

Blood Management Red Cell Transfusion

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April 8, 2010



Disclosure

- Dr. Thurer is an employee of the Haemonetics Corporation, Braintree, MA.

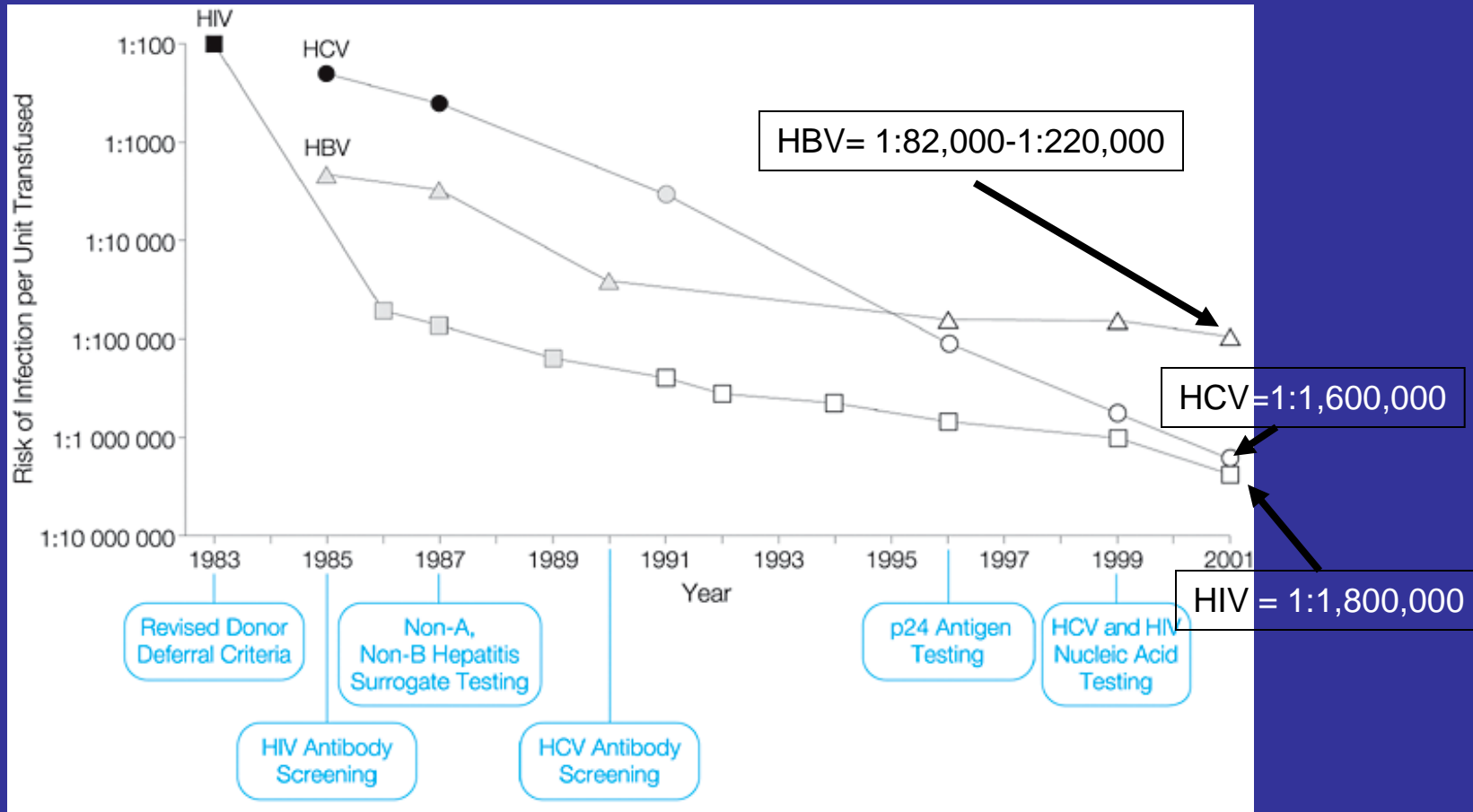


Objectives

- Risks of blood transfusion
 - Blood storage lesion
- Variability in the use of blood
- Are cardiac patients “special?”
- Proper utilization of RBC



Decline in Human Immunodeficiency Virus and Hepatitis B and Hepatitis C Risks of Transmission Through Transfusion



Busch MP, et al. *JAMA* 2003; 289:959-962



Transfusion-related Immunomodulation (TRIM)

