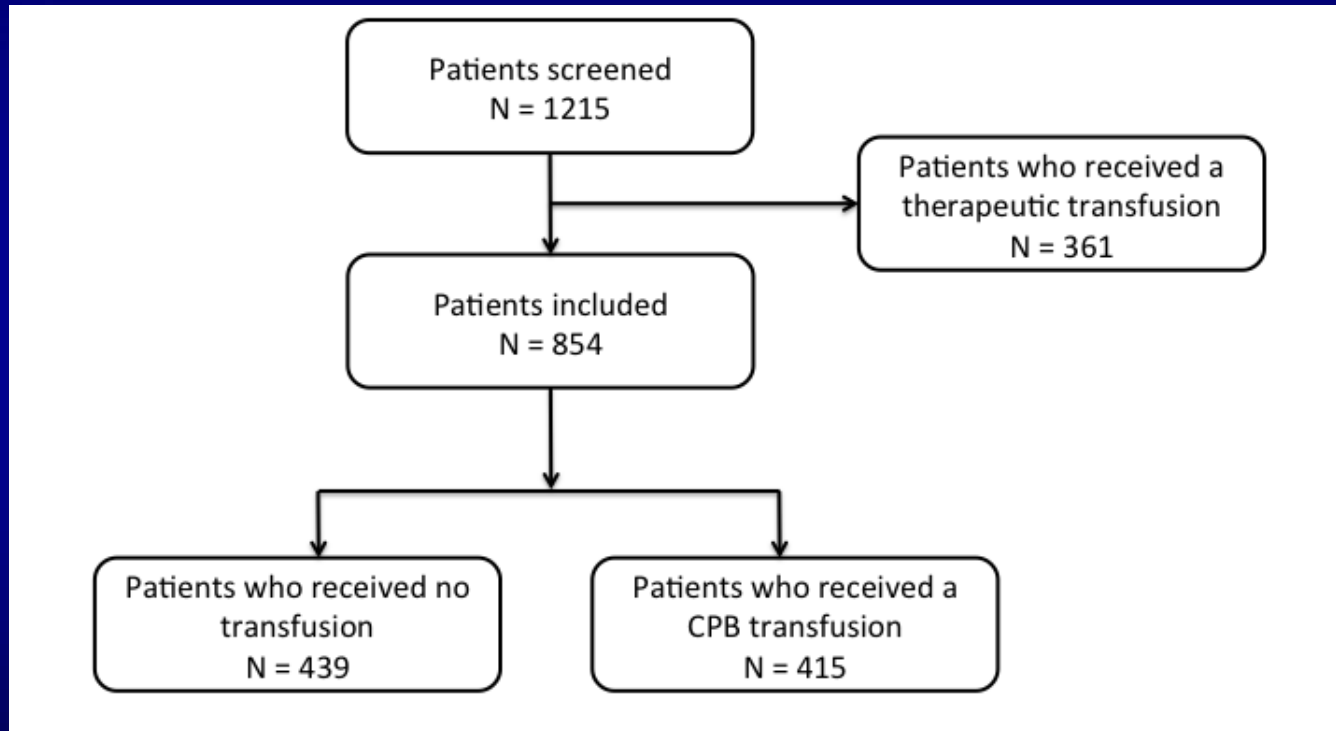
- ✓ RBC transfusion during CPB to maintained a predefined hct



- ✓ Hypothesis: on-bypass RBC transfusion does not affect postoperative morbi-mortality in pediatric cardiac surgery

Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

- ✓ Retrospective cohort study (2006-2012; N=1215)



