Experienced or Enfeebled?
Does Red Cell Storage Time Affect Patient Outcome?

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Experienced or Enfeebled?

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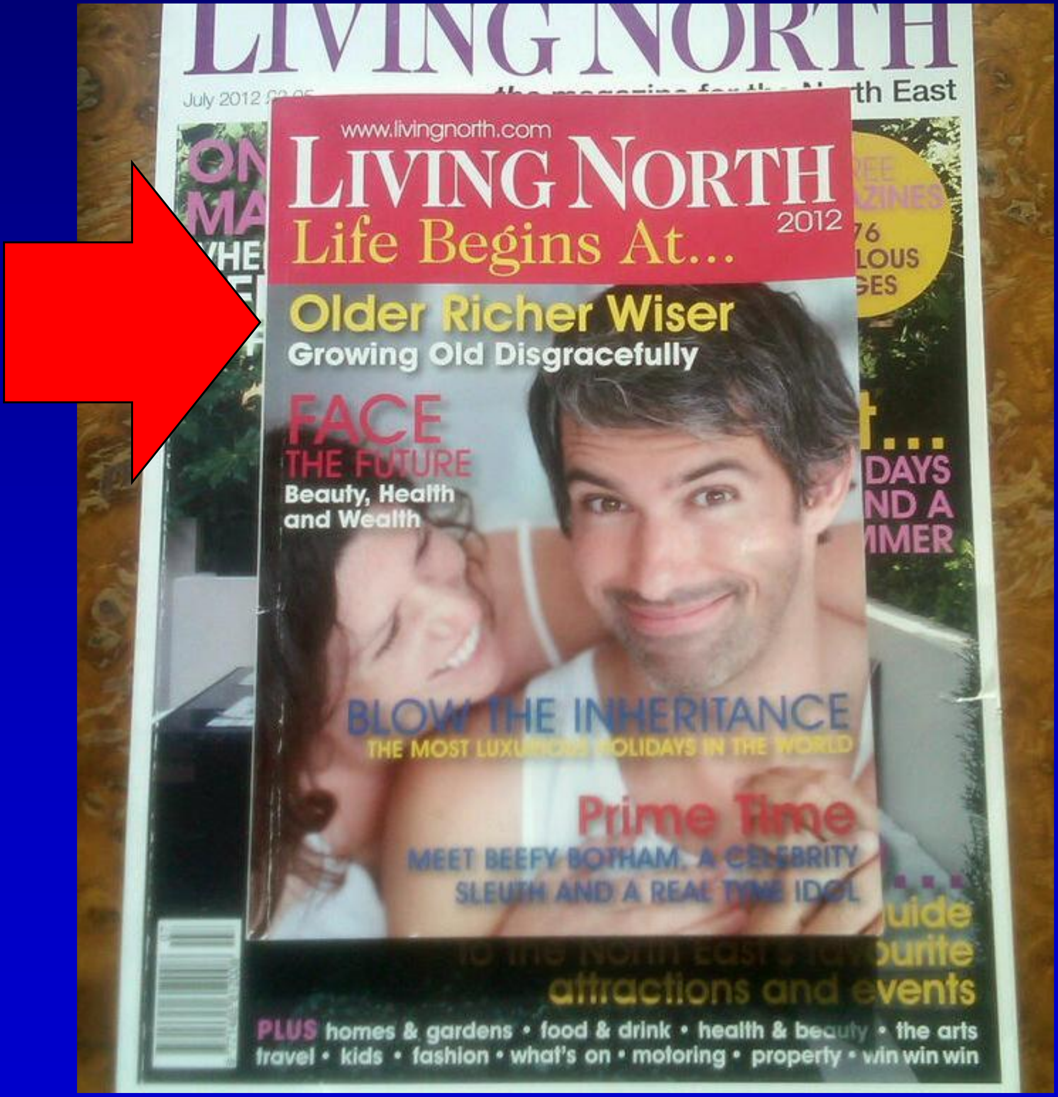
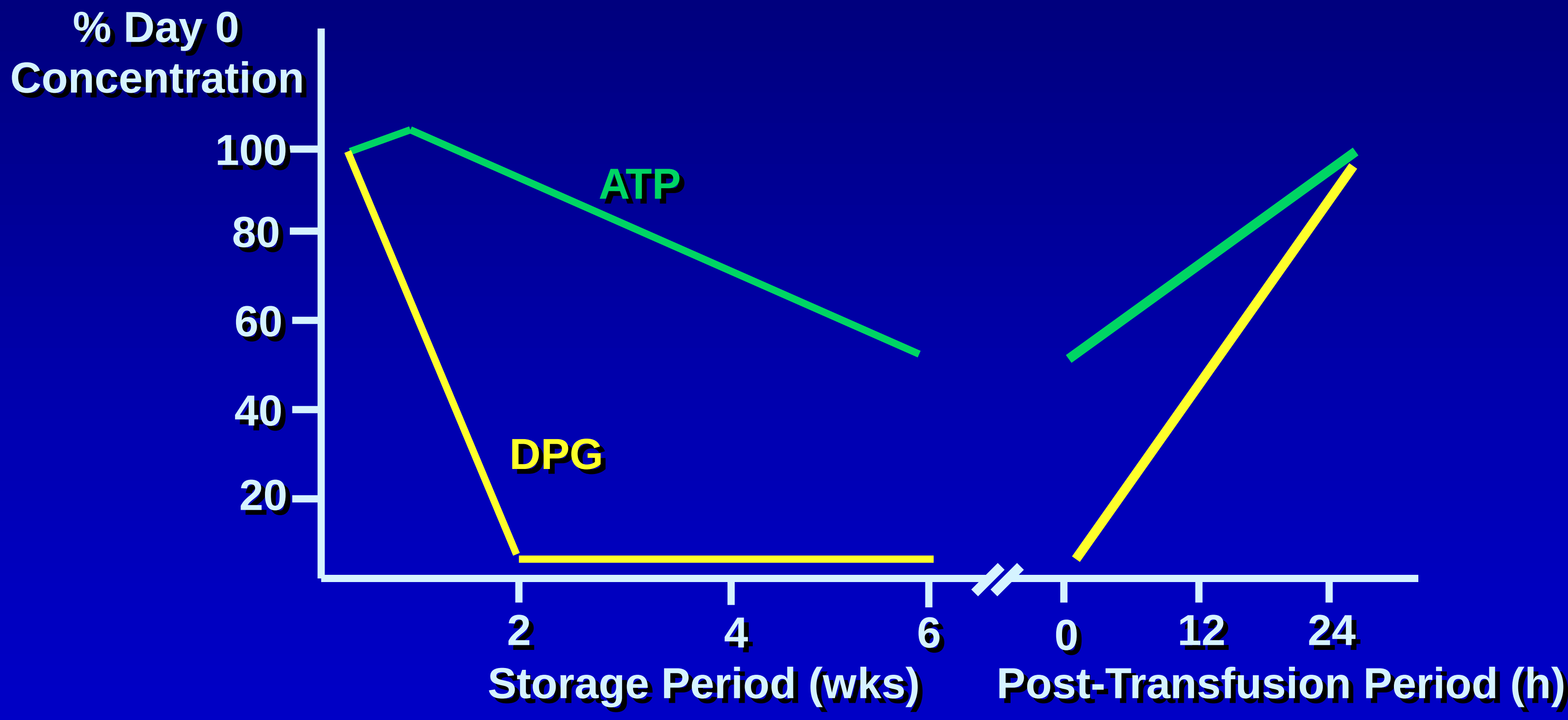


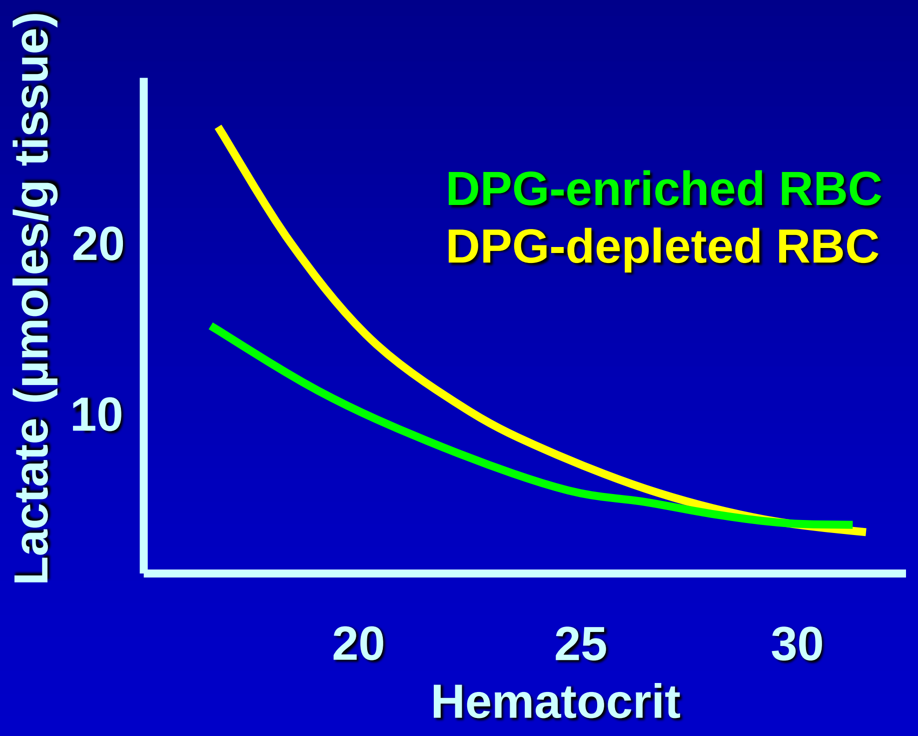
Red Cell Physiology and "The Storage Lesion"

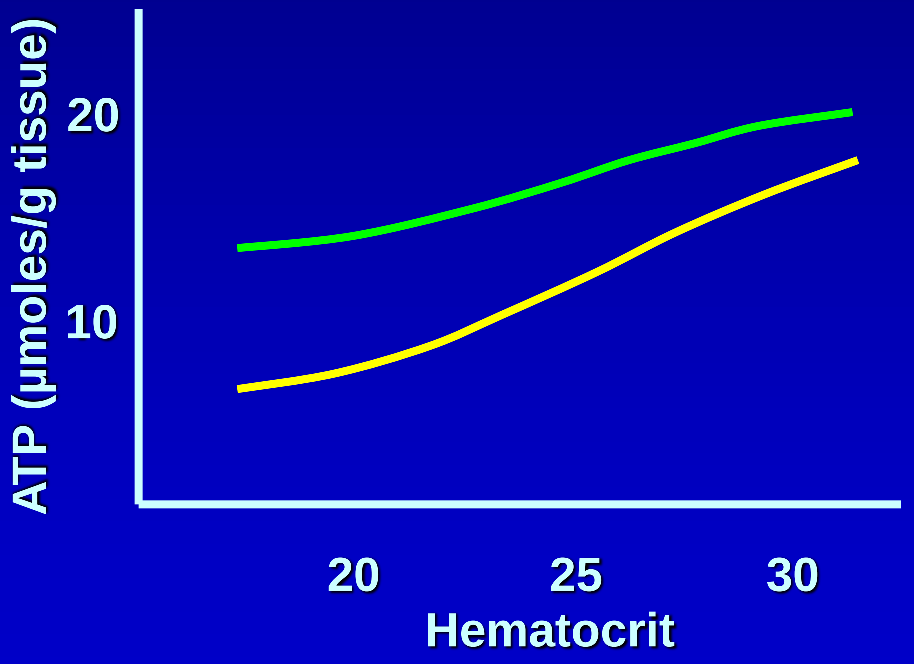


Heaton A *et al. Br J Haematol* 1989;71:131-6.

DPG Effect on Cerebral Metabolism

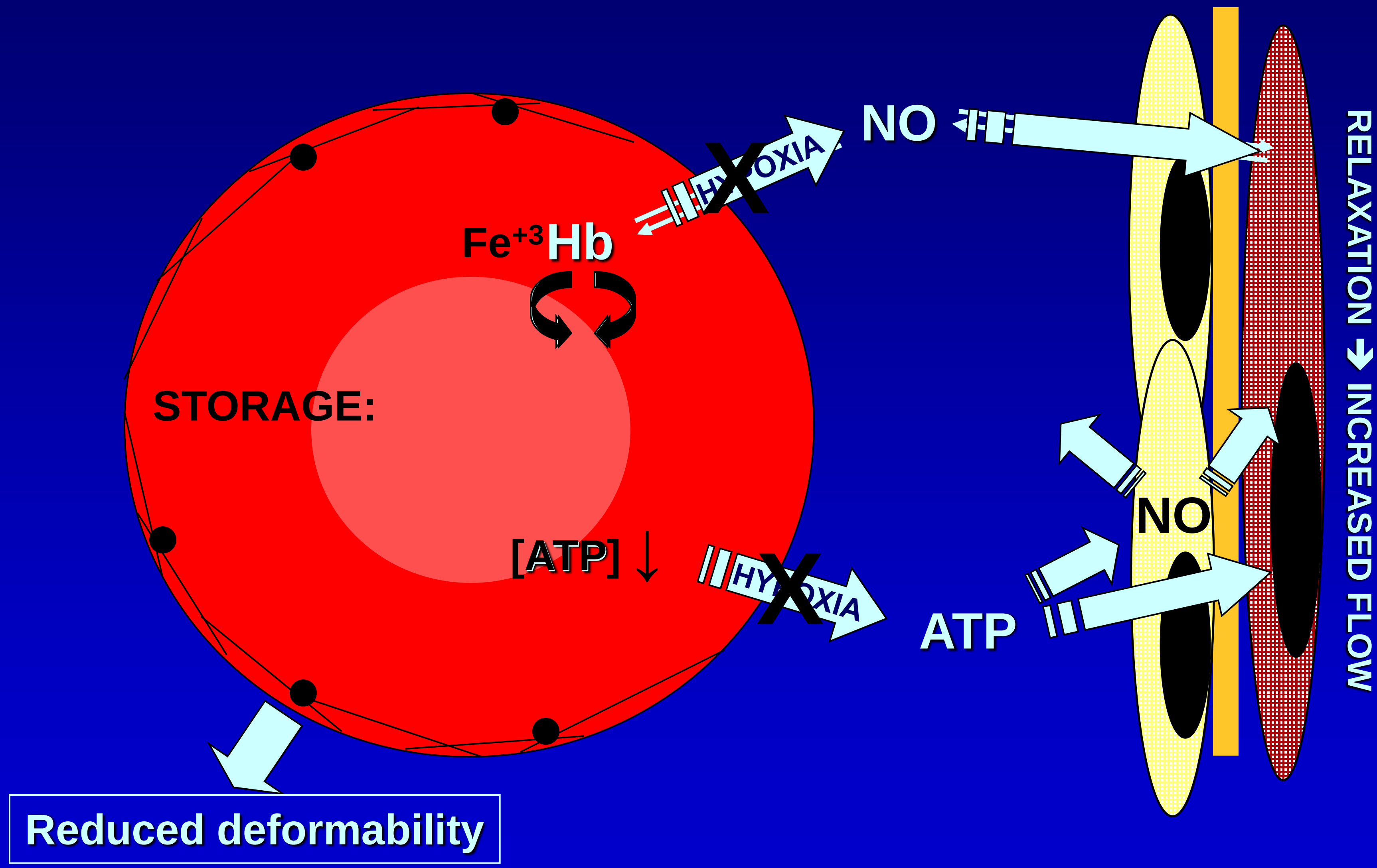
Murine Exchange Transfusion → Carotid Occlusion Model





Kimura H *et al. Stroke* 1995;26:1431-6.

Red Cell Physiology and "The Storage Lesion"

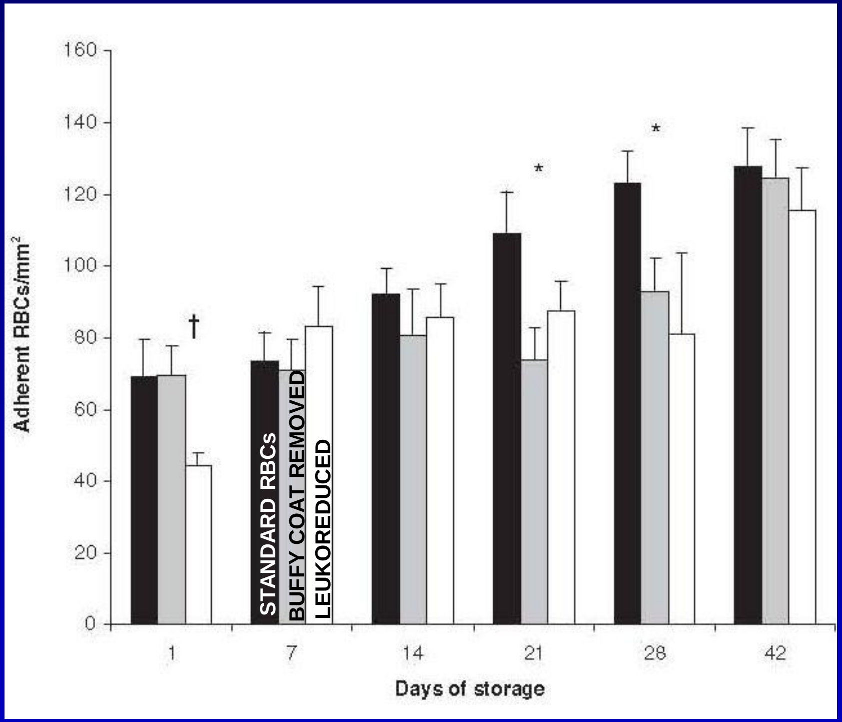


D'Amici GM *et al. J Proteome Res* 2007;6:3242-55.

Raat NJH and Ince C. *Vox Sang* 2007;93:12-18.

Red Cell Storage and Blood Flow

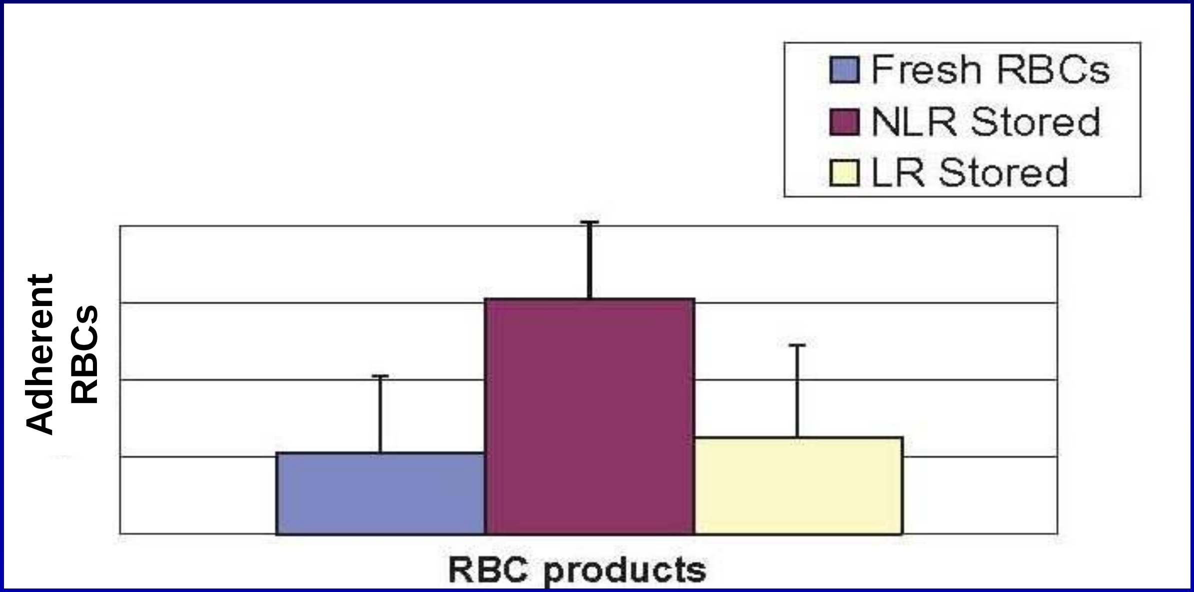
Adherence of RBCs to HUVECs with increasing storage time



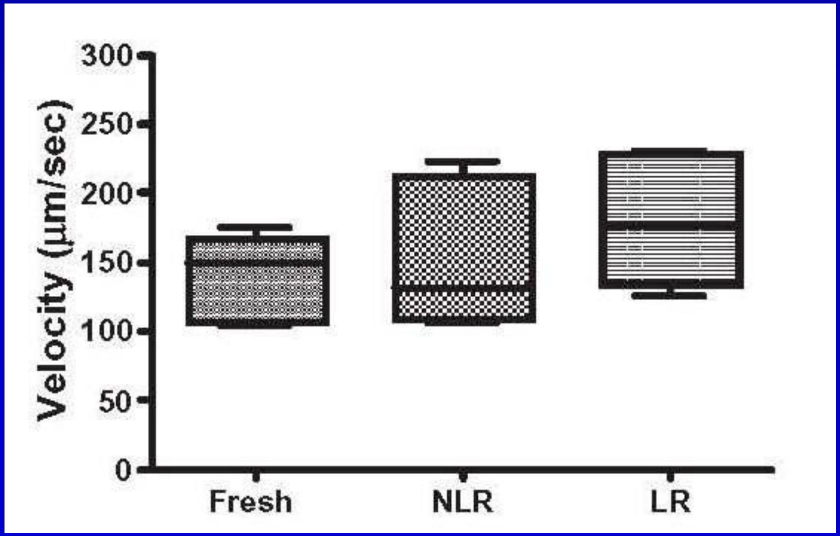
Increasing adherence with greater storage duration.