- Transfusion of allogeneic blood results in the infusion of large amounts of foreign cells, antigens, and biological response modifiers
- Leads to at temporary suppression of the immune system due to transfusion
- Dose - response relationship
 - Increased risk of mortality
 - Increased risk of infection
 - Increased length of stay



Allogeneic Blood & Length of Stay

- 576 trauma patients enrolled after 48 hours in ICU
- 74% Male, Mean Age 44
- Mean APACHE II score = 16.9
- Baseline Hgb = 11.1 ± 2.4 g/dL
- 55% transfused
- Mean pretransfusion Hgb = 8.9 ± 1.8 g/dL

Dose Response for Length of Stay in Critical Care

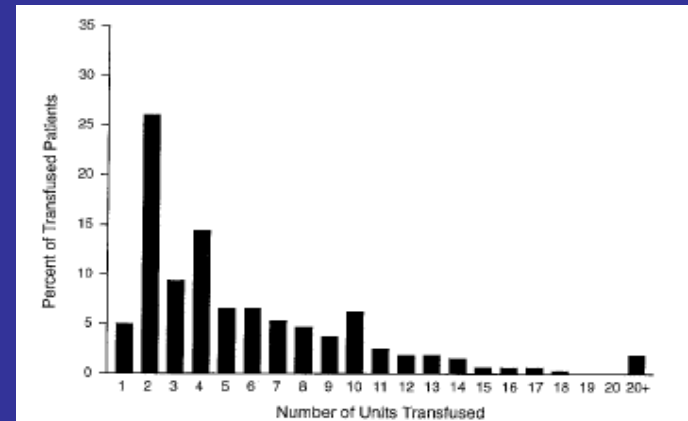
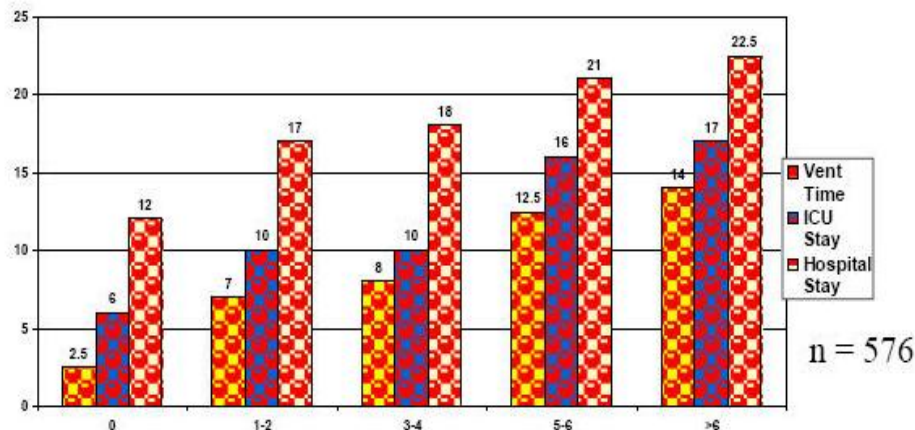


Fig. 1. Distribution of units transfused for transfused patients (in ICU).

Shapiro MJ, et al. *J Trauma* 2003; 55:269-73



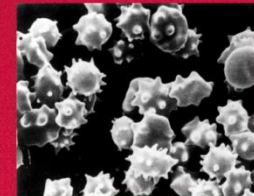
Blood Storage Lesion

- What is it?
 - RBC age more rapidly during refrigeration outside the body
 - At 24 hours, only 75% of the cells viable
 - ATP declines
 - RBC shape changes → stiffer
 - Loss of membrane lipid
 - 2, 3-DPG is undetectable at 1 week → 12-24 hours to regenerate after transfusion
- More difficult for RBC to deliver O₂ to tissues

