2025 Korean Society for Patient Blood Management Annual Symposium
10:00-10:20, Oct 24 2025
Session: Big Concerns and Controversies in PBM

Liberal vs. Restrictive Strategies: Strategies in MI

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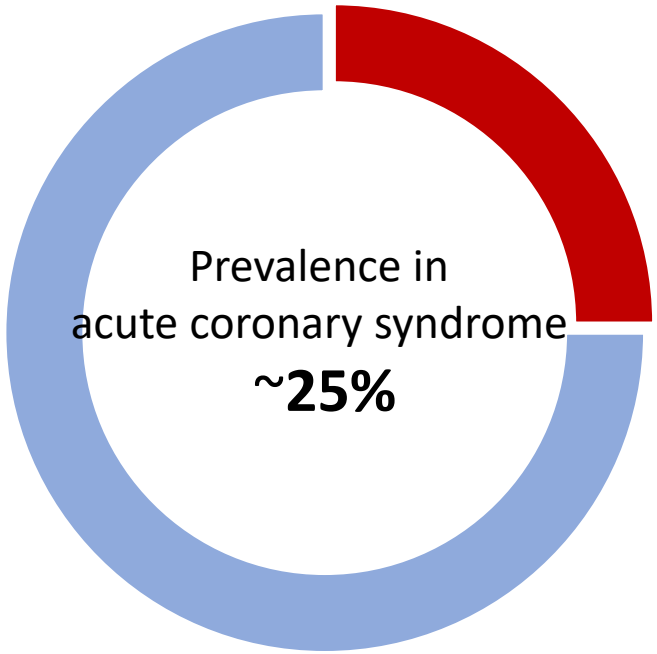
Prevalence and Impact of Anemia in AMI



OR & 95% CI for CV Death by 30 d

Hgb (g/dl)	n	*Unadjusted* OR	(95% CI)	*Adjusted for Baseline Characteristics* OR	(95% CI)	P value
>17	968	1.27	(0.90-1.79)	1.79	(1.18-2.71)	0.007
16-17	2783	0.85	(0.65-1.10)	1.08	(0.78-1.52)	0.637
15-16	5702	0.86	(0.70-1.05)	1.08	(0.84-1.39)	0.5302
14-15	6926	1.0	*reference*	1.0	*reference*	
13-14	5077	1.47	(1.22-1.77)	1.17	(0.93-1.47)	0.175
12-13	2502	2.22	(1.82-2.72)	1.40	(1.09-1.80)	0.009
11-12	962	3.29	(2.57-4.21)	1.63	(1.19-2.24)	0.003
10-11	288	3.97	(2.71-5.82)	1.98	(1.24-3.15)	0.004
<10	191	5.07	(3.32-7.73)	2.50	(1.42-4.39)	0.001

1. *Circulation*. 2005;111:2042–2049.

Observed Impact of RBC Transfusion in AMI

US national inpatient sample (NIS) selected by diagnostic code

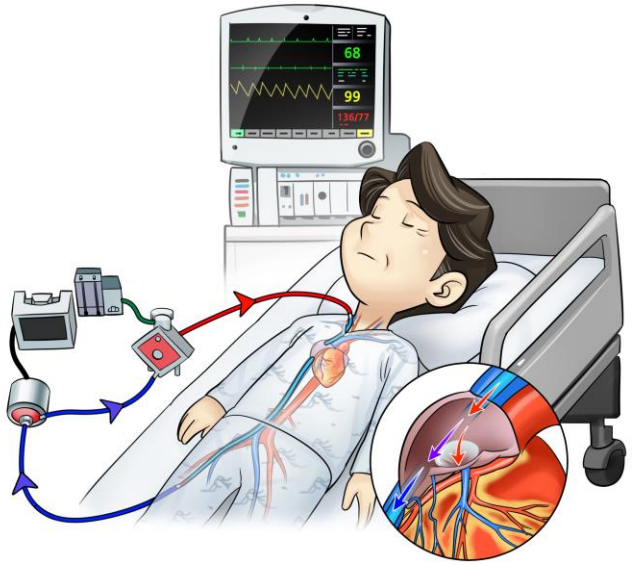
Effect of RBC transfusion on inpatient adverse events, mortality and resource utilization (n = 254,816).

	RBC transfusion		
	No (n = 208,171)	Yes (n = 46,645)	p-value
Length of stay (days), mean (SD)	7.37 (7.62)	10.69 (8.91)	< 0.001
Total cost ($), mean (SD)	31,400 (35,973)	44,100 (38,886)	< 0.001
Total charge ($), mean (SD)	134,212 (170,286)	187,519 (189,898)	< 0.001
Adverse Events, n (%)			
Any	111,586 (53.6)	29,112 (62.4)	< 0.001
Acute kidney injury	69,939 (33.6)	19,765 (42.4)	< 0.001
Cardiac arrest	8688 (4.2)	2437 (5.2)	< 0.001
Cardiogenic shock	16,472 (7.9)	4506 (9.7)	< 0.001
Hemorrhagic stroke	300 (0.1)	76 (0.2)	< 0.001
Ischemic stroke	3901 (1.9)	1163 (2.5)	< 0.001
TIA	882 (0.4)	227 (0.5)	< 0.001
Acute heart failure	63,960 (30.7)	16,310 (35.0)	< 0.001
Mortality, n (%)	14,261 (6.9)	3941(8.4)	< 0.001

Possible **reverse causality** due to disease severity and patient's clinical condition

Simple AMI and PCI

vs.



AMI requiring ECMO and CABG

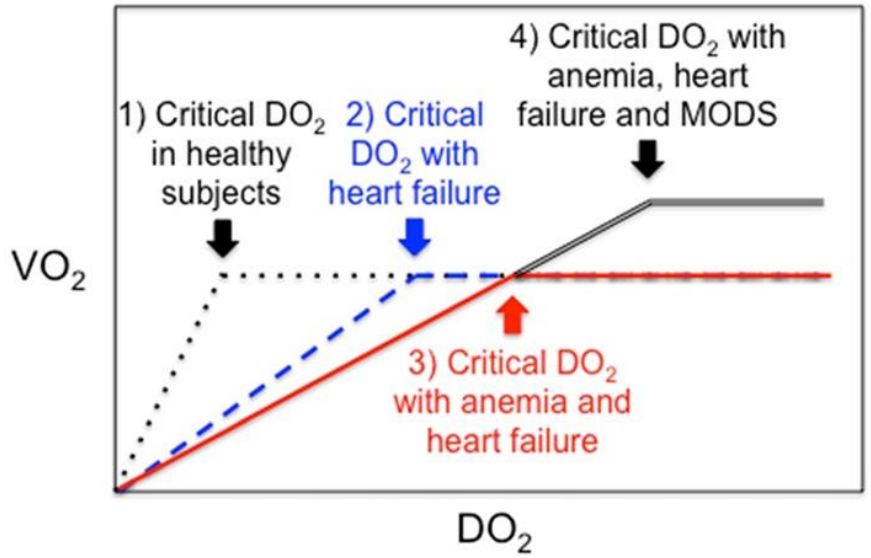
- Pneumonia combined with ABx use
- Numerous additional medications
- Bleeding, …

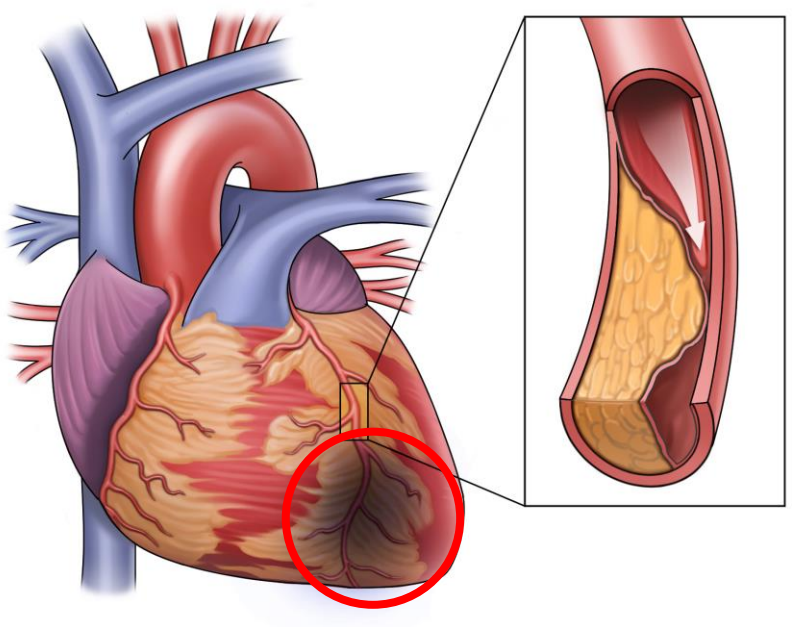
1. *Int J Cardiol*. 2024;408:132111.

