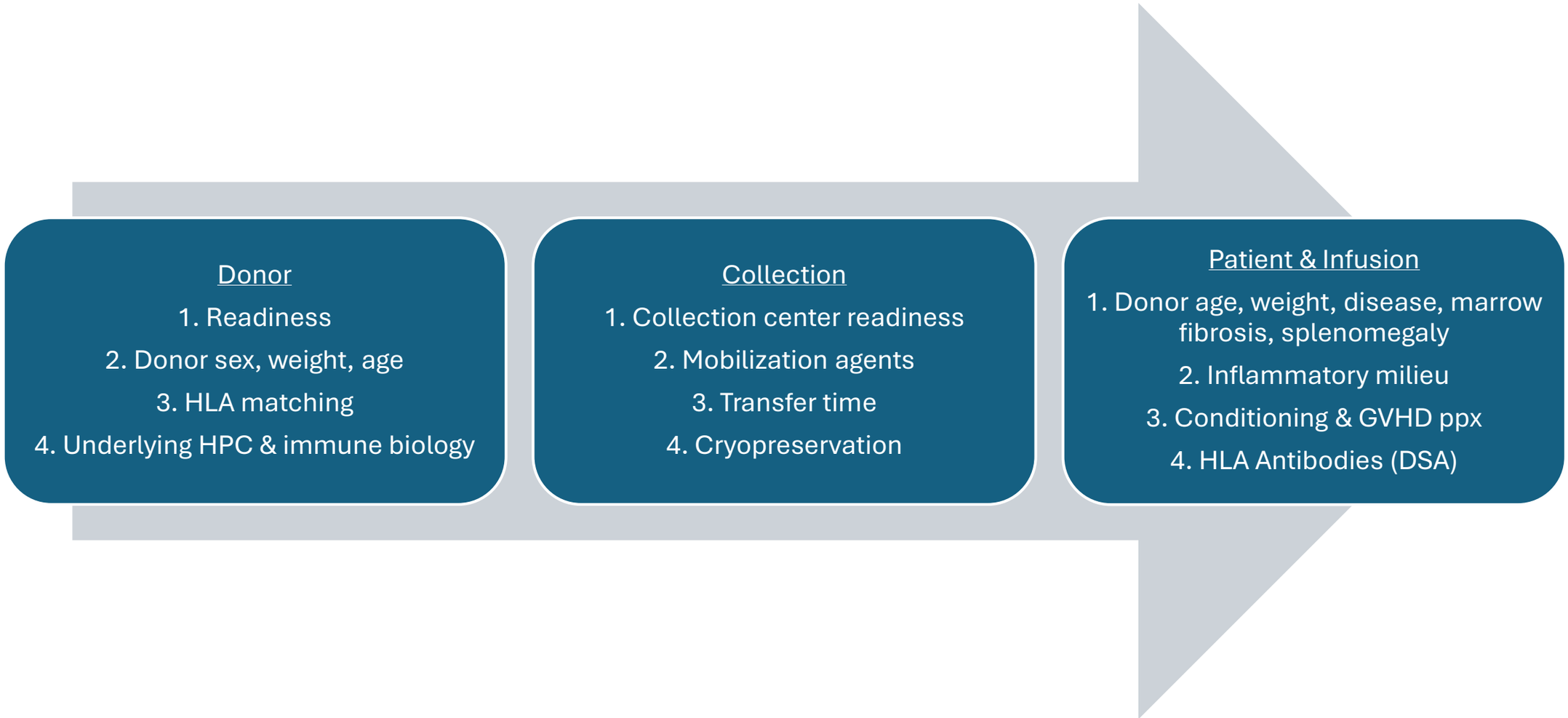
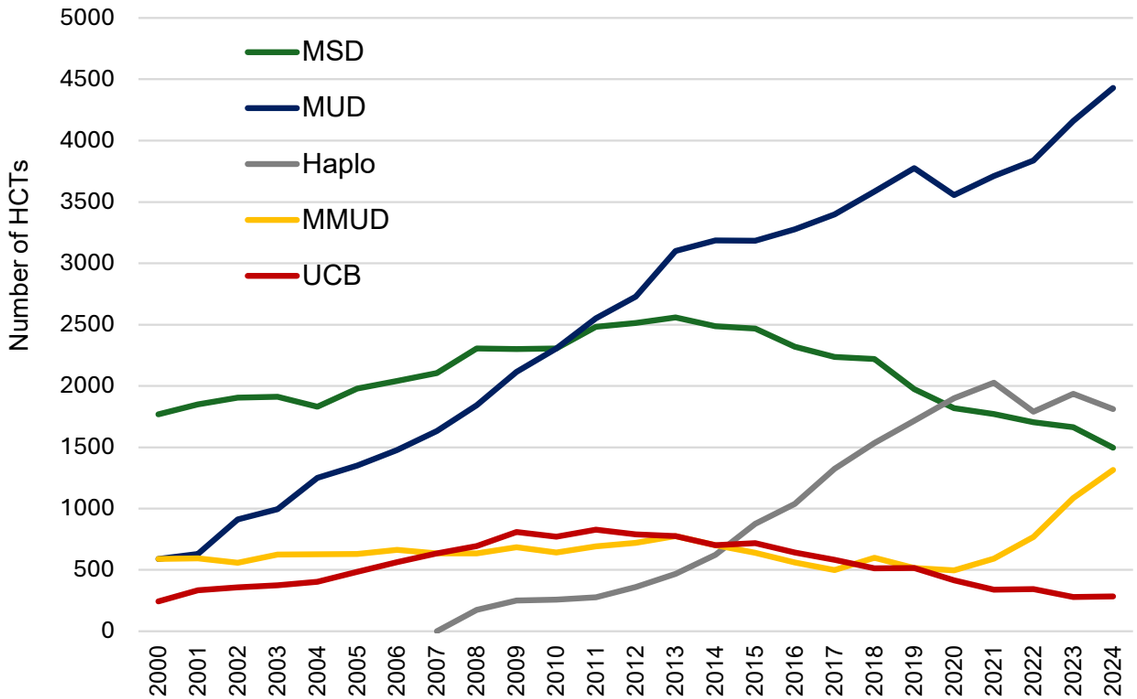
Donor Considerations, HCT Planning, and Outcomes

