What's New on Transfusion Medicine and Apheresis?

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Disclosure

- In the past 12 months, I have had a significant financial interest or other relationship with the manufacturer(s) of the following product(s) or provider(s) of the following service(s) that will be discussed in my presentation
  - Royalty for *Transfusion Medicine, Apheresis, and Hemostasis: Review Questions and Case Studies*

Objectives

- Outline restrictive vs. liberal transfusion strategy in patients with acute myocardial infarction
- Summarize the use of whole blood and other therapies in trauma resuscitation
- Review significant changes in the 2023 JCA guidelines on therapeutic apheresis
- Discuss potential pathway to have donors for all patients needing transplants

When to Transfuse Red Blood Cells?

Transfusion Red Blood Cells has Risks

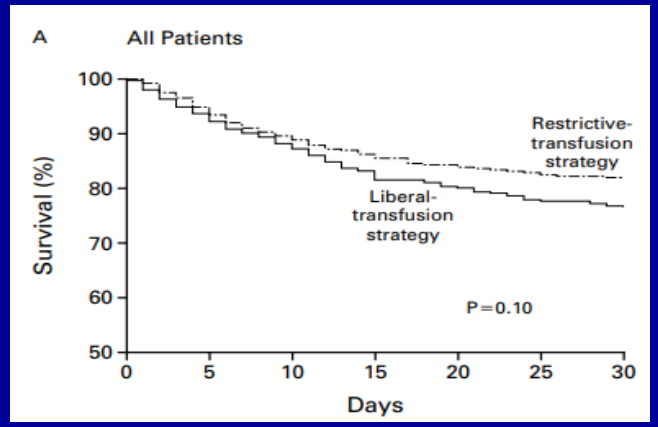
Table 1. Approximate Per-Unit Risk for Red Blood Cell (RBC) Transfusion in the US[a]

Adverse event	Approximate risk per RBC transfusion
Febrile reaction	1:161[3]
Allergic reaction	1:345[3]
Transfusion-associated circulatory overload	1:125[3]
Transfusion-related acute lung injury	1:1250[3]
Anaphylactic reactions	1:5000[3]
Hepatitis B virus	1:1 100 000[4]
Hepatitis C virus	1:1 200 000[4]
HIV	1:1 600 000[4]

Carson JL et al. JAMA 2023; 330: 1892-1902

Restrictive vs. Liberal Transfusion Strategy

- Liberal strategy
  - Transfusion when Hgb < 10 g/dL and maintain Hgb between 10 – 12 g/dL
- Restrictive strategy
  - Transfuse when Hgb < 7 g/dL and maintain Hgb between 7 – 9 g/dL
  - As effective as (possibly superior to) liberal strategy in critically ill patients (30-day mortality outcome) except for ones with acute myocardial infarction or unstable angina



Hebert PC et al. N Engl J Med 1999; 340: 409-417

Restrictive Strategy is Beneficial in Most Patients

- 45 randomized trials across range of settings

Outcome, No. of participants (No. of RCTs)	Relative effect (95% CI)	Absolute effects, %			Certainty	Plain language summary
		Restrictive	Liberal	Difference (95% CI)		
30-d Mortality, N = 16 092 (30)	RR, 1.00 (0.86-1.16)	8.3	8.3	0.0 Fewer (1.2 fewer to 1.3 more)	High	Transfusion threshold likely has little or no effect on mortality
MI, N = 14 370 (23)	RR, 1.04 (0.87-1.24)	3.3	3.2	0.1 More (0.4 fewer to 0.8 more)	High	Transfusion threshold has little or no effect on MI

Patient group (No. of RCTs)	30-d Mortality relative effect (95% CI)	Absolute effects, %			Certainty
		Restrictive	Liberal	Difference (95% CI)	
Hematologic malignancies, N = 149 (2)	RR, 0.37 (0.07-1.95)	2.4	6.6	4.1 fewer (6.1 fewer to 6.2 more)	Low[a]
Myocardial infarction, N = 820 (3)	RR, 0.99 (0.59-1.65)[b]	6.7	6.8	0.1 fewer (2.8 fewer to 4.4 more)	Low[c,d]

N = 4201 (13)				(0.5 fewer to 1.3 more)		or no effect on thromboembolism
Delirium, N = 6442 (9)	RR, 1.11 (0.88-1.40)	11.9	10.7	1.2 More (1.3 fewer to 4.3 more)	Moderate[b]	Transfusion threshold likely has little or no effect on delirium
Transfusion, N = 19 419 (41)	RR, 0.60 (0.54-0.66)	48.6	81.0	32.4 Fewer (37.3 to 27.5 fewer)	High	Restrictive transfusion threshold results in large reduction in transfusion

Carson JL et al. JAMA 2023; 330: 1892-1902

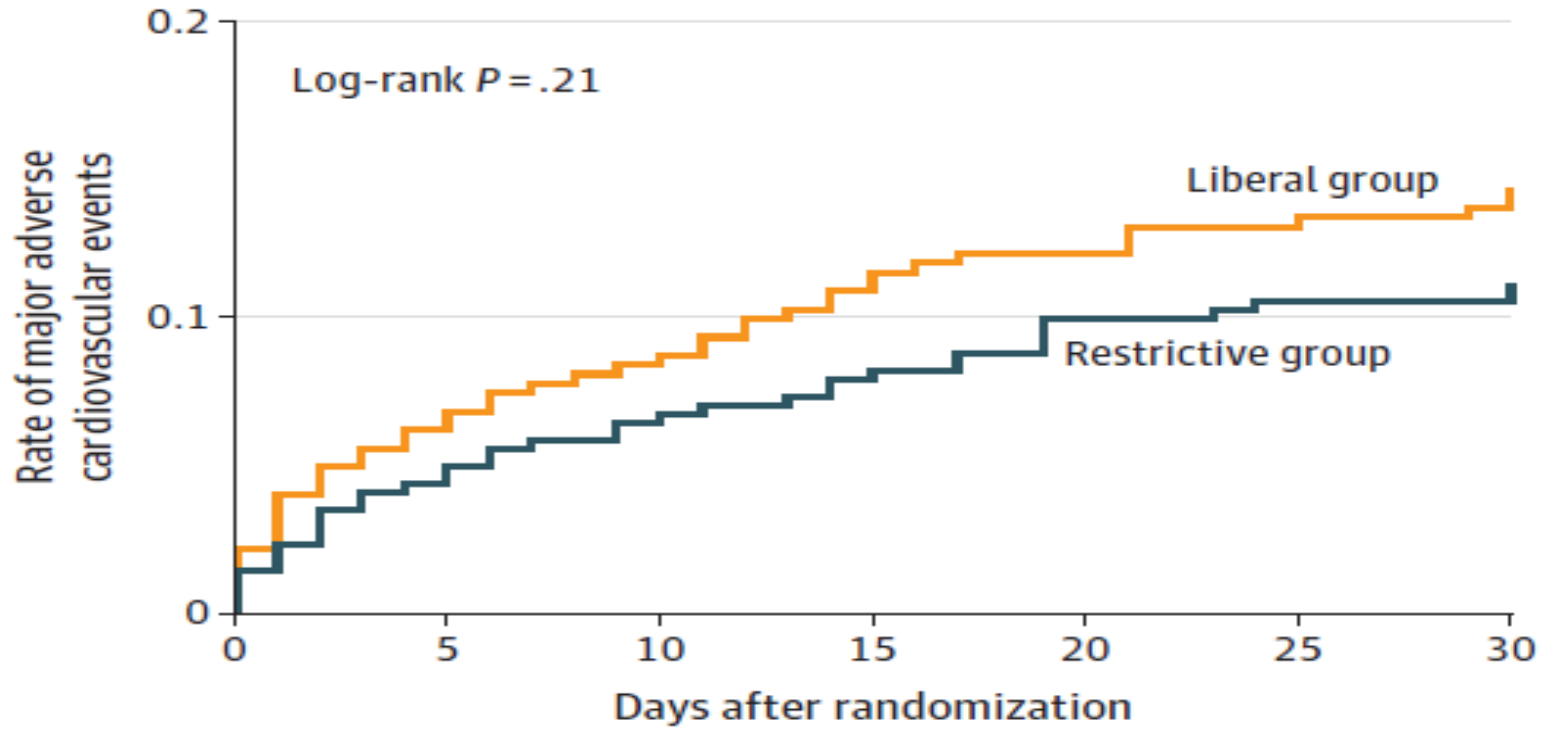
REALITY Randomized Clinical Trial

- Open-label, noninferiority trial in France and Spain (3/2016 – 9/2019)
- Patients with myocardial infarction and hemoglobin 7 – 10 g/dL
  - 668 patients randomized (median age 77 years, 42% females)
- Transfusion strategy
  - Threshold of 8 g/dL (n=342) vs. threshold of 10 g/dL (n=324)
- Composite outcome at 30 days
  - Major adverse cardiovascular events (all-cause death, stroke, recurrent myocardial infarction, or emergency revascularization due to ischemia)

Ducrocq G et al. JAMA 2021; 325: 552-560

Results

Figure 2. Rate of Major Adverse Cardiovascular Events in a Study of the Effect of a Restrictive vs Liberal Blood Transfusion Strategy Among Patients With Acute Myocardial Infarction and Anemia



No. of patients at risk							
Liberal group	324	301	293	285	281	278	275
Restrictive group	342	326	319	314	307	305	305