Anniss AM, Sparrow RL. *Transfusion* 2006;46:1561-7.

Red Cell Storage and Blood Flow



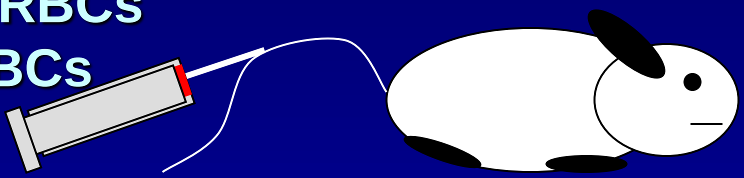
BUT…

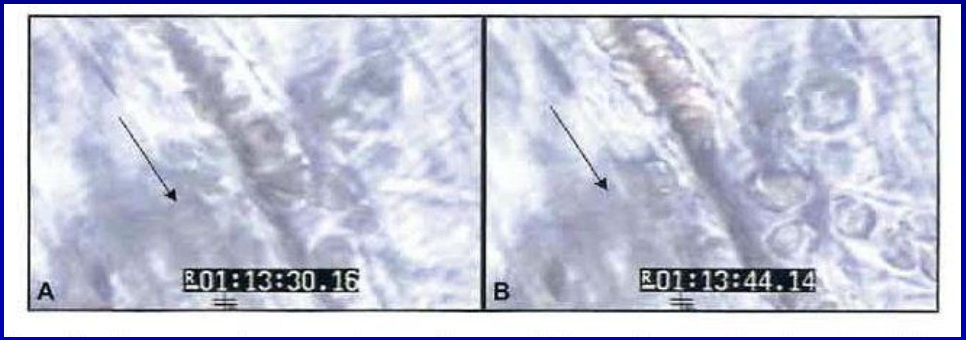


Chin-Yee IH *et al. Transfusion* 2009:49:2304-10.

Red Cell Storage and Blood Flow

+ 1 mL
  - *fresh* RBCs
  - *old* RBCs

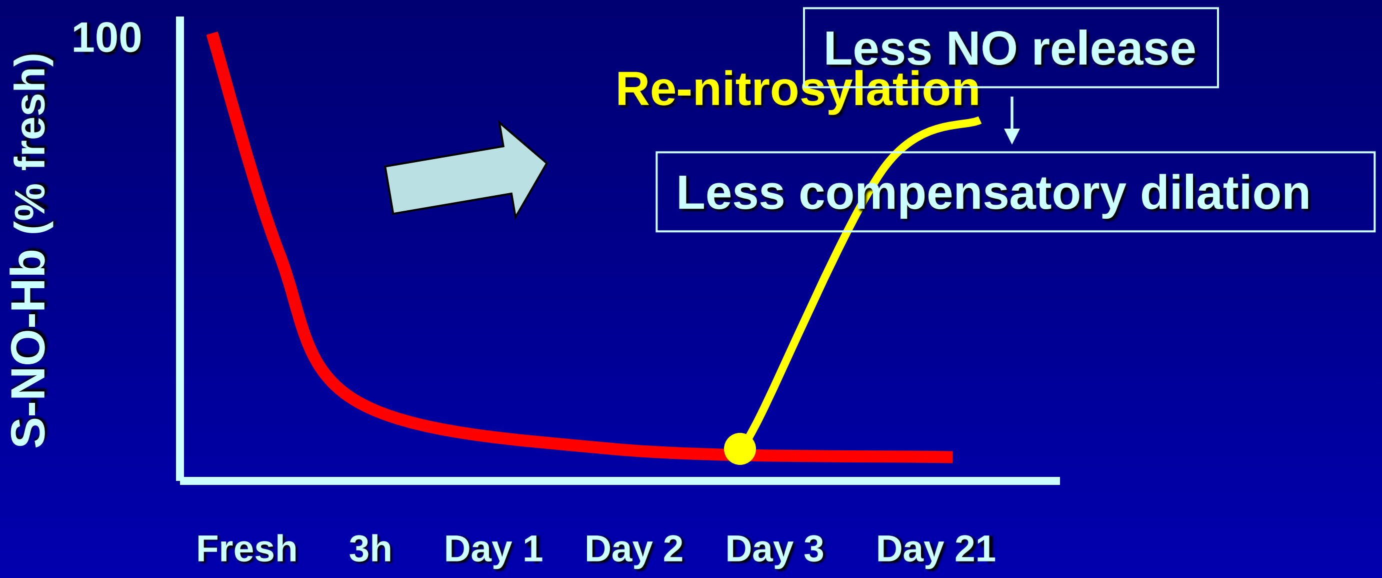




Reduction in capillary flow but not flow in arterioles

Arslan E *et al. Am J Surg* 2005;190:456-62.

Red Cell Physiology and “The Storage Lesion”



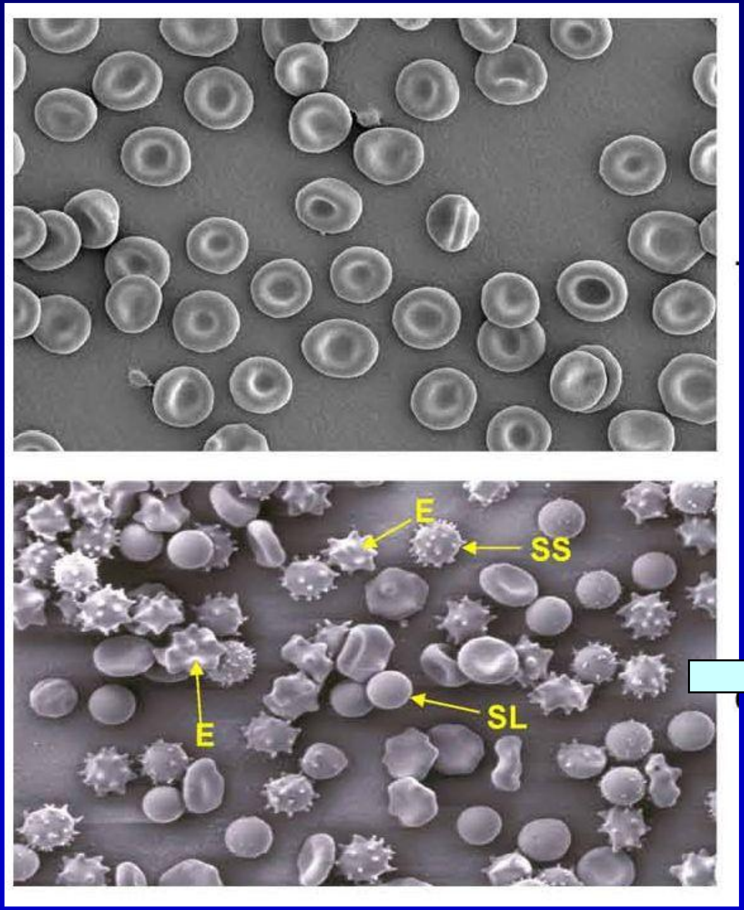
Alternative?

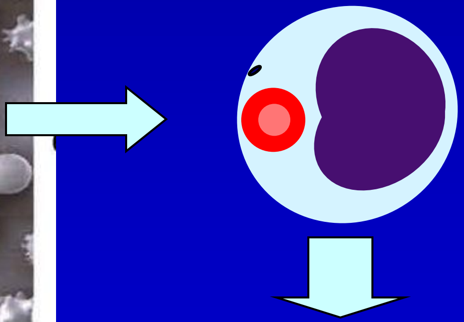
nary artery blood flow model

gnificant effect
clinically significant change

Bennett-Guerrera E *et al. PNAS* 2007.
Reynolds JD *et al. PNAS* 2007; Yuruk *et al. Transfusion* 2012;52:1410-22.

Red Cell Surface Changes During Storage

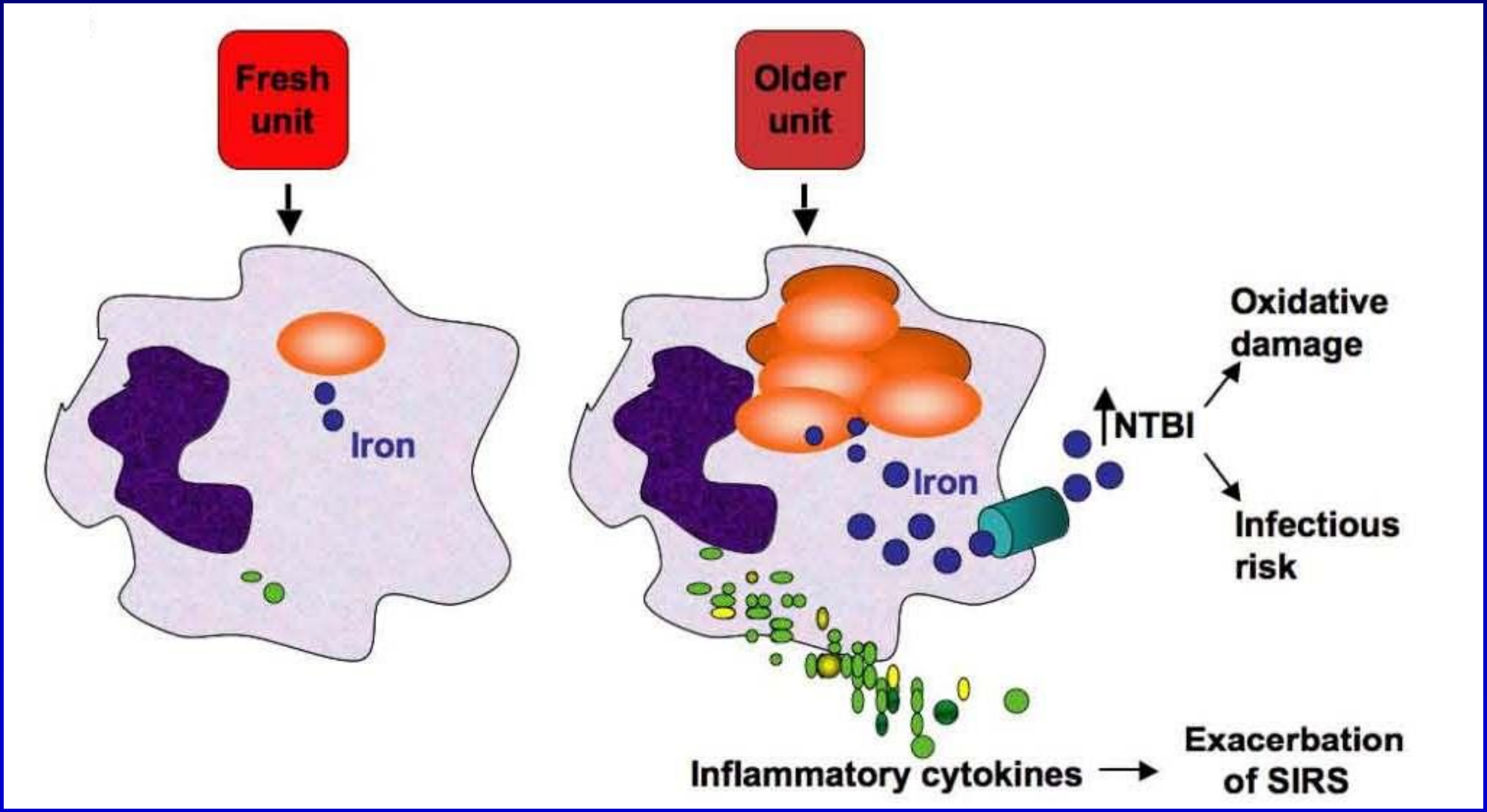




SECONDARY EFFECTS?

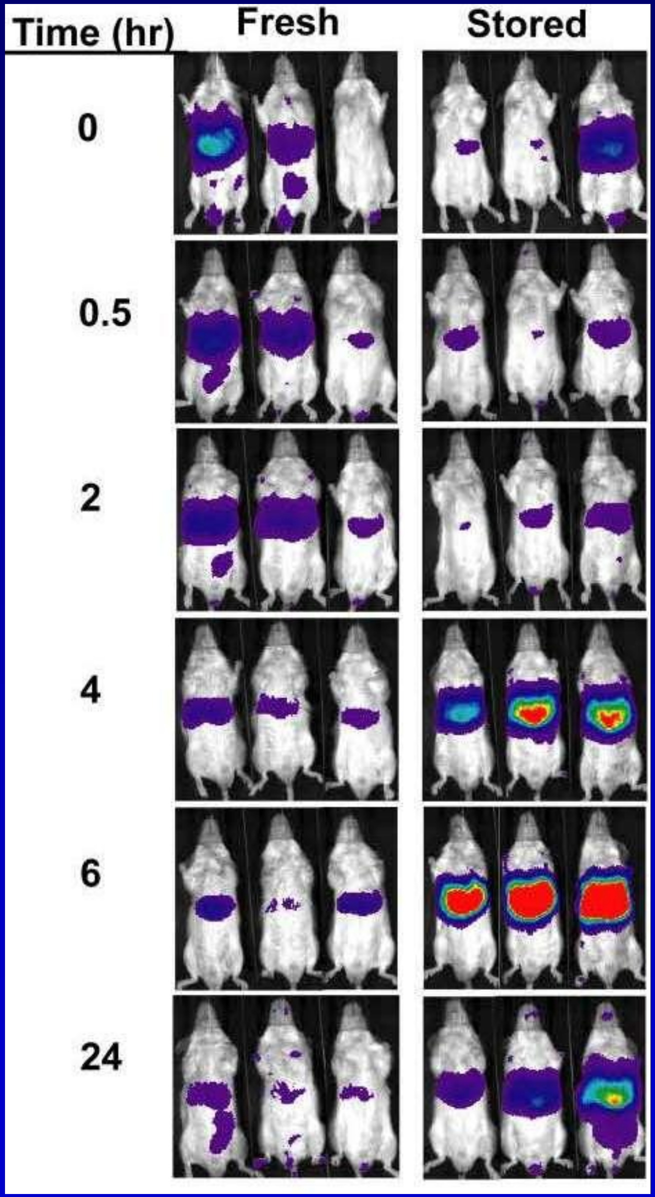
Mitrofan-Oprea L *et al. Transf Clin Biol* 2007 (epub).

The "Iron Hypothesis"



Hod EA *et al. Blood* 2010;115:4284-92.

Result: Inflammatory Response Induction



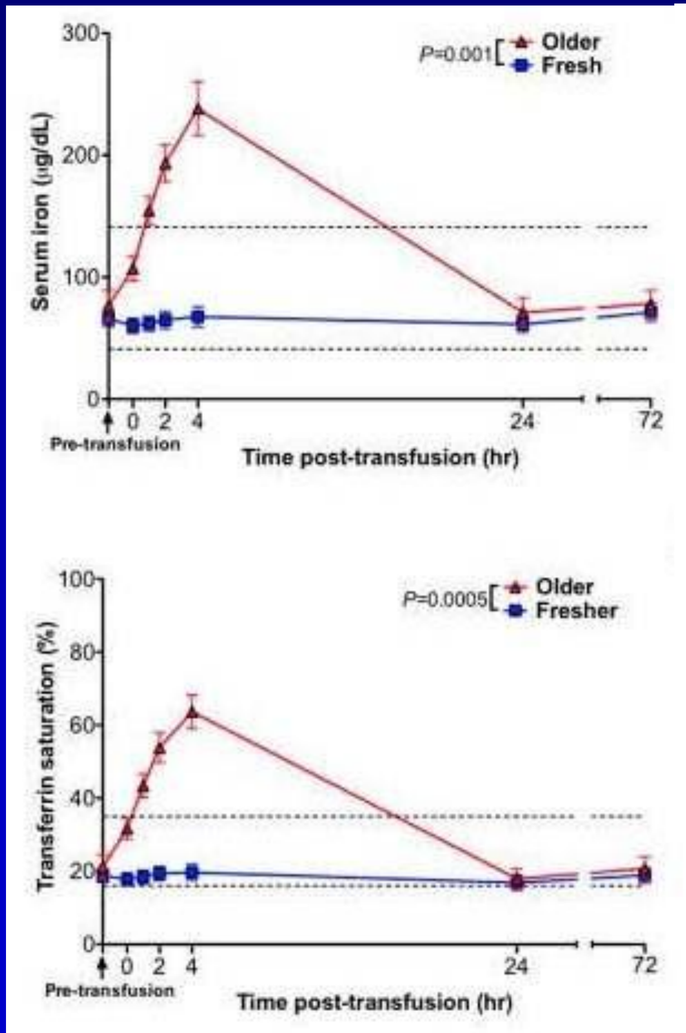
Seen with:
Washed RBCs

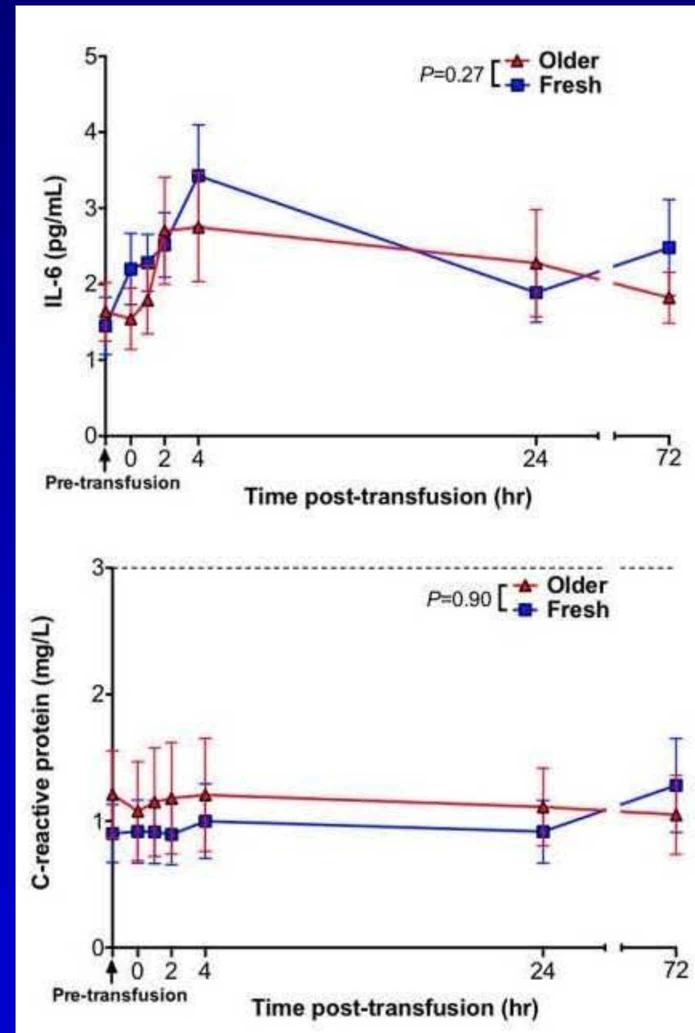
Not seen with:
RBC ghosts
Supernate
Stroma-free lysate

Hod EA *et al. Blood* 2010;115:4284-92.

Human Response

Different – or inadequate challenge?





n = 14   Storage: 3-7 vs 40-42 d
Txn: 1 autologous unit

Hod EA *et al. Blood* 2011;118:6675-82.