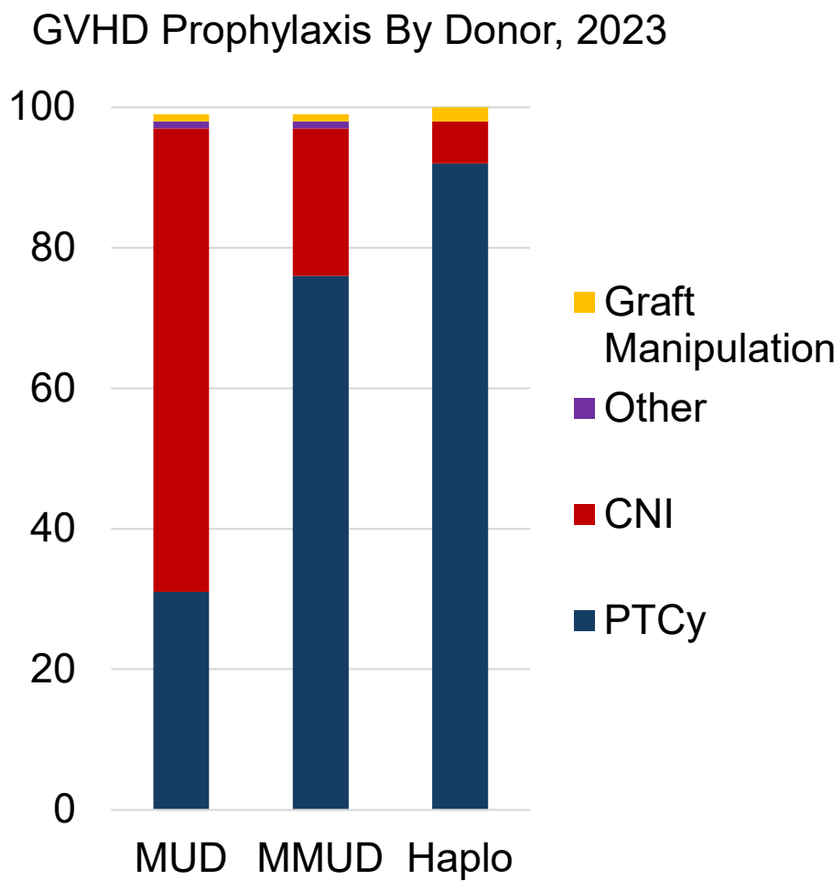


Emergent or Potential Changes Relevant to Donor Selection

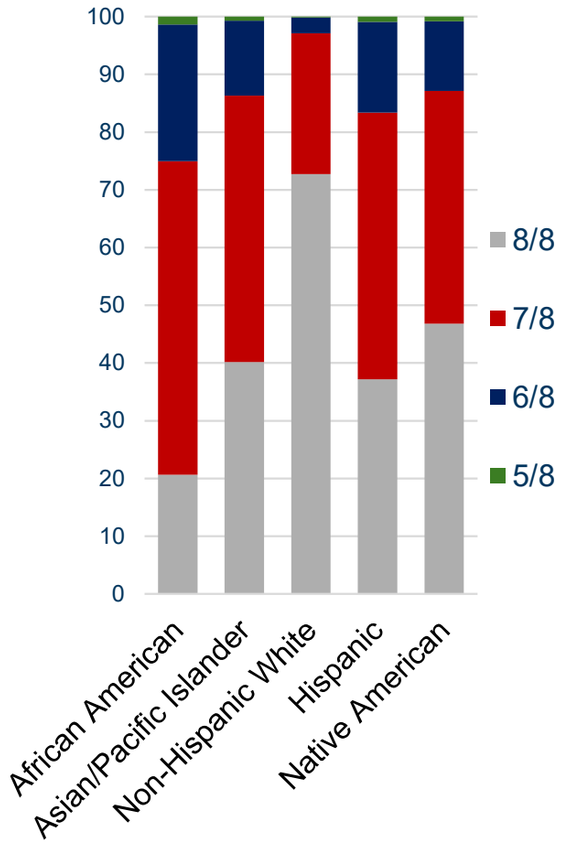
1. Increasing use of PTCy.
2. Increasing acceptance of unrelated donors, declining sibling donor use.
3. Decline in donor readiness.
4. Diversification and aging of US population, HCT population.