Ducrocq G et al. JAMA 2021; 325: 552-560

Results

Outcome	No. (%)		Difference (95% CI), %	Relative risk (1-sided 97.5% CI)
	Restrictive	Liberal		
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)
As-randomized population	38/342 (11.1) [7.6 to 14.6]	46/324 (14.2) [10.2 to 18.2]	−3.1 (−8.4 to 2.3)	0.78 (0.00 to 1.17)
Secondary (individual outcomes in the as-randomized population)[b]	**n = 342**	**n = 324**		
All-cause death	19 (5.6)	25 (7.7)		
Cardiovascular	13 (68.4)	21 (84.0)		
Noncardiovascular	3 (15.8)	2 (8.0)		
Unknown	3 (15.8)	2 (8.0)		

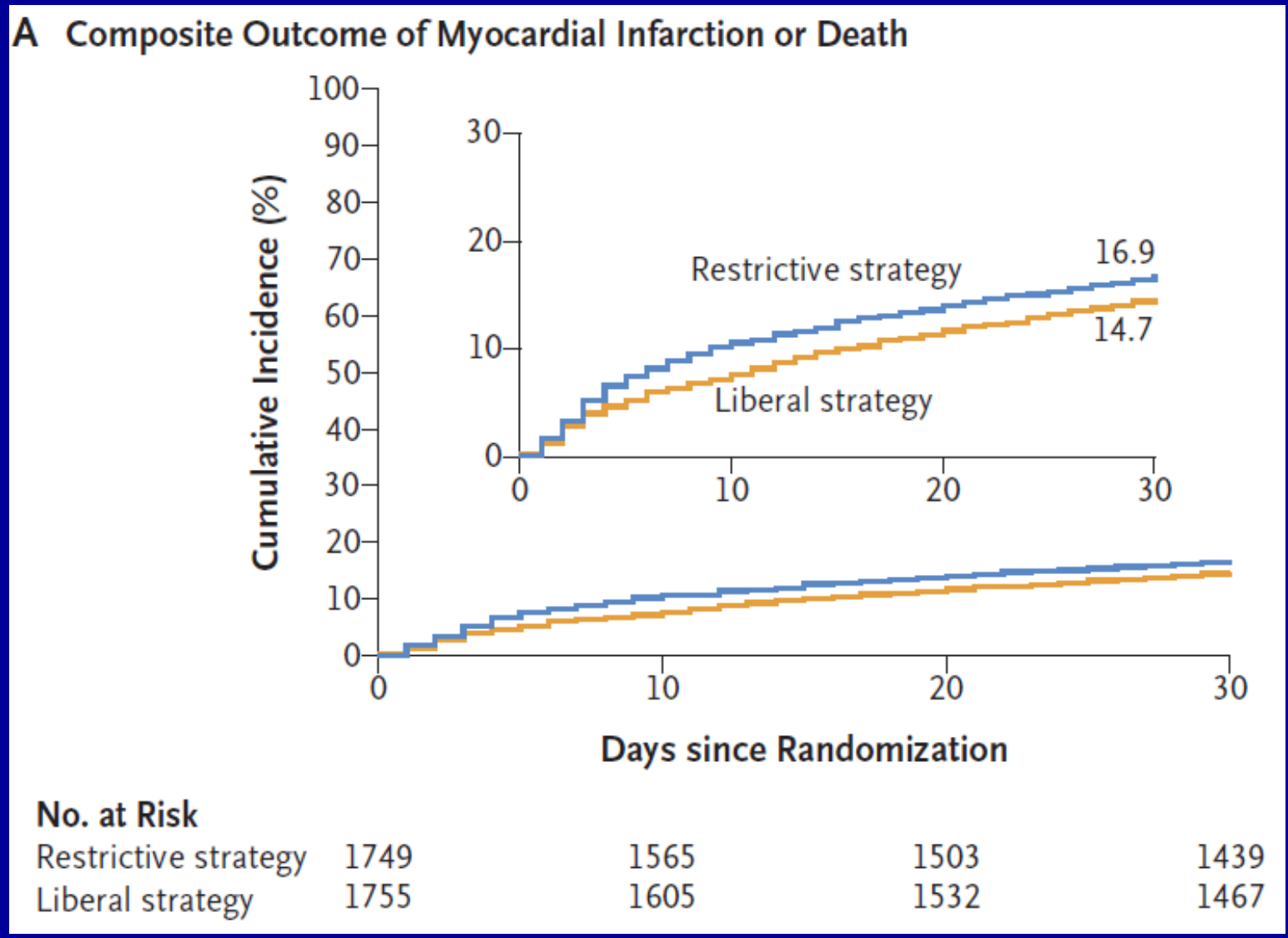
Ducrocq G et al. JAMA 2021; 325: 552-560

MINT Randomized Clinical Trial

- Open-label, noninferiority trial in US, Canada, France, Brazil, New Zealand, and Australia (4/2017 – 4/2023)
- Patients with myocardial infarction and hemoglobin <10 g/dL
  - 3504 patients randomized (median age 72 years, 46% females)
- Transfusion strategy
  - Threshold of 7 – 8 g/dL (n=1749) vs. threshold of 10 g/dL (n=1755)
- Composite outcome at 30 days
  - Myocardial and death from any cause

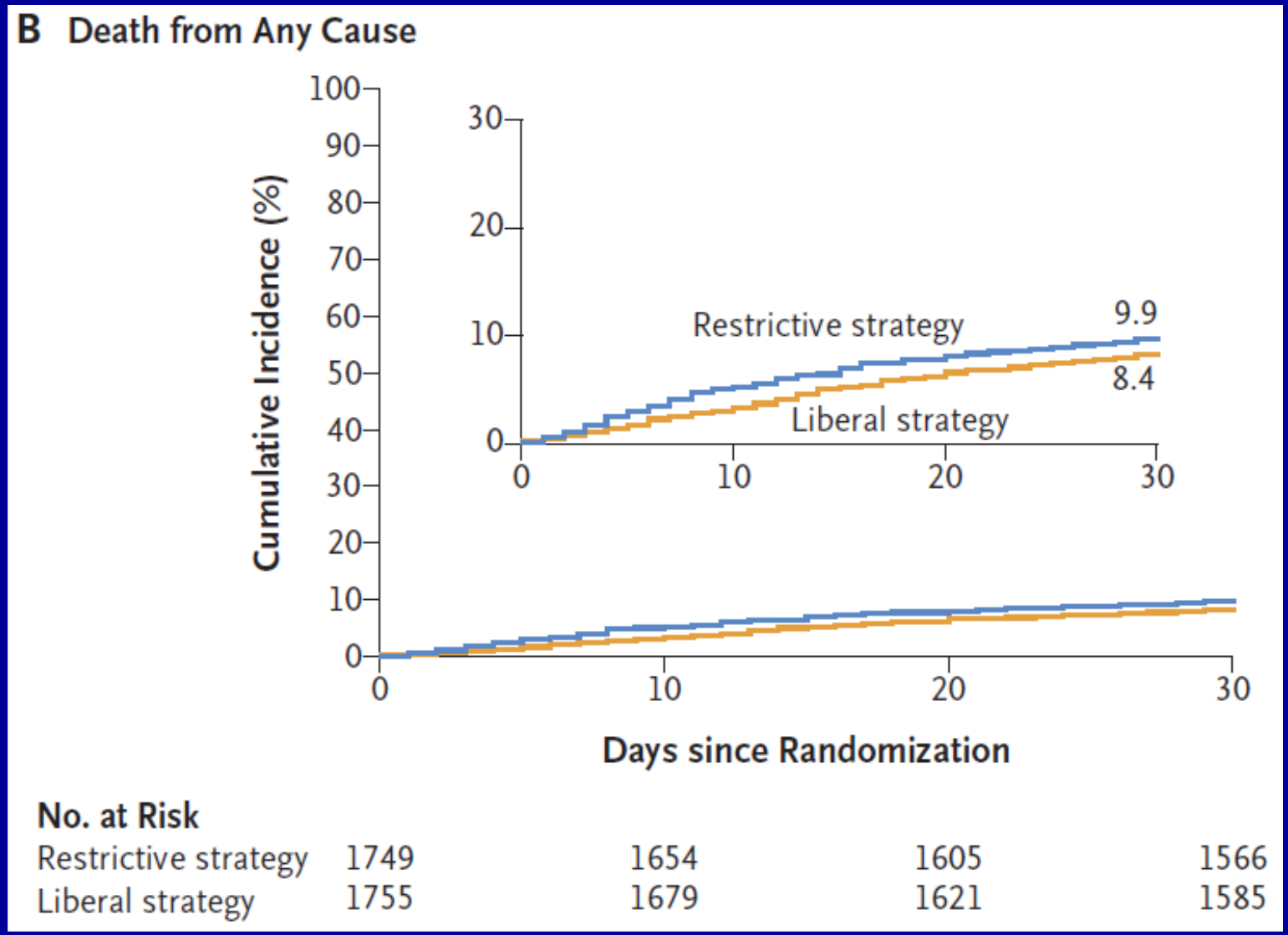
Carson JL et al. N Engl J Med 2023; 389: 2446-2456

Results – Composite Outcome



Carson JL et al. N Engl J Med 2023; 389: 2446-2456

Results – Mortality



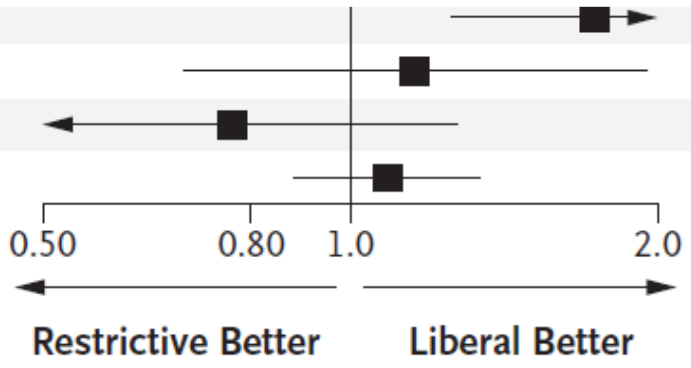
Carson JL et al. N Engl J Med 2023; 389: 2446-2456

Results – Risk Ratios

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)
Secon			
Dea			–1.47)
Myo			–1.49)
Dea or			–1.29)
Other			
Hea			–1.20)
Dea			–1.30)
Uns			–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)

CONCLUSIONS

In patients with acute myocardial infarction and anemia, a liberal transfusion strategy did not significantly reduce the risk of recurrent myocardial infarction or death at 30 days. However, potential harms of a restrictive transfusion strategy cannot be excluded. (Funded by the National Heart, Lung, and Blood Institute and others; MINT ClinicalTrials.gov number, NCT02981407.)