Mechanistic Aspects: Pros

DO2 (oxygen delivery) = Q (cardiac output) X CaO2 (arterial oxygen concentration)

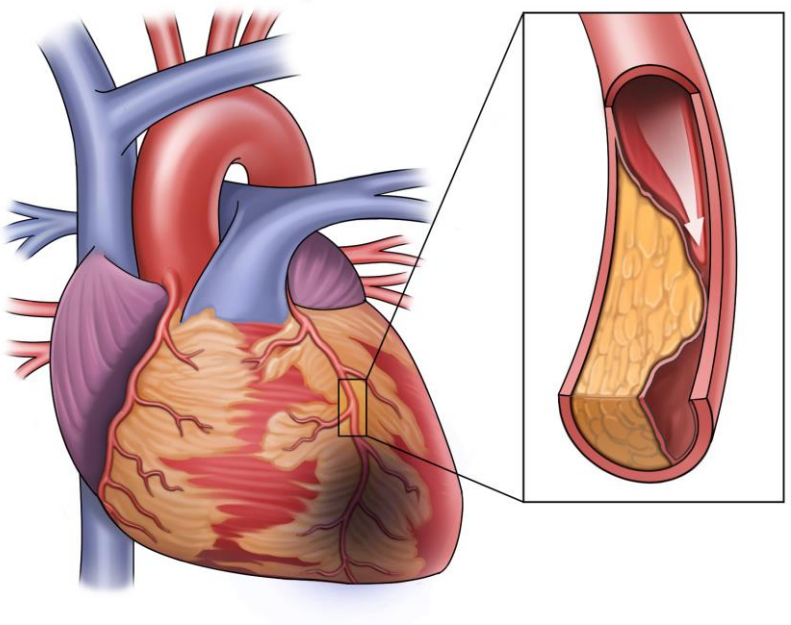
Anemia patients	② compensatory increase in CO	① Hb drops
AMI + anemia	↓ decrease in CO	↓ Hb drops



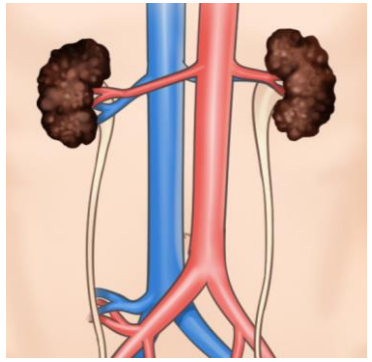


1. *Ann Intensive Care*. 2014;4:1

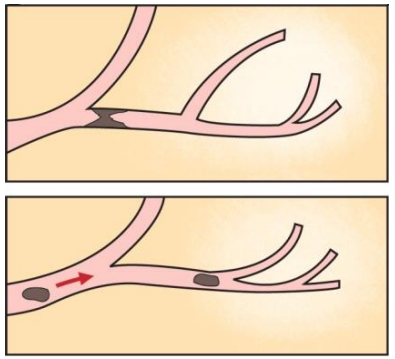
Mechanistic Aspects: Cons



Volume overload



Kidney, lung injury



Thrombosis due to increased viscosity

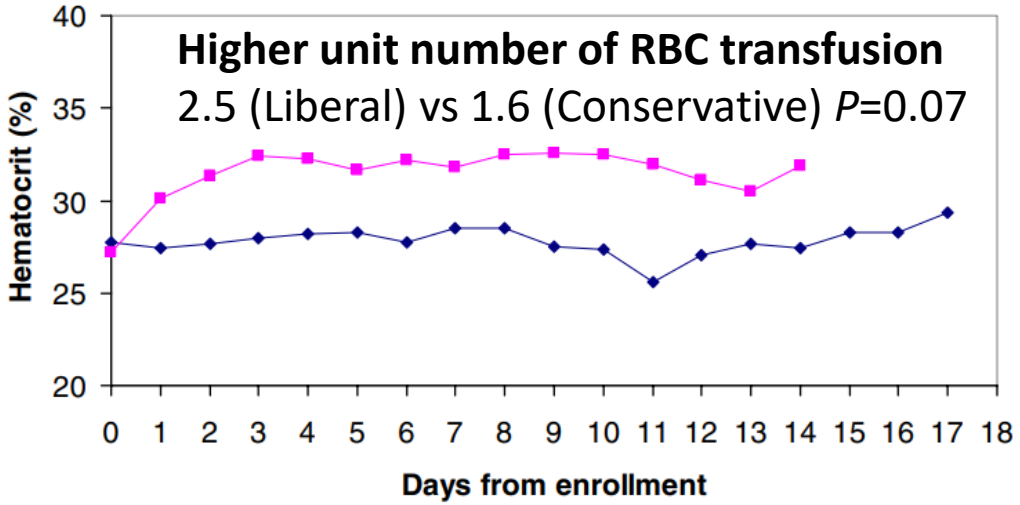
More transfusion needed, higher cost

Early Prospective Randomized Pilot Trials

Conservative Versus Liberal Red Cell Transfusion in Acute Myocardial Infarction (the CRIT Randomized Pilot Study)

Howard A. Cooper, MD[a,*], Sunil V. Rao, MD[b], Michael D. Greenberg, MD[c], Maria P. Rumsey, MD[a], Marcus McKenzie, MD[a], Kirsten W. Alcorn, MD[a], and Julio A. Panza, MD[a]

Liberal: HCT target 30%
Conservative: HCT target 24%



	Liberal (N=21)	Conservative (N=24)	*P*
In-hospital death, recurrent MI, HF	**38%**	**13%**	**0.046**
In-hospital death	5%	8%	1.0
HF	**38%**	**8%**	

1. *Am J Cardiol*. 2011;108:1108-11.

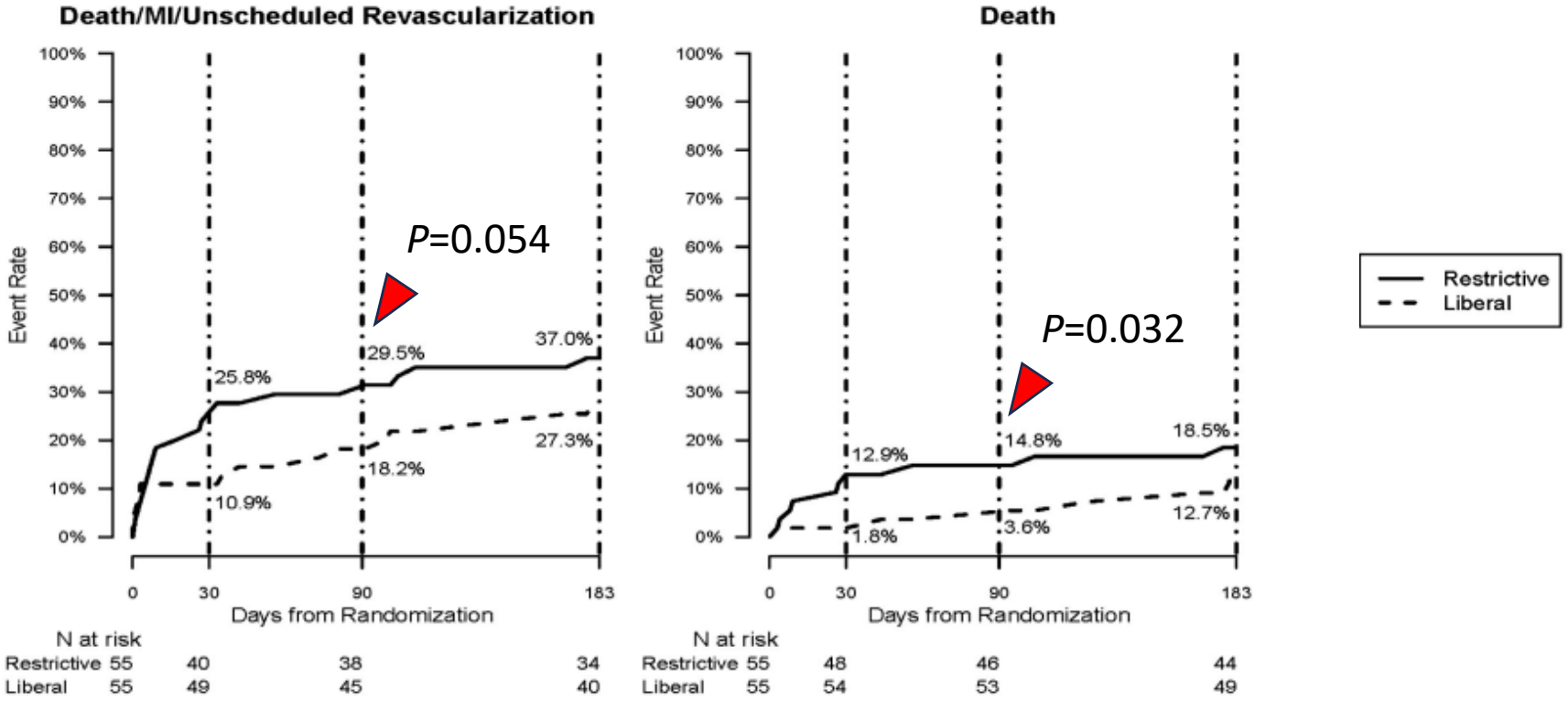
Early Prospective Randomized Pilot Trials

Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease

Jeffrey L. Carson, MD,[a] Maria Mori Brooks, PhD,[b] J. Dawn Abbott, MD,[c] Bernard Chaitman, MD,[d] Sheryl F. Kelsey, PhD,[b] Darrell J. Triulzi, MD,[e] Vankeepuram Srinivas, MD,[f] Mark A. Menegus, MD,[f] Oscar C. Marroquin, MD,[g] Sunil V. Rao, MD,[h] Helaine Noveck, MPH,[a] Elizabeth Passano, MS,[b] Regina M. Hardison, MS,[b] Thomas Smitherman, MD,[g] Tudor Vagaonescu, MD,[i] Neil J. Wimmer, MD,[j] and David O. Williams, MD[j] *New Brunswick, NJ; Pittsburgh, PA; Providence, RI; Saint Louis, MO; New York, NY; Durham, NC; and Boston, MA*

Liberal: Hb target 10 g/dL
Restrictive: Hb target 8 g/dL

Higher unit number of RBC transfusion
1.6 (Liberal) vs 0.6 (Restrictive)



1. *Am Heart J*. 2013;165:964-971.