5. Increasing use of bio-therapies in lieu of traditional chemotherapy for remission induction.

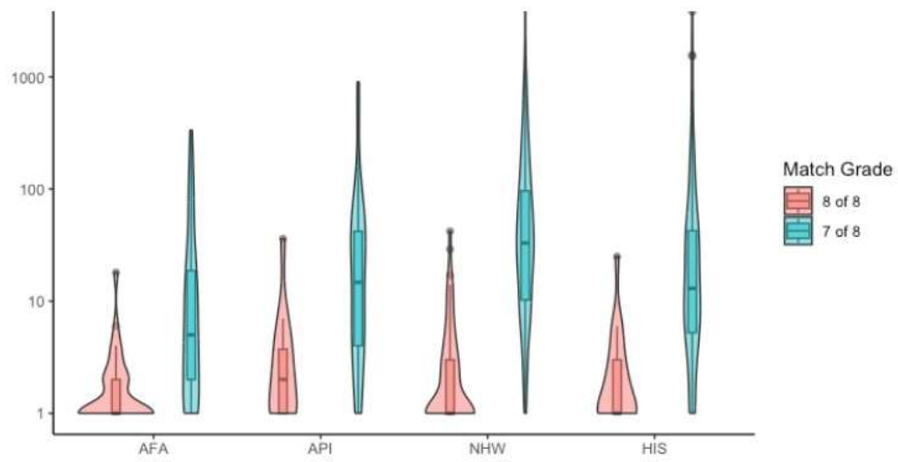
Graft Source and GVHD Prophylaxis Reported to CIBMTR, 2000-2024

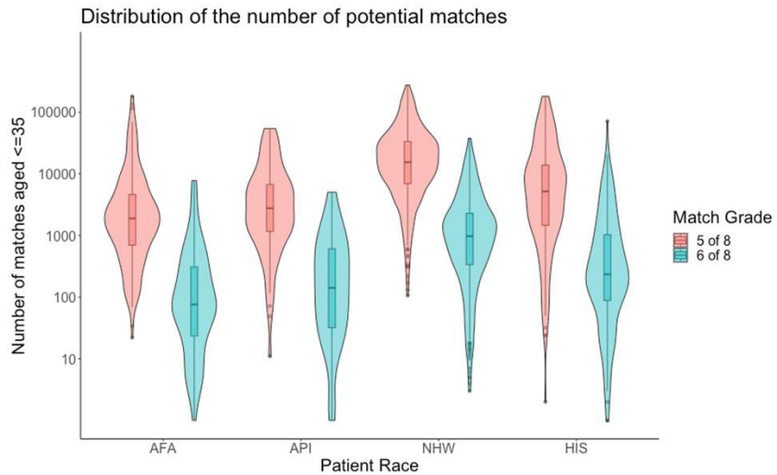




Preliminary URD search modeling (N=50,000)