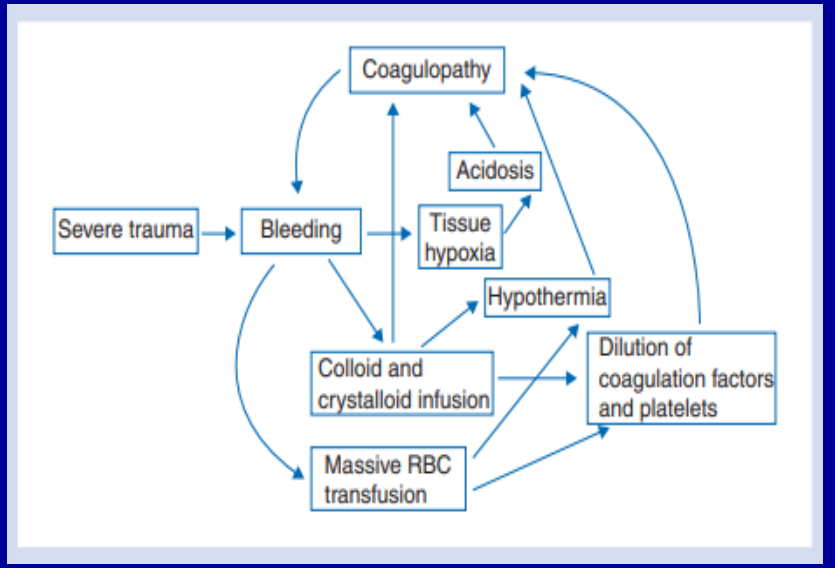


Carson JL et al. N Engl J Med 2023; 389: 2446-2456

What to Transfuse in Trauma Setting?

Trauma Resuscitation

- Hemorrhage in trauma
  - Accounts for 40% of deaths within 24 hours
  - Mainly causes by trauma-induced coagulopathy

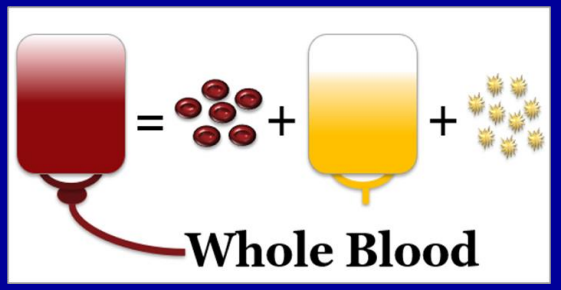


- Trauma resuscitation
  - Balanced transfusion approach of component therapy
  - Utilization of whole blood as initial transfusion product in some centers

Pham HP et al. Br J Anaesth 2013; 111(S1): i71-82
Torres CM et al. JAMA Surg 2023; 158: 532-540

Low Titer O Whole Blood (LTOWB)

- Whole blood collected from a group O donor with low titer (<200)
  - Cold stored (1-6ºC) without agitation
  - 21-day shelf life, 5 days fresh
  - Leukoreduced with platelet-sparing filter

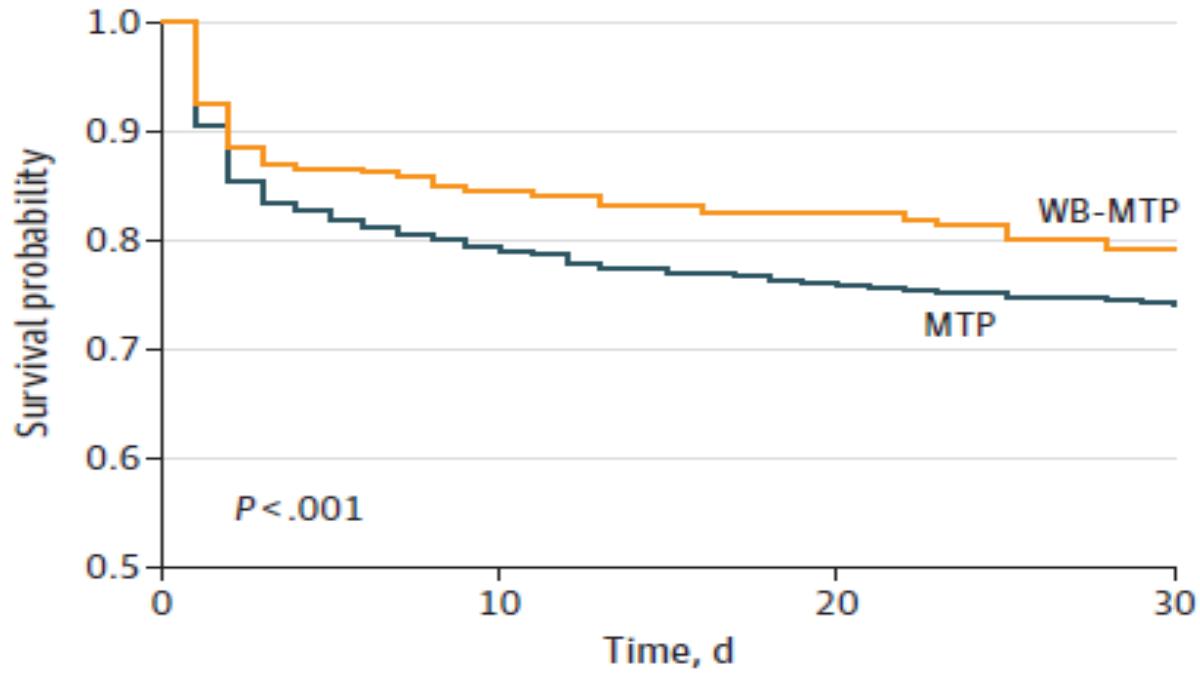


- Allows transfusion of all components simultaneously
- Primarily used to treat bleeding emergencies in adult trauma patients
  - AABB allows the use of LTOWB in bleeding emergencies, including before the patient's blood type is known
  - No evidence of significant hemolysis or transfusion reaction

Slide courtesy of Coberly E.