Two Pilot Trials with Conflicting Results

→ Larger number study with adequate power needed

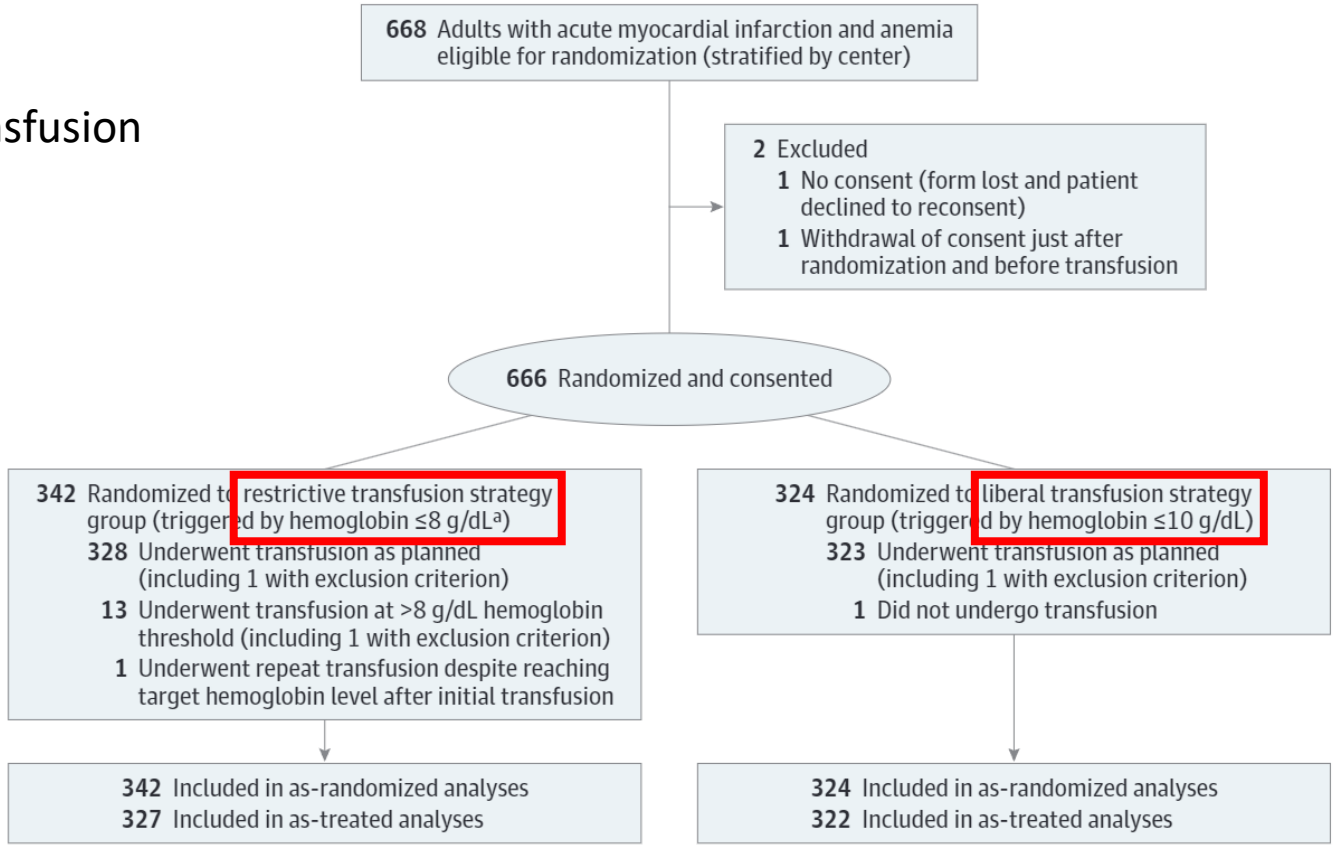
Non-Inferiority Trial of Restrictive Strategy

Non-inferiority trial
Restrictive transfusion would be non-inferior to liberal transfusion

JAMA | Original Investigation

Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia
The REALITY Randomized Clinical Trial

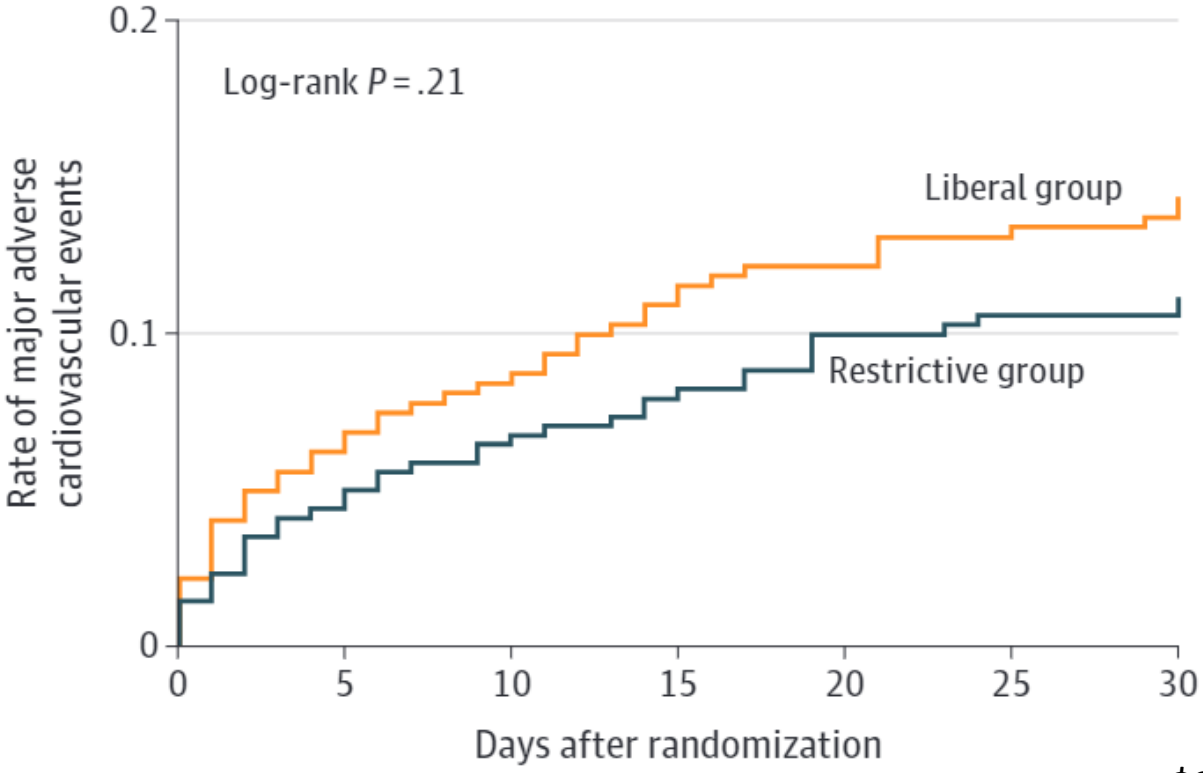
Gregory Ducrocq, MD, PhD; Jose R. Gonzalez-Juanatey, MD; Etienne Puymirat, MD; Gilles Lemesle, MD, PhD; Marine Cachanado, MSc; Isabelle Durand-Zaleski, MD, PhD; Joan Albert Arnaiz, MD, PhD; Manuel Martínez-Sellés, MD, PhD; Johanne Silvain, MD, PhD; Albert Ariza-Solé, MD; Emile Ferrari, MD; Gonzalo Calvo, MD, PhD; Nicolas Danchin, MD; Cristina Avendaño-Solá MD; Jerome Frenkiel, MD; Alexandra Rousseau, PhD; Eric Vicaut, MD, PhD; Tabassome Simon, MD, PhD; Philippe Gabriel Steg, MD; for the REALITY Investigators



1. *JAMA*. 2021;325(6):552-560.

Restrictive Strategy Can Be Non-Inferior, But..