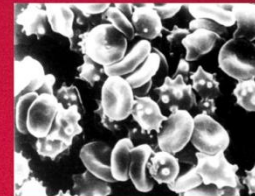
RBCs Change Shape During Storage¹



Day 1



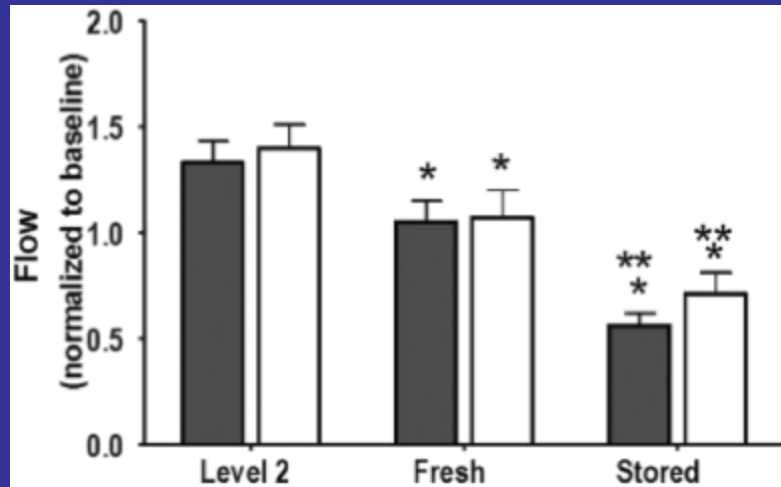
Day 21



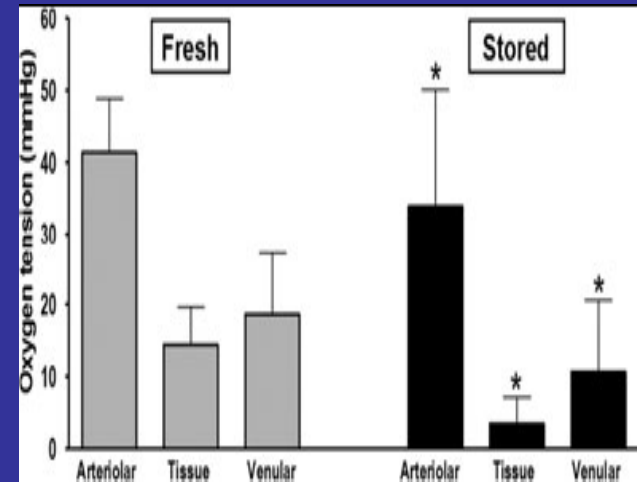
Day 35



Microvascular perfusion upon exchange transfusion with stored red blood cells in normovolemic anemic conditions (hamsters)



Changes in arteriolar (shaded bars) and venular (unshaded bars) blood flow after moderate hemodilution (Level 2) and in the two experimental groups: fresh and stored RBC.



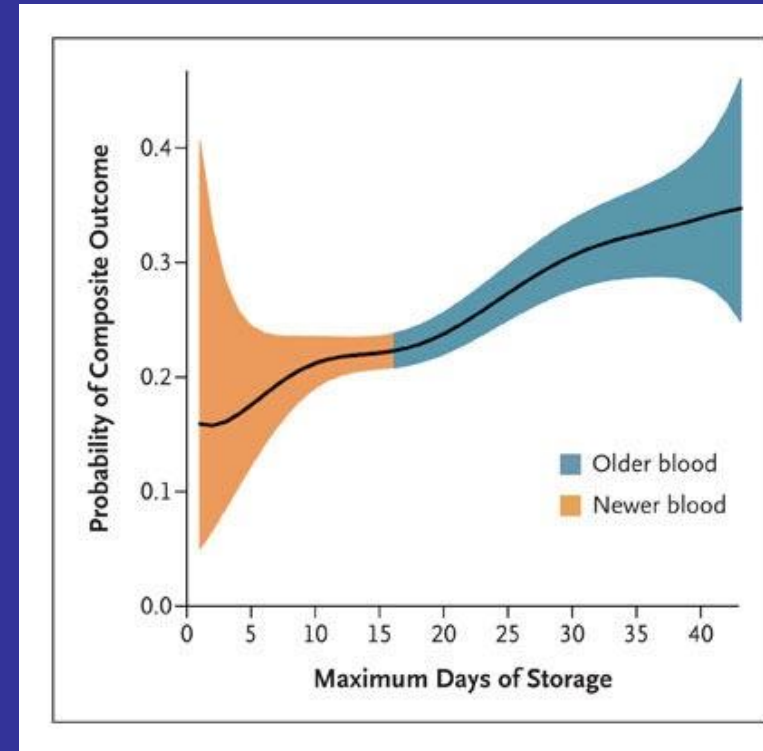
Comparison of microvascular oxygen distribution in arterioles, venules, and tissue after hemodilution and the two experimental groups: fresh (gray) and stored RBC (black).