Whole Blood in Civilian Trauma Setting

Figure 1. Unadjusted Kaplan-Meier Survival Estimates by Transfusion Group

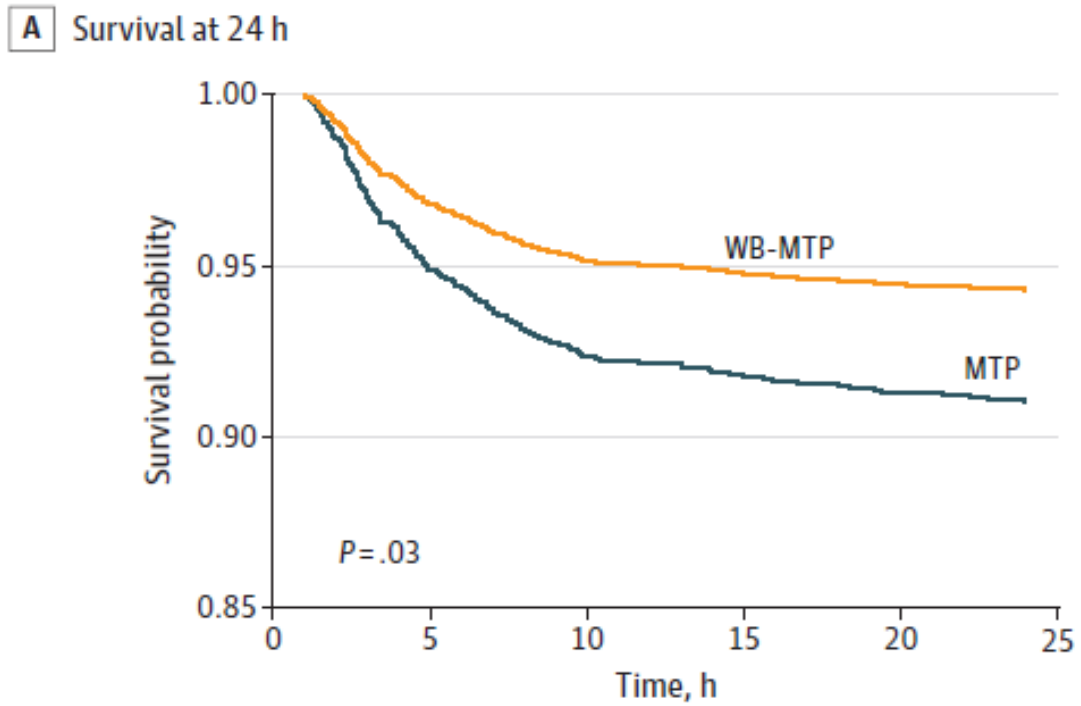


No. at risk				
MTP	2353	1505	932	585
WB-MTP	432	275	164	89

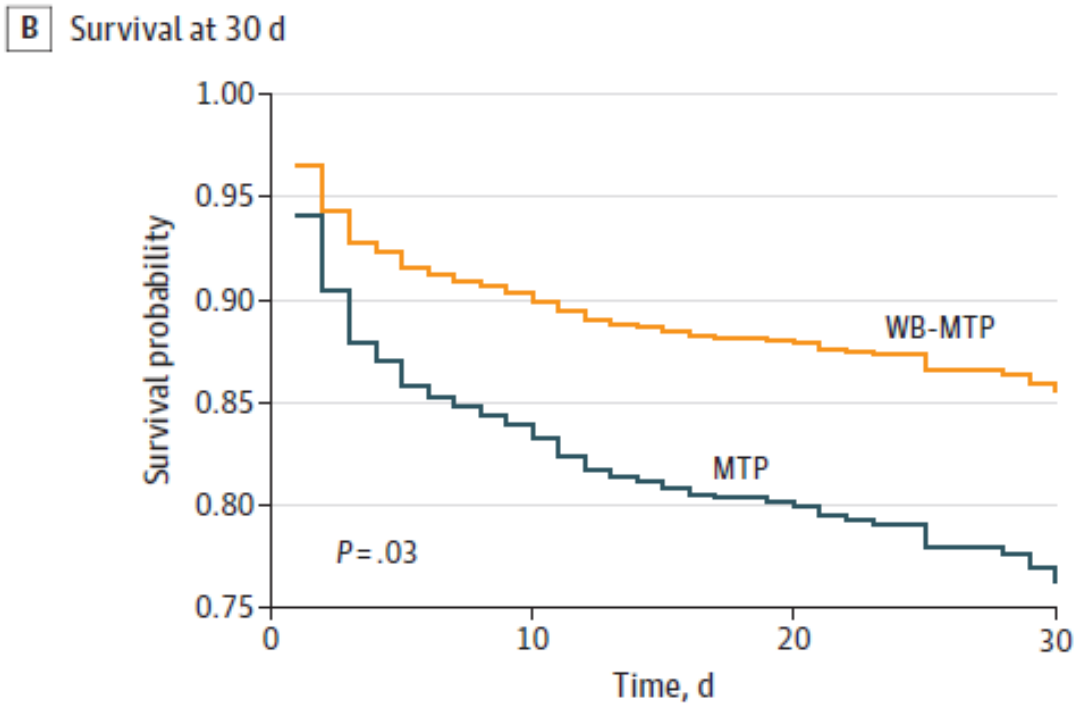
Torres CM et al. JAMA Surg 2023; 158: 532-540

Whole Blood in Civilian Trauma Setting

Figure 2. Adjusted Kaplan-Meier Survival Estimates by Transfusion Group



No. at risk						
WB-MTP	432	389	377	372	369	0
MTP	2353	2144	2039	2010	1990	0



No. at risk				
WB-MTP	432	275	164	89
MTP	2353	1505	932	585

Torres CM et al. JAMA Surg 2023; 158: 532-540

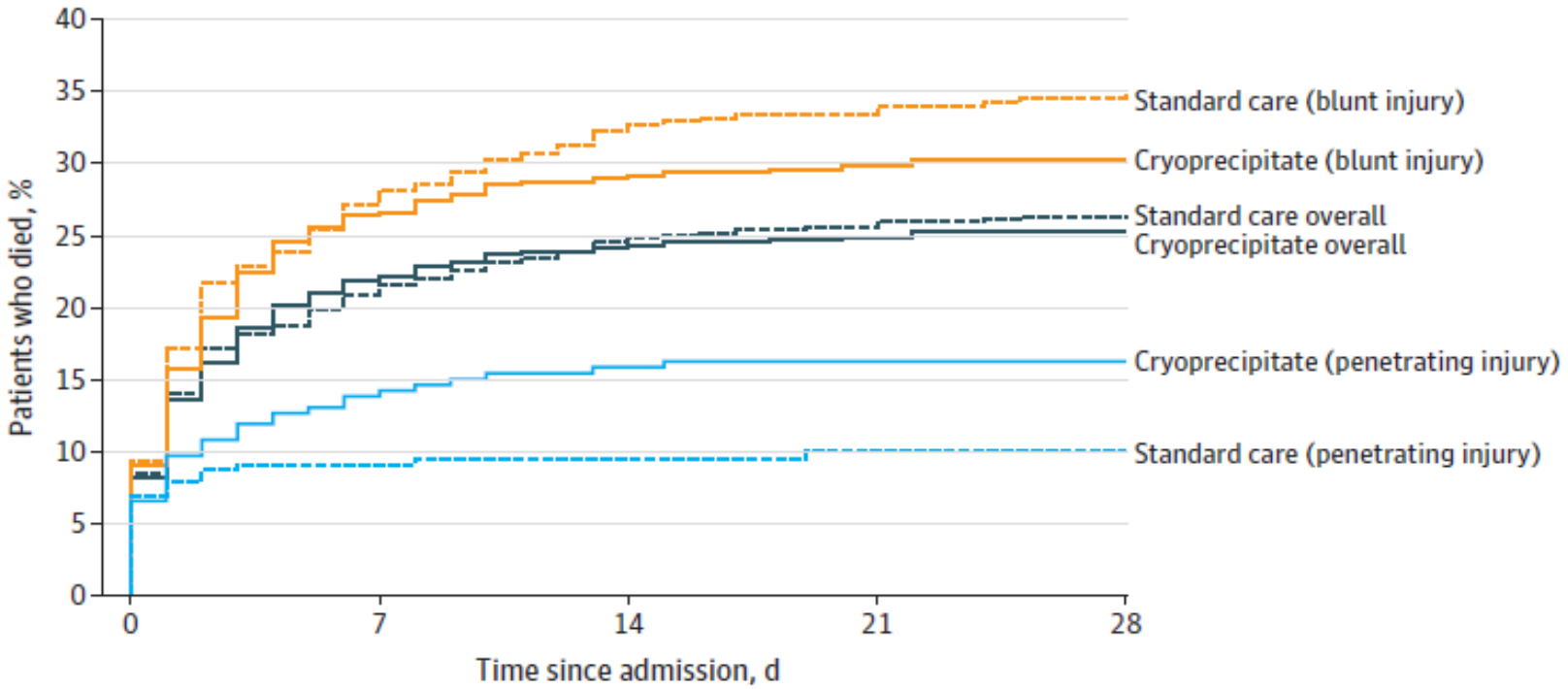
CRYOSTAT-2 Randomized Clinical Trial

- Open-label interventional trial in US and UK (8/2017 – 11/2021)
- Trauma patients required MTP activation and received at least 1 unit of blood component transfusion
  - 1604 patients randomized (median age 39 years, 79% males)
- Intervention
  - Standard of care (n=799) vs. standard of care and cryoprecipitate (3 pools, 6-gram equivalent, n=805) within 3 hours of injury
- All-cause mortality outcome at 28 days

Davenport R et al. JAMA 2023; 330: 1882-1891

Results

Figure 2. Mortality Overall and by Injury Type

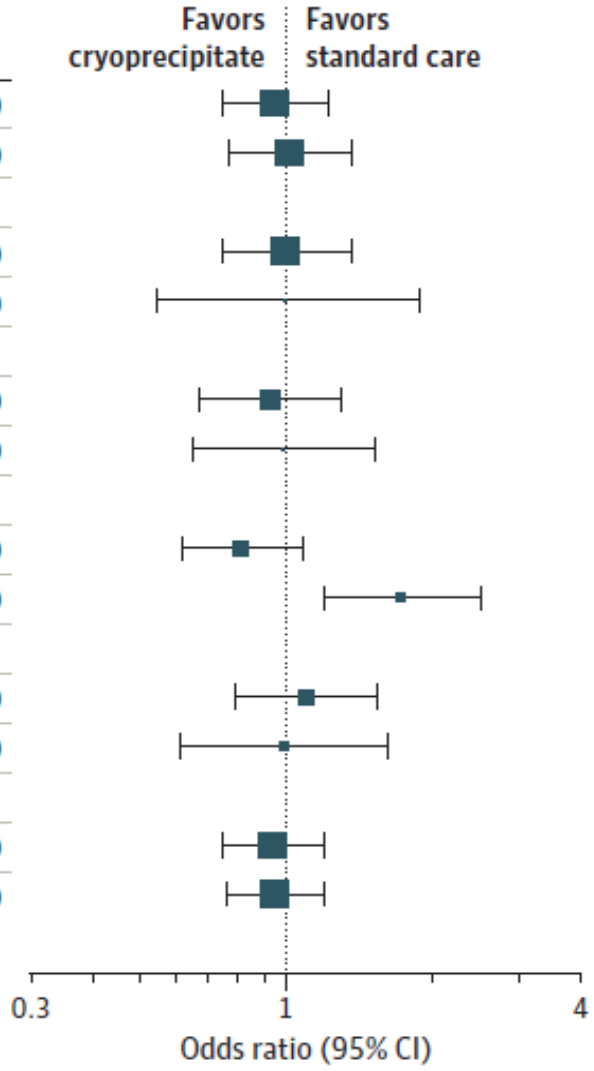


No. of patients at risk					
Cryoprecipitate overall	784	567	532	514	498
Standard care overall	795	569	518	501	479
Cryoprecipitate (blunt injury)	495	348	332	323	310
Standard care (blunt injury)	518	353	320	307	289
Cryoprecipitate (penetrating injury)	289	219	200	191	188
Standard care (penetrating injury)	277	216	198	194	190