Immunologic Effects of Red Cell Storage

T lymphocyte transcriptional response (at 72h) after *autologous* infusion of RBCs stored for 5 weeks:

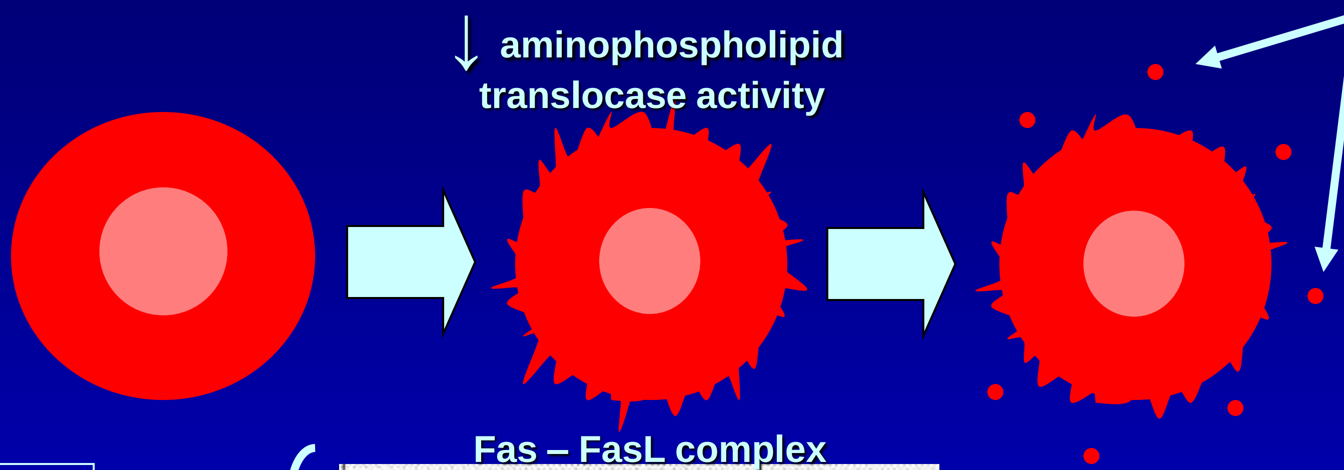
TLR4:	+9%
TLR5:	+6%
TLR6:	+5%
LRP1:	+12%
AATK:	+3%

TLR: Toll-like receptor
LPR: Low-density lipoprotein receptor related protein
AATK: Apoptosis-associated tyrosine kinase

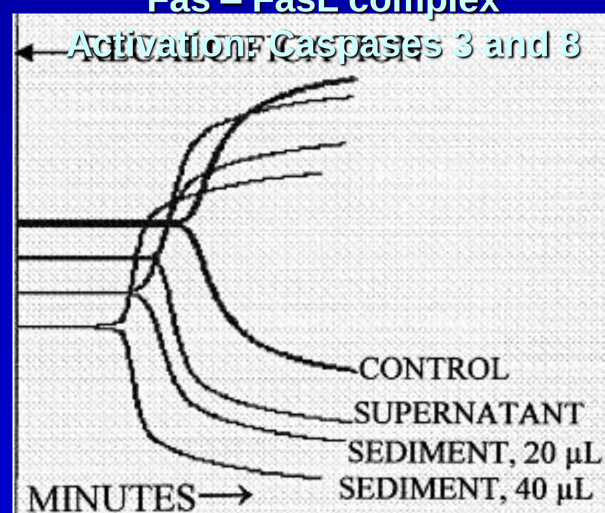
Pottgiesser T *et al. Vox Sang* 2009;96:333-6.

TRansfusion-Induced Facilitation of Thrombin

TRIFT



Fas – FasL complex
Activation: Caspases 3 and 8



THROMBIN

↓

PAR-1 RECEPTOR (DENDRITIC CELLS)

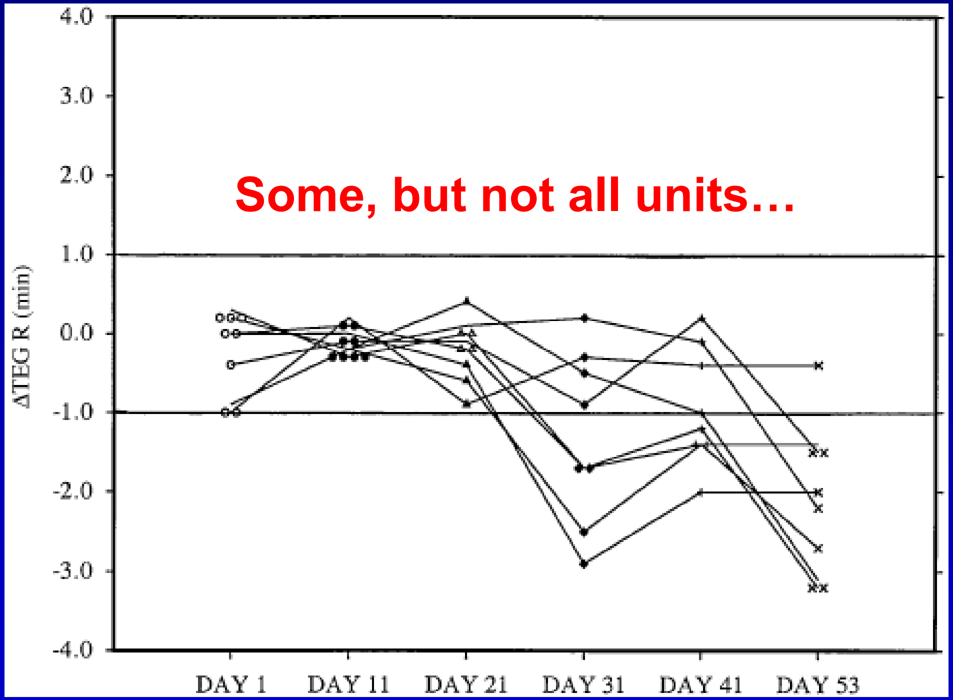
↓

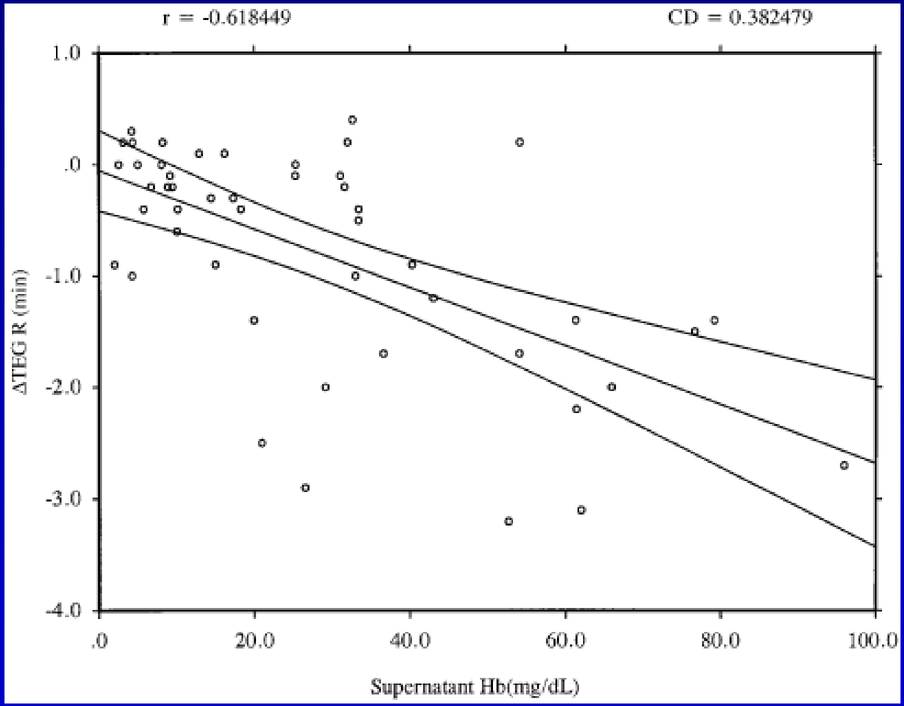
SYSTEMIC INFLAMMATORY RESPONSE

Ratio similar to 1 unit's supernate into adult blood volume

Mandal D *et al. J Biol Chem* 2005;280:39460-7.

TRansfusion-Induced Facilitation of Thrombin
TRIFT

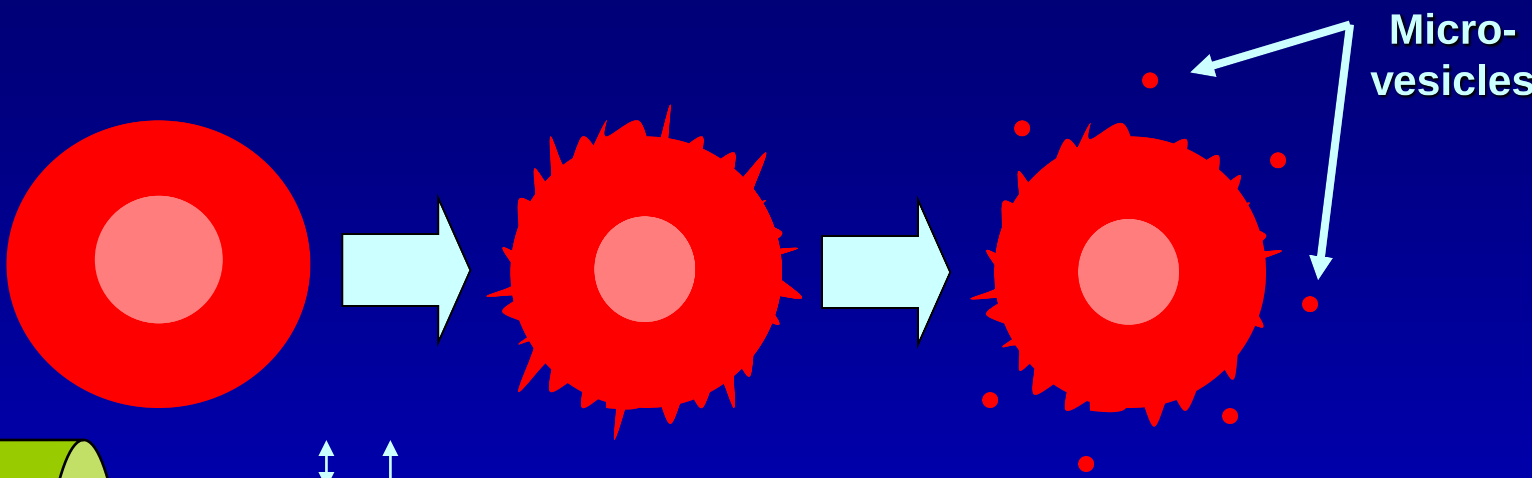


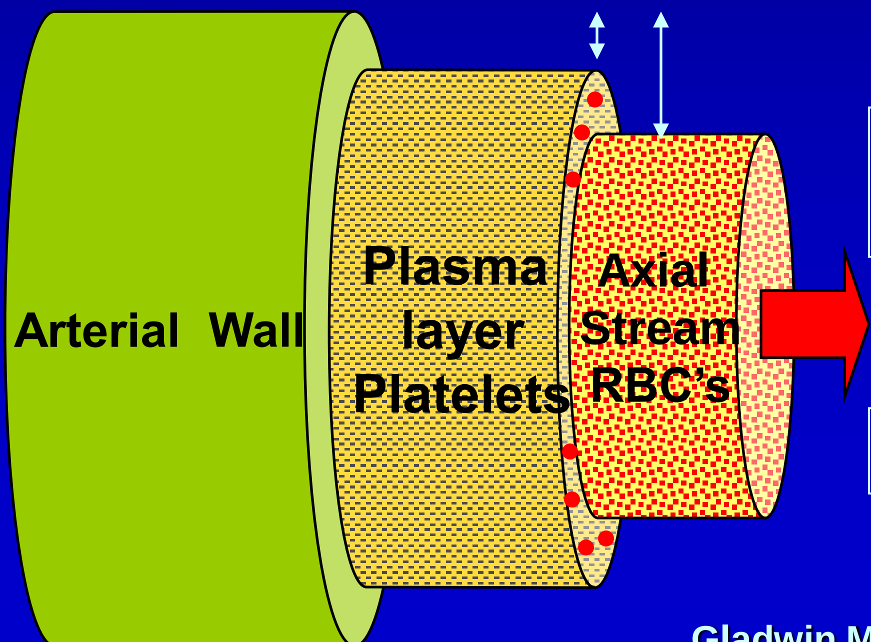


- after 21 days

Sweeney J *et al. Transfusion* 2009;49: epub.

Impact of Microvesicles: NO Dysregulation?



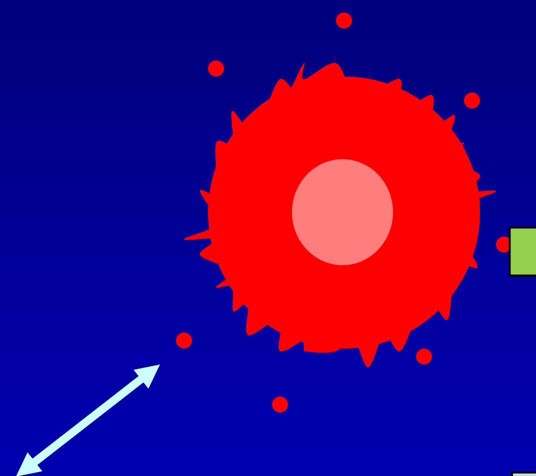


Reduced distance to NO synthesis <u>and</u> effector sites

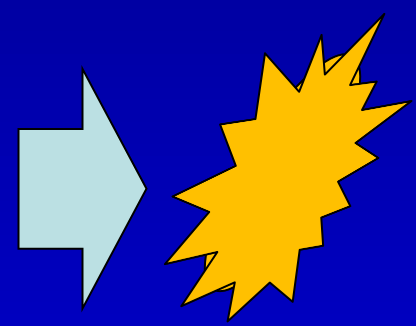
? Abnormal NO uptake

Gladwin MT, Kim-Shapiro DB. *Curr Opin Hematol* 2009;16:515-23.

Impact of Microvesicles: Chemokine Binding

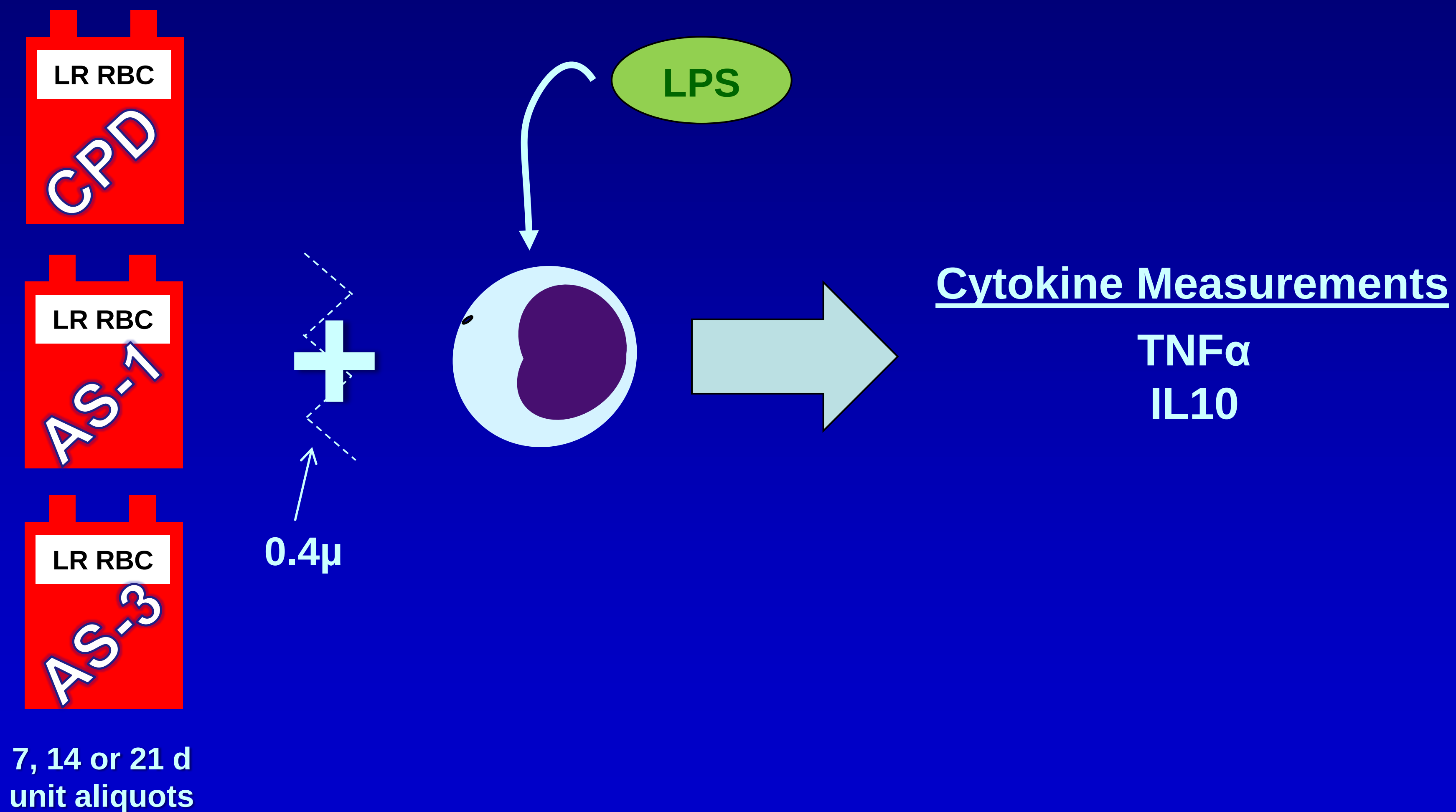


Reduced binding of chemokines



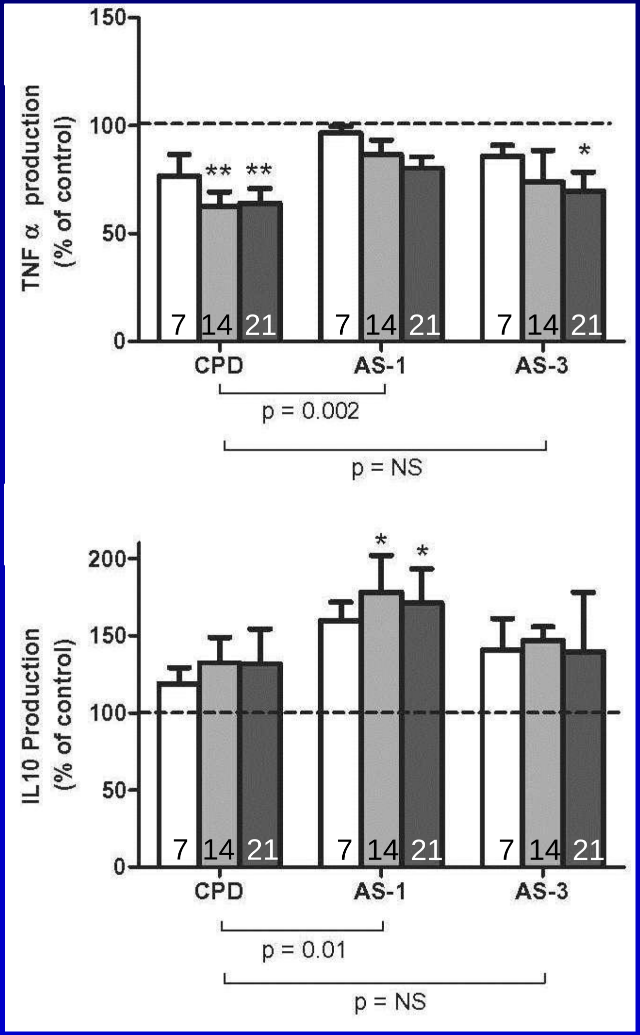
Xiong Z *et al. Transfusion* 2011;51:610-21.

RBC Storage and Monocytes: The Impact of the Storage Environment



Muszynski J *et al. Transfusion* 2012;52:794-802.

RBC Storage and Monocytes: The Impact of the Storage Environment



Greater effects with longer storage.

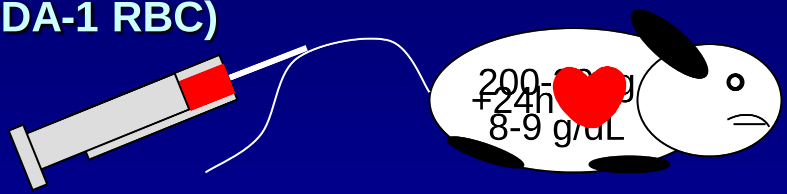
CONTROLS:
No media effect.