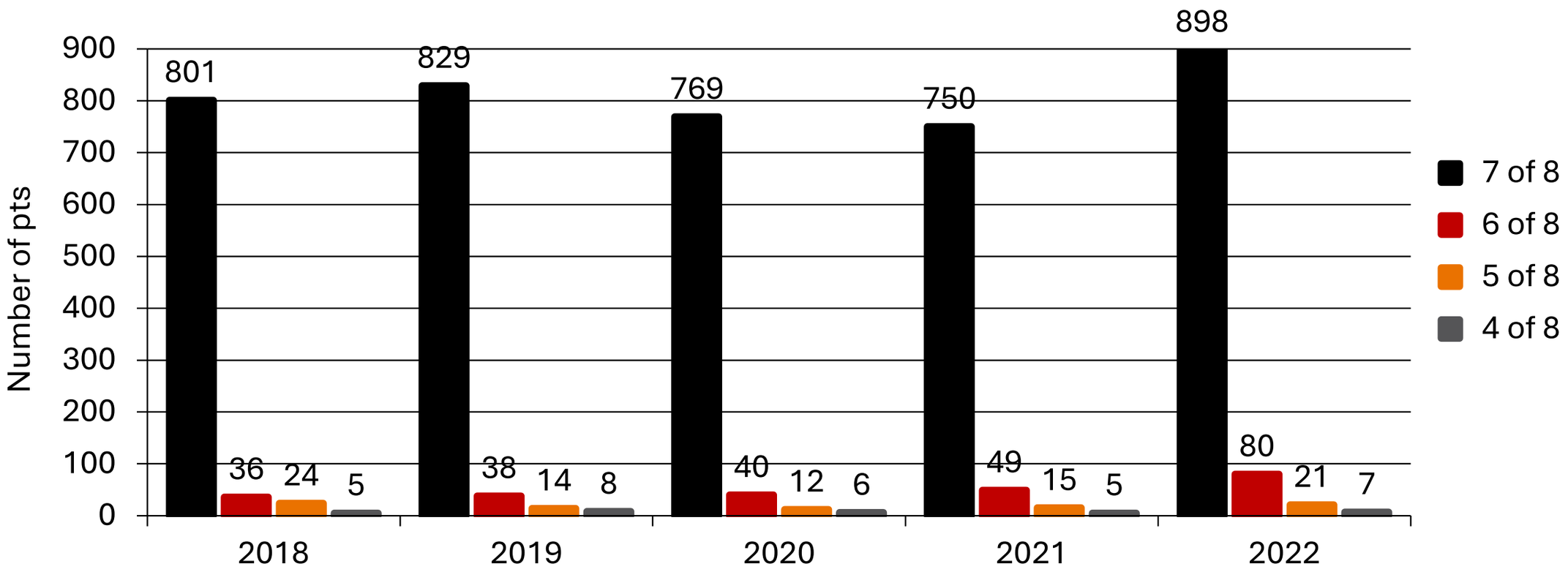






Adapted from Chowdhury JTCT 2023
Shaffer JCO 2024, c/o Martin Meiers

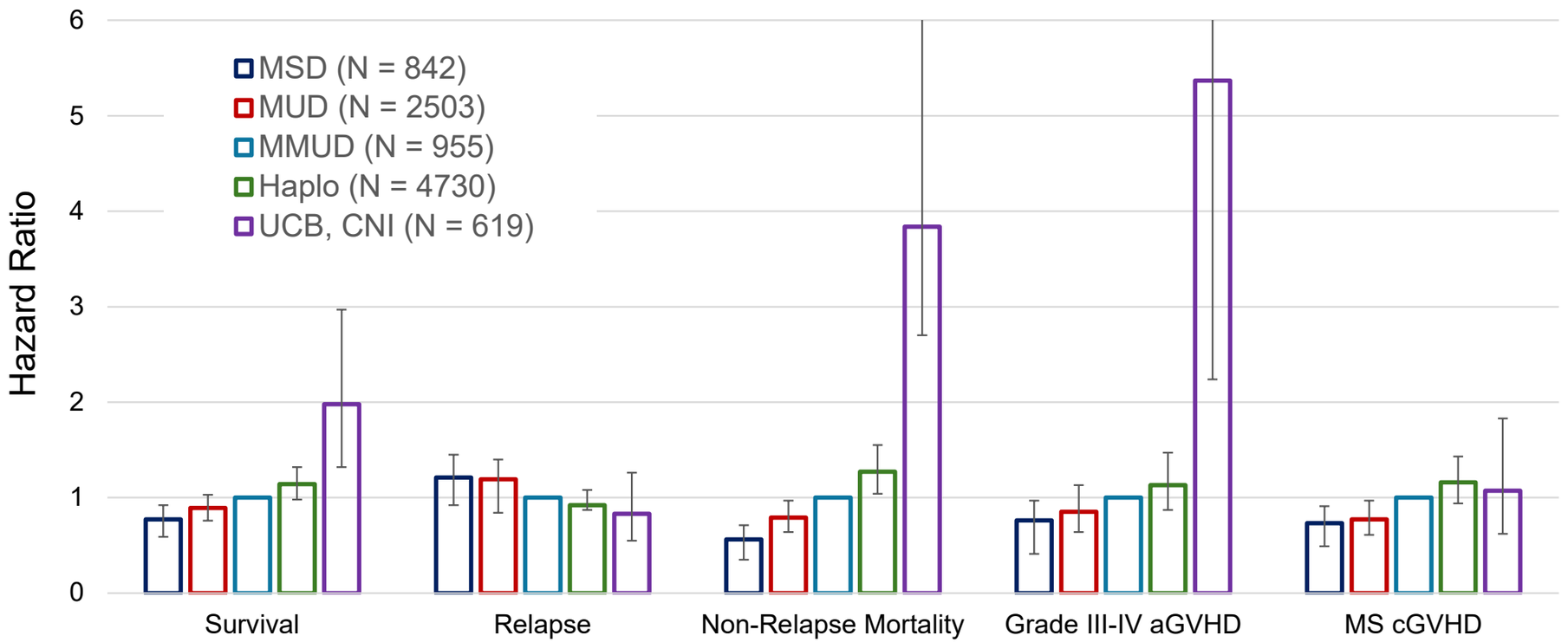
HLA match status in mmURD transplants reported to the CIBMTR, 2018-2022



NMDP Sponsored Clinical Trials in MMUD + PTCy: Expansion of MMUD HCT Uptake