Davenport R et al. JAMA 2023; 330: 1882-1891

Results

	No./total No. (%)		Odds ratio (95% CI)	*P* value
	Cryoprecipitate	Standard care		
Intent-to-treat population	192/760 (25.3)	201/771 (26.1)	0.96 (0.75-1.23)	.74[a]
Per-protocol population	163/706 (23.1)	154/683 (22.5)	1.03 (0.77-1.37)	.83[a]
Participant age, y				
<70	149/687 (21.7)	146/681 (21.4)	1.01 (0.75-1.37)	>.99[b]
≥70	40/69 (58.0)	49/84 (58.3)	1.01 (0.55-1.88)	
Participant sex				
Men	136/596 (22.8)	148/616 (24.0)	0.94 (0.67-1.31)	.82[b]
Women	56/164 (34.1)	53/155 (34.2)	1.00 (0.65-1.53)	
Injury type				
Blunt	147/483 (30.4)	174/500 (34.8)	0.82 (0.62-1.09)	.004[b]
Penetrating	45/277 (16.2)	27/271 (10.0)	1.74 (1.20-2.51)	
Head AIS score[c]				
<4	92/506 (18.2)	79/472 (16.7)	1.11 (0.79-1.55)	.74[b]
≥4	77/157 (49.0)	94/191 (49.2)	1.00 (0.61-1.63)	
Sensitivity analyses				
Switching 2% of outcomes inferred based on discharge	193/760 (25.4)	203/771 (26.3)	0.95 (0.75-1.21)	.69[a]
Unadjusted for center	192/760 (25.3)	201/771 (26.1)	0.96 (0.76-1.21)	.72[d]



Davenport R et al. JAMA 2023; 330: 1882-1891

PROCOAG Randomized Clinical Trial

- Double blinded, placebo-controlled trial in France (12/2017-8/2021)
- Trauma patients at risk of MTP activation
  - 324 patients randomized and analyzed (median age 39 years, 73% males)
  - Injury severity score 36; 69% required expedient hemorrhage control
- Intervention
  - Standard of care + 1 mL/kg saline (n=162) vs. standard of care + 25 IU/kg 4-factor PCC (n=162)
- 24-hour all blood product consumption

Bouzat P et al. JAMA 2023; 329: 1367-1375

Results

Outcome	No. (%) 4F-PCC (n = 164)	Placebo (n = 160)	Absolute difference (95% CI), %[a]	*P* value[b]
Primary outcome				
Total blood product consumption, median (IQR), U	12 (5 to 19)	11 (6 to 19)	0.2 (−2.99 to 3.33)	.72
Secondary outcomes				
Red blood cell consumption, median (IQR), U[c]	6 (3.5 to 10)	6 (4 to 10)	−0.3 (−1.8 to 1.3)	.93
Fresh frozen plasma consumption, median (IQR), U[d]	4 (1 to 8)	4 (2 to 8)	0.1 (−1.3 to 1.5)	.56
Platelet concentrate consumption, median (IQR), U[e]	1 (0 to 1)	1 (0 to 1)	0.0 (−0.3 to 0.3)	.83
Time to PTr <1.5, median (IQR) [No.], min[f]	0 (0 to 60) [154]	0 (0 to 60) [145]	−8.5 (−48.9 to 32.0)	.86
Mortality				
24-h	18 (11)	20 (13)	−2 (−9 to 5)	.67
28-d	26 (17)	30 (21)	−3 (−12 to 5)	.48
Time to achieve anatomic hemostasis, median (IQR) [No.], min[g]	309 (203 to 433) [121]	288 (219 to 404) [128]	22 (−72.2 to 72.8)	.96
Hospital-free days through day 28, median (IQR)	6.5 (0 to 22.5)	7 (0 to 22)	−0.15 (−1.65 to 1.35)	.78
Ventilator-free days through day 28, median (IQR)	4 (0.5 to 7)	4 (0 to 8)	0.33 (−1.0 to 1.6)	.51
ICU-free days through day 28, median (IQR)	6.5 (0 to 22.5)	7 (0 to 22)	1.22 (−5.93 to 8.37)	.78
Disposition at day 28				
Remained hospitalized	44 (33)	44 (35)	0 (−10 to 10)	.81
Intensive care unit	37 (28)	28 (23)	5 (−5 to 16)	
Home	31 (23)	29 (23)	−3 (−12 to 6)	
Died	26 (17)	30 (21)	−3 (−12 to 5)	
Rehabilitation	19 (14)	22 (18)	−2 (−14 to 9)	
Other	2 (2)	1 (1)	1 (−2 to 3)	
Unknown	5 (3)	6 (4)		
Glasgow Outcome Scale-Extended score, median (IQR) [No.][h]	3 (3 to 4) [36]	3 (3 to 5) [27]	−0.5 (−1.91 to 0.91)	.45

Bouzat P et al. JAMA 2023; 329: 1367-1375

Results

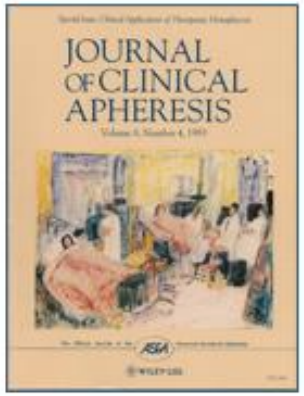
Table 3. Thromboembolic Events by Treatment Group

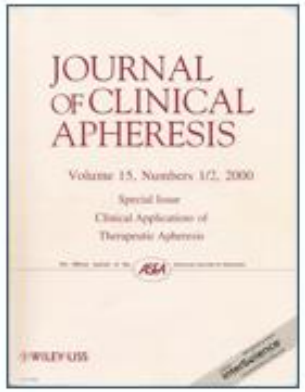
Thromboembolic event	No. (%)		Absolute difference (95% CI), %[a]	Relative risk (95% CI)	*P* value[b]
	4F-PCC (n = 164)	Placebo (n = 160)			
Patients with at least 1 thromboembolic event, No. (%) [No.]	56 (35) [161]	37 (24) [157]	11 (1 to 21)	1.48 (1.04 to 2.10)	.03
Superficial venous thrombosis	5 (3.1)	1 (0.6)	2 (−1 to 5)		
Deep venous thrombosis	27 (16.8)	23 (14.6)	2 (−6 to 10)		
Pulmonary embolism	20 (12.4)	17 (10.8)	2 (−5 to 9)		
Stroke[c]	2 (1.2)	0	1 (−1 to 3)		
Other[d]	9 (5.6)	5 (3.2)	2 (−2 to 7)		

Bouzat P et al. JAMA 2023; 329: 1367-1375

When to Perform Therapeutic Apheresis or Not

Apheresis Guidelines Evolution

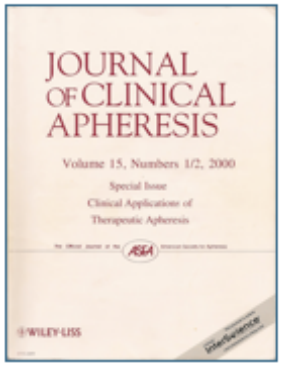




1986	1993	2000	2007
First edition	Category definitions introduced	Category definitions revised	Fact sheet format introduced

Slide courtesy of Dunbar NM.

