

# Transfusion Trigger and Erythropoietin Stimulating Agents

Jeffrey L. Carson, M.D.

Richard C. Reynolds Professor of Medicine  
Chief, Division of General Internal Medicine  
Robert Wood Johnson Medical School  
New Brunswick, New Jersey, USA

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# Presentation Outline

- Framework for transfusion decision
- Side effects of RBC transfusion
- Effect of anemia on mortality and morbidity
- Effect of blood transfusion on mortality and morbidity
  - Clinical trials
- Generalizability to ESA's

Transfuse vs No Transfuse

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graph TD; A[Transfuse vs No Transfuse] --> B[Benefit]; A --> C[Risks]; B --> D[Mortality]; D --> E[Morbidity]; E --> F[Functional Recovery]; C --> G[Blood Side Effects]; G --> H[Risks from Anemia];
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Benefit

Mortality

Morbidity

Functional Recovery

Risks

Blood Side  
Effects

Risks from Anemia

# Side Effects of Allogeneic Transfusion

	Estimated Risk
Urticaria or skin reaction	1 in 50-100
Febrile reaction	1 in 300
TRALI	1 in 5000
Hemolytic reaction	1 in 6000
Mistransfusion	1 in 14,000-19,000
Anaphylaxis	1 in 20,000-50,000
Hepatitis B	1 in 100,000-200,000
Fatal hemolysis	1 in 1 million
Hepatitis C	1 in 1-2 million
HIV	1 in 2-3 million

## Adverse Effects of RBC

Klein HG, Spahn DR, Carson JL Red Cell Transfusion in Clinical Practice. Lancet 2007

# Risk of Anemia

# Anemia in Animals

Group	Event	Hgb (g/dL)
Normal	ST segment changes	< 5
	Lactate production	< 3
	↓ Ventricular function	< 3
	Death	< 3
CAD	ST segment changes	7-10

# Effect of Anemia and CVD on Surgical Mortality and Morbidity

- Retrospective cohort study of patients who refuse blood transfusion for religious reasons
- Outcome-30-day mortality or morbidity
- CVD- patient with history of MI, angina, CHF, or PVD
- 1,958 patients age 18 or older