Outcome	No. (%) Restrictive	Liberal	Difference (95% CI), %	Relative risk (1-sided 97.5% CI)
Primary (major adverse cardiovascular events), No./total No. (%) [95% CI][a]				
As-treated population	36/327 (11.0) [7.5 to 14.6]	45/322 (14.0) [10.0 to 17.9]	−3.0 (−8.4 to 2.4)	0.79 (0.00 to 1.19)

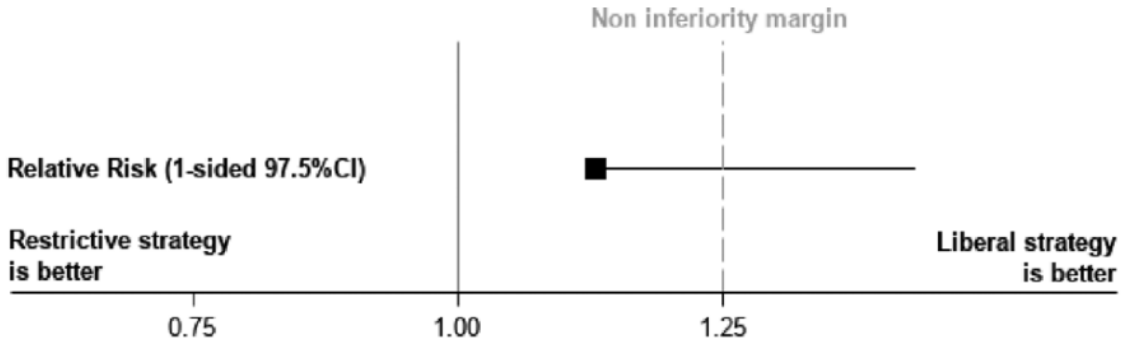


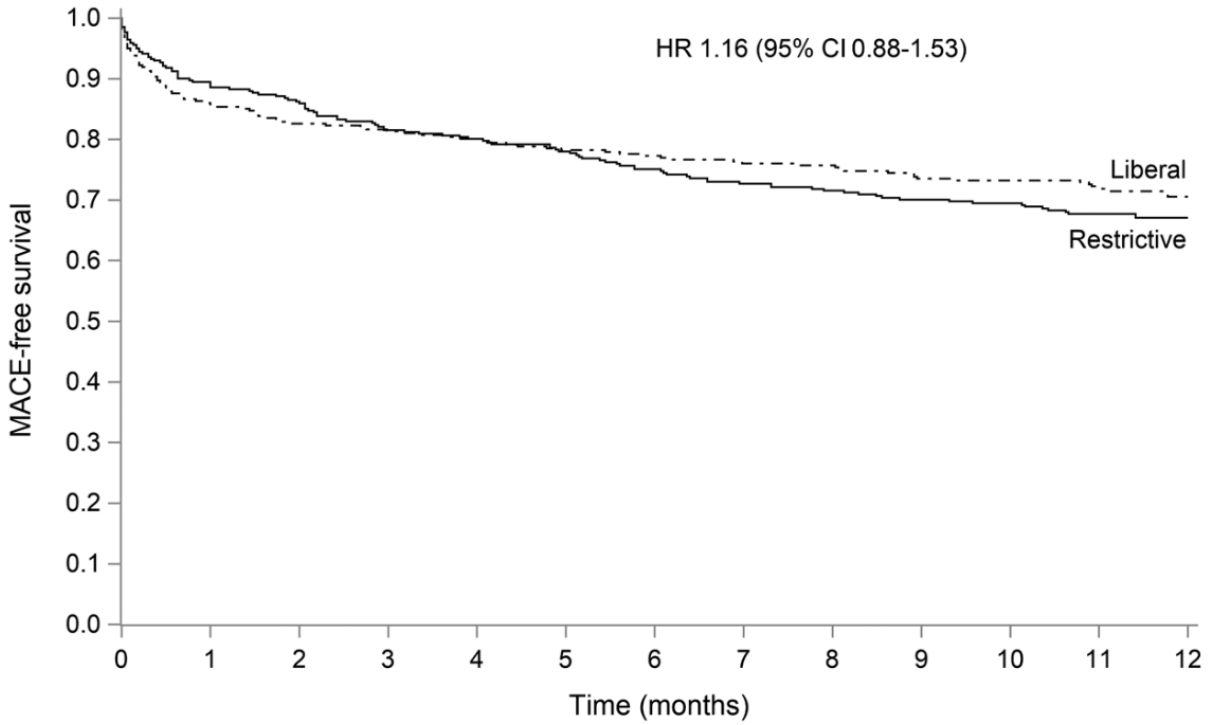
Adverse event	No. (%) Restrictive (n = 342)	Liberal (n = 324)	
At least 1 adverse event	40 (11.7)	36 (11.1)	
Acute kidney injury[a]	33 (9.7)	23 (7.1)	
Acute heart failure[b]	11 (3.2)	12 (3.7)	
Severe allergic reaction[a]	3 (0.9)	0	
Acute lung injury/ARDS[a]	1 (0.3)	7 (2.2)	*P*=0.03
Multiorgan system dysfunction[a]	1 (0.3)	3 (0.9)	
Infection[a,c]	0	5 (1.5)	*P*=0.03

>$39,000 cost-saving with restrictive strategy per additional MACE

1. *JAMA*. 2021;325(6):552-560.

Prespecified One-Year Extension of The REALITY Trial





1. *Circulation*. 2022;145(6):486-488.

Potential harmful signal with restrictive transfusion strategy in AMI Population

Pilot to Large-Number Randomized Trial

Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease

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MINT pilot trial

ORIGINAL ARTICLE

Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia

J.L. Carson, M.M. Brooks, P.C. Hébert, S.G. Goodman, M. Bertolet, S.A. Glynn, B.R. Chaitman, T. Simon, R.D. Lopes, A.M. Goldsweig, A.P. DeFilippis, J.D. Abbott, B.J. Potter, F.M. Carrier, S.V. Rao, H.A. Cooper, S. Ghafghazi, D.A. Fergusson, W.J. Kostis, H. Noveck, S. Kim, M. Tessalee, G. Ducrocq, P. Gabriel Melo de Barros e Silva, D.J. Triulzi, C. Alsweiler, M.A. Menegus, J.D. Neary, L. Uhl, J.B. Strom, C.B. Fordyce, E. Ferrari, J. Silvain, F.O. Wood, B. Daneault, T.S. Polonsky, M. Senaratne, E. Puymirat, C. Bouleti, B. Lattuca, H.D. White, S.F. Kelsey, P.G. Steg, and J.H. Alexander, for the MINT Investigators*