Apheresis Guidelines Evolution



2010 — Grade system adopted

2013 — Separately categorize/ grade disease presentations

2016 — Retire category IV indications with no new information

2019 — Criteria for new fact sheets introduced

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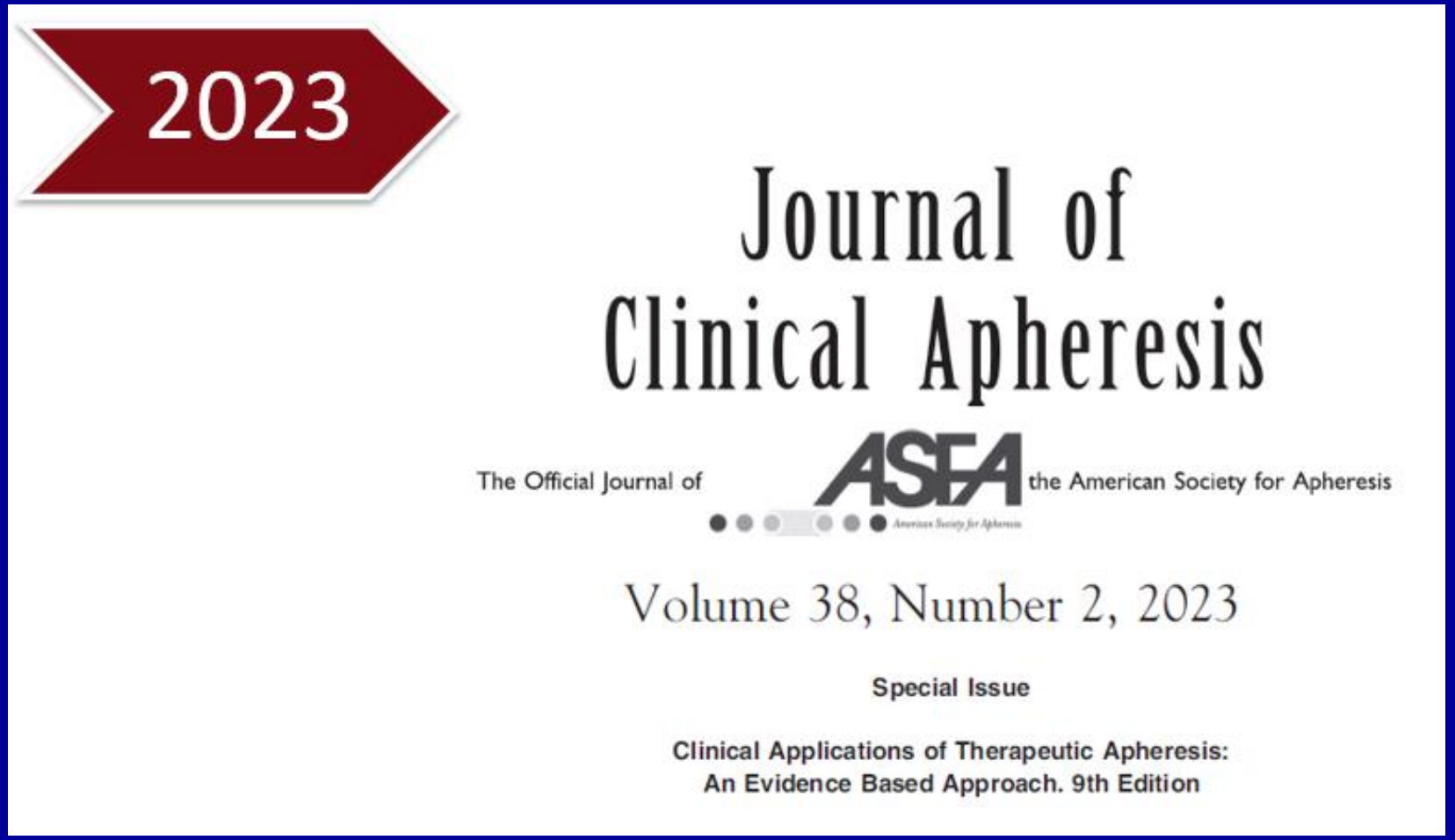
Apheresis Guidelines Evolution



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2023 Special Issue Highlights

- 91 diseases / conditions, 166 indications

TABLE 1 Category and grade recommendations for therapeutic apheresis.

Disease/condition	Indication	Procedure	Category	Grade	Page
Acute disseminated encephalomyelitis	Steroid refractory	TPE	II	2C	95
Acute inflammatory demyelinating polyradiculoneuropathy	Primary treatment	TPE	I	1A	97
		IA	I	1B	
Acute liver failure	Acute liver failure	TPE-HV	I	1A	99
		TPE	III	2B	
	Acute fatty liver of pregnancy[a]	TPE	III	2B	
Acute toxins, venoms and poisons	Mushroom poisoning	TPE	II	2C	101
	Envenomation	TPE	III	2C	
	Other[a]	TPE/RBC exchange	III	2C	
Age related macular degeneration	Dry, high risk	DFPP	III	2B	103
Alzheimer's disease[a]	Mild or moderate	TPE	III	2A	105

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278

ASFA Category

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision-making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB/Ethics Committee approval is desirable if apheresis treatment is undertaken in these circumstances.

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Grade of Recommendation

Recommendation	Description	Methodological quality of supporting evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
Grade 2A	Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

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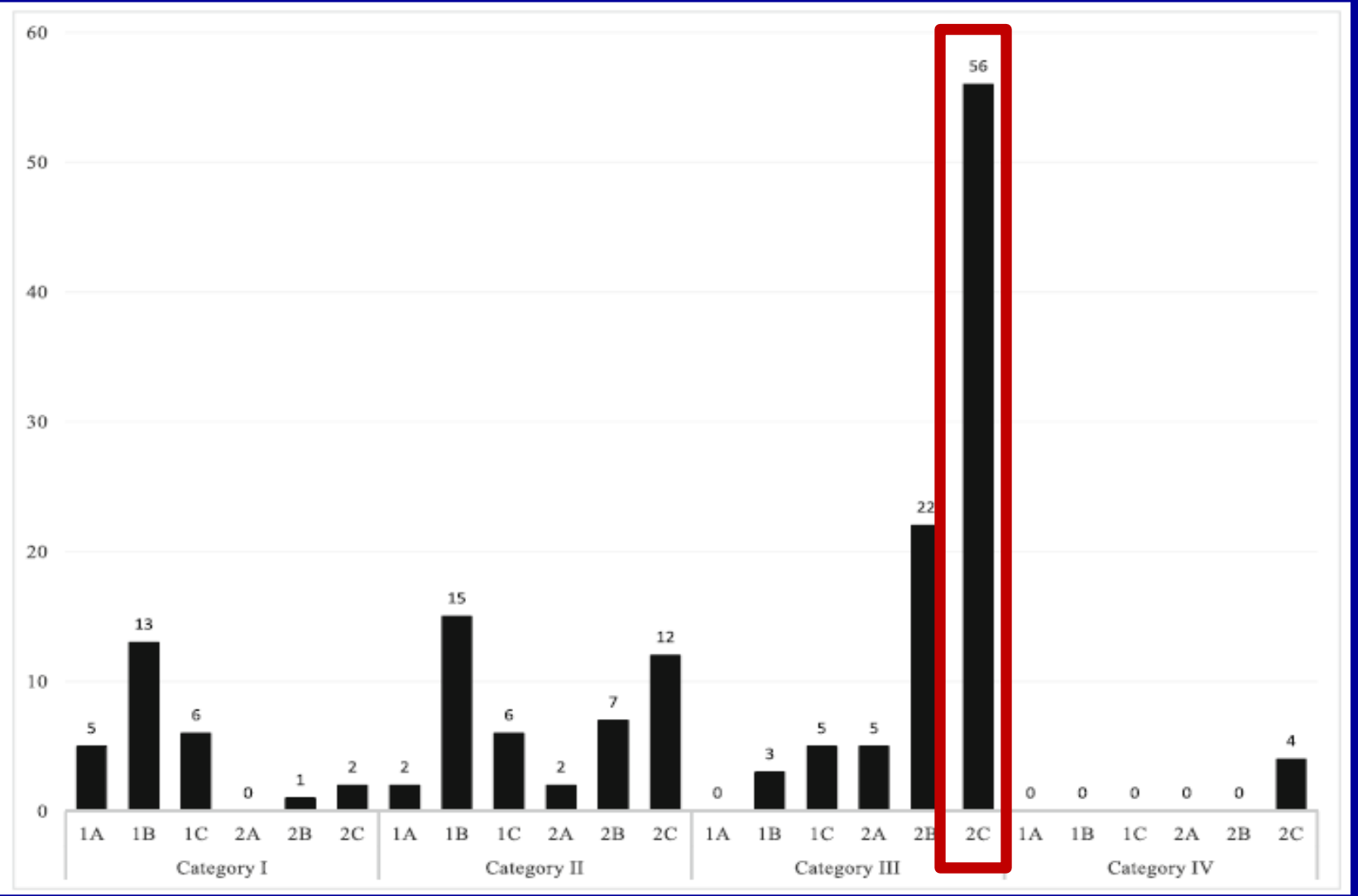

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New Fact Sheets

Incorporated as new fact sheets
Alzheimer's disease
Autoimmune dysautonomia
Idiopathic inflammatory myopathies
Immune checkpoint inhibitors, immune-related adverse events
Paraneoplastic autoimmune retinopathies
Transplantation, intestine
Vaccine-induced immune thrombotic thrombocytopenia

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278

New Indications in Existing Fact Sheets

Incorporated into existing fact sheets
Mechanical hemolysis incorporated into acute toxins, venoms and poisons
Methemoglobinemia incorporated into acute toxins, venoms and poisons
Bone marrow necrosis/fat embolism syndrome incorporated into sickle cell disease, acute

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278

Insufficient Evidence for New Fact Sheets

Insufficient evidence at time of review
Autoimmune myofasciitis
Autoimmune recurrent pregnancy failure
Hyperbilirubinemia, kidney failure/bile cast nephropathy
Pancreatic transplantation
Platelet refractoriness due to human leukocyte antigen (HLA) antibodies
Transplantation, composite tissue

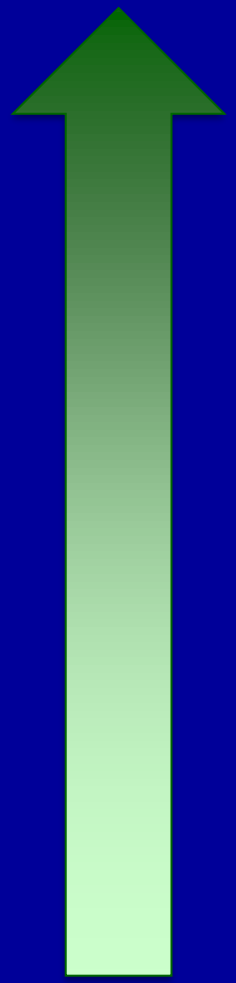
Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278