Carson JL, et al. Lancet 1996;348:1055-60

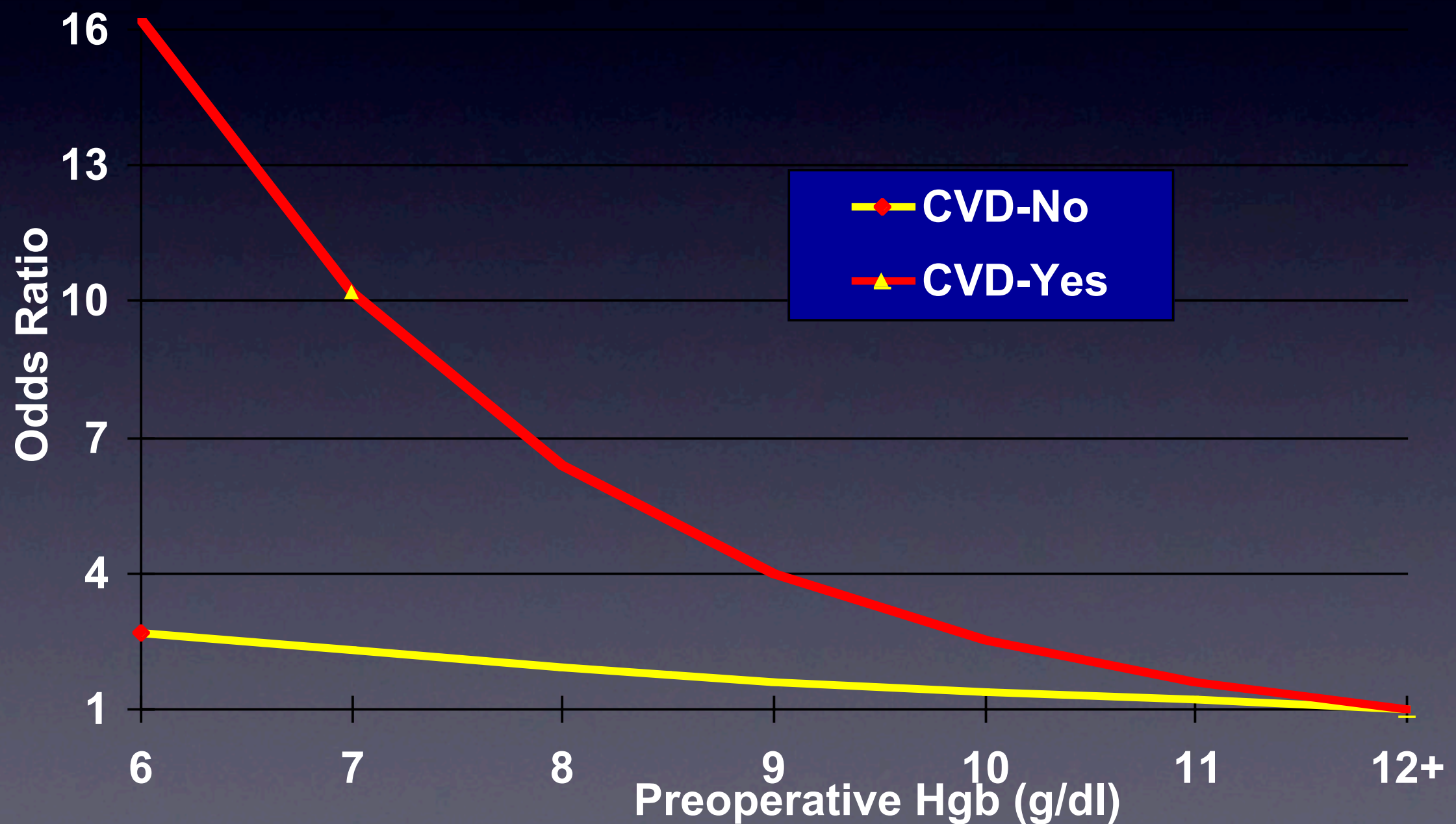


# Preop Hgb and Mortality

Preop Hgb	N	% Dead	95% CI
0-5.9	36	33.3	18.6-51.0
6.0-6.9	27	18.5	6.3-38.1
7.0-7.9	49	12.2	4.6-24.7
8.0-8.9	39	12.8	4.3-27.4
9.0-9.9	75	8.0	3.0-16.6
10.0-10.9	109	4.6	1.5-10.4
11.0-11.9	212	2.4	0.8-5.4
12+	1411	1.3	0.8-2.0