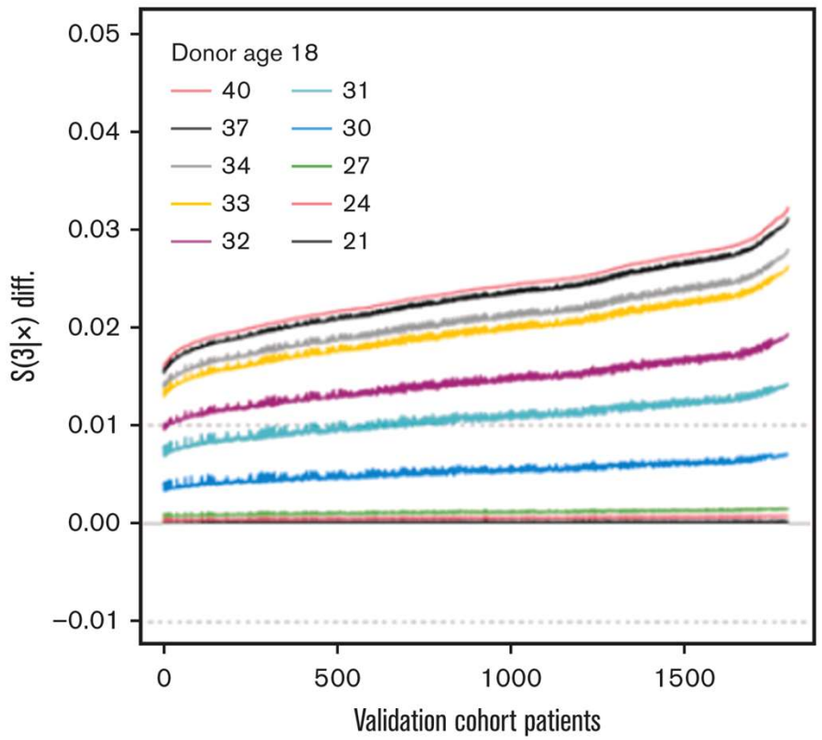
Trial Name	Accrual Start	Key Question	N Patients	N Centers
15-MMUD	2016	Marrow MMUD w PTCy + siro	80	11
ACCESS	2021	PBSC MMUD w PTCy + tacro	263	16-33
OPTIMIZE	2024	Reduced dose PTCy	157	33
ACCELERATE	2025	Platform Study	40+ per arm	60+