“Old” RBC Worsen Clinical Outcomes

- All transfusions ≤ 14 Days 2,872 patients 8,802 units
- All transfusions ≥ 15 Days 3,130 patients 10,782 units

	≤ 14 Days	≥ 15 Days	p
In-hospital mortality	1.7%	2.8%	0.0004
Prolonged ventilation	5.6%	9.7%	0.001
Renal failure	1.6%	2.7%	0.003
1 year mortality	7%	11%	0.001

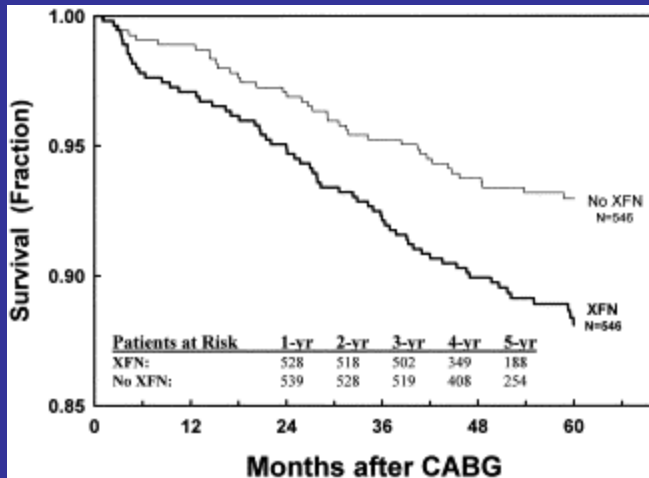


Koch CG, et al. *N Engl J Med* 2008; 358:1229-39



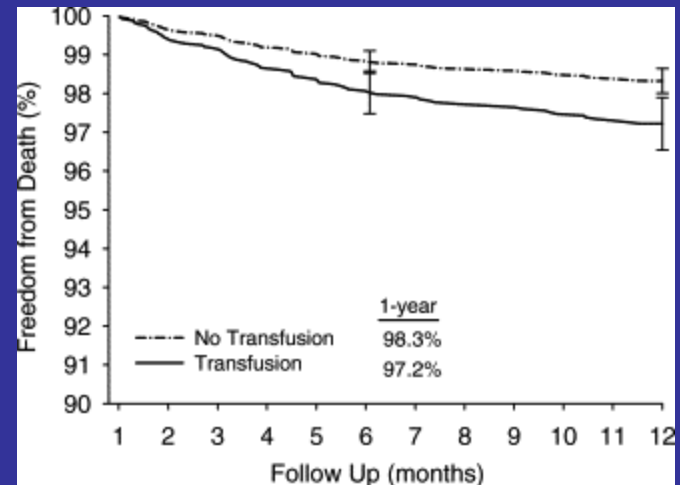
Effect of Blood Transfusion on Long-Term Survival After Cardiac Operation

- 1,915 first-time isolated coronary artery bypass patients (34% transfused)



Estimates of survival based on **equal propensity scores** of any transfusion (XFN) versus no transfusion (No XFN).

- 3024 consecutive isolated CABG patients 1999 – 2001 Liverpool, UK



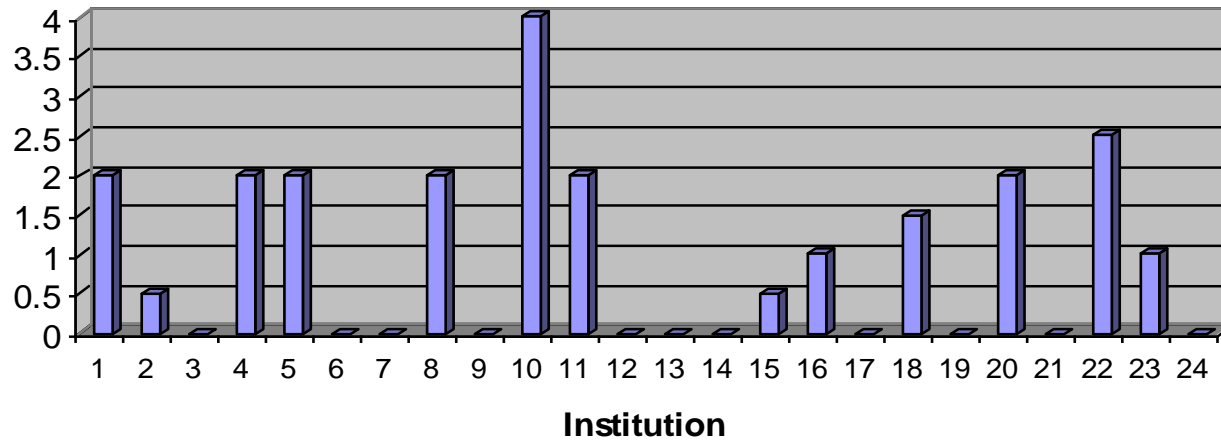
Risk adjusted survival following CABG - Excluding 30-day mortality