Same results with cellular barrier: Soluble mediator

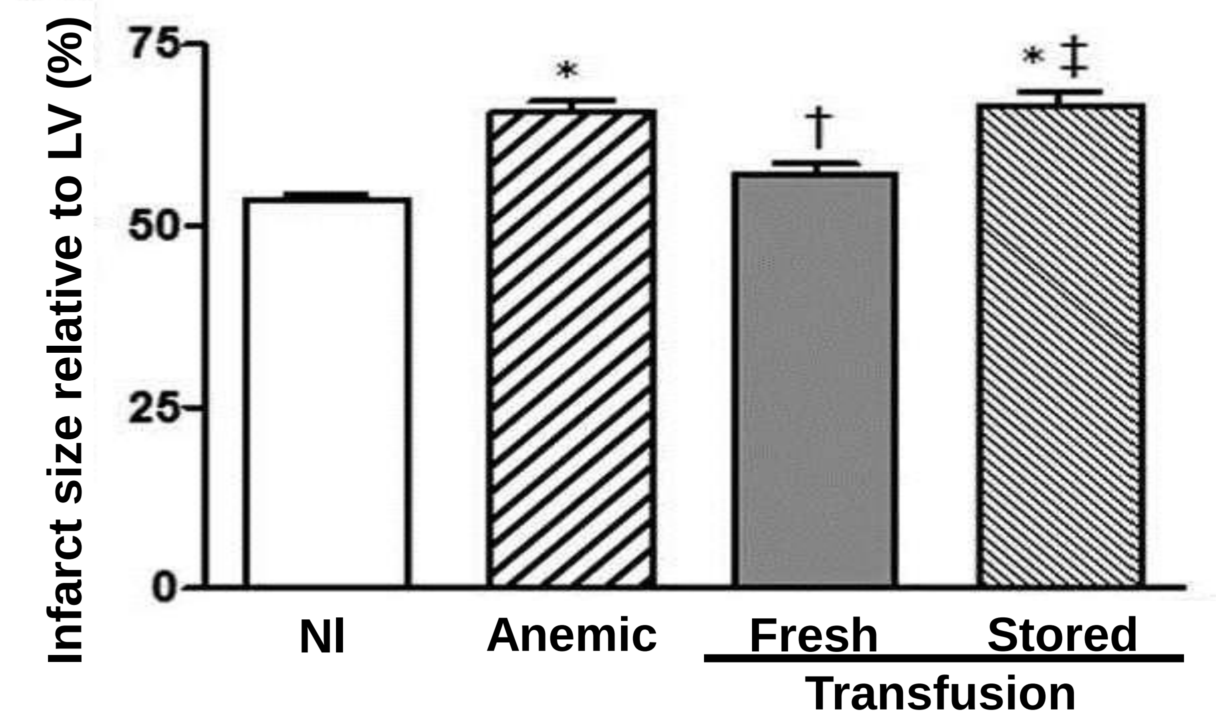
Muszynski J *et al. Transfusion* 2012;52:794-802.

Transfusion after Myocardial Infarction

± Transfusion to 10 g/dL
(NLR CPDA-1 RBC)



Storage:
4 hr
7d (“≈ 29d”)



Hu H *et al. Crit Care Med* 2012;40:740-6.

Transfusion after Myocardial Infarction

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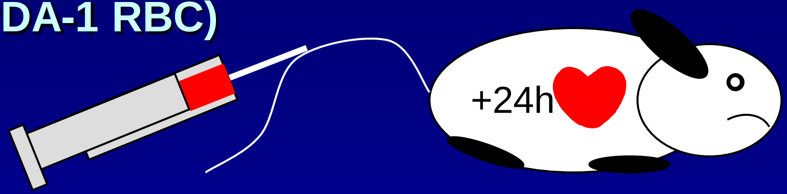

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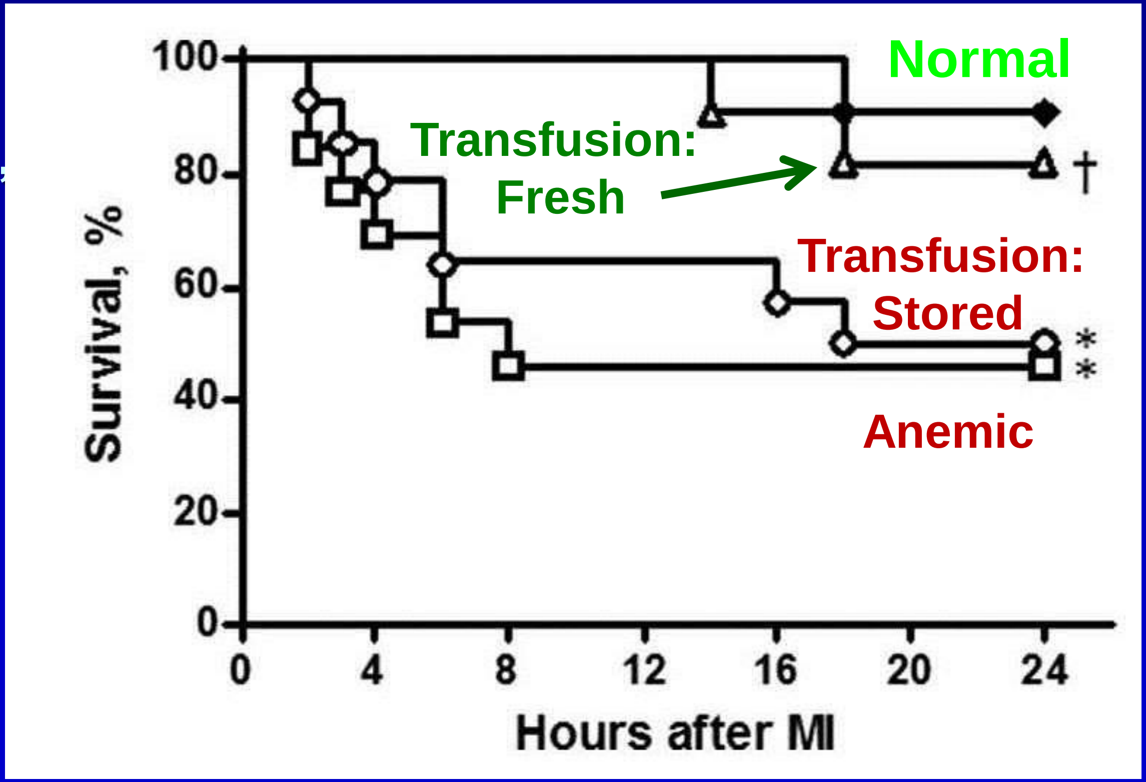
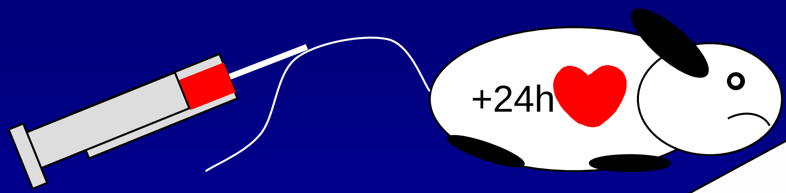


Hu H *et al. Crit Care Med* 2012;40:740-6.

Transfusion after Myocardial Infarction



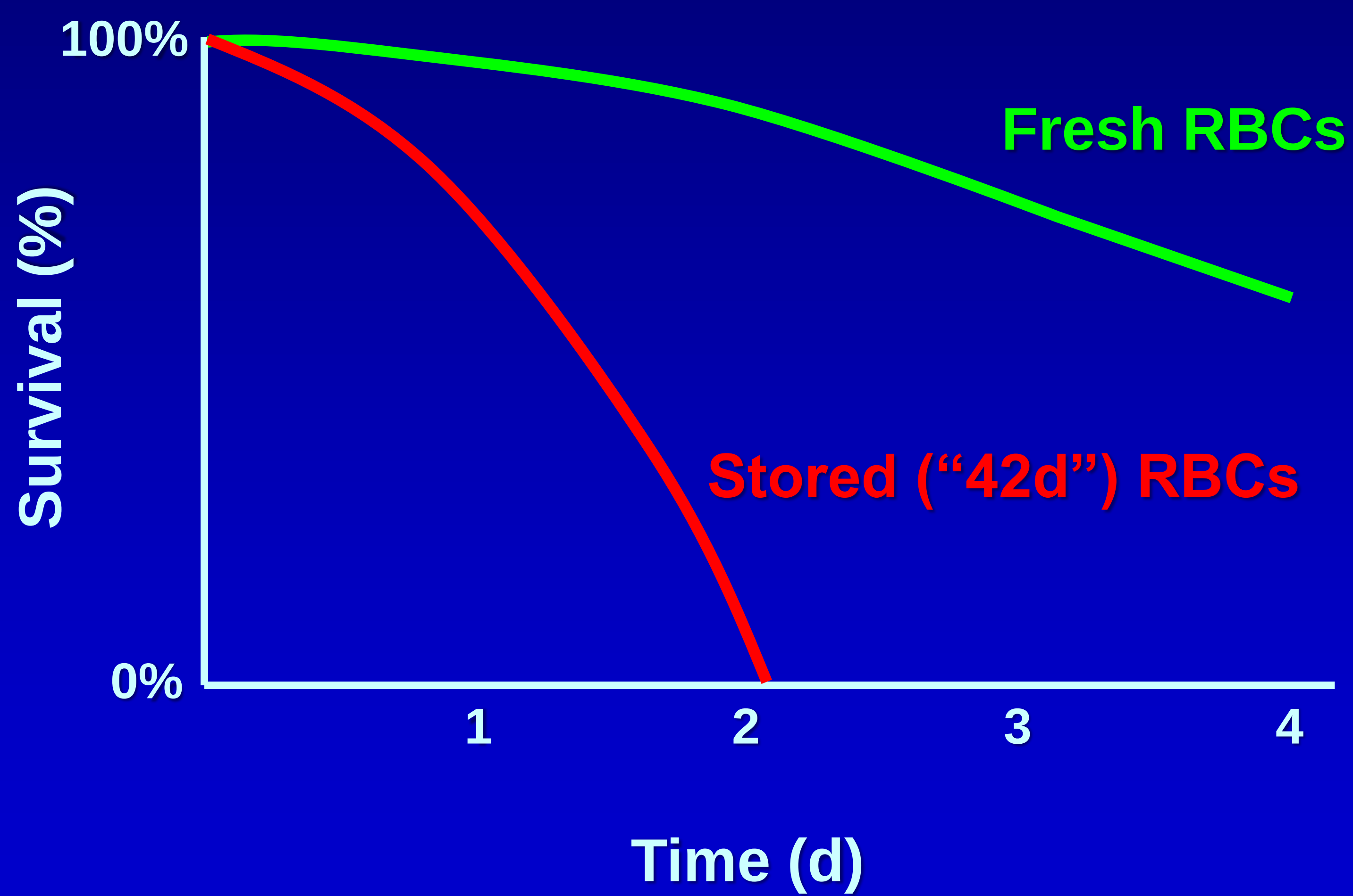
Do you ask your blood banker to transfuse only fresh red blood cells in cardiac patients?

Note: Differences in rheology, biochemistry, coagulation by species

Piagnerelli M *et al. Crit Care Med* 2012;40:983-4.

Transfusion after Pneumonia

Canine Model – Complete Exchange Transfusion

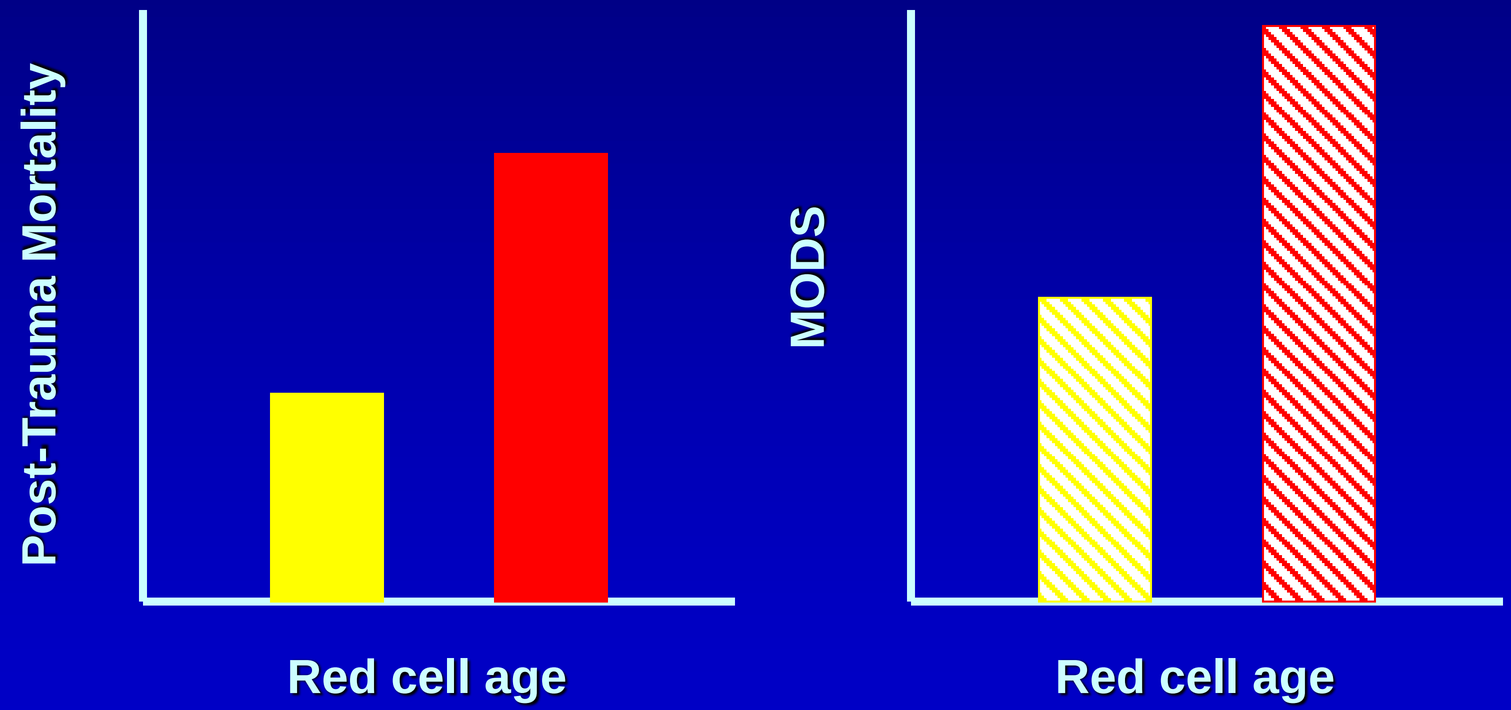


Natanson C *et al. 2012*.

There are multiple animal models demonstrating worse outcomes with red cell storage.

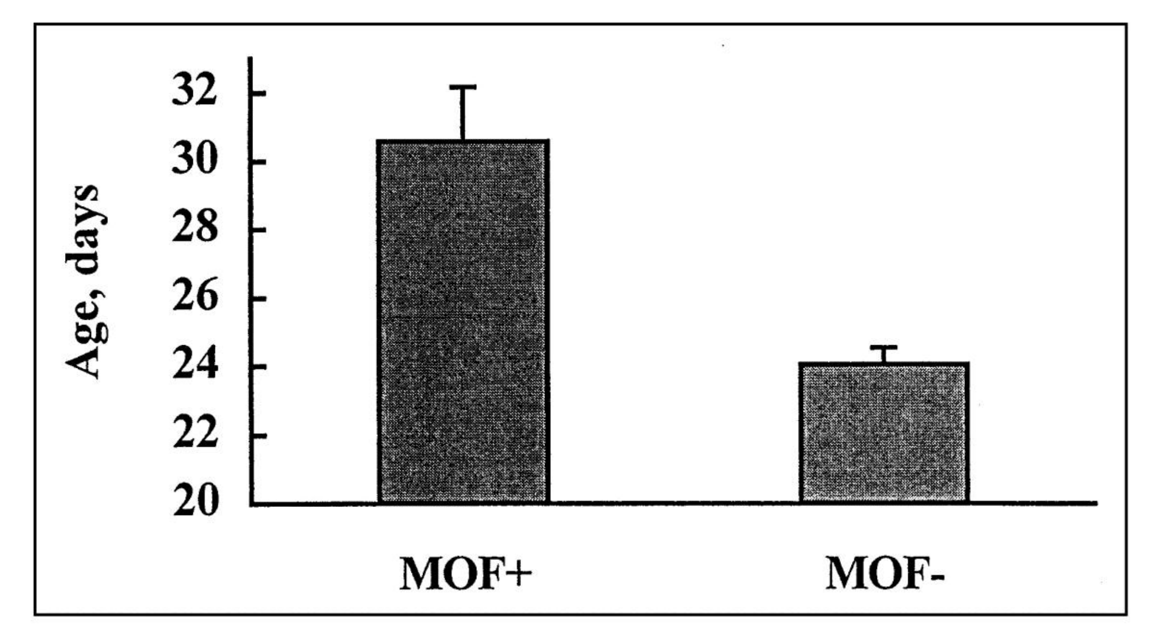
Do we see this with (human) clinical care?

Are Old Red Cell Units Dangerous?



Retrospective Analyses

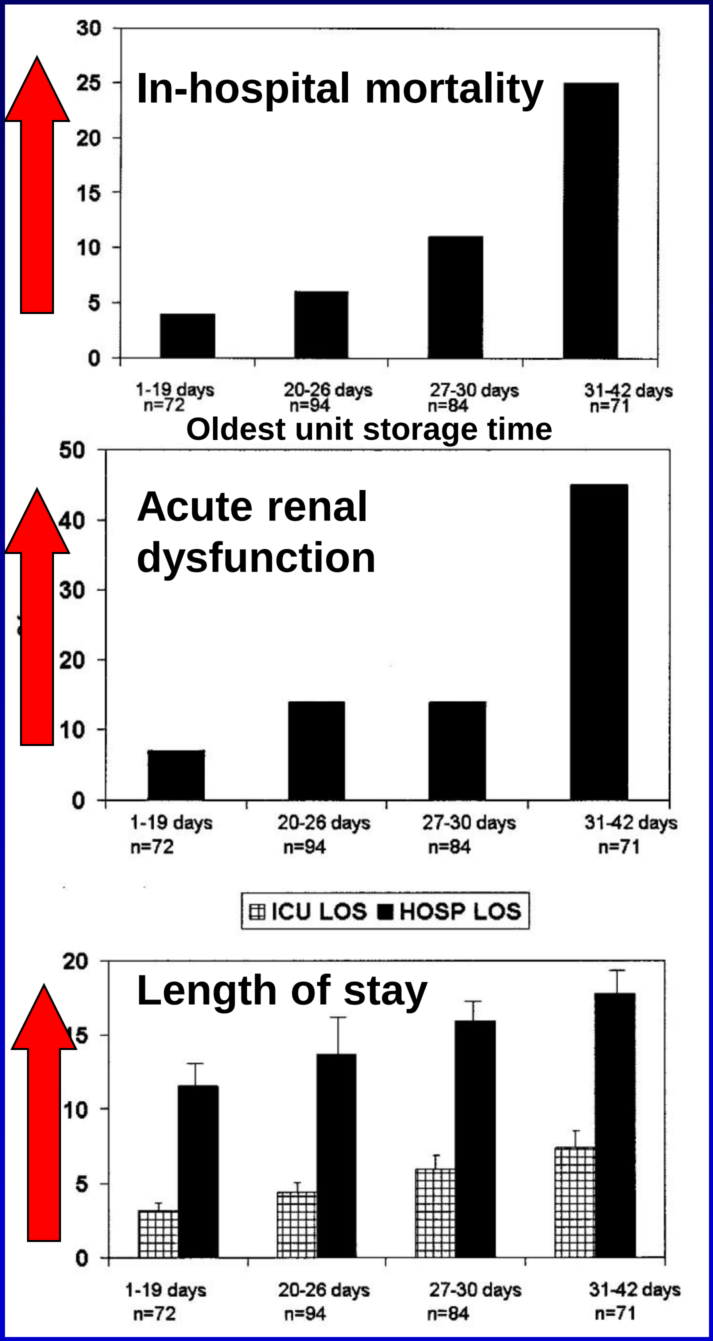
RBC Storage and MOF
A cohort analysis in trauma



Zallen G *et al. Am J Surg* 1999;178:570-2.