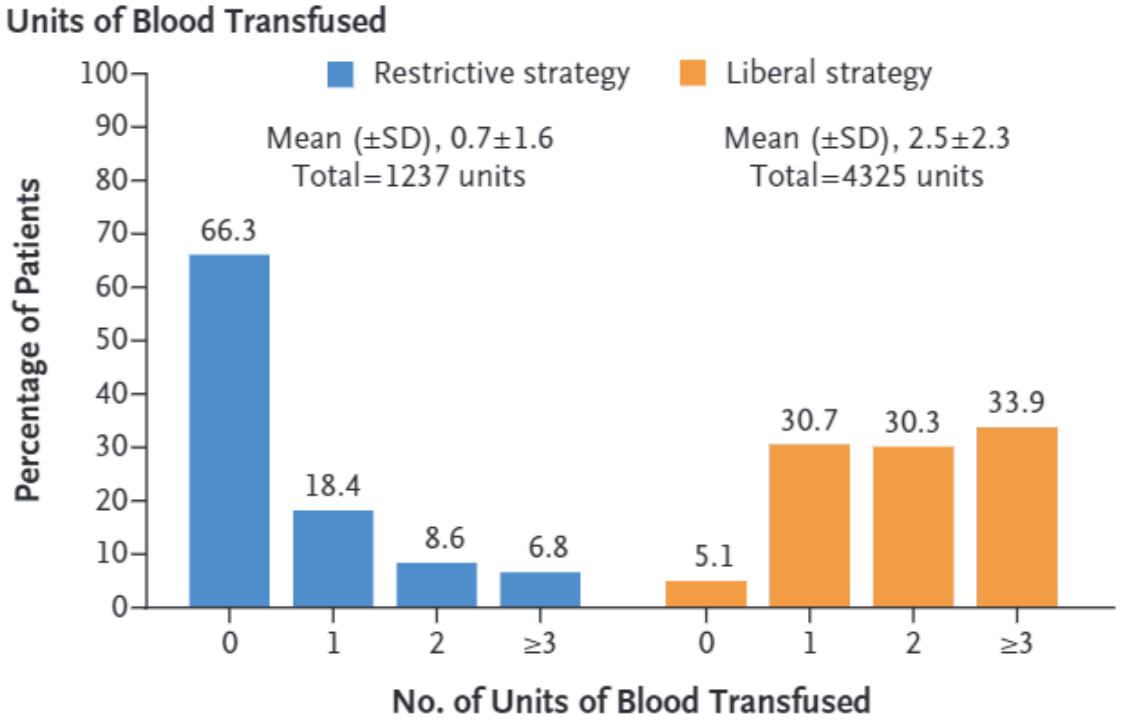
MINT RCT

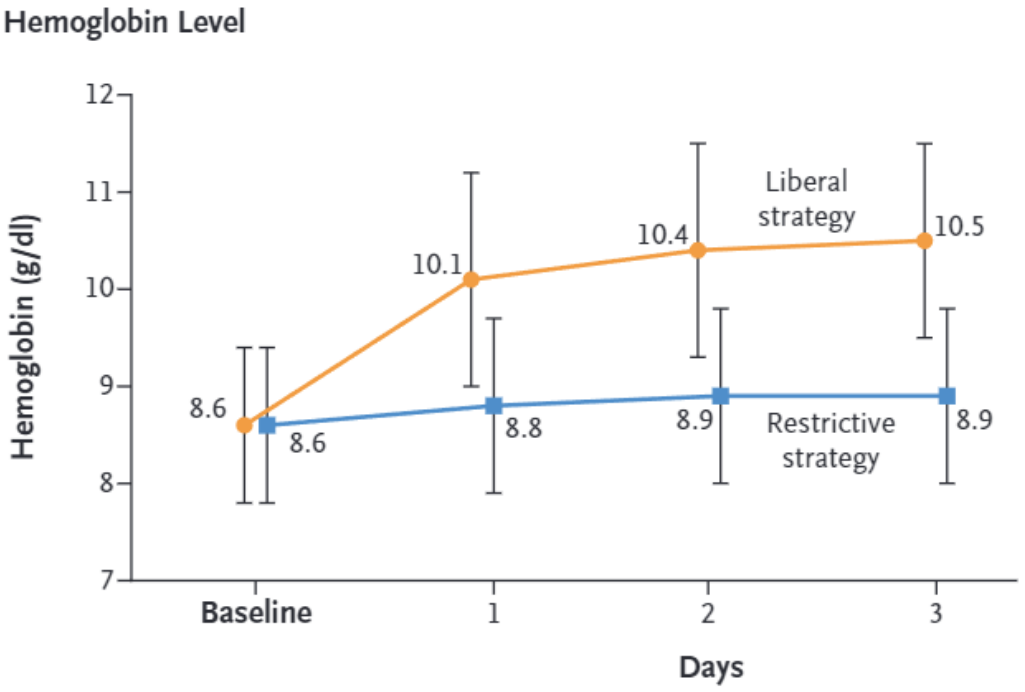
1. *Am Heart J*. 2013;165:964-971. **2**. *N Engl J Med*. 2023;389:2446-56.

MINT Trial Details

AMI patients with Hb <10 g/dL
Target Hb in the liberal group (7 g/dL) and the restrictive group (10 g/dL)

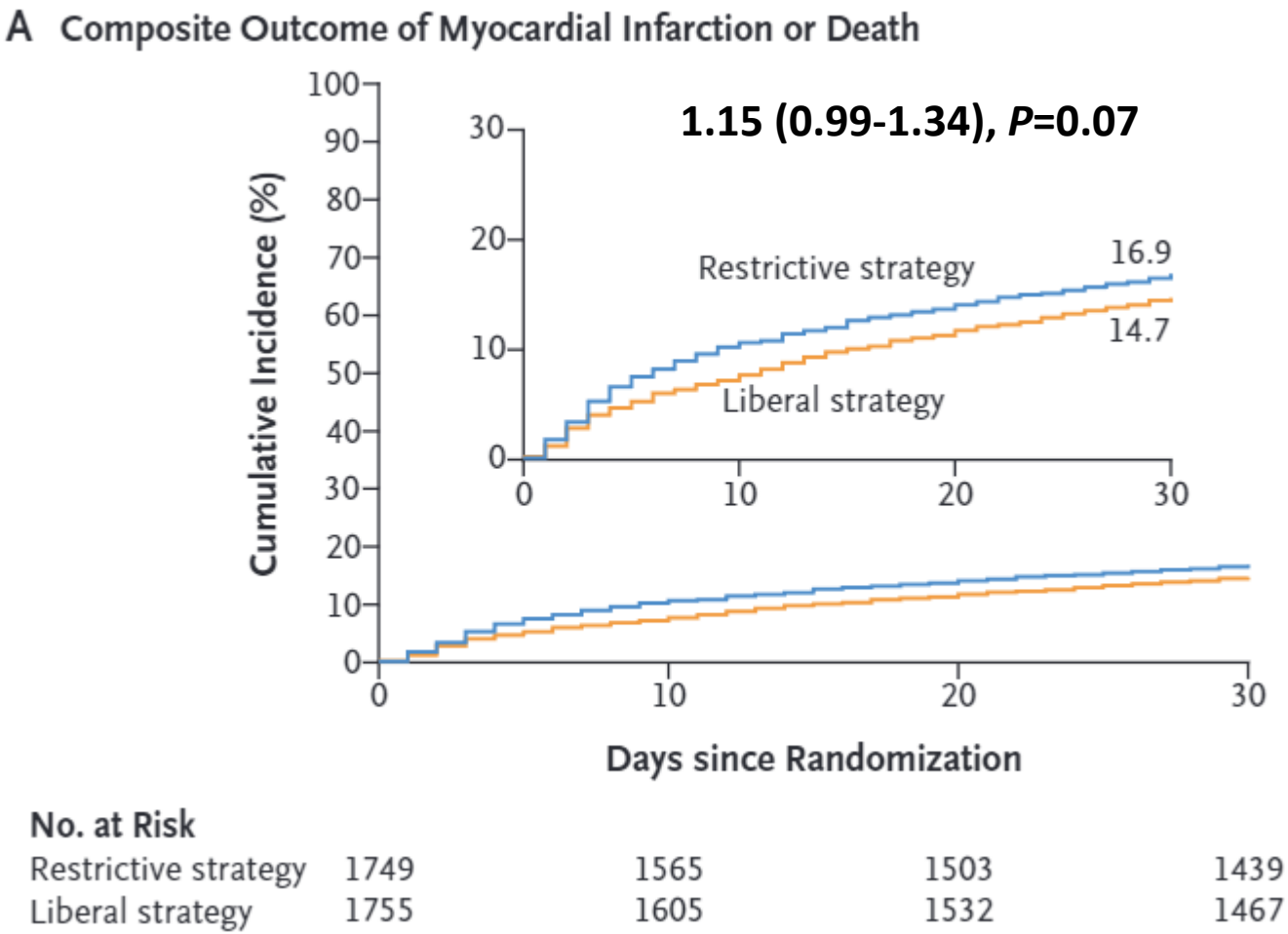
3.5 times of transfusion number





1. *N Engl J Med*. 2023;389:2446-56.

Close Miss in Superiority and No Harmful Signals

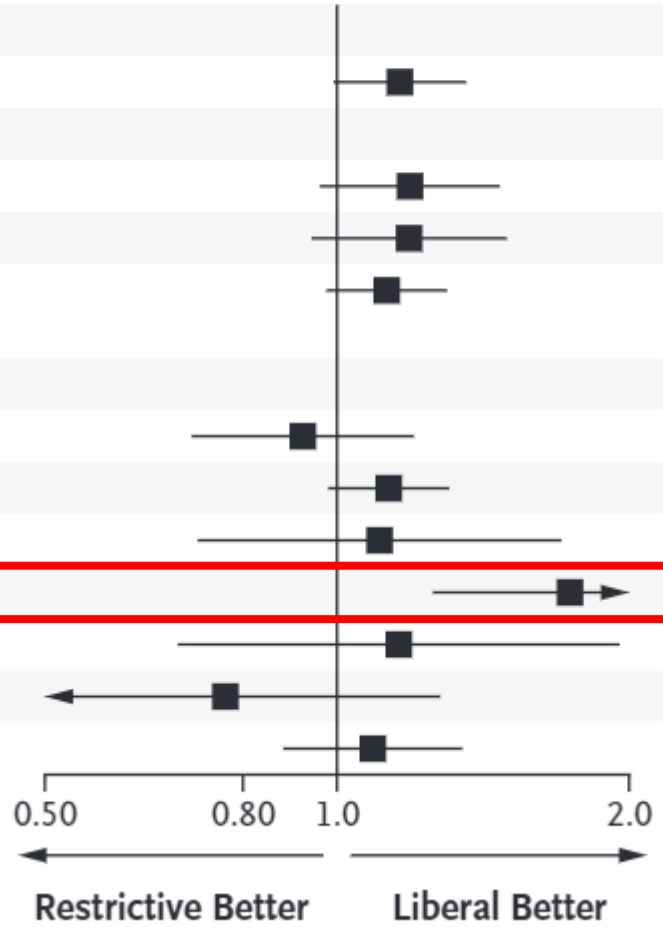


Outcome	Restrictive	Liberal	Relative Risk
Acute respiratory failure	148/1749 (8.5%)	153/1755 (8.7%)	0.97 (0.78,1.20)
Acute renal failure	233/1749 (13.3%)	233/1755 (13.3%)	1.00 (0.85,1.19)
Transfusion Related Adverse Events			
Transfusion related acute lung injury (TRALI)	0/1748 (0.0%)	6/1754 (0.3%)	- (-.-)
Transfusion associated cardiac overload (TACO)	8/1749 (0.5%)	23/1755 (1.3%)	0.35 (0.16,0.78)
Acute hemolytic transfusion reaction	0/1748 (0.0%)	4/1754 (0.2%)	- (-.-)
Transfusion associated sepsis	0/1748 (0.0%)	1/1754 (0.1%)	- (-.-)
Anaphylactic transfusion reaction	2/1748 (0.1%)	2/1754 (0.1%)	1.00 (0.14,7.12)
Urticarial transfusion reaction	0/1748 (0.0%)	2/1754 (0.1%)	- (-.-)
Febrile non-hemolytic transfusion reaction	1/1748 (0.1%)	14/1754 (0.8%)	0.07 (0.01,0.54)

1. *N Engl J Med*. 2023;389:2446-56.