Engoren MC, et al. *Ann Thorac Surg* 2002; 74:1180–6

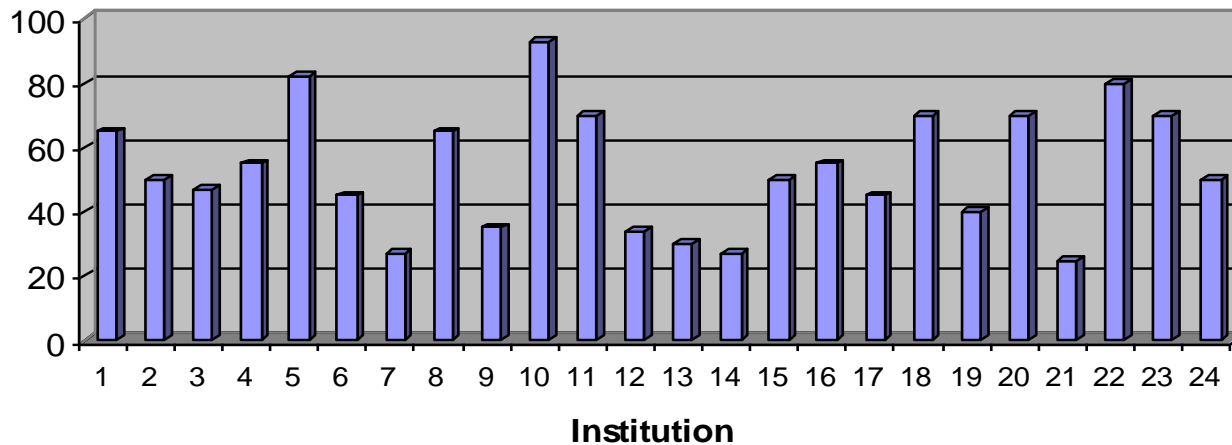
Kuduvalli M, et al. *Eur J Cardiothorac Surg* 2005; 27:592-8



Median Units Transfused



Percentage of Patients Receiving Transfusion



Variability of Blood Transfusion in Cardiac Surgery

Stover EP, et al. *Anesthesiology* 1998; 88:327-333

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Avoiding RBC transfusion

- Transfusion risks + lack of benefit + poorer outcomes in transfused patients + variability = need to avoid transfusion

HOW?

- Response to anemia
 - Increased cardiac output
 - Increased oxygen extraction
- Lower (eliminate) transfusion triggers
- Blood conservation strategies – limit blood loss, blood salvage, targeted treatment of coagulopathy, etc.