RBC Storage in CABG Patients

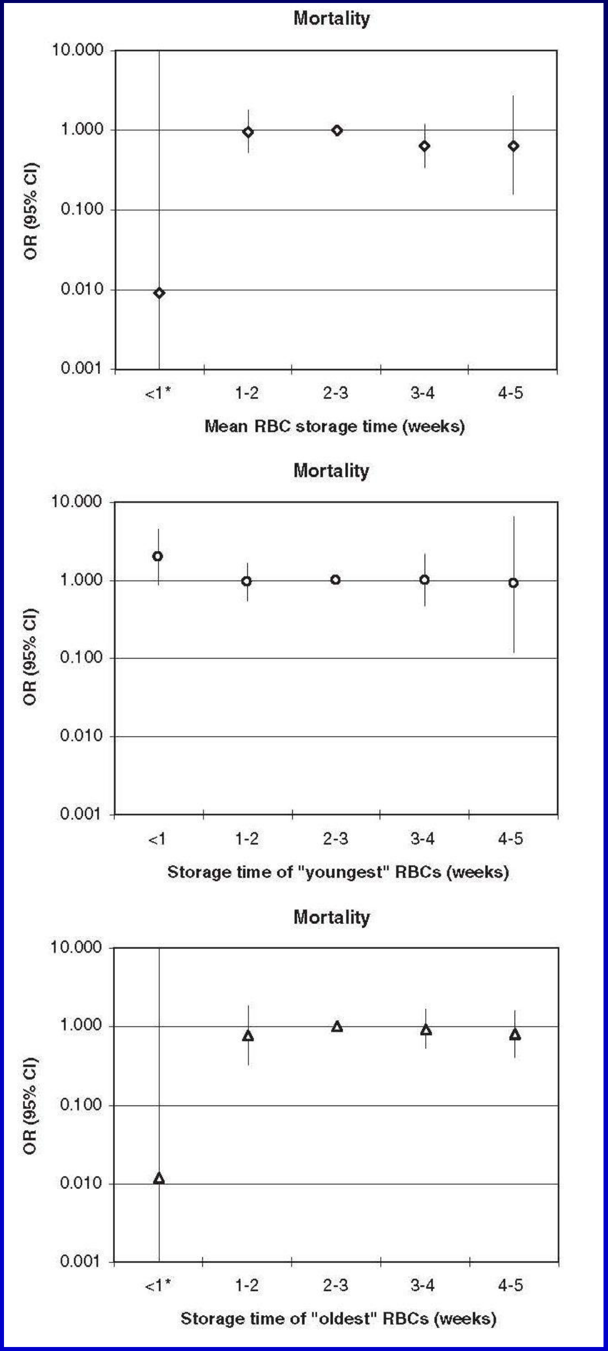
n=321



Confounding variables accounted for:

- FFP, platelet transfusions
- Number of RBCs transfused
- Gender
- NYHA class
- Diabetes
- LV EF
- COPD
- HTN
- Hct
- Cr
- Procedure, times
- Post-op inotropes

Basran S *et al. Anesth Analg* 2006;103:15-20.



RBC Storage in CABG Patients

n=2732

No correlation between RBC storage time and
- **Mortality**
- **ICU LOS**

Note: LR AS RBCs

Van de Watering L *et al. Transfusion* 2006;46:1712-8.

RBC Storage in CABG Patients

Risk of pneumonia increased 1% per day of RBC storage

Twenty factors correlated with LOS; transfusion still an independent predictor of LOS: 0.84% ↑ per unit.

Are there other factors not being accounted for that correlate with transfusion and are more important?

FACTOR	VARIANCE EXPLAINED
Intubation	33%
Impaired consciousness	25%
Wound drainage	17%
Chest tube drainage > 1300 mL	17%
Age > 74 y	12%
Repeat surgery	10%
Other cardiac procedure	8%
Bypass > 135 min	8%
Female gender	5%
Single IM bypass	4%

Vamvakas EC, Carven JH. *Transfusion* 1999;39:701-10.
Vamvakas EC, Carven JH. *Transfusion* 2000;40:101-9.

RBC Storage in Cardiac Surgery Patients

Retrospective analysis of 6002 patients

Storage time:	≤14d	>14d
In-hospital mortality	1.7%	2.8%
Intubation > 72h	9.7%	5.6%
Renal dysfunction	1.6%	2.7%
1yr mortality	7.4%	11.0%

Differences in:

- ABO group distribution
- ABO group usage (> distribution)
- LV dysfunction
- Mitral regurgitation; prior MI
- Body size
- NYHA class
- Peripheral vascular disease

Koch CG *et al. NEJM* 2008;358:1229-39.

Patient Groups

Table 1. Characteristics of Transfused Blood and Demographic and Clinical Features of the Patients.*

Variable	Patients Receiving Newer Blood (N=2872)†	Patients Receiving Older Blood (N=3130)‡	P Value
Transfused blood			
Duration of storage — days			
Median	11	20	
Interquartile range	9–3	17–25	
No. of red-cell units per patient			0.99
Median	2	2	
Interquartile range	2–4	2–4	
Blood group — no. of units/total no. of units (%)			<0.001
A	3340/8802 (37.9)	6116/10,782 (56.7)	
B	778/8802 (8.8)	1291/10,782 (12.0)	
O	4674/8802 (53.1)	3349/10,782 (31.1)	
AB	10/8802 (0.1)	26/10,782 (0.2)	
Leukocyte reduction — no. of patients (%)			<0.001
Yes	1037 (36.1)	1723 (55.0)	
No	1724 (60.0)	1050 (33.5)	
Mixed	111 (3.9)	357 (11.4)	
Fresh frozen plasma — no. of patients (%)	301 (10.5)	335 (10.7)	0.78
Platelets — no. of patients (%)	454 (15.8)	509 (16.3)	0.63
Demographic features			
Race — no. of patients (%)§			0.09
White	2421 (84.3)	2700 (86.3)	
Black	189 (6.6)	188 (6.0)	
Other	262 (9.1)	242 (7.7)	
Age — yr			0.05
Median	69	70	
Interquartile range	60–76	61–77	
Female sex — no. of patients (%)	1208 (42.1)	1311 (41.9)	0.89
Body-surface area — m²			0.03
Median	1.93	1.94	
Interquartile range	1.75–2.09	1.77–2.10	
Blood group — no. of patients/total no. of patients (%)			<0.001
A	992/2860 (34.7)	1542/3120 (49.4)	
B	303/2860 (10.6)	449/3120 (14.4)	
O	1456/2860 (50.9)	949/3120 (30.4)	
AB	109/2860 (3.8)	180/3120 (5.8)	
Clinical features			
Preoperative laboratory values			
Hematocrit — %			0.41
Median	38.2	38.0	
Interquartile range	34.4–41.1	34.3–41.0	
Creatinine — mg/dl			0.12
Median	1.0	1.0	
Interquartile range	0.8–1.3	0.8–1.3	

Table 1. (Continued.)

Variable		Patients Receiving Older Blood (N=3130)‡	P Value
Bilirubin — m…			0.81
Median		0.6	
Interquart…		0.4–0.8	
Cardiac featur…			
Abnormal … pat…		1975 (63.1)	<0.001
Heart failu…		1469 (46.9)	0.15
NYHA cla…			<0.001
I		370 (11.8)	
II	1474 (51.3)	1622 (51.8)	
III	700 (24.4)	827 (26.4)	
IV	382 (13.3)	311 (9.9)	
Prior myocardial infarction — no. of patients (%)	1502 (52.3)	1564 (50.0)	0.07
Aortic regurgitation — no. of patients (%)	1102 (38.4)	1157 (37.0)	0.27
Mitral regurgitation — no. of patients (%)	1842 (64.1)	2105 (67.3)	0.01
>70% Stenosis of left main trunk — no. of patients (%)¶	353 (12.7)	367 (12.2)	0.55
Clinical presentation — no. of patients (%)			
Preoperative IABP	63 (2.2)	68 (2.2)	0.96
Emergency surgery	37 (1.3)	48 (1.5)	0.42
Coexisting conditions			
Hypertension — no. of patients (%)‖	2135 (75.3)	2402 (77.1)	0.11
COPD — no. of patients (%)	345 (12.0)	391 (12.5)	0.57
Smoking — no. of patients (%)	1649 (57.4)	1751 (55.9)	0.25
Diabetes — no. of patients (%)**	843 (29.5)	968 (31.1)	[illegible]
Stroke — no. of patients (%)	307 (10.7)	376 (12.0)	0.11
Peripheral vascular disease — no. of patients (%)	1563 (54.4)	1830 (58.5)	0.002
Perioperative factors			
Cardiopulmonary-bypass time — min			0.55
Median	101	100	
Interquartile range	80–126	78–127	
Aortic-clamp time — min			0.98
Median	78	78	
Interquartile range	62–97	60–98	
Reoperation — no. of patients (%)	916 (31.9)	1040 (33.2)	0.27
Operative procedure — no. of patients (%)			
Isolated CABG	1251 (43.6)	1336 (42.7)	0.49
Isolated valve replacement	754 (26.3)	844 (27.0)	0.53
Use of internal thoracic artery as bypass conduit	1407 (49.0)	1552 (49.6)	0.65

Blood is not issued randomly!

Comparison of very different patient groups gives different results !

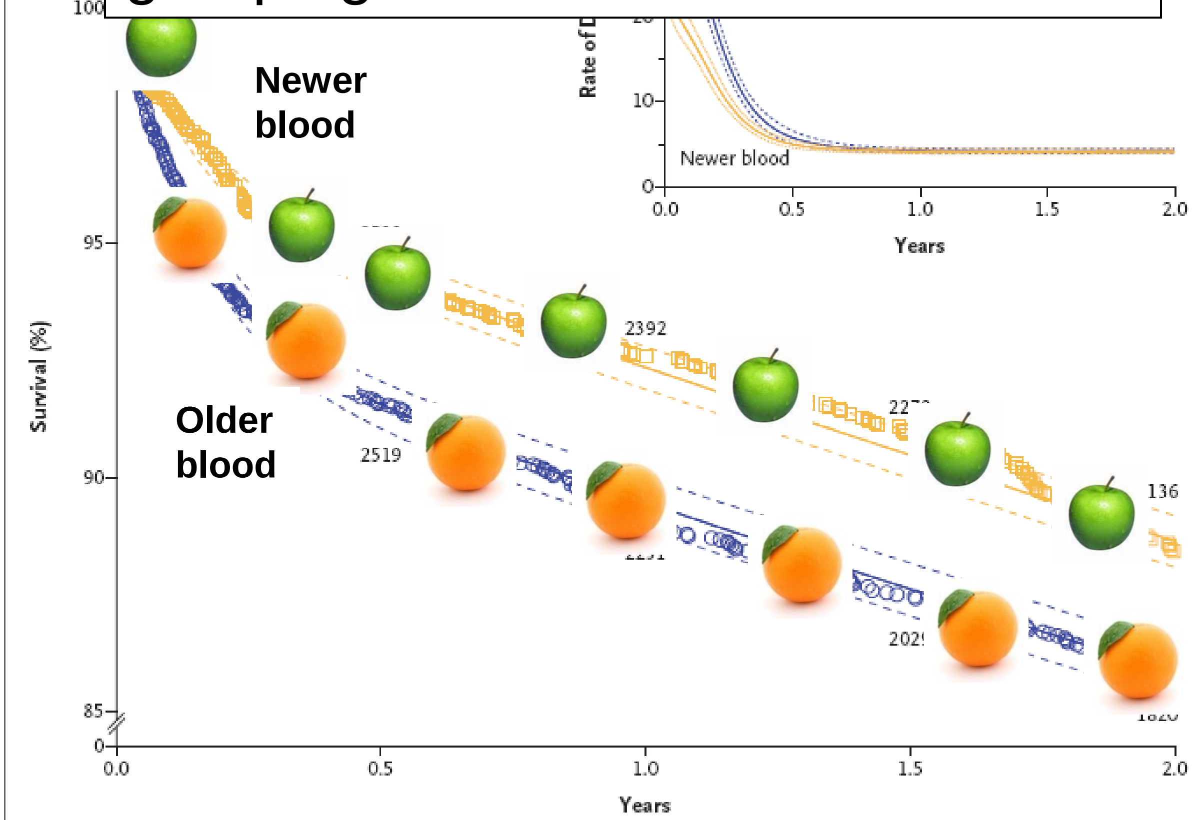


Figure 3. **Kaplan–Meier Estimates of Survival and Death.**

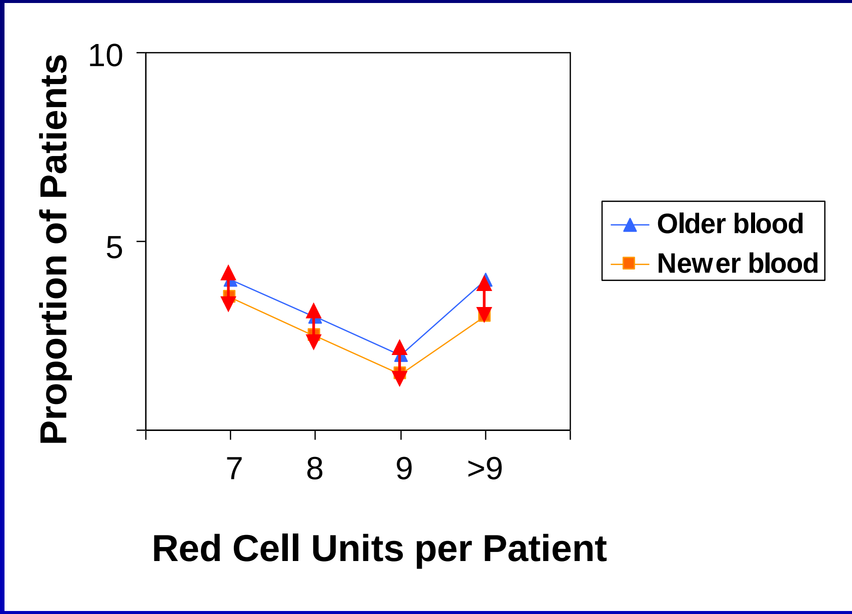
The curves show data from 2872 patients who were given exclusively newer blood (stored for 14 days or less) and 3130 patients given exclusively older blood (stored for more than 14 days). The numbers above and below the curves represent the numbers of patients who were alive and under follow-up observation in each group at that time. The solid lines of the same color represent estimated survival or the rate of death, and the dotted lines represent pointwise 95% confidence intervals. The nonparametric survival estimator (orange squares or blue circles), as determined by the Kaplan–Meier method, is superimposed on the parametric survival function estimator. In this unadjusted comparison, the percentage of patients receiving older blood who survived was lower than the percentage of those receiving newer blood who survived, especially during the initial follow-up period.

Data un-adjusted for differences in patient groups shown in Table 1 !

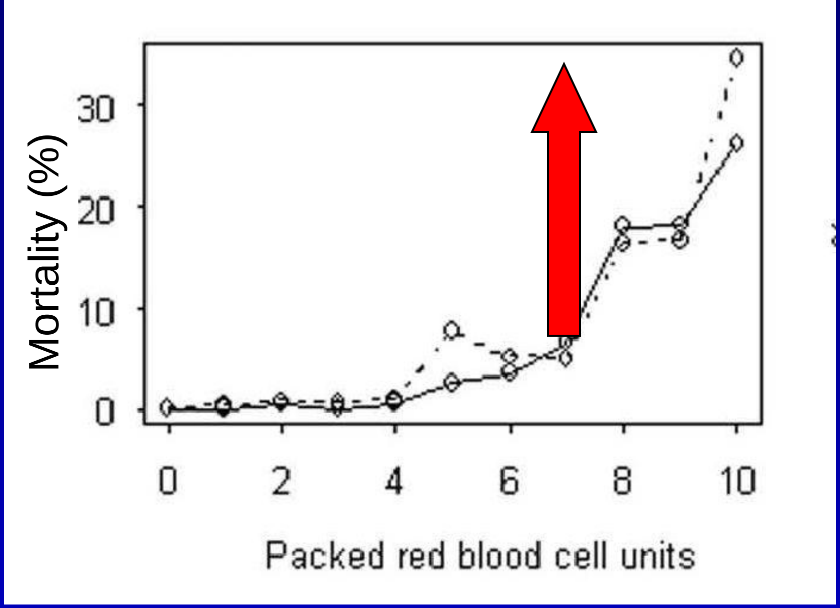
Koch CG *et al.*
***NEJM* 2008;358:1229-39.**
as modified by Sunny Dzik

RBC Storage in Cardiac Surgery Patients

Is there really a difference?

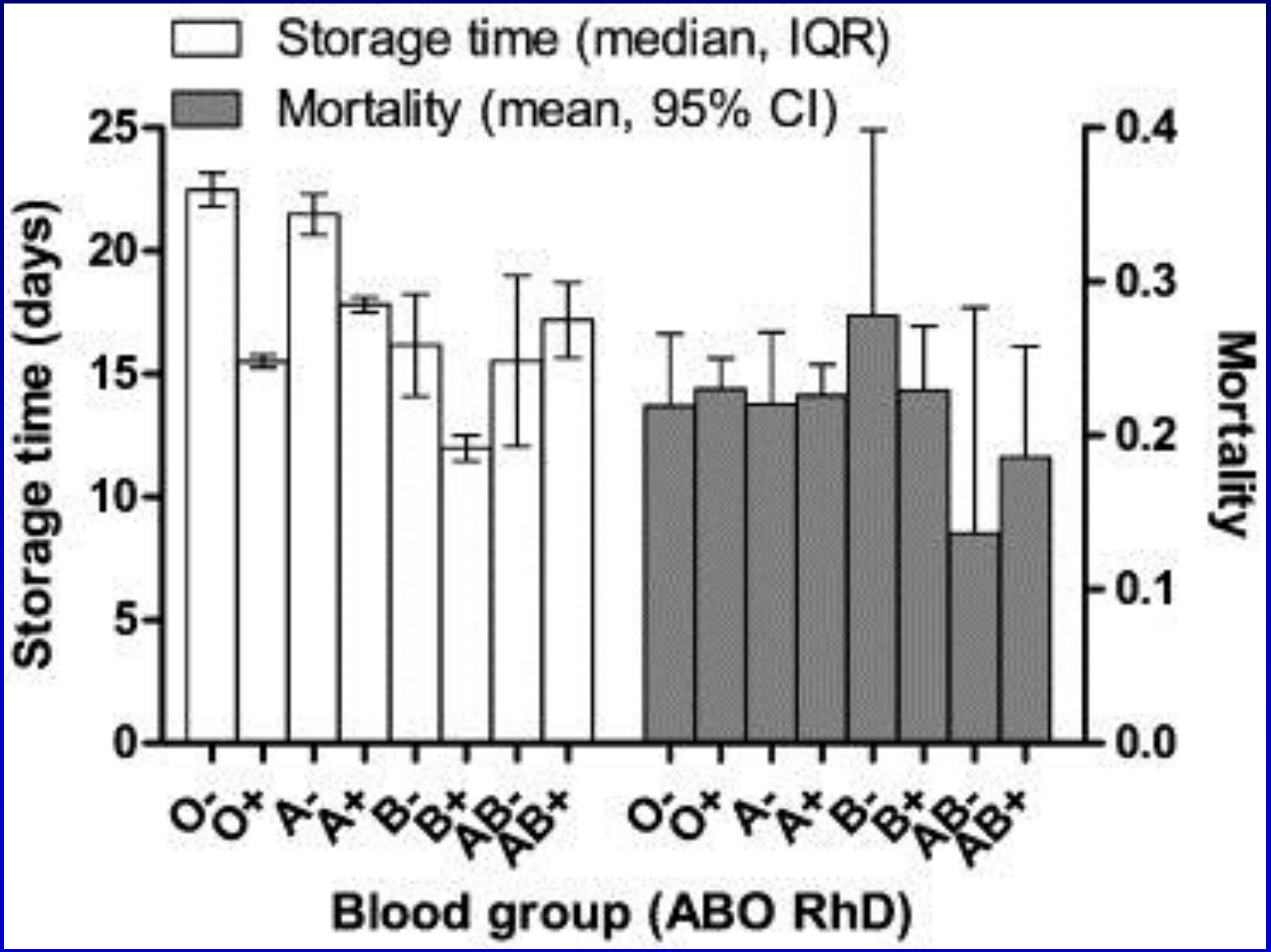


Koch CG *et al. NEJM* 2008;358:1229-39.



Koch CG *et al. Crit Care Med* 2006;34:1608-16.

Yes, blood group and type do matter!



Middelburg RA *et al. Transf Med Rev* 2012.

RBC Storage in Cardiac Surgery Patients

Is there really a difference?