Potential Increased Risk of Cardiac Death

Outcome	Restrictive Strategy	Liberal Strategy	Risk Ratio (95% CI)
	no. of patients/total no. (%)		
Primary outcome			
Myocardial infarction or death	295/1749 (16.9)	255/1755 (14.5)	1.16 (1.00–1.35)
Secondary outcomes			
Death	173/1749 (9.9)	146/1755 (8.3)	1.19 (0.96–1.47)
Myocardial infarction	149/1749 (8.5)	126/1755 (7.2)	1.19 (0.94–1.49)
Death, myocardial infarction, revascularization, or rehospitalization	342/1749 (19.6)	305/1755 (17.4)	1.13 (0.98–1.29)
Other outcomes			
Heart failure	102/1749 (5.8)	111/1755 (6.3)	0.92 (0.71–1.20)
Death, myocardial infarction, or unstable angina	338/1749 (19.3)	300/1755 (17.1)	1.13 (0.98–1.30)
Unscheduled revascularization	43/1749 (2.5)	39/1755 (2.2)	1.11 (0.72–1.70)
Cardiac death	97/1749 (5.5)	56/1755 (3.2)	1.74 (1.26–2.40)
Stroke	30/1749 (1.7)	26/1755 (1.5)	1.16 (0.69–1.95)
Pulmonary embolism or deep venous thrombosis	26/1749 (1.5)	34/1755 (1.9)	0.77 (0.46–1.27)
Pneumonia or bacteremia	166/1749 (9.5)	153/1755 (8.7)	1.09 (0.88–1.34)

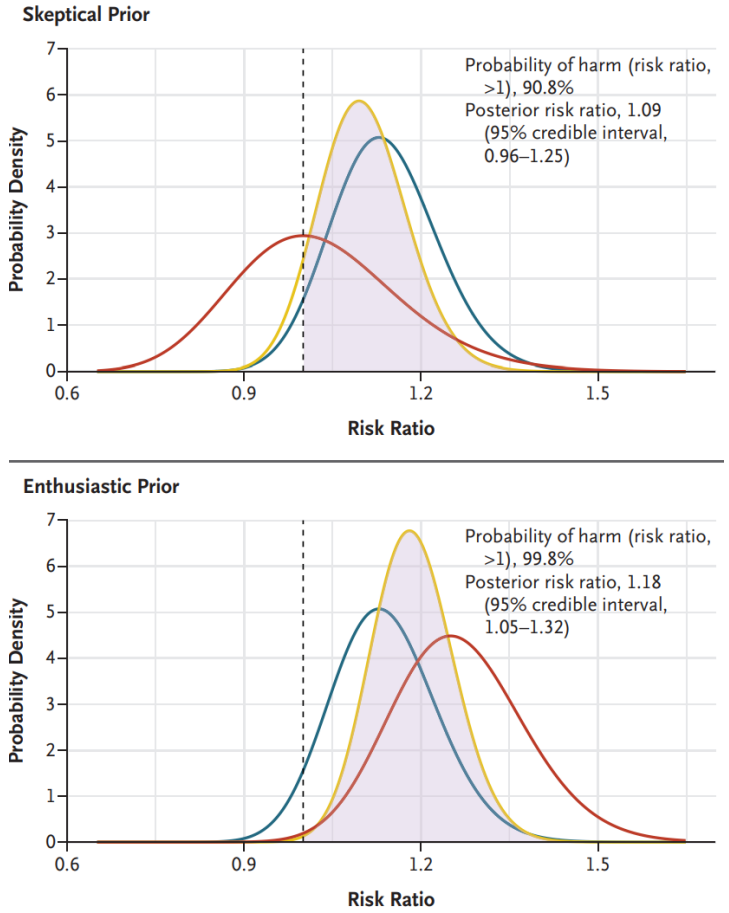


1. *N Engl J Med*. 2023;389:2446-56.

Significant Findings from Non-Significant Results

significant one.[2] In the MINT trial, if 2 additional patients among the 1749 in the restrictive-strategy group had had a primary-outcome event — or 2 additional patients among the 1755 in the liberal-strategy group had not had a primary-outcome event — the results would have been significant in favor of the liberal transfusion strategy. This information allows us to better understand how fragile the absence of significance was in the analysis of the primary outcome.

Probable harmful effect of restrictive strategy, ranging 90.8% ~ 99.8% based on Bayesian analysis

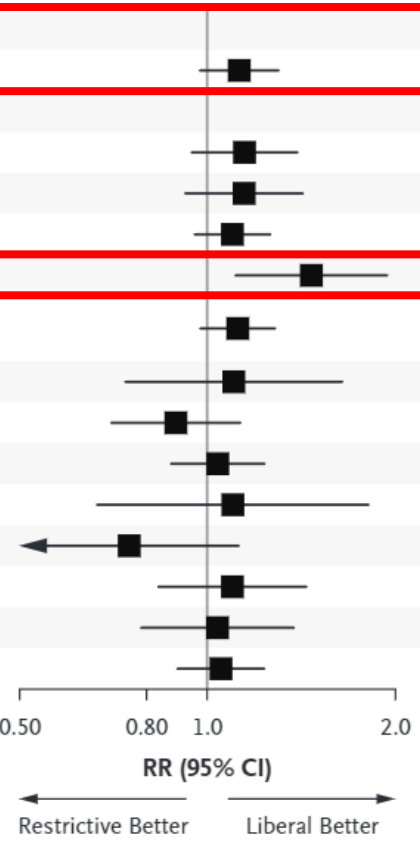


1. *N Engl J Med*. 2023;390(10):960-961.

Meta-Analysis from 4 RCTs

	Trial Name	Restrictive N	Liberal N
Cooper et al. 2011	CRIT†	24	21
Carson et al. 2013	MINT Pilot‡	50	46
Ducrocq et al. 2021	REALITY§	342	324
Carson et al. 2023	MINT¶	1749	1755

Outcome	Restrictive n/N (%)	Liberal n/N (%)	Absolute Difference (95% CI)	RR (95% CI)
Primary Outcome				
Death or MI	334/2165 (15.4)	296/2146 (13.8)	1.3% (–0.7 to 3.4)	1.13 (0.97 to 1.30)
Other Outcomes				
Death within 30 days	201/2165 (9.3)	174/2146 (8.1)	1.1% (–0.5 to 2.8)	1.15 (0.95 to 1.39)
MI	163/2165 (7.5)	142/2146 (6.6)	0.5% (–0.9 to 1.9)	1.15 (0.92 to 1.42)
MACE (death, MI, or stroke)	351/2165 (16.2)	319/2146 (14.9)	1.1% (–1.1 to 3.2)	1.10 (0.96 to 1.26)
Cardiac death	117/2141 (5.5)	79/2125 (3.7)	1.8% (0.6 to 3.1)	1.47 (1.11 to 1.94)
Death, MI, or unscheduled revascularization	361/2141 (16.9)	322/2125 (15.2)	1.4% (–0.7 to 3.6)	1.12 (0.98 to 1.28)
Unscheduled revascularization	50/2141 (2.3)	45/2125 (2.1)	0.2% (–0.7 to 1.1)	1.10 (0.74 to 1.64)
Heart failure	122/2165 (5.6)	134/2146 (6.2)	–0.5% (–1.8 to 0.9)	0.89 (0.70 to 1.13)
Acute renal failure/dialysis	235/1883 (12.5)	223/1854 (12.0)	0.6% (–1.4 to 2.7)	1.04 (0.88 to 1.23)
Stroke	32/2165 (1.5)	29/2146 (1.4)	0.1% (–0.6 to 0.8)	1.10 (0.67 to 1.81)
PE/DVT	26/2141 (1.2)	38/2125 (1.8)	–0.7% (–1.4 to –0.1)	0.68 (0.42 to 1.12)
Pneumonia	103/1799 (5.7)	94/1801 (5.2)	0.6% (–0.9 to 2.1)	1.10 (0.84 to 1.44)
Bacteremia	95/2141 (4.4)	91/2125 (4.3)	0.2% (–1.1 to 1.4)	1.04 (0.78 to 1.38)
Bleeding	272/2165 (12.6)	255/2146 (11.9)	0.7% (–1.2 to 2.6)	1.05 (0.90 to 1.23)

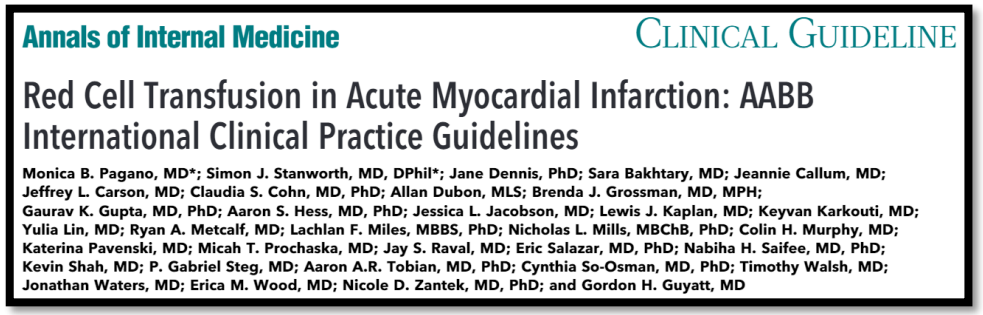


1. *NEJM Evid.* 2025;4(2):EVIDoa2400223.