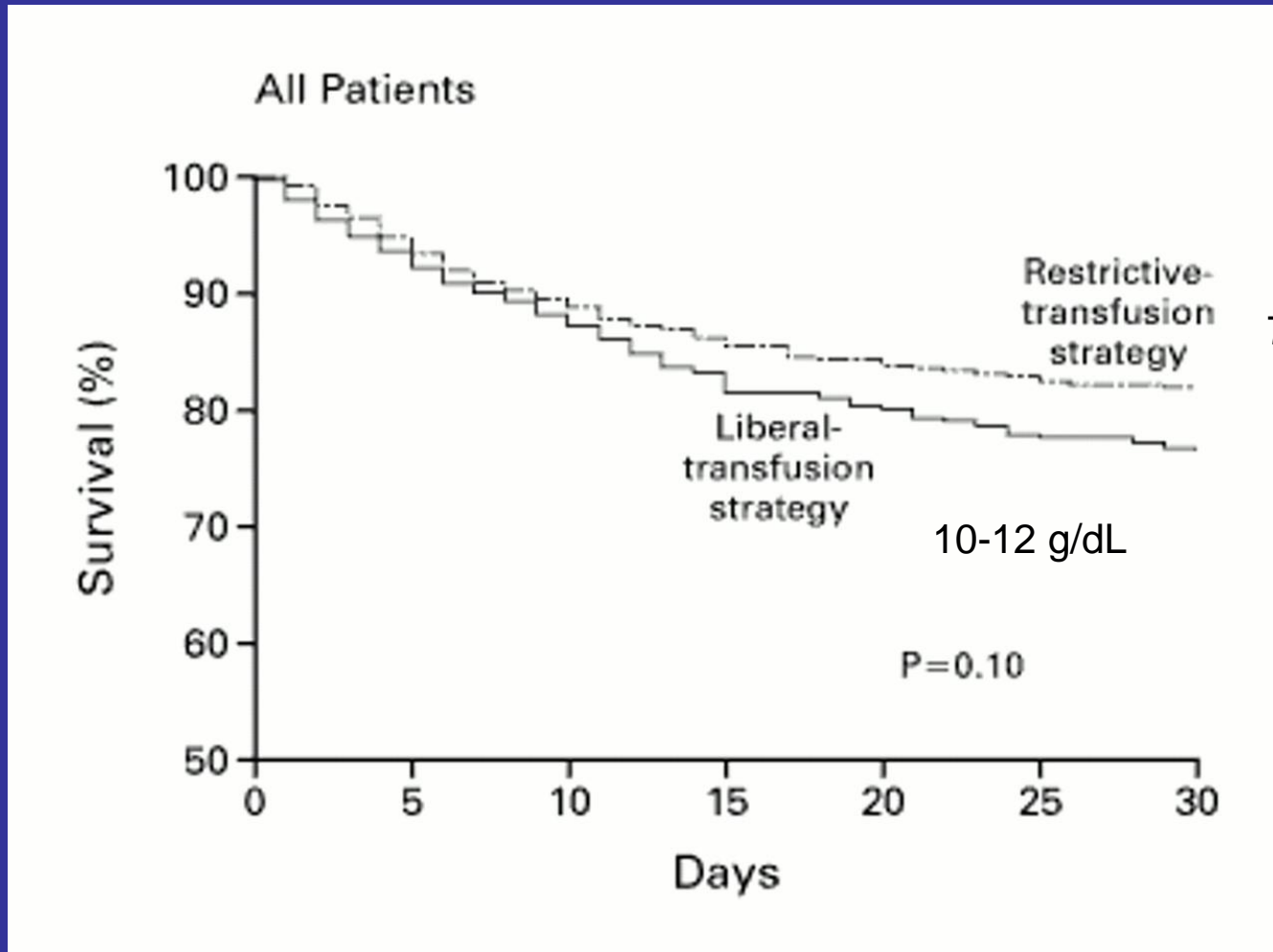
What About Hgb 6 – 10 g/dL?

- The use of allogeneic transfusion is variable
- Few randomized clinical trials (only 10 met criteria for Cochrane Review)
- **Carson JL, et al. Transfusion Triggers: A Systematic Review of the Literature. *Transfusion Medicine Reviews* 2002; 16:187-189**
 - Restrictive practice
 - Reduced the probability of receiving RBC by 48%
 - Reduced the volume of RBC received by 0.93 units
 - Hct values were 5.6% lower
 - Mortality, cardiac events, morbidity and LOS were not affected



TRICC Study

Kaplan-Meier Estimates of Survival in the 30 Days after Admission to the Intensive Care Unit in the Restrictive-Strategy and Liberal-Strategy Groups



Secondary end points in FOCUS trial

In-hospital events

End point	Liberal ^a , n=1005 (%)	Restrictive ^b , n=1008 (%)
Isolated troponin elevation	6.2	5.9
In-hospital mortality	2.0	1.4
MI, unstable angina, or death	4.3	5.2

a. Hgb 10g/dL threshold

b. Transfusion symptom driven (Hgb < 8.0 g/dL)



How should ischemic heart disease influence transfusion decisions?



- Anemia is an independent predictor of CV mortality, AMI, and recurrent ischemia in patients with acute coronary syndromes