Excluded patients were moribund (ASA5) or Jehovah's witness patients

Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

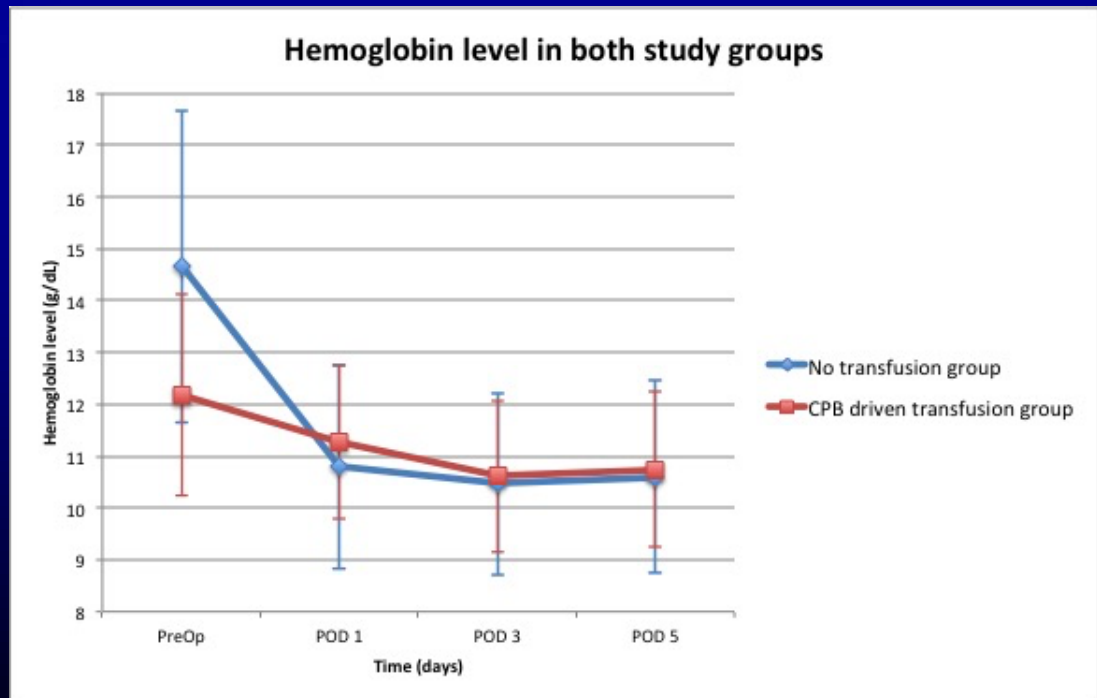
- ✓ Retrospective cohort study (2006-2012; N=1215)
- ✓ Studied population (N=854)
 - No transfusion (N=439)
 - Transfused to maintain an on-bypass hct of 24% (N= 415)
- ✓ Primary outcome: composite measure including either hospital death and/or the presence of at least 2 of the following events:
 - Pulmonary failure (mechanical ventilation duration > 75th percentile)
 - Prolonged inotropic support (inotropes > 5 µg/kg.min for more than 48h)
 - Renal failure (reduction of postop creat clearance ≥ 75% from baseline)

Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

- ✓ Retrospective cohort study (2006-2012; N=1215)
- ✓ Studied population (N=854)
 - No transfusion (N=439)
 - Transfused to maintain an on-bypass hct of 24% (N= 415)
- ✓ Statistics: a propensity score analysis, using genetic matching followed by a logistic regression for binary outcomes variables and weighted least squares linear regression for continuous outcomes

Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

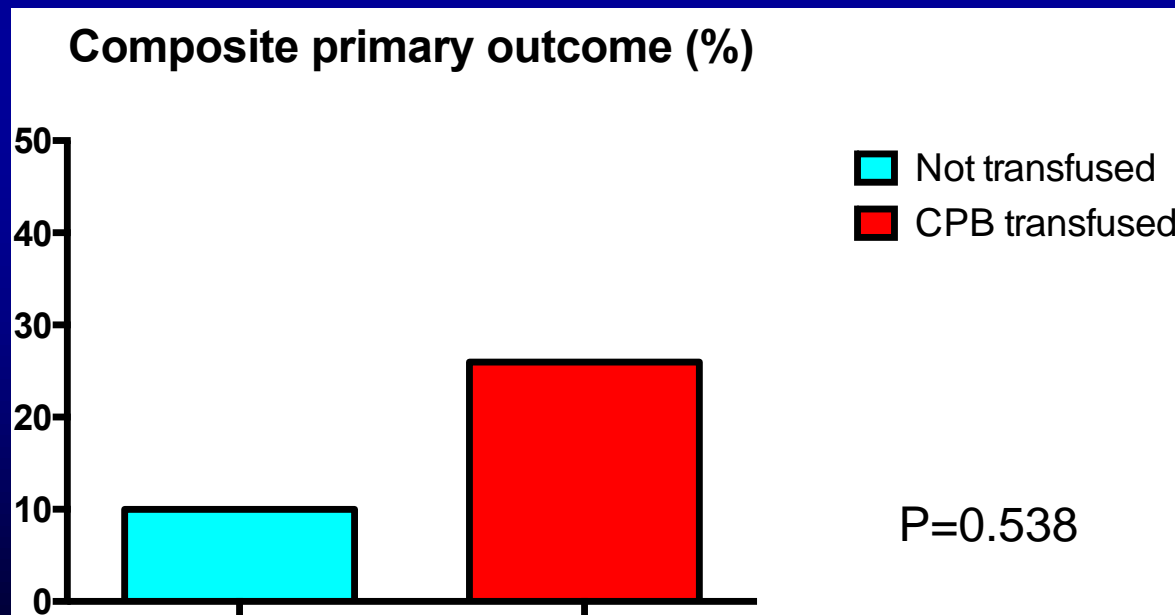
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From Willems A et al.
Anesth Analg 123:420-9, 2016.