No significant benefit with liberal transfusion strategy

But, potential benefit regarding cardiac death

MINT Trial Outcomes and Changes in Recommendation



Annals of Internal Medicine CLINICAL GUIDELINE

Red Cell Transfusion in Acute Myocardial Infarction: AABB International Clinical Practice Guidelines

Monica B. Pagano, MD*; Simon J. Stanworth, MD, DPhil*; Jane Dennis, PhD; Sara Bakhtary, MD; Jeannie Callum, MD; Jeffrey L. Carson, MD; Claudia S. Cohn, MD, PhD; Allan Dubon, MLS; Brenda J. Grossman, MD, MPH; Gaurav K. Gupta, MD, PhD; Aaron S. Hess, MD, PhD; Jessica L. Jacobson, MD; Lewis J. Kaplan, MD; Keyvan Karkouti, MD; Yulia Lin, MD; Ryan A. Metcalf, MD; Lachlan F. Miles, MBBS, PhD; Nicholas L. Mills, MBChB, PhD; Colin H. Murphy, MD; Katerina Pavenski, MD; Micah T. Prochaska, MD; Jay S. Raval, MD; Eric Salazar, MD, PhD; Nabiha H. Saifee, MD, PhD; Kevin Shah, MD; P. Gabriel Steg, MD; Aaron A.R. Tobian, MD, PhD; Cynthia So-Osman, MD, PhD; Timothy Walsh, MD; Jonathan Waters, MD; Erica M. Wood, MD; Nicole D. Zantek, MD, PhD; and Gordon H. Guyatt, MD

Recommendation

For hospitalized patients with AMI, the international panel suggests RBC transfusion when the Hb is less than 10 g/dL (conditional recommendation, low-certainty evidence).

Good Practice Statement

For hospitalized adult patients with AMI, it is important to incorporate the clinical context (e.g., patients' history, signs, symptoms, hemodynamic status) and patients' preferences when weighing RBC transfusion decisions.

Remark

In accordance with the increased risks of severe adverse events in the liberal transfusion strategy, clinicians should consider strategies for mitigation of adverse transfusion events. Strategies include optimizing fluid status peri-transfusion, slowing transfusion rate, prescribing diuretics, achieving the target Hb more gradually, and transfusing during renal replacement therapy sessions for renal failure.

1. *Ann Intern Med*. Published online 2025.

Interpretation and Perspectives

Restrictive Transfusion as a Universal Criteria

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D., CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.SC., ELIZABETH YETISIR, M.SC., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

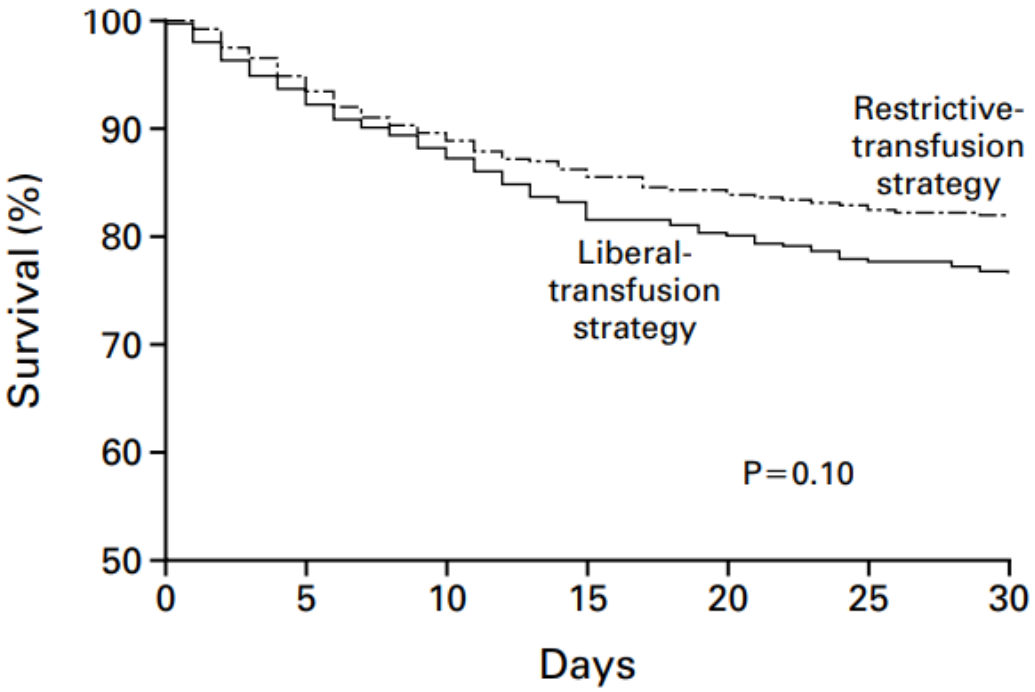


Table 1. Hemoglobin Threshold for a Restrictive Transfusion Strategy, as Recommended by Clinical Practice Guidelines for Various Populations.*

Variable	AABB†	FCC‡	U.K.‡	ESA§	SCA¶	PCC‖
			grams of hemoglobin per deciliter			
Hospitalization with hemodynamic stability	7	7	7			
Severe perioperative bleeding				7–9		
Cardiac surgery	7.5	7.5	7		7.5	
Orthopedic surgery	8	8	7			
Previous cardiovascular disease	8	8				
Hematologic or oncologic disorder	7	Insufficient data	7			
Pediatrics	7			7–9		7
Acute myocardial infarction	Insufficient data	Insufficient data	8			
Acute gastrointestinal bleeding		7–8				
Brain injury		Insufficient data				

Hb level of 7.0 ~ 8.0 g/dL

1. *N Engl J Med*. 1999;340:409-17. **2**. *N Engl J Med*. 2023;389:2483-85.

Evidence Gap in Myocardial Infarction

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

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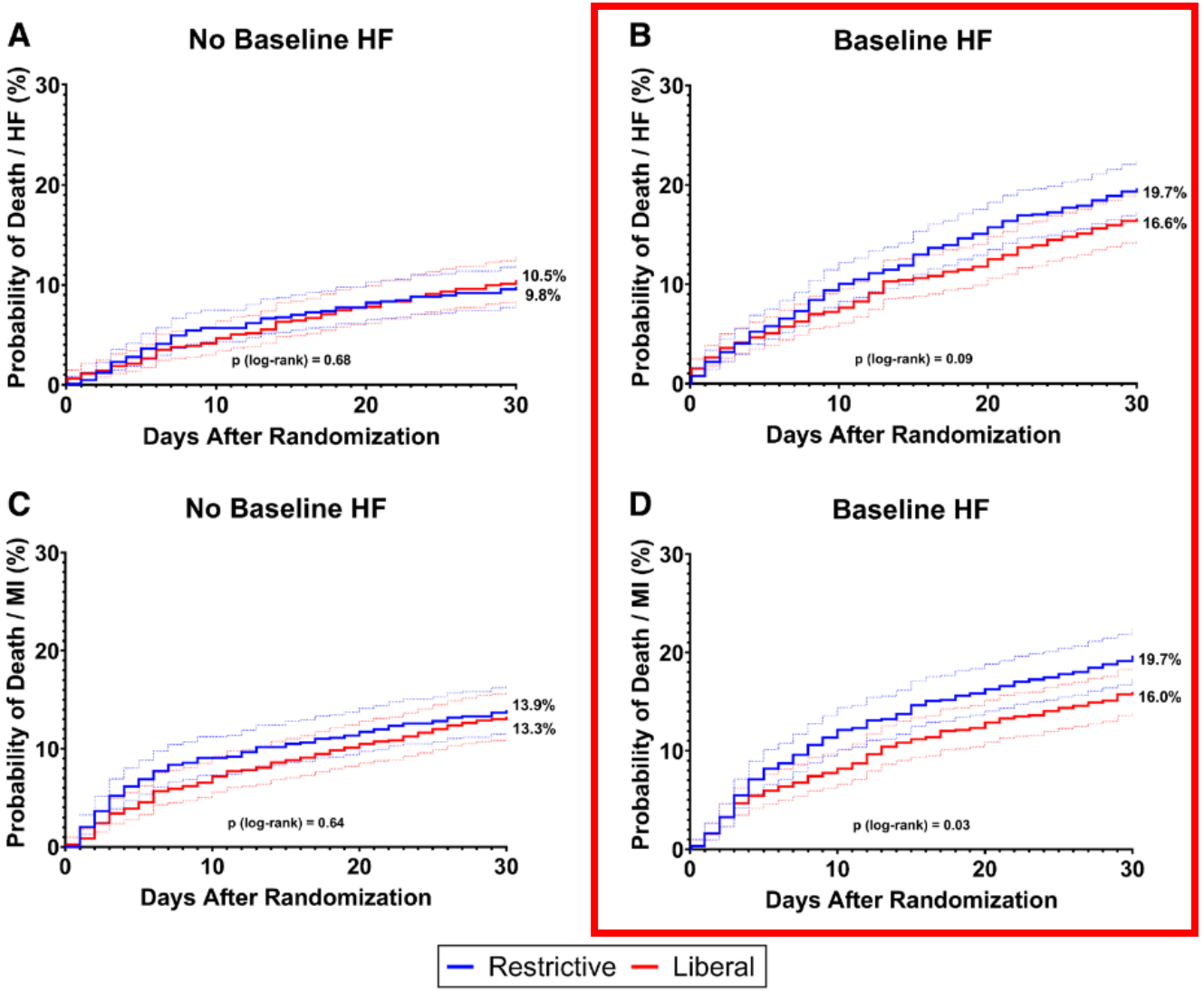
TABLE 4. CHARACTERISTICS OF THE 176 PATIENTS WHO DIED.*

CHARACTERISTIC	RESTRICTED-TRANSFUSION STRATEGY (N=78)	LIBERAL-TRANSFUSION STRATEGY (N=98)	P VALUE
Demographic and diagnostic variables			
Age — yr	68.7±12.0	65.9±15.2	0.16
Male sex — no. (%)	48 (62)	58 (59)	0.76
APACHE II score	25.3±7.0	24.6±8.5	0.53
Primary diagnosis at death — no. (%)			0.27
Cardiovascular disease	15 (19)	15 (15)	
Respiratory disease	28 (36)	44 (45)	
Gastrointestinal disease	11 (14)	9 (9)	
Neurologic abnormality	9 (12)	6 (6)	
Other	15 (19)	25 (26)	

The diversity of the patients enrolled in this trial and the consistency of the results suggest that our conclusions may be generalized to most critically ill patients, with the possible exception of patients with active coronary ischemic syndromes.