Impact of COVID-19

- New fact sheet for “Vaccine-induced immune thrombotic thrombocytopenia (VITT)”
- New indications in “Sepsis with multiorgan failure” and “Vasculitis, other” fact sheets
- Comments concerning associations with COVID-19 in several fact sheets

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Upgraded ASFA Category Indications



ERYTHROPOIETIC PROTOPORPHYRIA, LIVER DISEASE

Incidence: 2-5/1,000,000		**Procedure**	**Recommendation**	**Category**
		TPE	Grade 2C	III
		RBC Exchange	Grade 2C	III
# reported patients: <100	**RCT**	**CT**	**CS**	**CR**
TPE	0	0	1(3)	15(16)
RBC Exchange	0	0	1(3)	7(9)

ERYTHROPOIETIC PROTOPORPHYRIA, LIVER DISEASE

Incidence: ~2 to 5/1,000,000/year				
Procedure	**Category**		**Grade**	
TPE/RBC exchange	II		2C	
# reported patients: <100	**RCT**	**CT**	**CS**	**CR**
	0	0	2 (8)*	17 (18)**

*includes patients who received both TPE and RBC exchange; **6 TPE only, 10 RBC exchange only, 2 TPE in combination with RBC exchange.

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Upgraded ASFA Category Indications

INFLAMMATORY BOWEL DISEASE

Incidence: UC: 35--100/100,000; CD: 27-48/100,000		**Indication**	**Procedure**	**Recommendation**	**Category**
		UC/CD	Adsorptive cytapheresis	Grade 1B	III
		CD	ECP	Grade 2C	III
# reported patients: >300		**RCT**	**CT**	**CS**	**CR**
UC	Adsorptive cytapheresis	12(724)	9(92)	NA	NA
CD	Adsorptive cytaphereis	2(258)	1(104)	NA	NA
CD	ECP	0	0	3(69)	2(3)

INFLAMMATORY BOWEL DISEASE

Incidence: ulcerative colitis: 35 to 100/100,000; Crohn's disease: 27 to 48/100,000

Indication	**Procedure**	**Category**		**Grade**	
Ulcerative colitis	Adsorptive cytapheresis	II		1B	
Crohn's disease	Adsorptive cytapheresis	III		1B	
	ECP	III		2C	
# reported patients: >300	**Procedure**	**RCT**	**CT**	**CS**	**CR**
Ulcerative colitis	Adsorptive cytapheresis	14 (982)	12 (300)	NA	NA
Crohn's disease	Adsorptive cytapheresis	2 (258)	1 (104)	NA	NA
	ECP	0	0	3 (69)	2 (3)

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Downgraded ASFA Category Indications

AGE RELATED MACULAR DEGENERATION, DRY

Prevalence: 2% (dry AMD and soft drusen, US population)	**Indication**	**Procedure**	**Recommendation**	**Category**
	High-risk	Rheopheresis	Grade 2B	II
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	6(433)	3(396)	NA	NA

AGE RELATED MACULAR DEGENERATION

Prevalence: 30% of individuals over age 85

Indication	**Procedure**		**Category**	**Grade**
Dry, high risk	DFPP		III	2B
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	6 (433)	3 (396)	NA	NA

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Downgraded ASFA Category Indications

RED CELL ALLOIMMUNIZATION, PREVENTION AND TREATMENT

Incidence: 15% of population is RhD negative; Pregnancy: 35/10,000 live births/yr (US)	**Indication**	**Procedure**	**Recommendation**	**Category**
	Exposure to RhD + RBCs	RBC exchange	Grade 2C	III
	Pregnancy, GA <20 wks	TPE	Grade 2C	III
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
Exposure to RhD + RBCs	0	0	0	6(8)
Pregnancy, GA <20 wks	0	0	14(312)	29(33)

RED BLOOD CELL ALLOIMMUNIZATION, PREGNANCY COMPLICATIONS

Incidence: hemolytic disease of the fetus and newborn: 1,700 cases/100,000 newborns (United States)

Indication	**Procedure**		**Category**	**Grade**
Hemolytic disease of the fetus and newborn	TPE		III	2C
RhD alloimmunization prophylaxis after transfusion	RBC exchange		IV	2C
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
Hemolytic disease of the fetus and newborn	0	0	>10 (>200)	NA
RhD alloimmunization prophylaxis after transfusion	0	0	0	6 (8)

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Downgraded ASFA Category Indications

APPENDIX: VASCULITIS, ANCA-ASSOCIATED (AAV)

Incidence: 1-3/100000/year (geographical and ethnic differences; MPA: 48%-65%, GPA: 25%-40%, EGPA: 10%-12%)

Indication	Procedure		Category	Grade
MPA/GPA/RLV				
RPGN, Cr ≥5.7 mg/dL*	TPE		II	1B
RPGN, Cr <5.7 mg/dL*	TPE		III	2C
DAH	TPE		I	1C
EGPA	TPE		III	2C
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	10(1091)	5(345)	NA	NA

VASCULITIS, ANCA-ASSOCIATED

Incidence: 1 to 3/100,000/year (geographical, age, and ethnic differences)

Indication	Procedure		Category	Grade
Microscopic polyangiitis	TPE		III	1B
Granulomatosis with polyangiitis				
Eosinophilic granulomatosis with polyangiitis	TPE		III	2C
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	10 (1091)	5 (345)	NA	NA

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Downgraded ASFA Category Indications

BABESIOSIS

Incidence: 4,600 cases in the US since 1986; endemic in Northeast and Great Lakes regions	**Indication**	**Procedure**	**Recommendation**	**Category**
	Severe	RBC exchange	Grade 2C	II
# reported patients: <100	**RCT**	**CT**	**CS**	**CR**
	0	3	4(20)	19(20)

New data shows unclear benefit compared to antibiotics alone

BABESIOSIS

Incidence: endemic in United States Northeast and upper Midwest regions

Indication	**Procedure**		**Category**	**Grade**
Severe	RBC exchange		III	2C
# reported patients: 100 to 300	**RCT**	**CT**	**CS**	**CR**
	0	1 (28)	9 (157)	NA

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278
Slide courtesy of Dunbar NM.

Downgraded ASFA Category Indications

HYPERLEUKOCYTOSIS

Incidence: AML: WBC >100×10^9/L; 5-13% adults; ALL: WBC >400×10^9/L; 10-30% adults	**Indication**	**Procedure**	**Recommendation**	**Category**
	Symptomatic	Leukocytapheresis	Grade 2B	II
	Prophylactic or secondary	Leukocytapheresis	Grade 2C	III
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
AML	0	14(2400)	NA	NA
ALL	0	6(578)	NA	NA

HYPERLEUKOCYTOSIS

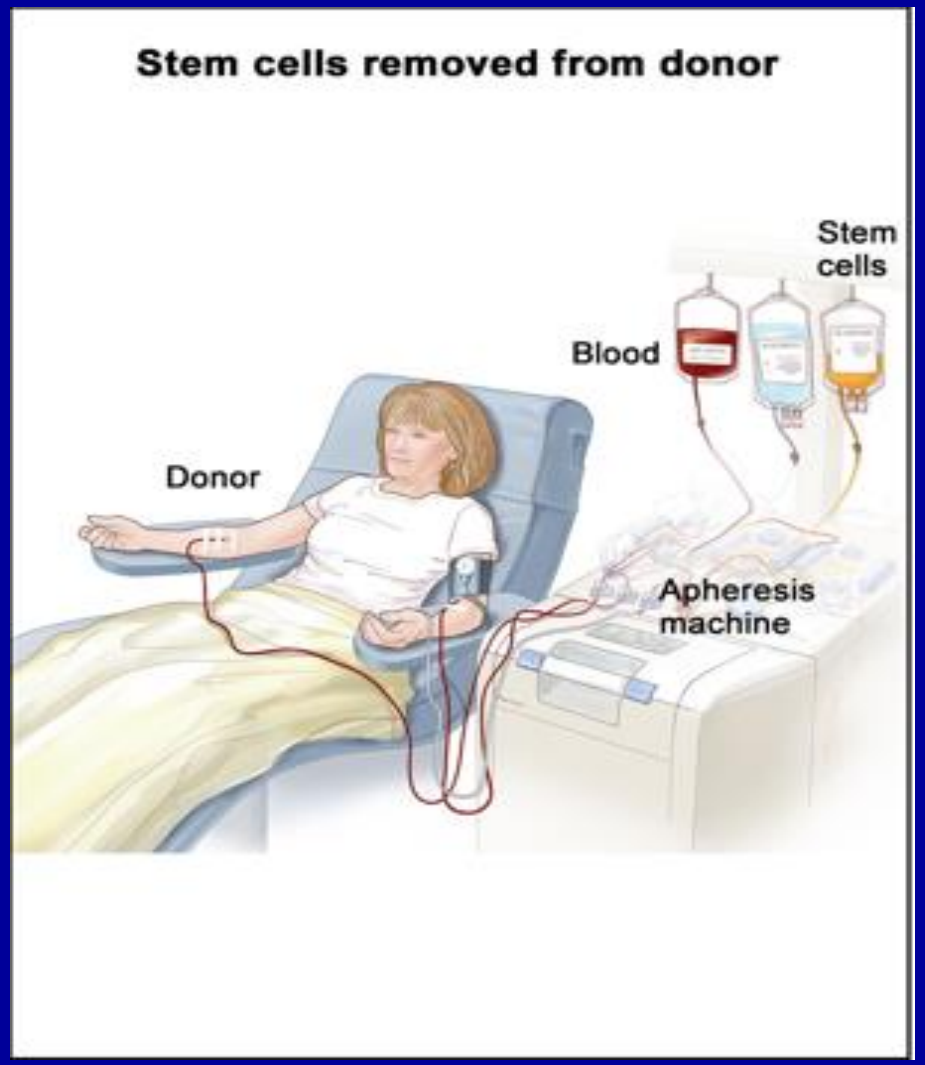
Incidence: AML: WBC >100 × 10^9/L; 5% to 13% adults; ALL: WBC >400 × 10^9/L; 10% to 30% adults

Indication	**Procedure**		**Category**	**Grade**
	Leukocytapheresis		III	2B
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
AML	0	20 (3602)	NA	NA
ALL	0	9 (710)	NA	NA

Connelly-Smith L et al. J Clin Apher 2023; 38: 77-278

Slide courtesy of Dunbar NM.