Carson JL, et al. Lancet 1996;348:1055-60

# Preop Hgb by Cardiovascular Disease Interaction $P=0.03$



# Postop Hgb Level and Mortality in Patients with Hgb < 8 g/dL

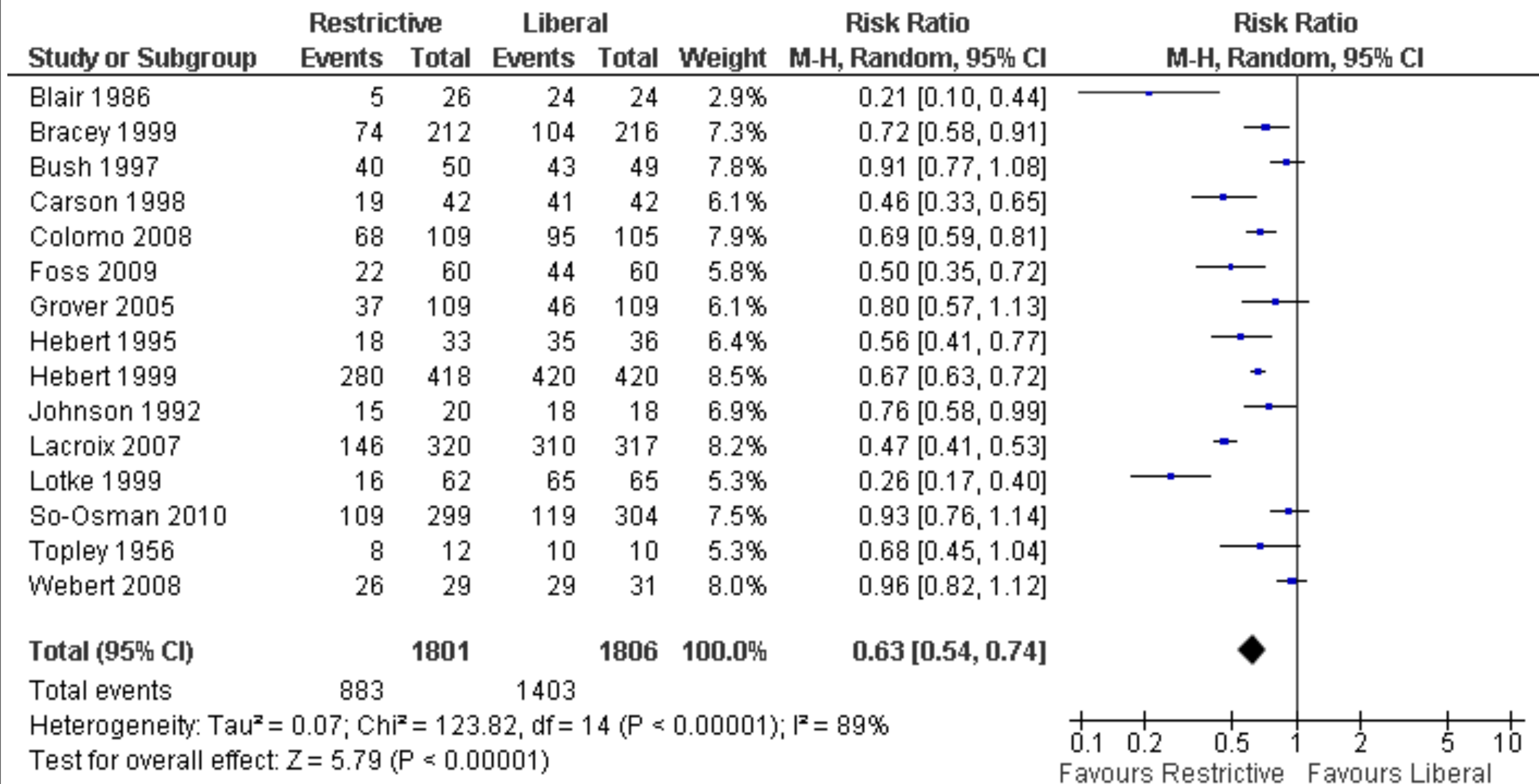
Postop Hgb	N(300)	% 30 day Mortality	% 30 day Mortality Morbidity
1.1-2	7	100	100
2.1-3	24	54.2	91.7
3.1-4	28	25	52.6
4.1-5	32	34.4	57.7
5.1-6	54	9.3	28.6
6.1-7	56	8.9	22
7.1-8	99	0	9.4

Carson JL, et al. Transfusion 2002

# Conclusions-Risk of Anemia

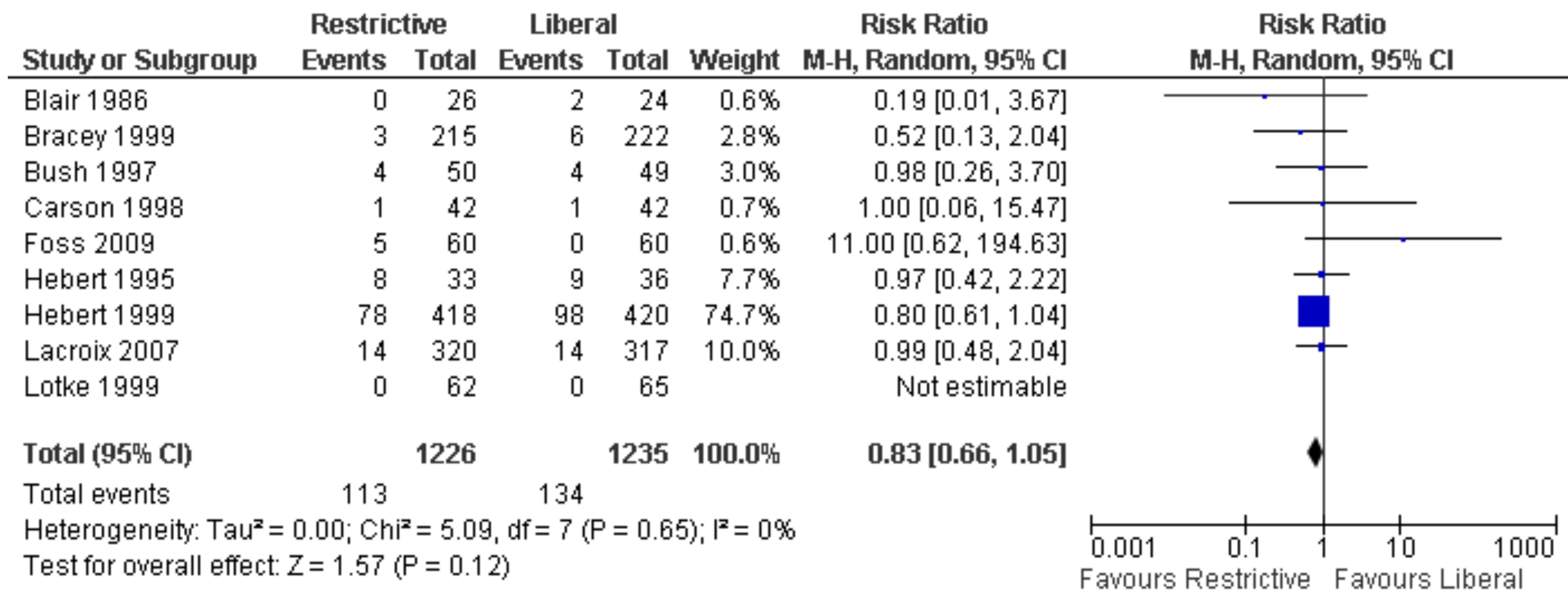
- Mortality and morbidity rises as preoperative hemoglobin falls
- Animal and human data suggest that patients with CVD may be less tolerant of anemia than patients without CVD