1. *N Engl J Med*. 1999;340:409-17.

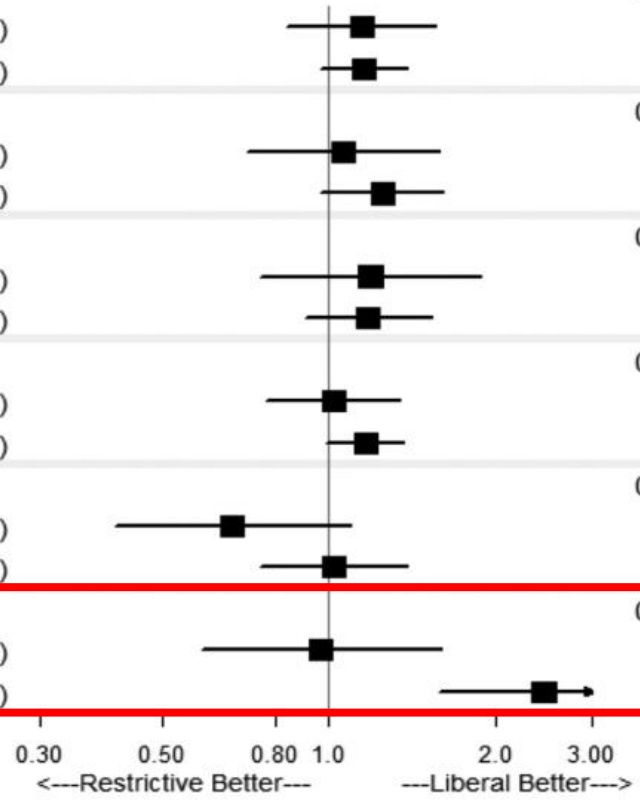
MI Occurring in the Background of HF



1. *Circ: Heart Fail*. 2025;18(4):e012495.

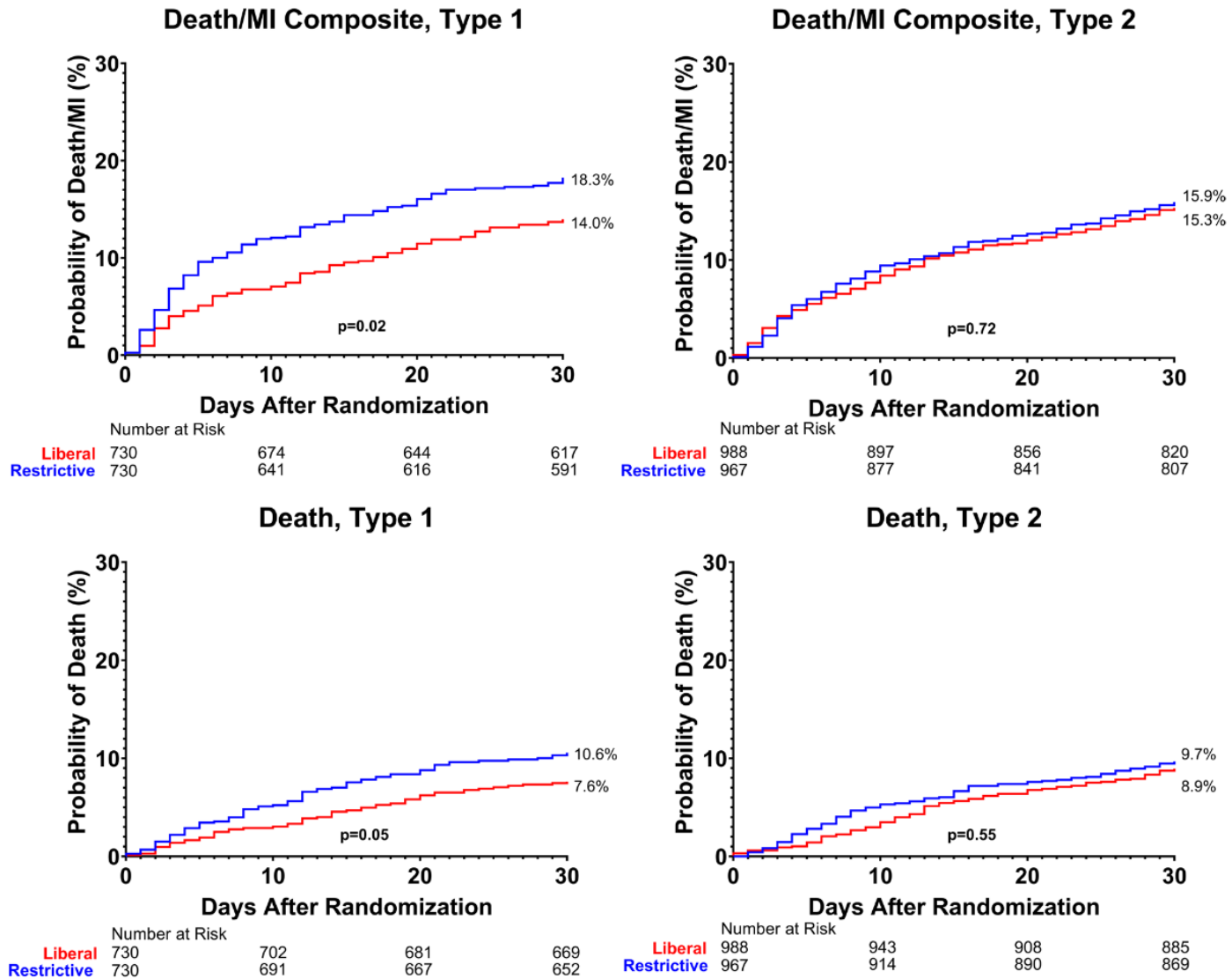
MI without Revascularization May Benefit Liberal Strategy

Subgroup	Restrictive n / N (%)	Liberal n / N (%)	Relative Risk RR (95% CI)	p-value
Death/MI				0.953
Revascularization	77/509 (15.1%)	65/493 (13.2%)	1.15 (0.84, 1.56)	
No Revascularization	213/1210 (17.6%)	187/1232 (15.2%)	1.16 (0.97, 1.39)	
Death				0.495
Revascularization	46/509 (9.0%)	42/493 (8.5%)	1.06 (0.71, 1.58)	
No Revascularization	124/1210 (10.2%)	101/1232 (8.2%)	1.25 (0.97, 1.61)	
MI				0.983
Revascularization	38/509 (7.5%)	31/493 (6.3%)	1.19 (0.75, 1.88)	
No Revascularization	109/1210 (9.0%)	94/1232 (7.6%)	1.18 (0.91, 1.54)	
Death/MI/Revasc/Readmit				0.396
Revascularization	86/509 (16.9%)	82/493 (16.6%)	1.02 (0.77, 1.34)	
No Revascularization	251/1210 (20.7%)	219/1232 (17.8%)	1.17 (0.99, 1.37)	
Heart Failure				0.165
Revascularization	25/509 (4.9%)	36/493 (7.3%)	0.67 (0.41, 1.10)	
No Revascularization	74/1210 (6.1%)	74/1232 (6.0%)	1.02 (0.75, 1.39)	
Cardiac Death				0.006
Revascularization	29/509 (5.7%)	29/493 (5.9%)	0.97 (0.59, 1.60)	
No Revascularization	65/1210 (5.4%)	27/1232 (2.2%)	2.45 (1.58, 3.81)	



1. *Circ: Cardiovasc Interv*. 2025;18(5):e015249.

Potential Harmful Signal for Type I Than Type II MI



1. *Circulation*. 2024;150(23):1826-1836.

Summary

Myocardial Infarction

Distinctive disease entity with high importance of oxygen delivery
Results from old RCTs cannot apply to this disease entity

Findings from Recent Trials

No significant benefits of liberal transfusion strategy
Potential benefits exist
- esp. for type I MI, Pts without revascularization, and baseline history of HF

Individualized Approaches

Rather than unselected liberal transfusion strategy
Incorporating risk of volume overload
Necessitating further strategies mitigating transfusion-related adverse events

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Asan Medical Center

Thank You