Population: 670 first-time CABG patients; ≥ 2u in 48h

80% power to detect a LOS difference ≥ 5d

<u>Outcomes</u>

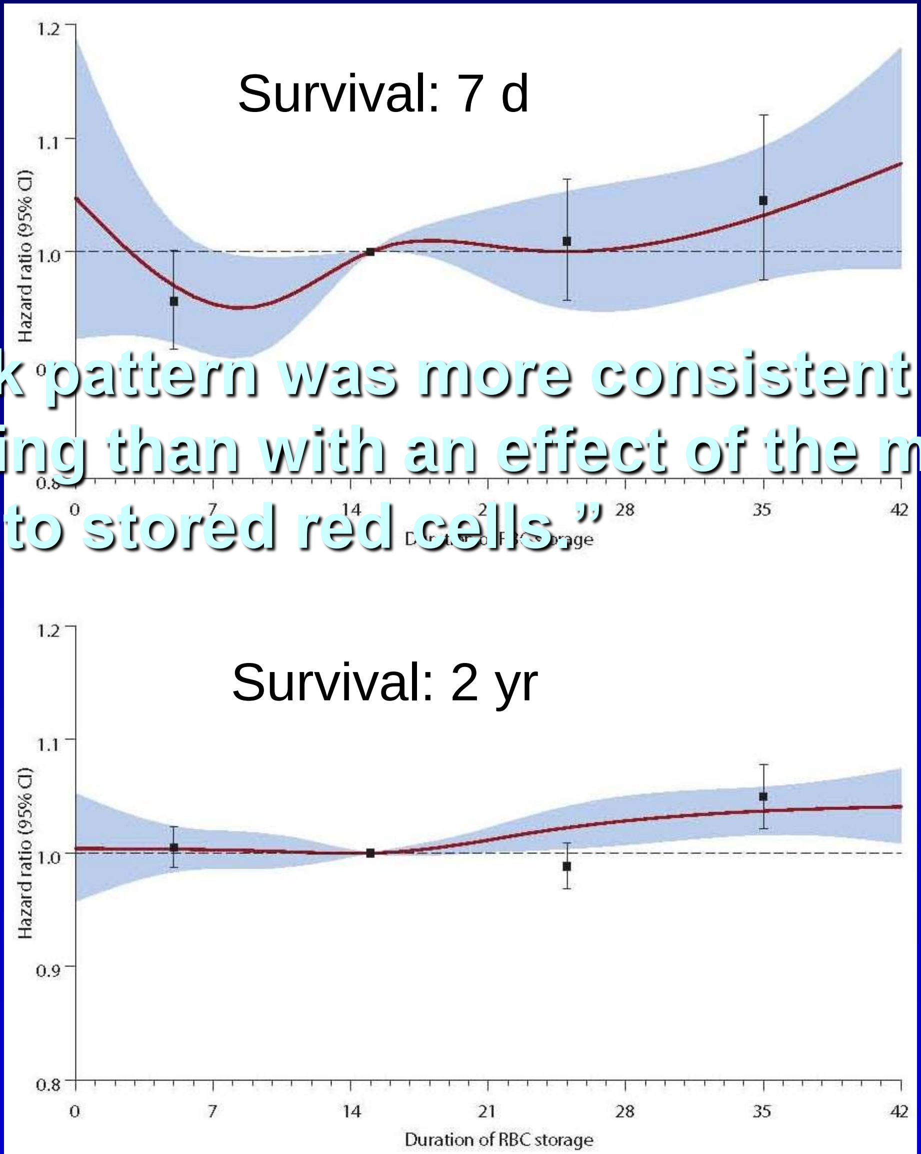
Post-op mortality
New renal failure
Pneumonia
ICU LOS
Ventilation time

No effect of storage time
oldest unit age
units > 30d old

after adjustment for operative risk and volume transfused

Yap C-H *et al. Ann Thorac Surg* 2008;86:554-9.

Scandinavian Observational Study



"…the risk pattern was more consistent with weak confounding than with an effect of the momentary exposure to stored red cells."

n = 405,000 transfusions

Edgren G *et al. Transfusion* 2010;50:1185-95.

RBC Storage - Critically Ill Children

Outcomes
Oxygenation
Ventilation time
Mortality

No effect of storage time
for singly or multiply patients
(n = 67)

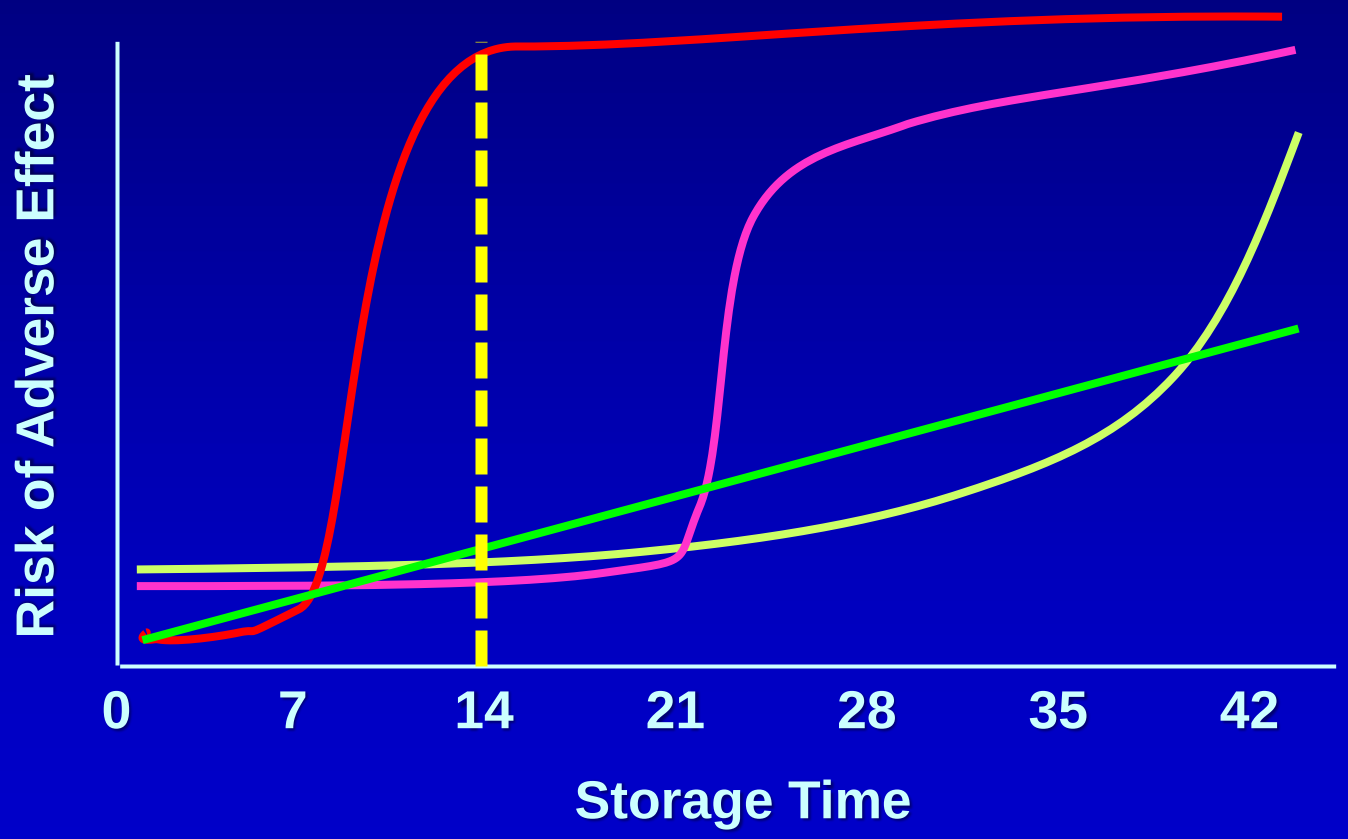
Kneyber MCJ *et al. Intens Care Med* 2009;35:170-80.

Pitfalls of Retrospective Studies Assessing the Effect of Storage Time

- Lack of accounting for association with number of units (total; beyond a particular age)
- Using non-transfused patients as a reference
- Analyzing a "storage score" (time * number)
- Stratifying analysis with open upper end (effect seen only > x units)
- Analysis based on oldest unit (➔ selects high transfusion volume)
- Failure to account for ABO differences
- Historic controls
- Failure to correct for co-linearity error
- Post hoc subgroup analyses
- Incorrect math!

van de Watering L. *Vox Sang* 2011;100:36-45.
Transfusion 2011;51:1847-54.

Pitfalls of Retrospective Studies Assessing the Effect of Storage Time



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Pitfalls of Retrospective Studies Assessing the Effect of Storage Time

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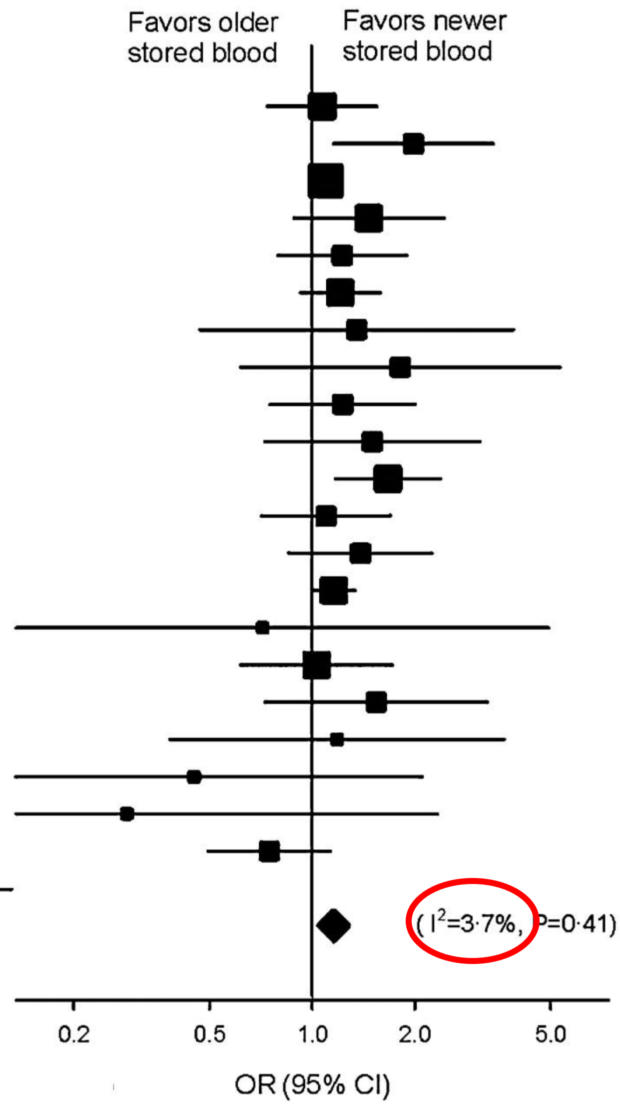
Historic controls
Failure to correct for co-linearity error
Post hoc subgroup analyses
Incorrect math!

If you torture data long enough, it will eventually confess!

van de Watering L. *Vox Sang* 2011;100:36-45.
Transfusion 2011;51:1847-54.

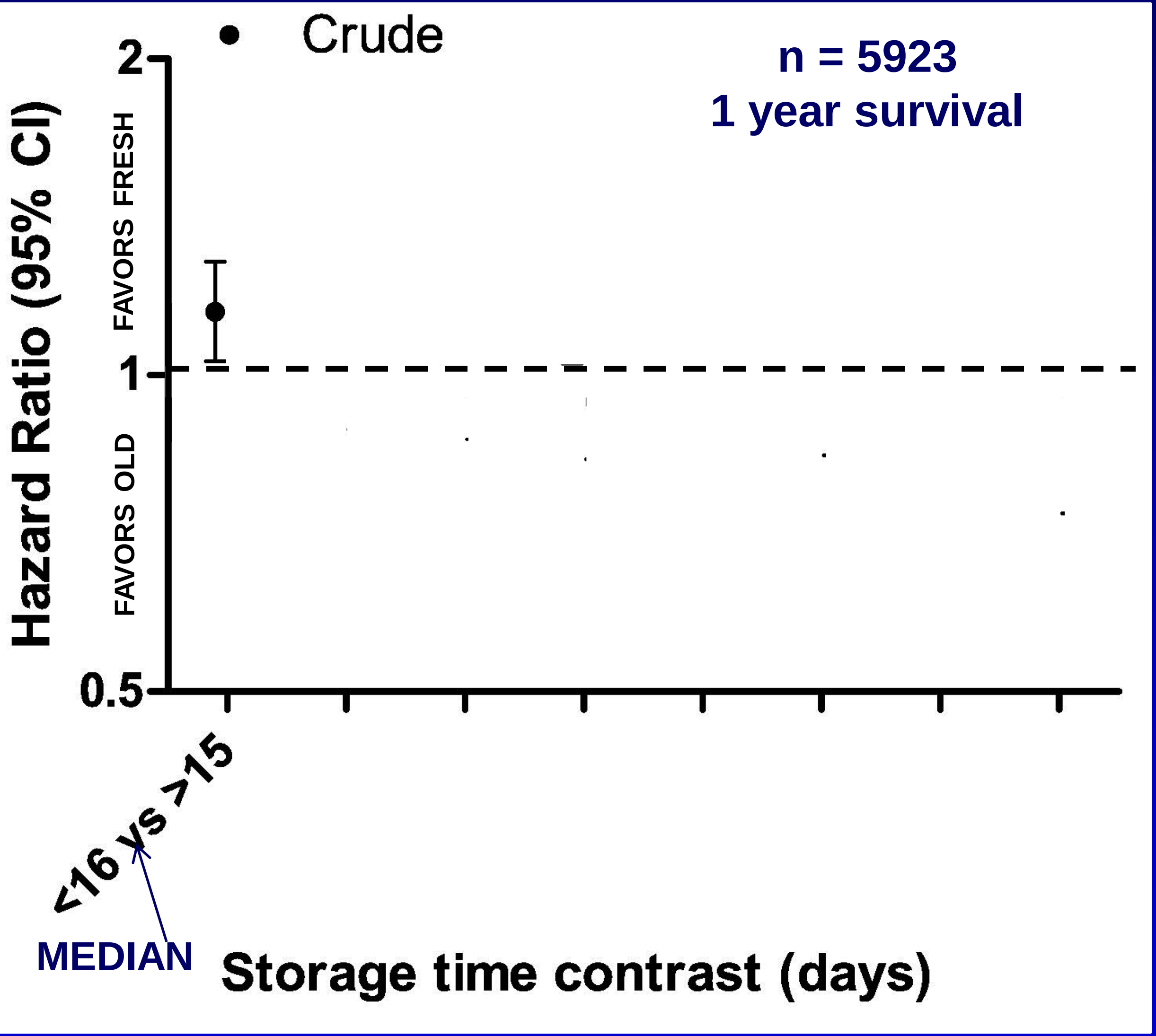
Meta-Analysis: Storage Time and Mortality

Study/ Year (Reference)	OR (95% CI)	p value
Van Straten/ 2011 [14]	1·07 (0·74, 1·55)	0·72
Pettila/ 2011 [15]	1·98 (1·15, 3·39)	0·01
Edgren/ 2010 [22]	1·09 (1·00, 1·19)	0·04
Eikelboom/ 2010 [21]	1·43 (0·90, 2·28)	0·13
Robinson/ 2010 [20]	1·22 (0·79, 1·90)	0·37
Weinberg/ 2010 [13]	1·21 (0·92, 1·58)	0·17
Karam/ 2010 [10]	1·35 (0·47, 3·89)	0·58
Gauvin/ 2010 [24]	1·81 (0·62, 5·32)	0·28
Van Buskirk/ 2009 [32]	1·23 (0·75, 2·00)	0·41
Spinella/ 2009 [17]	1·50 (0·73, 3·10)	0·27
Koch/ 2008 [16]	1·67 (1·17, 2·37)	0·005
Weinberg/ 2008 [26]	1·10 (0·71, 1·69)	0·68
Yap/ 2008 [25]	1·38 (0·85, 2·25)	0·19
Weinberg/ 2008 [19]	1·16 (1·00, 1·33)	0·05
Leal-Noval/ 2008 [23]	0·71 (0·10, 4·93)	0·73
Van-De-Watering/ 2006 [18]	1·03 (0·62, 1·71)	0·91
Murrell/ 2005 [27]	1·54 (0·73, 3·26)	0·26
Fernandes-Da-Cunha/ 2005 [33]	1·18 (0·38, 3·65)	0·77
Hebert/ 2005 [34]	0·45 (0·10, 2·10)	0·31
Schulman/ 2002 [35]	0·29 (0·04, 2·32)	0·24
Mynster/ 2001 [12]	0·75 (0·49, 1·13)	0·17
All Studies	**1·16 (1·07, 1·24)**	**0·0001**



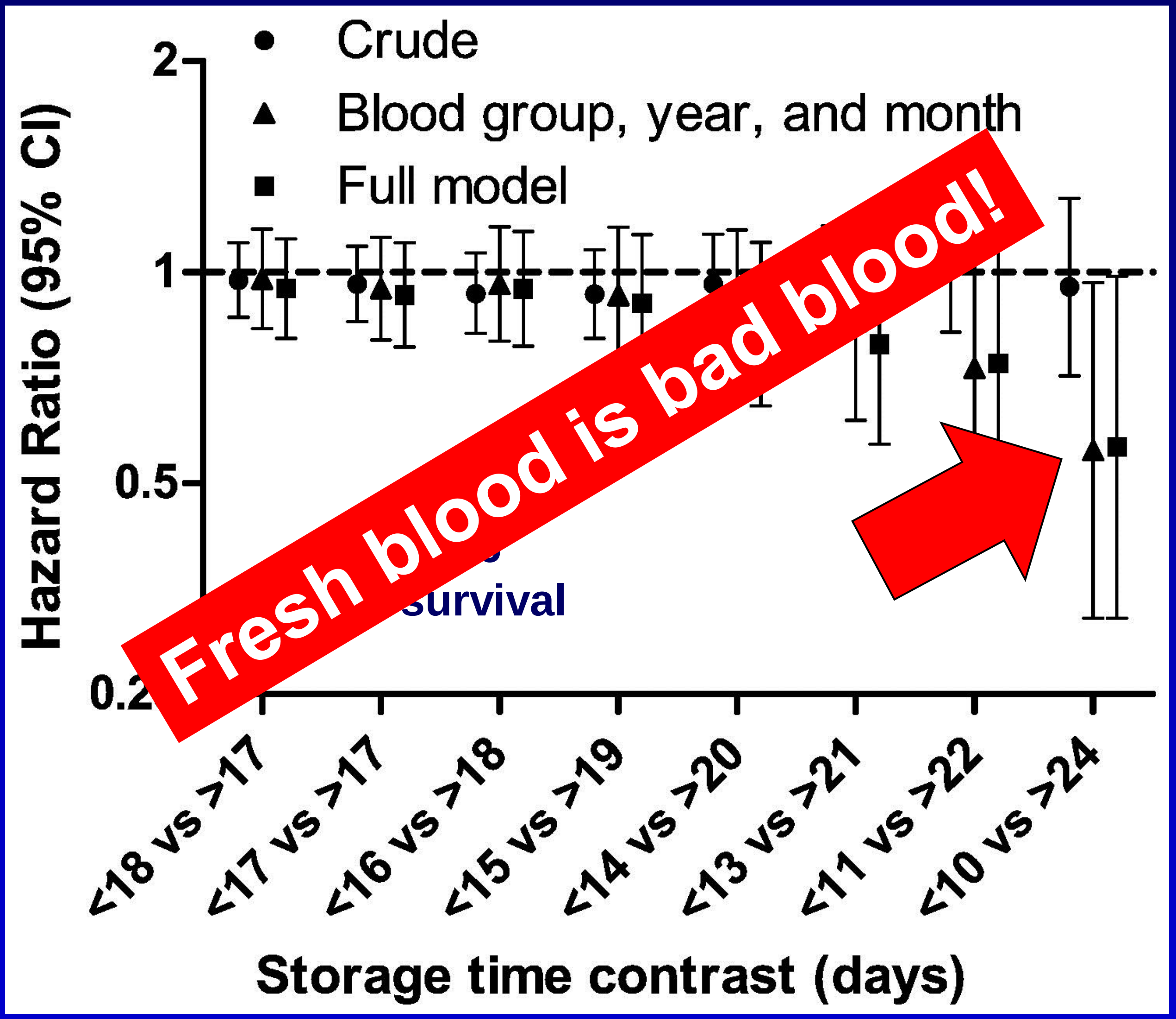
Wang D *et al. Transfusion* 2012;52:1184-95.

Transfusion and Survival



Middelburg RA *et al. Transf Med Rev* 2012.

Transfusion and Survival



Middelburg RA *et al. Transf Med Rev* 2012.