# Efficacy of Transfusion Clinical Trials



# Exposure to Blood Transfusion

Carless P, Henry D, Carson JL, Hebert PC, McClelland, B Ker K. Cochrane Database of Systematic Reviews 2010



# 30-Day Mortality

Carless P, Henry D, Carson JL, Hebert PC, McClelland, B Ker K. Cochrane Database of Systematic Reviews 2010

# Transfusion in Critical Care

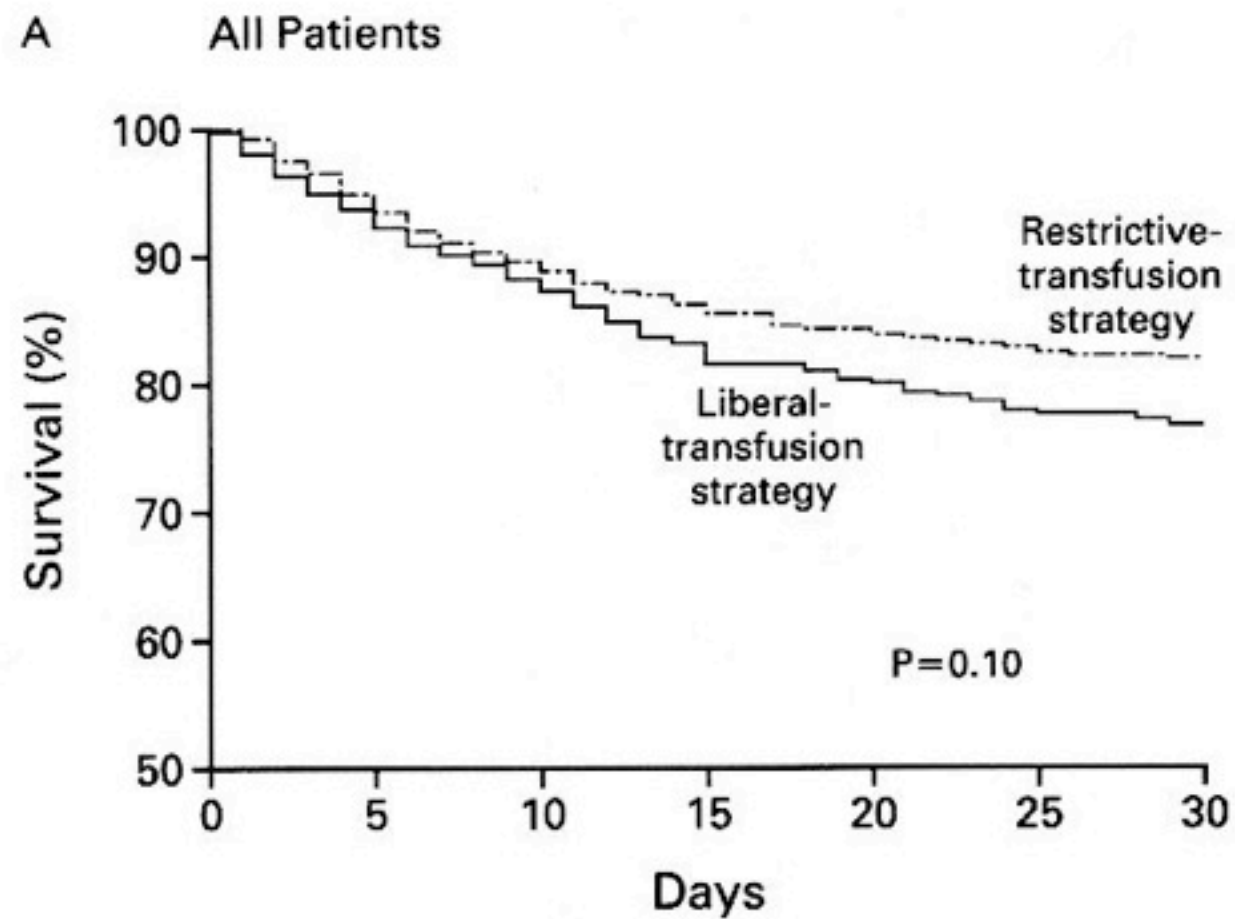
- Clinical trial in consecutive ICU patients with Hgb < 9.0 g/dL and euvolemia
- Restrictive: blood given when Hgb < 7.0 g/dL and maintained between 7-9 g/dL
- Liberal: blood given when Hgb < 10 g/dL and maintained between 10-12 g/dL
- Primary outcome 30 day mortality