How to Have Donors Available for All Patients?



HLA Match Likelihood for HPC Transplants

U.S. Racial and Ethnic Group	Likelihood of Identifying an Adult Donor*		Likelihood of Identifying a Cord-Blood Unit for Patients ≥20 Yr of Age†			Likelihood of Identifying a Cord-Blood Unit for Patients <20 Yr of Age†		
	8/8 HLA Match	≥7/8 HLA Match	6/6 HLA Match	≥5/6 HLA Match	≥4/6 HLA Match	6/6 HLA Match	≥5/6 HLA Match	≥4/6 HLA Match
				percent				
White European	75	97	17	66	96	38	87	99
Middle Eastern or North African	46	90	6	46	91	18	75	98
African American	19	76	2	24	81	6	58	95
African	18	71	1	23	81	5	56	95
Black South or Central American	16	66	2	27	82	7	58	96
Black Caribbean	19	74	1	24	81	6	58	95
Chinese	41	88	6	44	91	19	77	98
Korean	40	87	5	39	89	17	73	98
South Asian	33	84	4	41	90	14	73	98
Japanese	37	87	4	37	88	16	72	97
Filipino	40	83	5	42	89	19	76	98
Southeast Asian	27	76	3	37	89	12	70	98
Vietnamese	42	84	6	44	89	20	76	98
Hawaiian or Pacific Islander	27	72	3	32	84	10	64	96
Mexican	37	87	6	45	91	19	75	98
Hispanic South or Central American	34	80	5	43	90	17	73	98
Hispanic Caribbean	40	83	5	40	89	17	71	98
Native North American	52	91	10	54	93	25	80	99
Native South or Central American	49	87	11	53	93	26	79	98
Native Caribbean	32	77	4	35	86	14	66	97
Native Alaskan	36	83	7	47	91	18	75	98

Gragert L et al. N Engl J Med 2014;371: 339-348

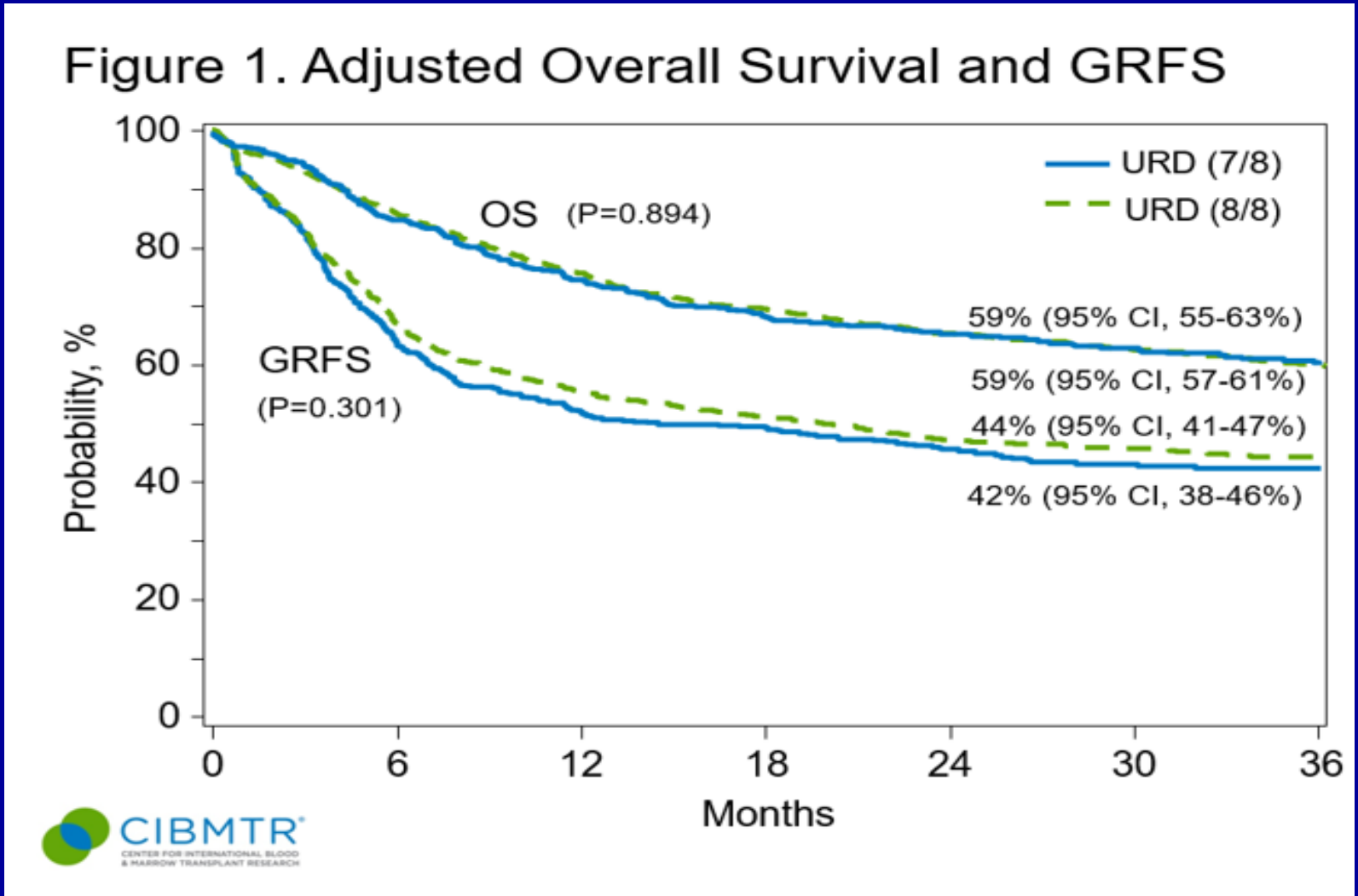
Mismatched Unrelated Bone Marrow Transplants

- HLA Mismatched unrelated transplants (MMUD)
  - Increase risk of GVHD and graft failure with standard calcineurin inhibitor-based GVHD prophylaxis

- Post-transplant high dose cyclophosphamide (PTCy)
  - Selectively (toxic) sensitive to activated alloreactive effector T cells
  - Preserve regulatory T-cell function
  - Have been use successfully in haploidentical transplants

Shaw BE et al. J Clin Oncol 2021; 39: 1971-1982

MMUD Transplants with PTCy



Auletta JJ et al. ASH 2023

HLA Match Likelihood for HPC Transplants

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	8/8 HLA Match	≥7/8 HLA Match	6/6 HLA Match	≥5/6 HLA Match	≥4/6 HLA Match	6/6 HLA Match	≥5/6 HLA Match	≥4/6 HLA Match
				percent				
White European	75	97	17	66	96	38	87	99
Middle Eastern or North African	46	90	6	46	91	18	75	98
African American	19	76	2	24	81	6	58	95
African	18	71	1	23	81	5	56	95
Black South or Central American	16	66	2	27	82	7	58	96
Black Caribbean	19	74	1	24	81	6	58	95
Chinese	41	88	6	44	91	19	77	98
Korean	40	87	5	39	89	17	73	98
South Asian	33	84	4	41	90	14	73	98
Japanese	37	87	4	37	88	16	72	97
Filipino	40	83	5	42	89	19	76	98
Southeast Asian	27	76	3	37	89	12	70	98
Vietnamese	42	84	6	44	89	20	76	98
Hawaiian or Pacific Islander	27	72	3	32	84	10	64	96
Mexican	37	87	6	45	91	19	75	98
Hispanic South or Central American	34	80	5	43	90	17	73	98
Hispanic Caribbean	40	83	5	40	89	17	71	98
Native North American	52	91	10	54	93	25	80	99
Native South or Central American	49	87	11	53	93	26	79	98
Native Caribbean	32	77	4	35	86	14	66	97
Native Alaskan	36	83	7	47	91	18	75	98

Gragert L et al. N Engl J Med 2014;371: 339-348

Thank you for your attention

- Email: hpham2@nmdp.org or huy.pham@redcross.org
- Donate blood: https://www.redcross.org/give-blood.html
- Join the NMDP registry: https://my.bethematch.org/s/?language=en_US