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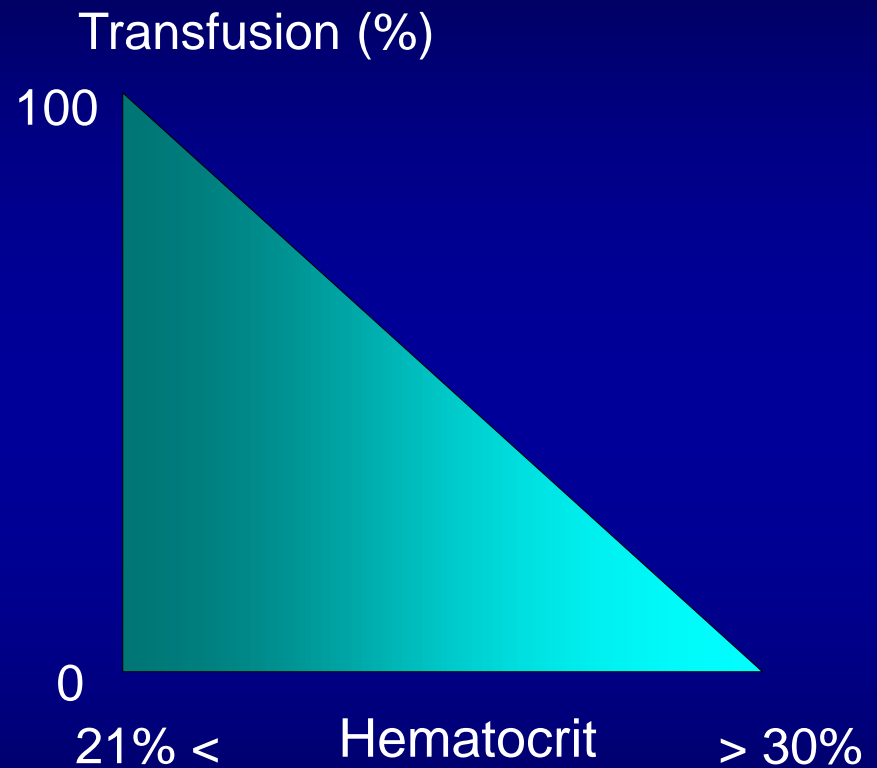
Does RBC Transfusion Transfused on Bypass Affect Outcome In Pediatric Cardiac Surgery

There is no evidence that on-bypass RBC transfusion affect outcome in pediatric cardiac surgery.

The real impact of RBC transfusion on postoperative morbidity remains to be determined.

Perioperative Transfusion Trigger

- ✓ Transfusion practice largely individualized for each patient
- ✓ Transfusion policy based on a “one by one unit” strategy



Development of a patient's blood management program:

- Optimization of preoperative RBC mass
- “Restrictive” blood loss strategy


Merci de votre attention



Patient Blood Management

- ✓ Defined as “the appropriate use of blood and blood components with a goal of minimized their use”.
- ✓ Encompasses an evidence-based medical and surgical approach that is multidisciplinary (transfusion medicine specialists, surgeons, anesthesiologists, and critical care specialists) and multiprofessional (physicians, nurses pump technologists and pharmacists)

Patient Blood Management: Motivation

- ✓ Known (and unknown) risk associated with blood products
 - ✓ Constraints from escalating costs
 - ✓ Preservation of the national blood inventory
 - Decreased donors' population
 - Increased demand of products
 - Mismatch between recipients and donors regarding ABO blood groups
(i.e. sickle cell disease)
-  Aging of the population
Changes in travel pattern