Hebert et al NEJM 1999

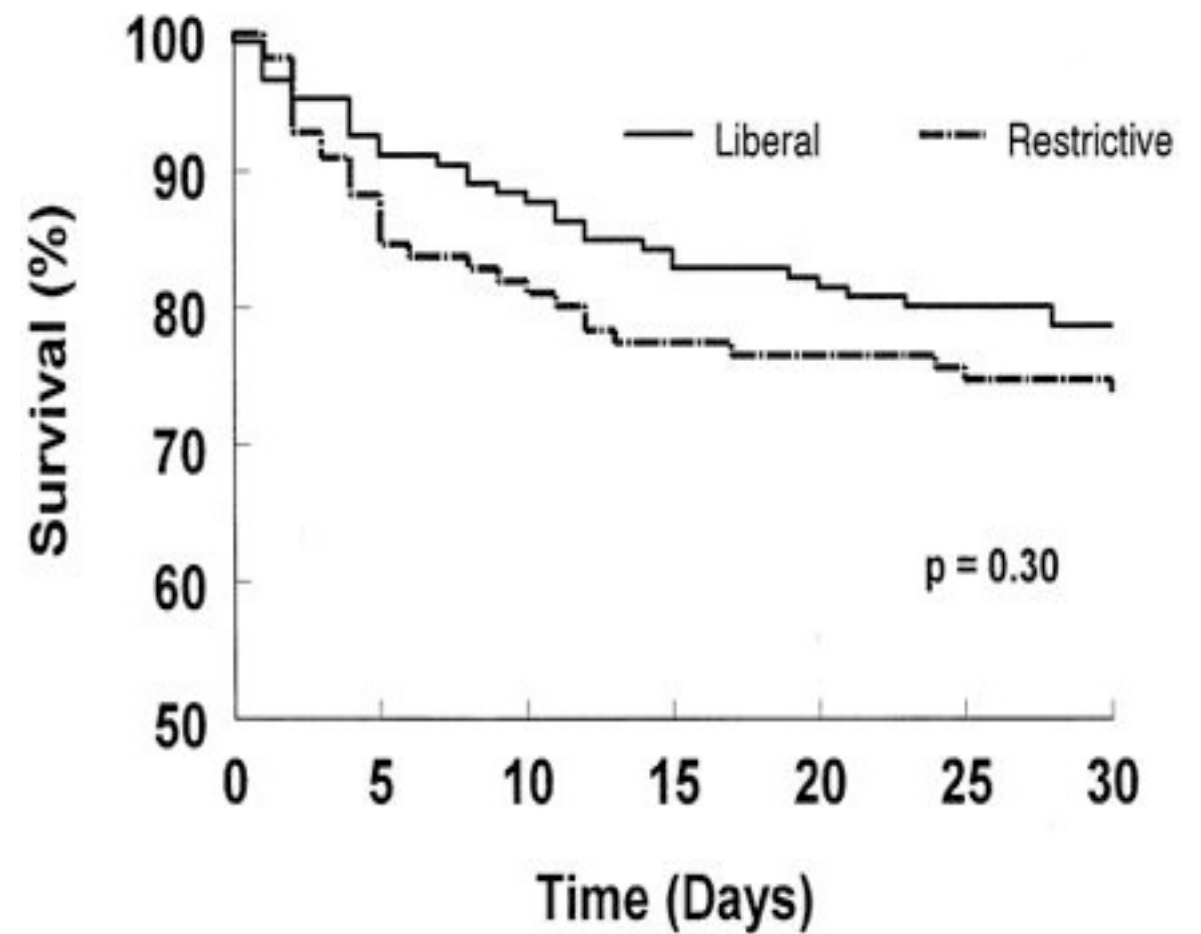


# Outcomes TRICC Trial

Outcome	Restrictive N=418	Liberal N=420	Difference (95% CI)
30 day death	18.7%	23.3%	4.7% (0.8-10.2)



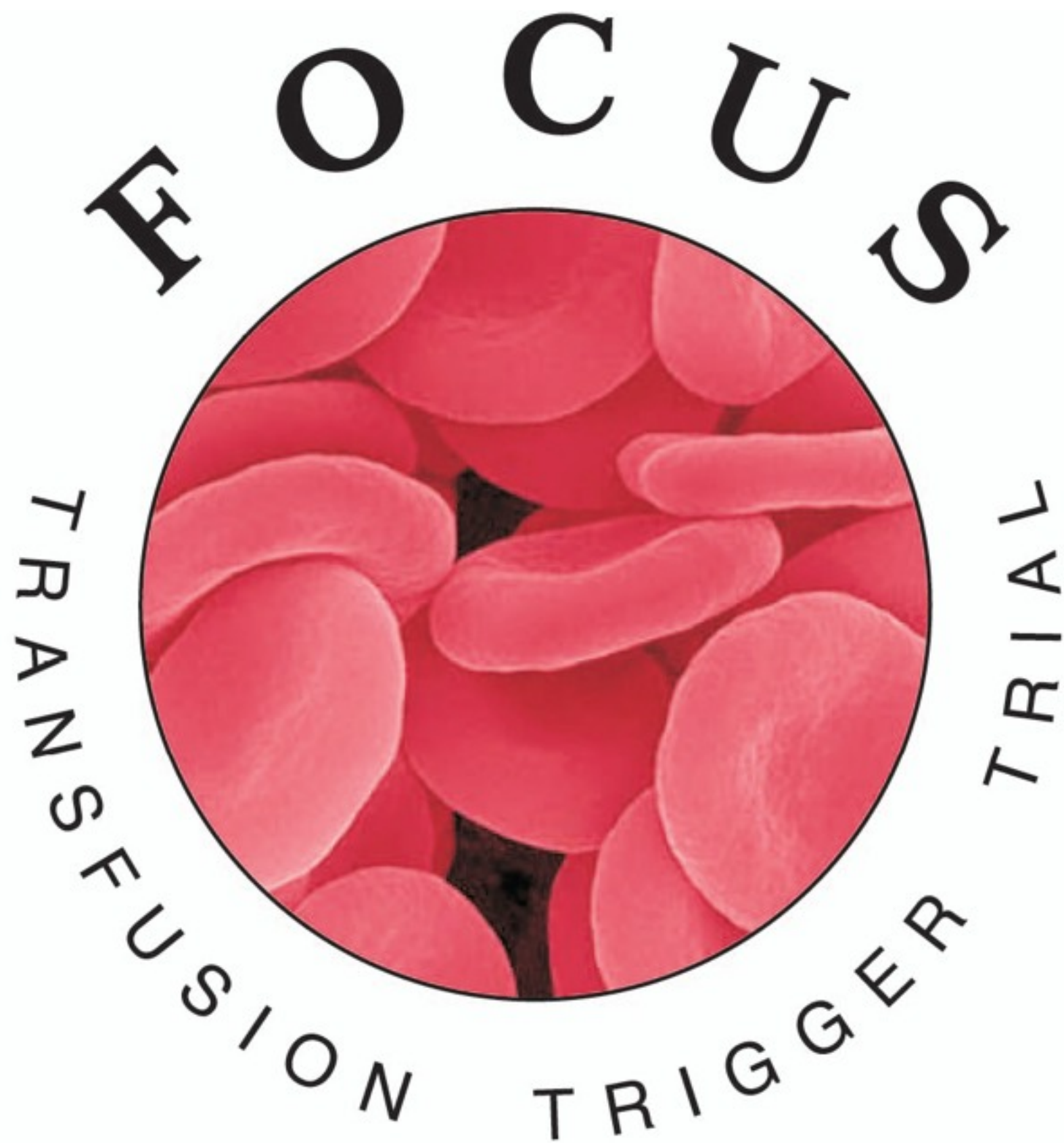
Overall



Ischemic Heart Disease

# Morbidity Outcomes in TRICC

	Restrictive N (%)	Liberal N (%)	P Value
MI	3 (0.7)	12 (2.9)	0.02
Pulmonary Edema	22 (5.3)	45 (10.7)	0.01
ARDS	32 (7.7)	48 (11.4)	0.06