Fresh vs. Stored Red Cells

in critically ill patients

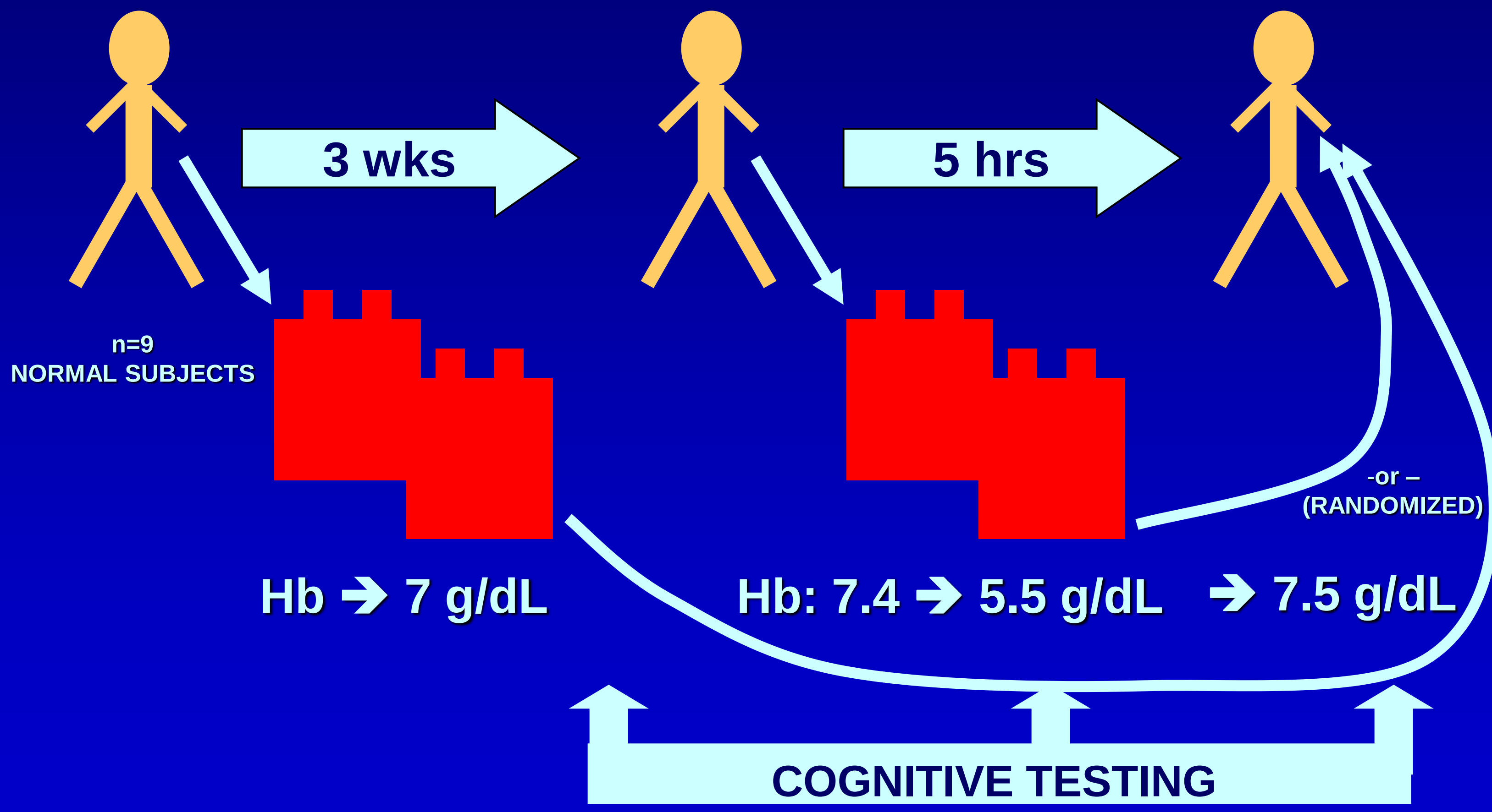
	Fresh Blood (2d)	**Stored Blood** (28d)
Gastric-arterial pCO_2 Gastric intramucosal pH Arterial pH Arterial lactate	During transfusion and 5h after ***No differences***	

Our data do not support the hypothesis that transfusing stored red cells adversely affects tissue oxygenation in anemic, euvolemic, critically ill patients with no evidence of bleeding.

Walsh TS *et al. Crit Care Med* 2004;32:364-71.

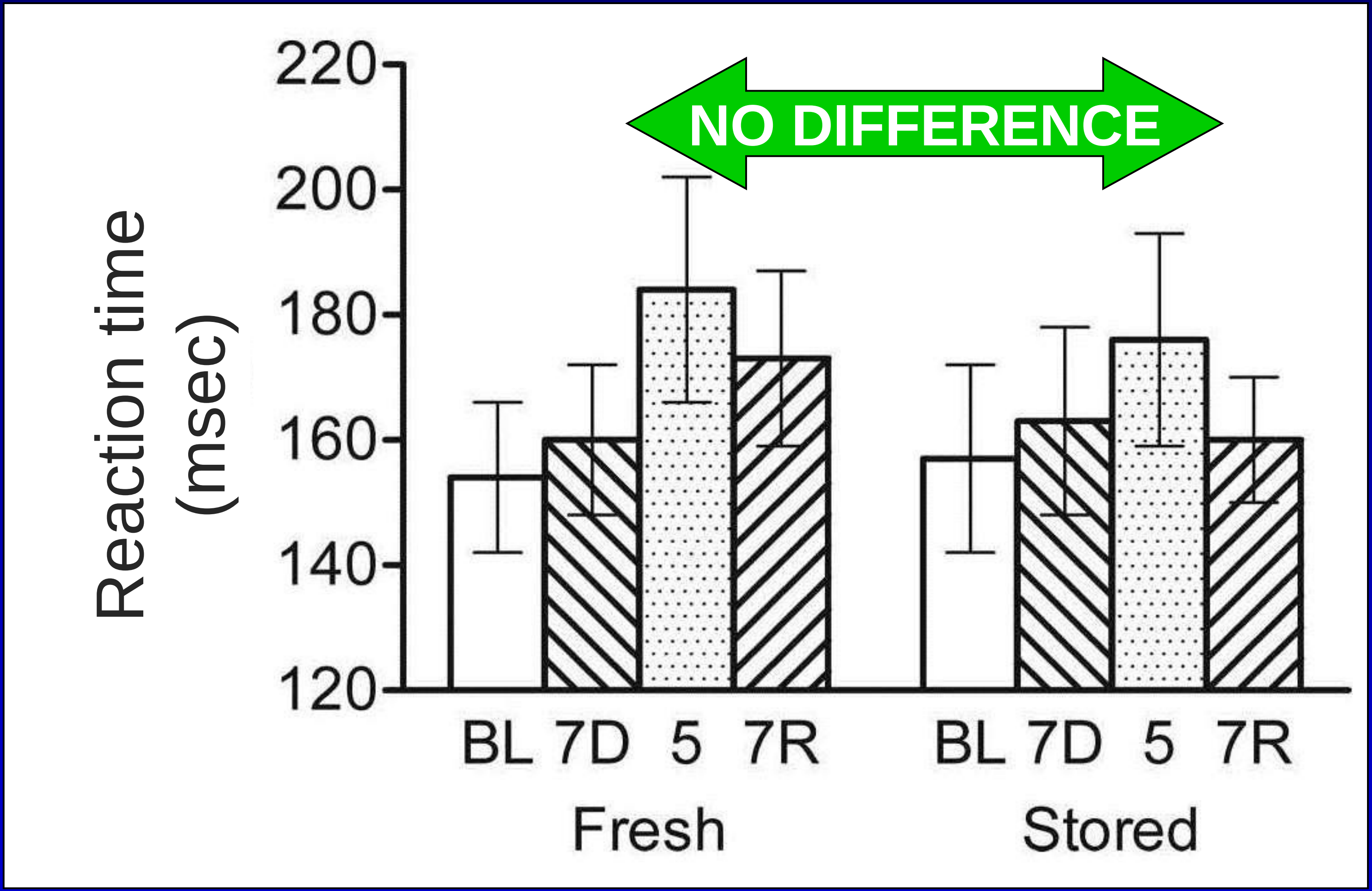
Fresh vs. Stored Red Cells

in normal, anemic subjects



Weiskopf R *et al. Anesthesiology* 2006; 104:911-20.

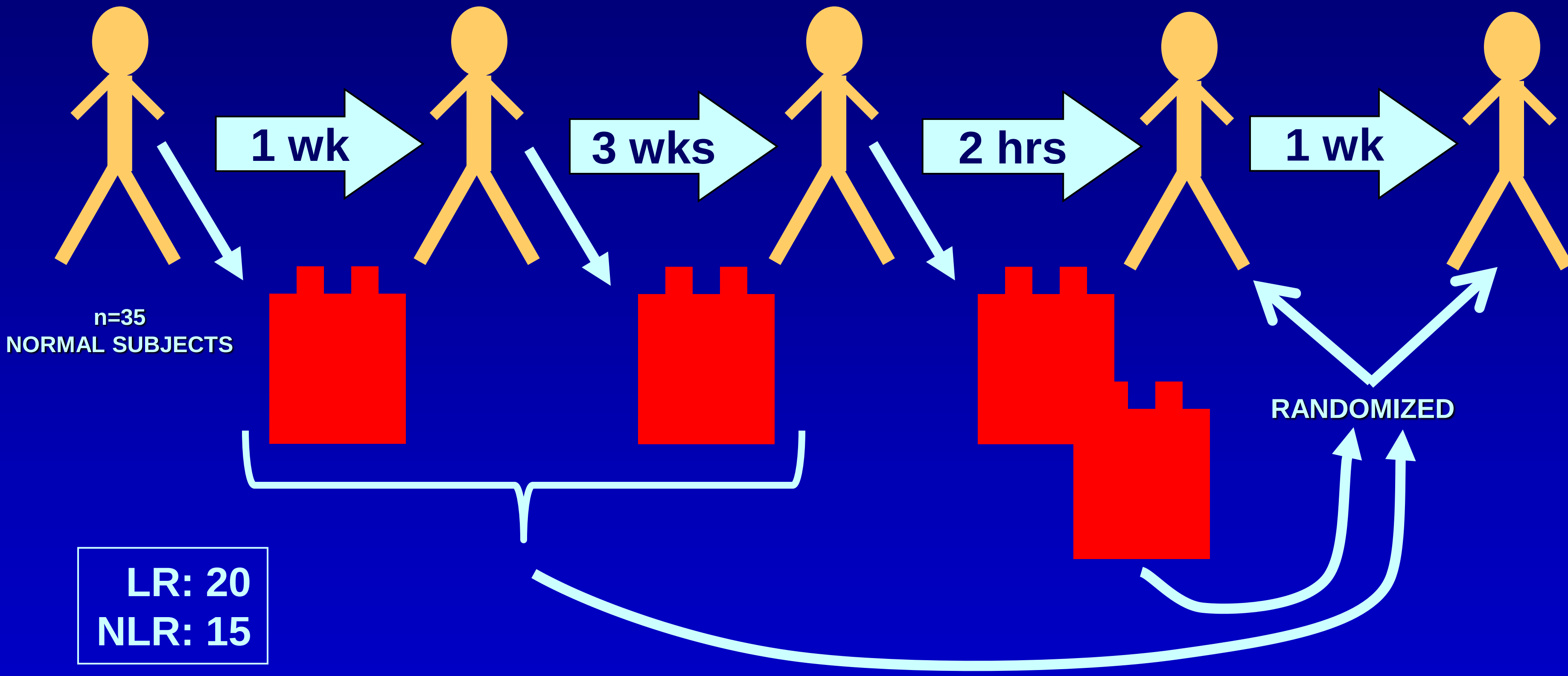
Fresh vs. Stored Red Cells



Weiskopf R *et al. Anesthesiology* 2006; 104:911-20.

Fresh vs. Stored Red Cells

and Pulmonary Function



AaD_{O_2} Pre- vs. 60 min post-transfusion

STORED vs. FRESH

Weiskopf RB *et al. Anesth Analg* 2012;114:511-9.

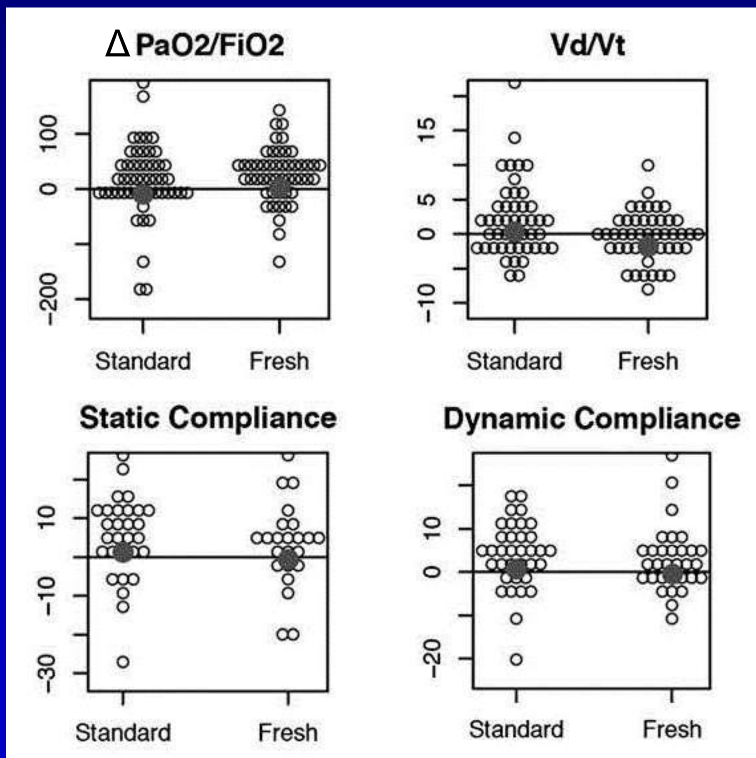
Fresh vs. Stored Red Cells
and Pulmonary Function

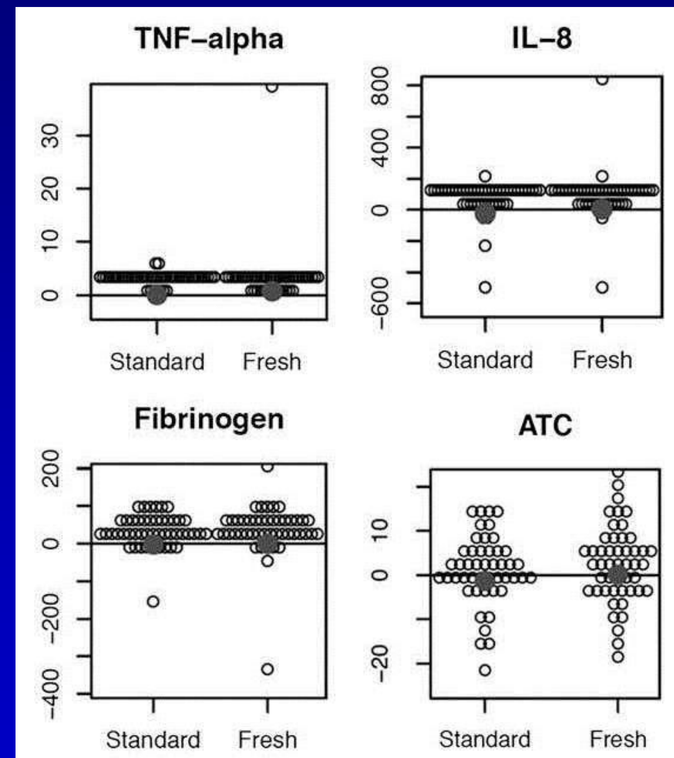
Transfusion of either:
Δ = 3 mm Hg
(= 8% ≈ "equivalence")

LR = NLR ➔ Data pooled

Weiskopf RB *et al. Anesth Analg* 2012;114:511-9.

Fresh vs. Stored Red Cells
and Pulmonary Function





Storage: 27d (median) 4d (<5d)

n = 50/group, randomized

Kor DJ *et al. Am J Resp Crit Care Med* 2012;185:842-50.

Is Old Blood Bad Blood?

Prospective, Randomized (Pilot) Trial

Cardiac surgery and Intensive care patients

RANDOMIZE

YOUNG ***vs.*** **OLD**

Group receiving "fresh" red cells (≤ 8d) had <u>higher</u> mortality.

Hébert *et al*.,*Anesth Analg* 2005;100:1433-8.

Is Old Blood Bad Blood?

ABLE

Intensive care patients
n = 2500

RANDOMIZE

< 8d

vs.

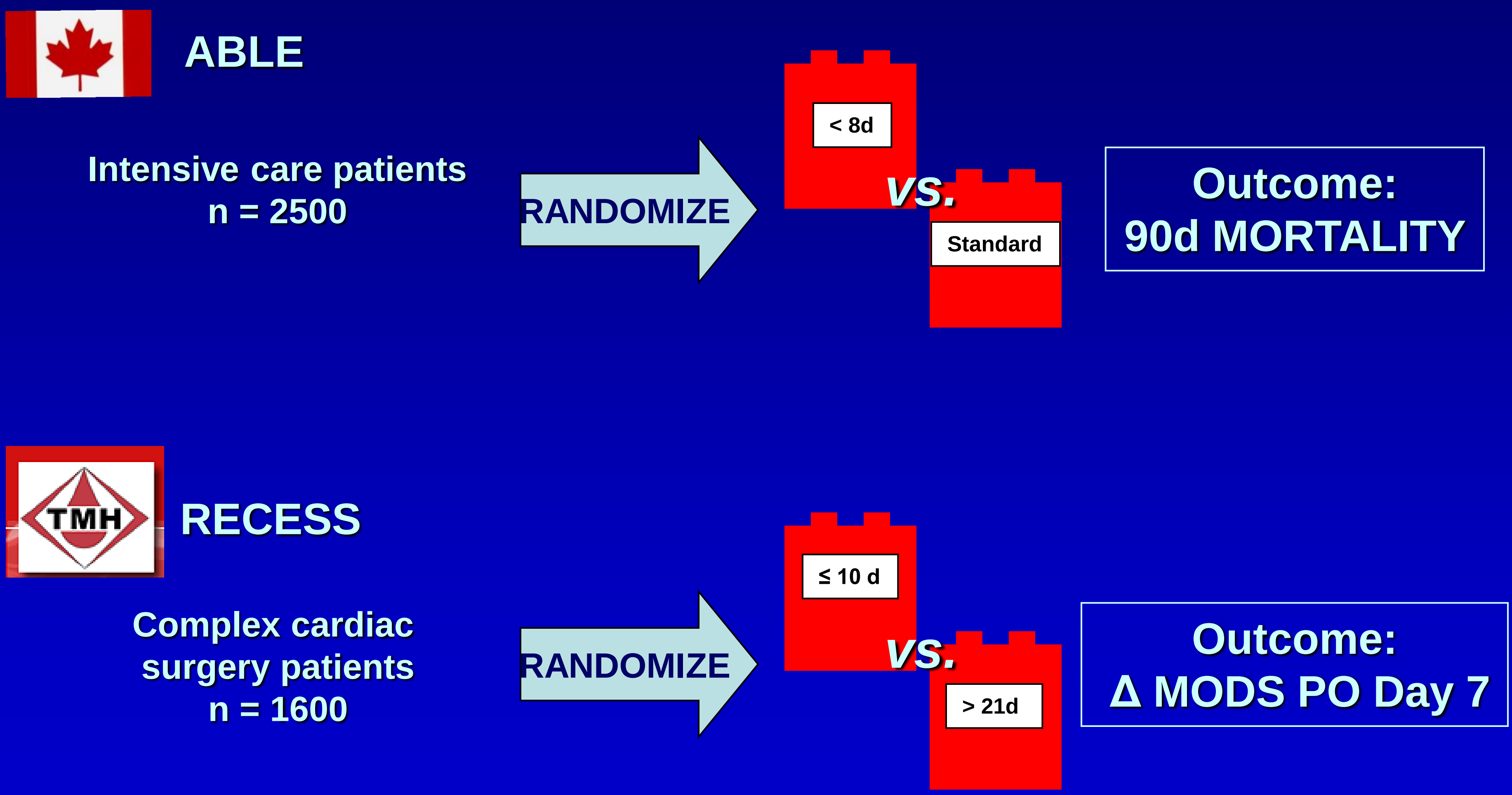
Standard

Outcome:
90d MORTALITY

MEAN STORAGE TIMES: 5d 22d

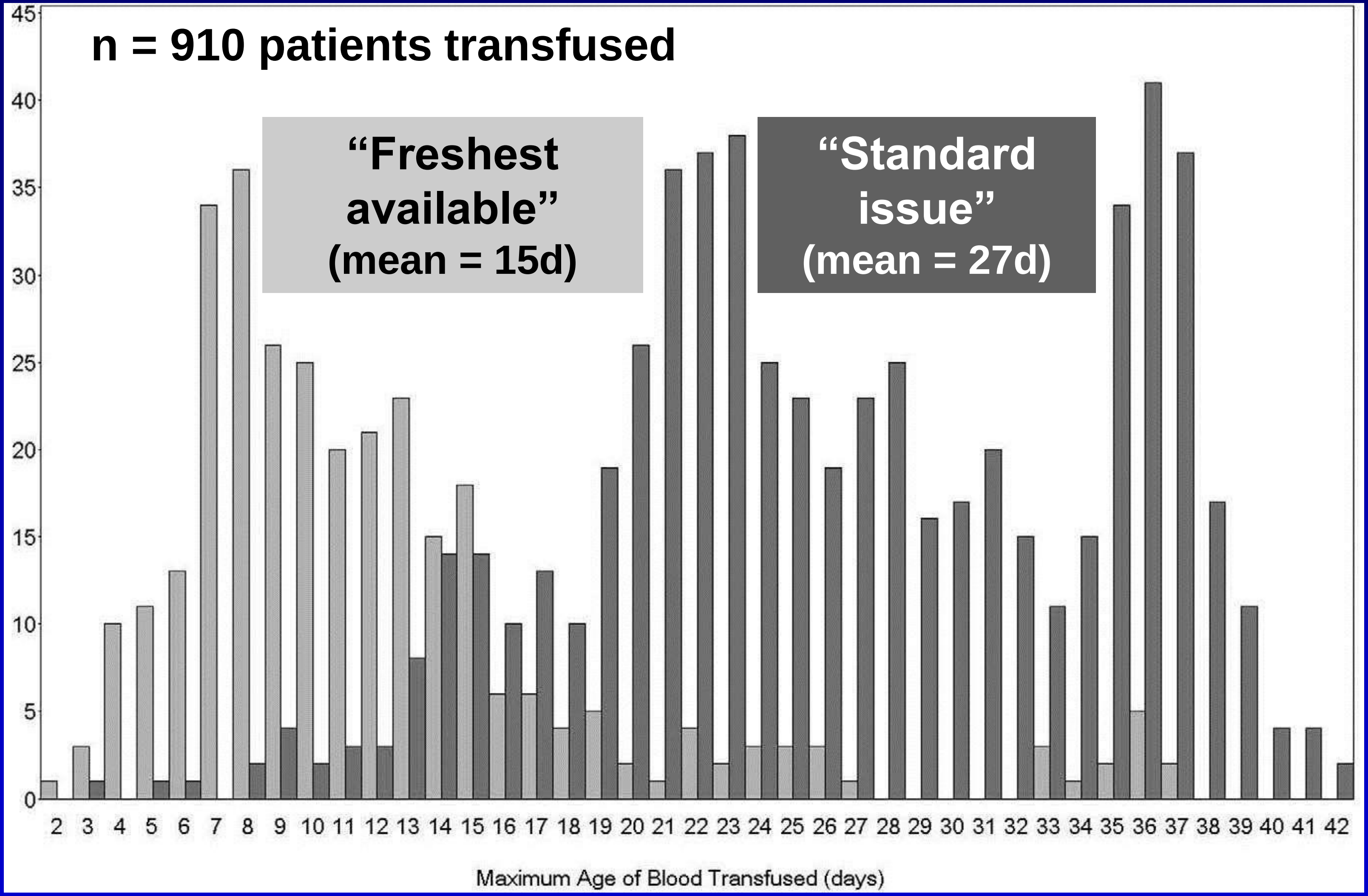
As of August: 1207 enrolled
Compliance = 94% (small overlap)

Is Old Blood Bad Blood?