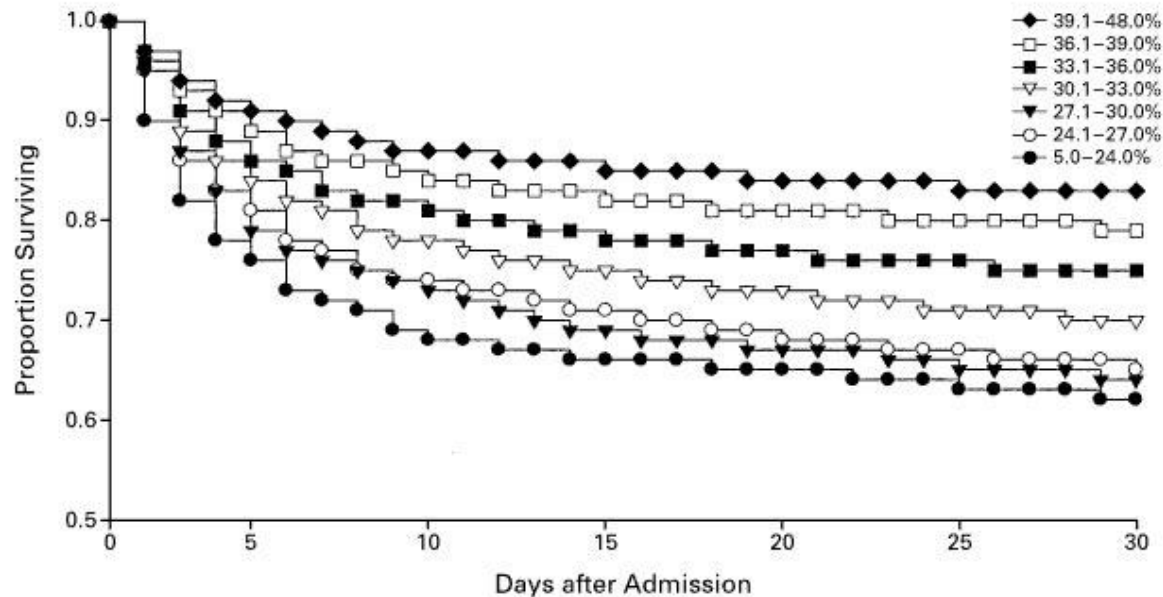
Wu WC, et al. *N Engl J Med* 2001; 345:1230-1236
Sabatine MS, et al. *Circulation* 2005; 111:2042-2049

Slides adapted from Gross I. Transfusion “triggers” in ischemic heart disease. SABM 2009 New England Regional Blood Management Conference



Kaplan-Meier 30-Day Survival Curves According to Hematocrit Category

78,974 patients with acute myocardial infarction



HEMATOCRIT CATEGORY	no. (%) at risk						
5.0-24.0%	380 (100.0)	277 (72.9)	257 (67.6)	250 (65.8)	247 (65.0)	240 (63.2)	233 (61.3)
24.1-27.0%	838 (100.0)	655 (78.2)	611 (72.9)	587 (70.0)	570 (68.0)	557 (66.5)	543 (64.8)
27.1-30.0%	2,106 (100.0)	1,618 (76.8)	1,507 (71.6)	1,442 (68.5)	1,405 (66.7)	1,375 (65.3)	1,350 (64.1)
30.1-33.0%	4,848 (100.0)	3,972 (81.9)	3,727 (76.9)	3,597 (74.2)	3,508 (72.4)	3,437 (70.9)	3,392 (70.0)
33.1-36.0%	9,885 (100.0)	8,382 (84.8)	7,938 (80.3)	7,692 (77.8)	7,559 (76.5)	7,456 (75.4)	7,353 (74.4)
36.1-39.0%	16,218 (100.0)	14,176 (87.4)	13,589 (83.8)	13,294 (82.0)	13,091 (80.7)	12,950 (79.8)	12,825 (79.1)
39.1-48.0%	44,699 (100.0)	40,132 (89.8)	38,670 (86.5)	38,007 (85.0)	37,544 (84.0)	37,267 (83.4)	37,002 (82.8)



The NEW ENGLAND
JOURNAL of MEDICINE



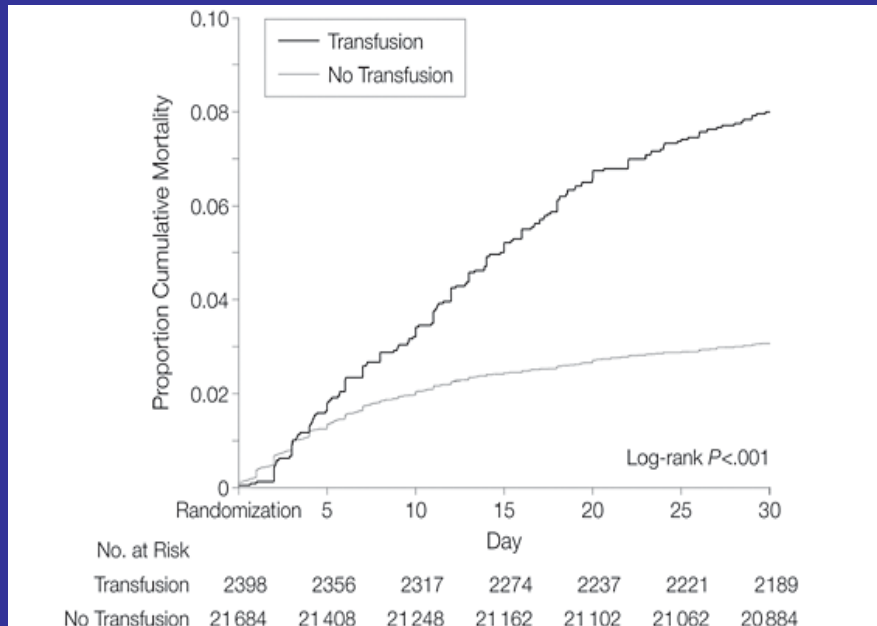
The Heart's Response to Anemia

- Anaerobic metabolic state.
- Coronary blood flow is shifted from the endocardium to the epicardium
- Increased risk of ischemia and subendocardial infarction.