# FOCUS Methods

- RCT in hip fracture patients
- CVD or CVD risk factors
- Hemoglobin < 10 g/dL
- Liberal (10 g/dL) vs Restrictive (Symptomatic) Transfusion
- Function, mortality, myocardial infarction, morbidity
- 2016 patients from 47 centers in US and Canada

**Unpublished FOCUS  
Results Will Be Presented  
at the Meeting**

# Generalizability to ESA's?

# Clinical Differences

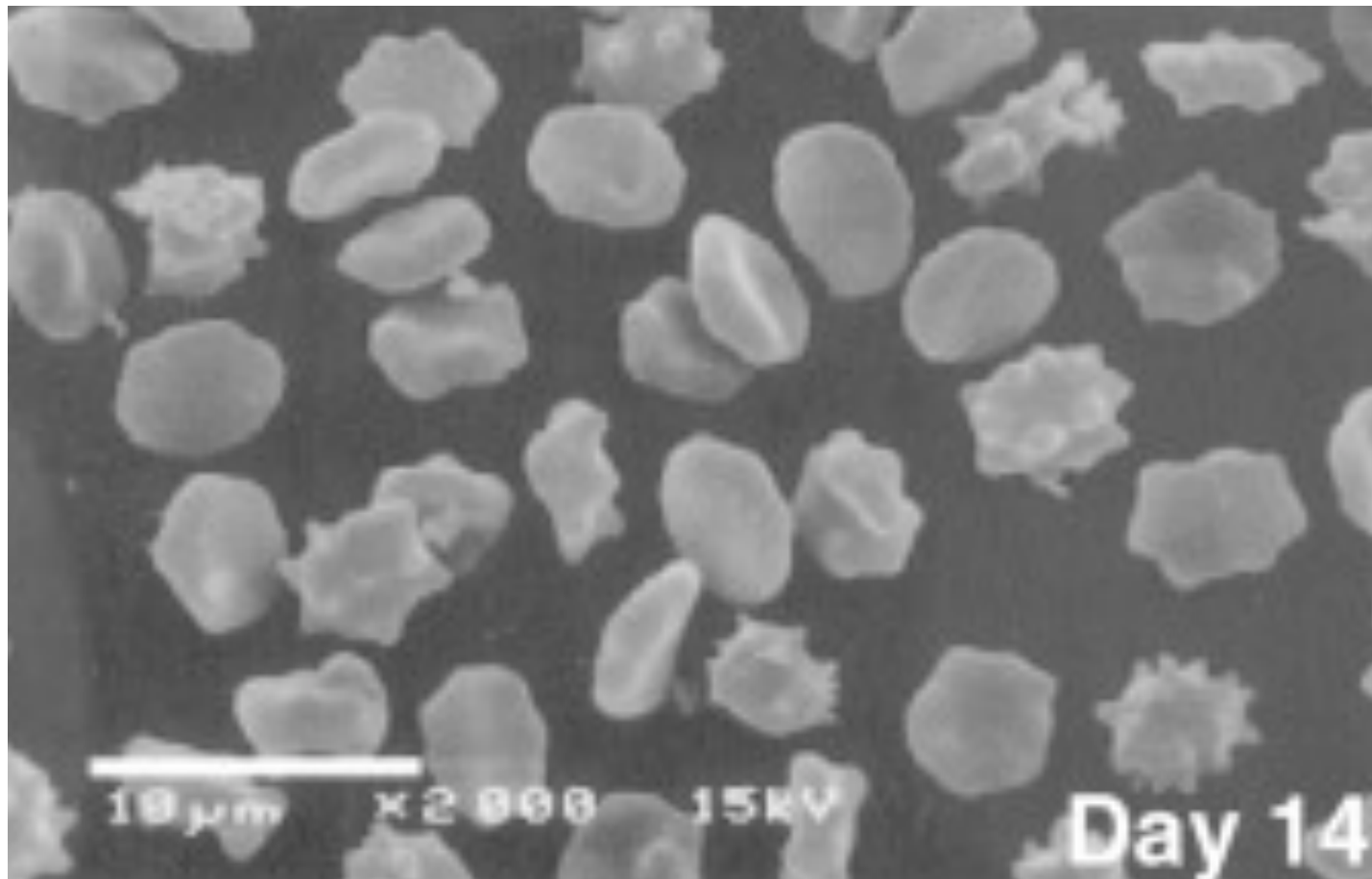
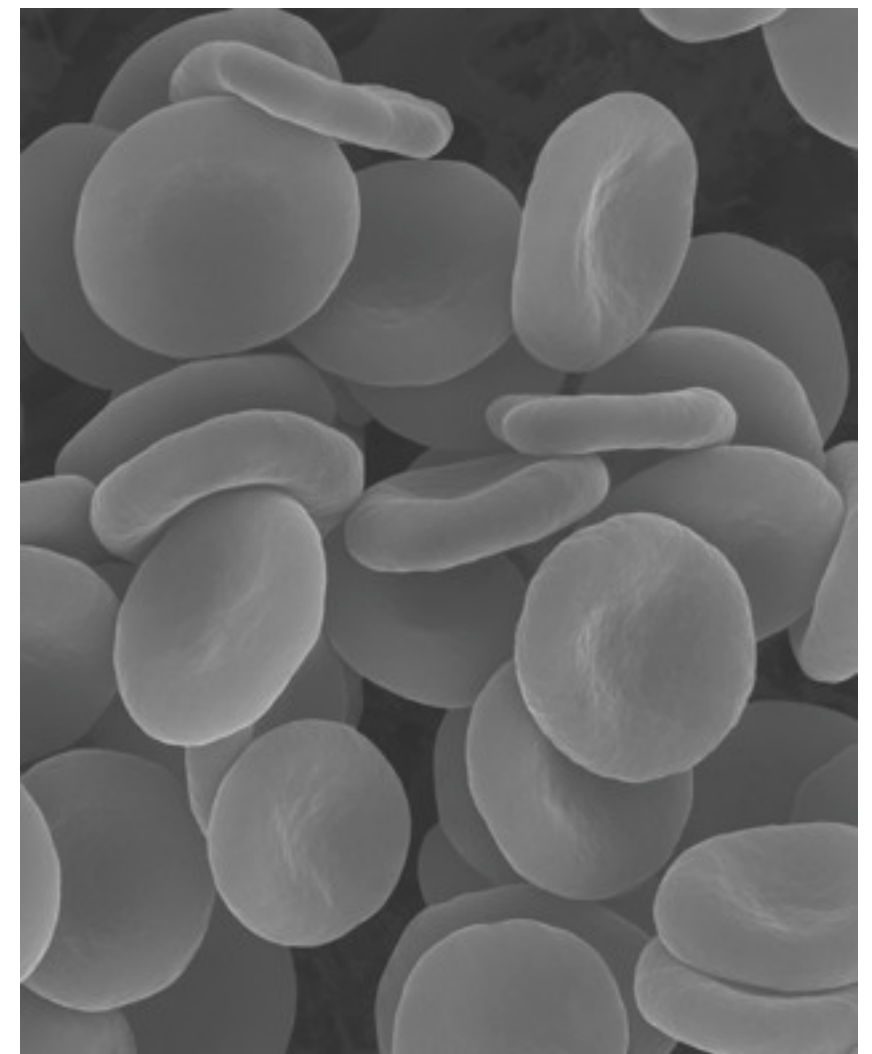
	Transfusion	Erythropoietin Stimulating Agents
Anemia	Acute	Chronic
Time Course	Short-term	Long-term
Outcomes	Mortality Morbidity (MI, CHF, Infection) Function Transfusion Fatigue	Transfusion Fatigue Function Morbidity (MI, CHF, Clot) Mortality



# Clinical Differences

	Transfusion	Erythropoietin Stimulating Agents
Side Effects	Infections (Viral) Infections (Bacterial) TRALI TACO Hemolytic Allergic	Thrombosis Stroke Cancer progression

# Fresh



# Stored

# Overall Summary

- The risk of transfusion appears to be low
- Patients with cardiovascular disease appear to be less tolerant of anemia
- Clinical trials.....
- The generalizability of transfusion data to ESA's is uncertain because of differences in potential benefits and risks, and time course of anemia