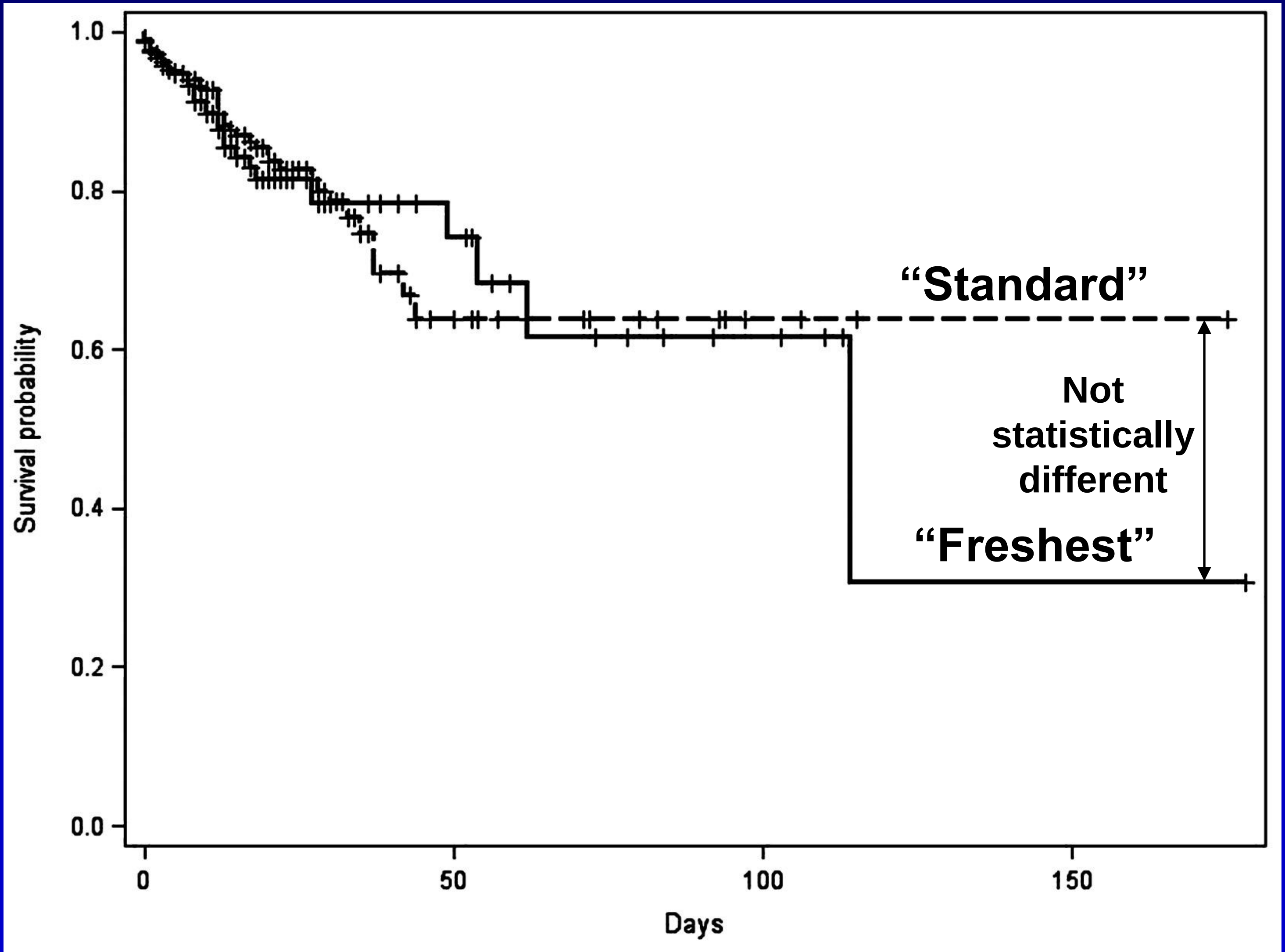
(Both with companion biomarker studies)

Comparative Effectiveness: Pilot Trial



Heddle NM *et al. Transfusion* 2012;52:1203-12.

Comparative Effectiveness: Pilot Trial



Heddle NM *et al. Transfusion* 2012;52:1203-12.

Are Old Red Cell Units Dangerous?

Cleveland Clinic

Cardiac Surgery Redux

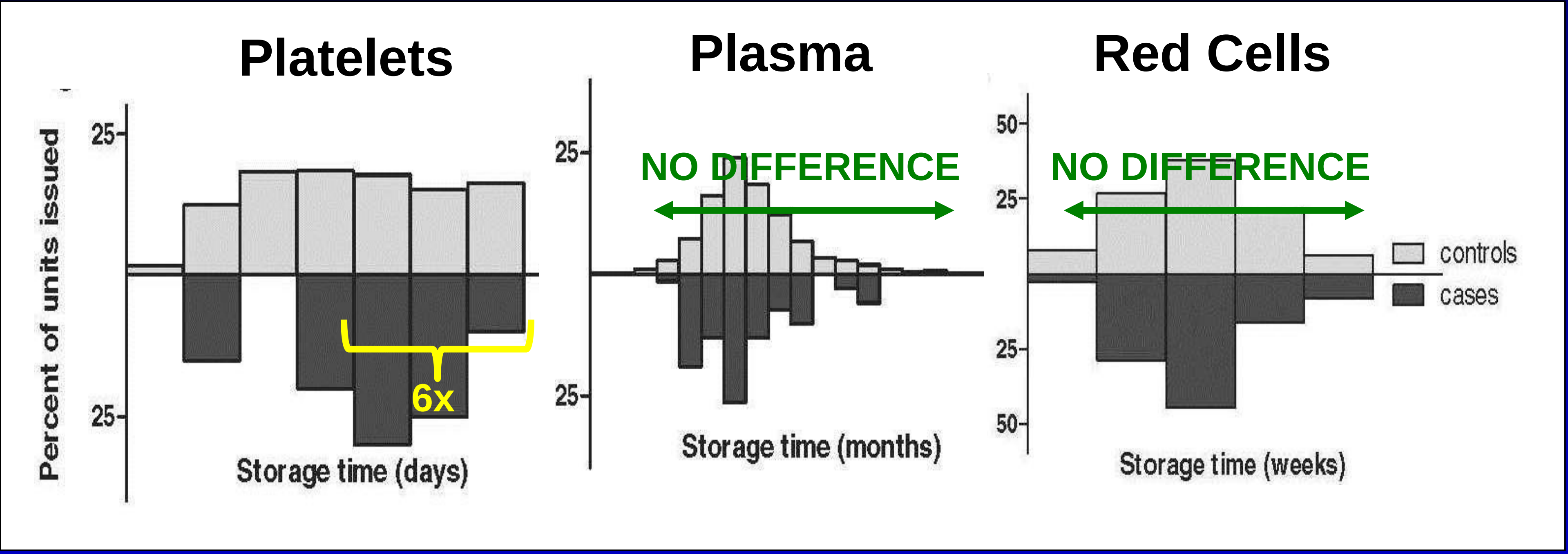
n = 2800
Storage: < 14 d vs. >20 d
Outcome: Morbidity

ARIPI

n = 2500 NICU patients (450 < 1250 g)
Storage: < 8 d vs. “standard”
Outcome: 90 d mortality+combined

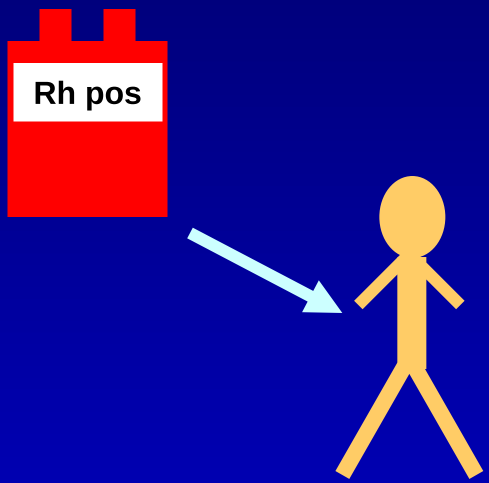
Outcome: No difference.

Storage Time and TRALI



Middelburg RA *et al. Transfusion* 2012;52:658-67.

Storage Time and Alloimmunization



Rh neg

n = 87

No association between length of storage and anti-D alloimmunization

Yazer MH, Triulzi DJ. *AJCP* 2010;134:443-7.

Meta-analysis of clinical studies of the purported deleterious effects of "old" (versus "fresh") red blood cells: are we at equipoise?

Eleftherios C. Vamvakas

BACKGROUND: A meta-analysis examined wh
the available data support an adequate suspici
transfusion of old red blood cells (RBCs) is ass
with increased mortality, organ failure, infection
longed mechanical ventilation, and prolonged s
the hospital or the intensive care unit. Such su
required for intentionally exposing patients enro
randomized controlled trials (RCTs) to the know
probable—but rare—risks of old RBCs, to docu
(and prevent) purported common adverse effec
RBCs.
STUDY DESIGN AND METHODS: Observatio
studies presenting adjusted results were eligibl
analysis if the adequacy of the adjustment for c
founding factors could be assessed. Three RC
24 observational studies were retrieved. Medic
statistically homogeneous studies were integrated by
fixed-effects methods. Otherwise homogeneous studies
conducted in different clinical settings were inte
by random-effects methods.
RESULTS: Based on "as-treated" analysis, tra
of old RBCs was associated with a significant
in mortality (summary odds ratio, 0.38; 95% co
interval, 0.14-0.99; $p < 0.05$) across two small
Integration of *adjusted* findings on the same ou
from observational studies conducted in the sa
setting, produced summary results that were e
negative (in six analyses) or impossible to eval
owing to uncontrolled confounding by the numb
transfused RBCs (in two analyses).
CONCLUSION: The available data do not supp
adequate suspicion that old RBCs may be associated
with common adverse morbidity and/or mortality outcomes, so as to justify exposing experimental subjects
to the other known or probable—but rare—risks of old
RBCs.

Transfusion of red blood cells (RBCs) stored for

non–WBC-reduced[19,20] RBCs to such adverse outcomes.
The biologic plausibility of this hypothesis,[15-19] and the

…there is a predictable association between the number of transfused RBCs and the length of storage of the oldest unit…Authors have erred overwhelmingly in the direction of not adjusting for the number of transfused RBCs.

Given the paucity of evidence on any association between transfusion of old RBCs and common adverse outcomes, the ongoing RCTs will most likely generate *null* findings….

From the Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California.
Address reprint requests to: Eleftherios C. Vamvakas, MD, PhD, Pathology and Laboratory Medicine, South Tower, Room 3733, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Los Angeles, CA 90048; e-mail: vamvakase@cshs.org.

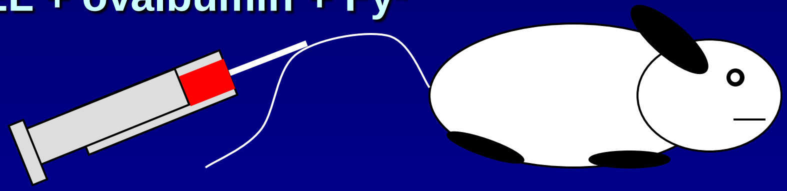
Received for publication June 17, 2009; revision received August 20, 2009; and accepted August 20, 2009.
doi: 10.1111/j.1537-2995.2009.02465.x
TRANSFUSION 2010;50:600-610.

- and then what?

A Simple Way Out?

Transfusion with transgenic RBCs

HOD: HEL + ovalbumin + Fy^b



Storage: | **In vitro cytokine analyses**

“Fresh” → Tolerated (No anti-HOD response)

“Old” (14d) → Cytokine “storm” + anti-HOD ↑ IL6, IL8,MCP-1

Fresh + Old → “Storm” blunted (but ↑ TNFα) ↓ anti-HOD Ab

MCP-1 = monocyte chemoattractant protein-1.

Hendrickson JE *et al. Transfusion* 2011;51:2695-702

What If? → Inventory Modeling

TRANSFUSION ORDER

↓

OLDEST BELOW THRESHOLD

↓ None younger?

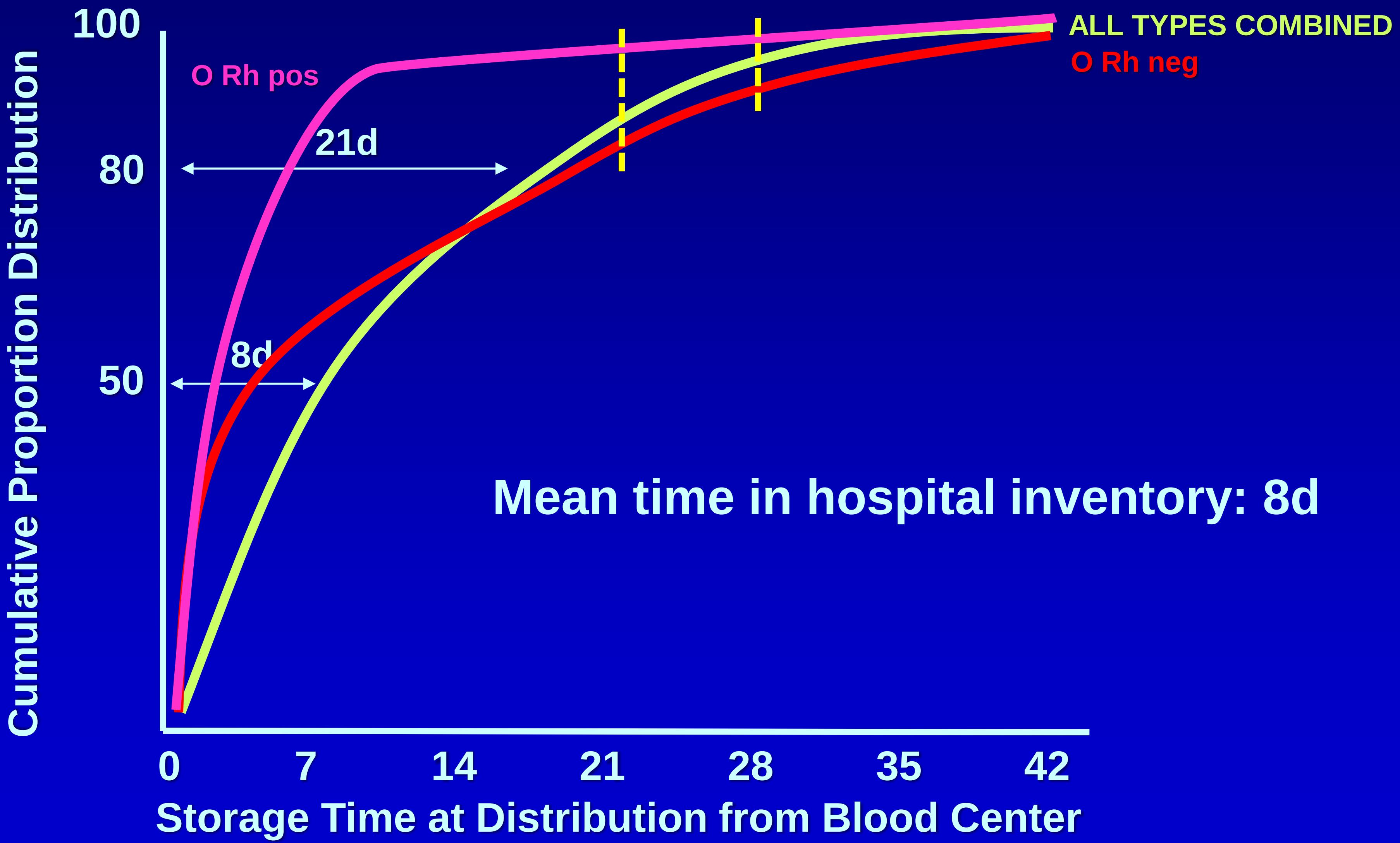
YOUNGEST OVER THRESHOLD

"Worked" in a *highly unusual, constrained* situation

Would it work across a regional system?

Atkinson MP *et al. Transfusion* 2012;52:108-17.

Regional RBC Distribution Patterns



Sayers M, Centilli J. *Transfusion* 2012;52:201-6.

What If? ➔ Inventory Coercion

Storage Period	Fee
2d	$400
3d	$390
4d	$380
⋮	⋮
10d	$320
⋮	⋮
21d	$210
⋮	⋮
41d	Free!

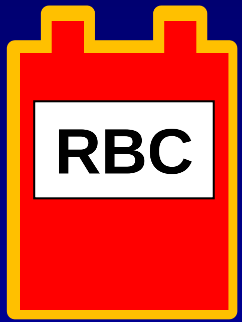
What About Donor Differences?

Some donors are “poor storers”

- GDP/GTP pathway?
- G6PD deficiency?

Female donors have lower hemolysis

The Gold-Plated Red Cell Unit



- O negative
- Genotypically matched (35 antigens)
- Selected donor (female?); HbS negative
- Leukoreduced
- Pathogen reduced/Prion reduced
- Optimal additive solution
- G6PD augmented
- Reducing environment/Hypoxic storage
- Storage with plasticizer without recipient effects
- Stored ≤ 7d
- Renitrosylated
- Washed/Filtered
- Qualified by functional parameters and biomarker analysis
- Transfused according to evidence-based decision making
- Followed by: Inhaled NO, ADAMTS-13 activator, anti-inflammatories, and a chaser of rHaptoglobin

Improved outcome – not longer storage

Predicting the Future

ABLE

RECESS

ARIPI

The power of one's own data is enormous.

The comprehension of statistics is minimal.

Secondary endpoint differences <u>will</u> be found.

REGULATORY INTEREST

CLINICIANS' INTEREST

Hospitals: Will it cost me less overall? ***Prove it!***

Experienced or Enfeebled?

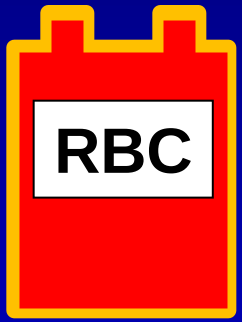
Does Red Cell Storage Time Affect Patient Outcome?

Yes, storage lesions are there…

…but what is their clinical significance, and what can we do about it?

Experienced or Enfeebled?

Does Red Cell Storage Time Affect Patient Outcome?



What parameters are most important in improving the quality of the red cells we transfuse?