Does transfusion improve the outcome of IHD patients with anemia?



Relationship of Blood Transfusion and Clinical Outcomes in Patients with Acute Coronary Syndromes



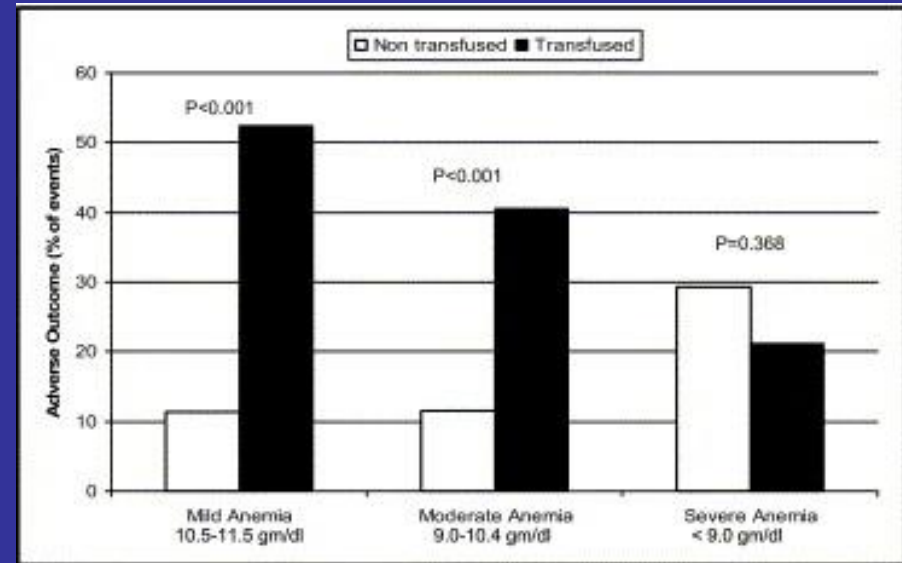
Kaplan-Meier Estimates of 30-Day Mortality Among Patients Who Did and Did Not Receive Blood Transfusion

- Retrospective analysis of 24,112 patients (GUSTO, PURSUIT, PARAGON B)
- Utilized Cox proportional hazards modeling that incorporated transfusion as a time-dependent covariate
- Transfusion was associated with an **adjusted hazard ratio** for death of 3.94 (3.26-4.25)
- Probability of 30-day mortality was higher with transfusion at nadir Hct > 25%.
- No association below Hct = 25%



Impact of Blood Transfusions in Patients Presenting with Anemia and Suspected Acute Coronary Syndrome

- Prospective registry of patients with ACS/non-STEMI
 - 1,410 patients, 370 anemic on presentation
 - 110/370 (30%) transfused
- Transfusion was associated with a **risk adjusted** odds ratio for 30 day recurrent MI or death of 2.57



Multivariate analysis for predictors of death or myocardial infarction at 30 days

Variable	Odds Ratio	95% Confidence Interval	p Value
Pulmonary edema at admission	2.51	1.27–4.96	0.008
Systolic blood pressure < 90 mm Hg	3.05	1.70–5.45	0.001
↑ Troponin	3.48	1.75–6.92	0.001
Red blood cell transfusion	2.57	1.41–4.69	0.001

Singla I, et al. *Am J Cardiol* 2007; 99:1119-21



Surgical Transfusion Decision

- History - anemia, hematologic disorders
- Meds - antiplatelet, anticoagulants
- Symptoms - dyspnea, angina
- Oxygen delivery/consumption
 - Oxygen saturation
 - Oxygen extraction
 - Serum lactate
 - Base deficit
- Procedure/Estimated blood loss
- Potential for continuing blood loss
- Anesthetized patients
 - Increase in cardiac output mostly from increase in stroke volume
- Awake patients
 - Increase in cardiac output from increases in both heart rate and stroke volume