NMDP/CIBMTR ”Pan-Donor” Multivariable Regression Results

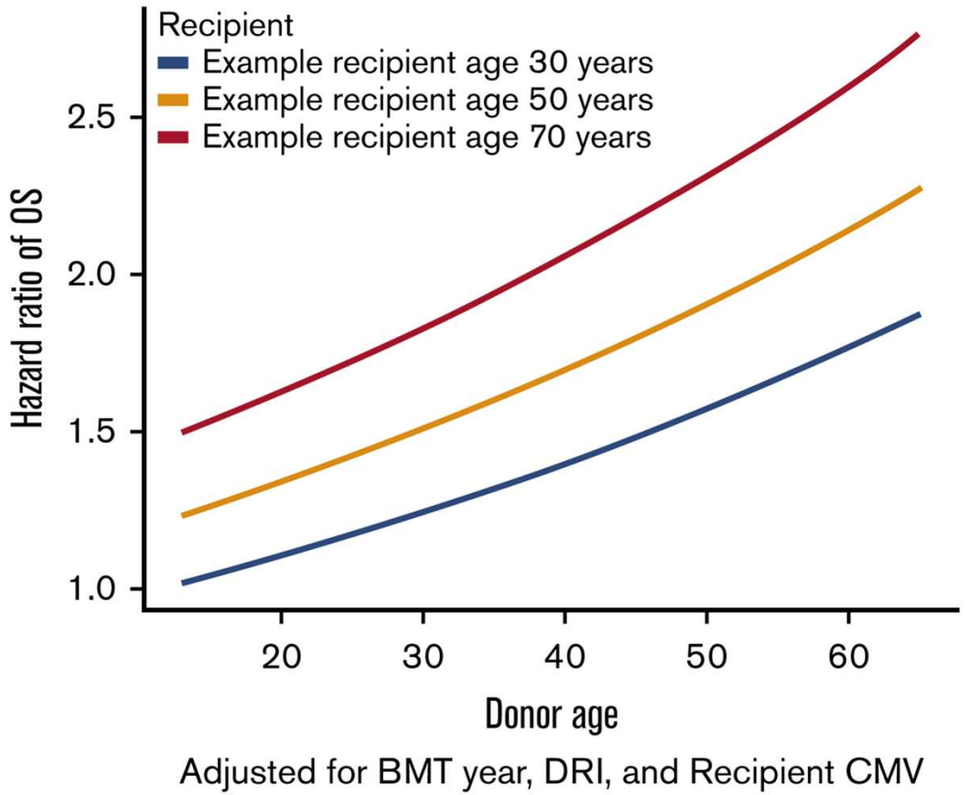


Devine EBMT 2025

Relationship Between Age and Outcomes

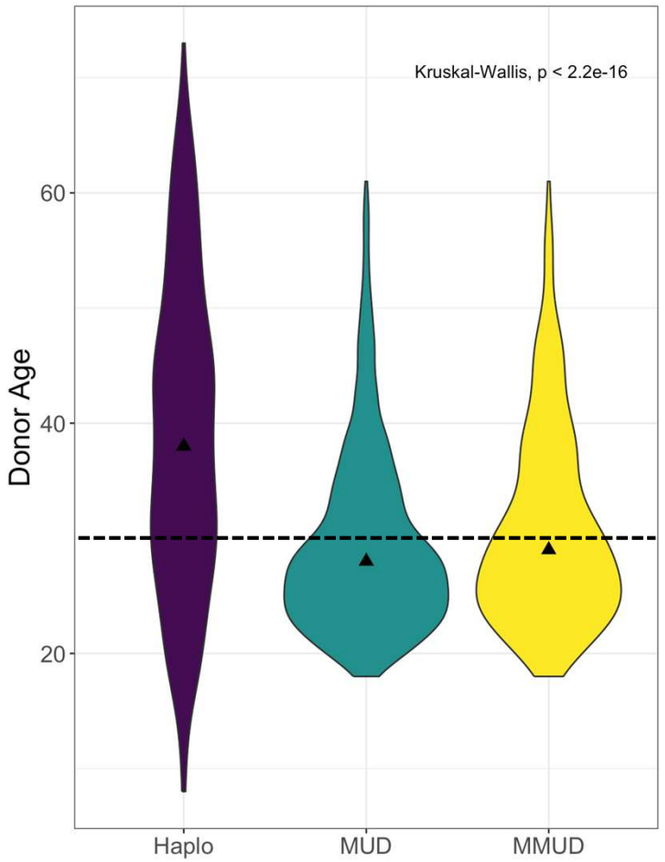


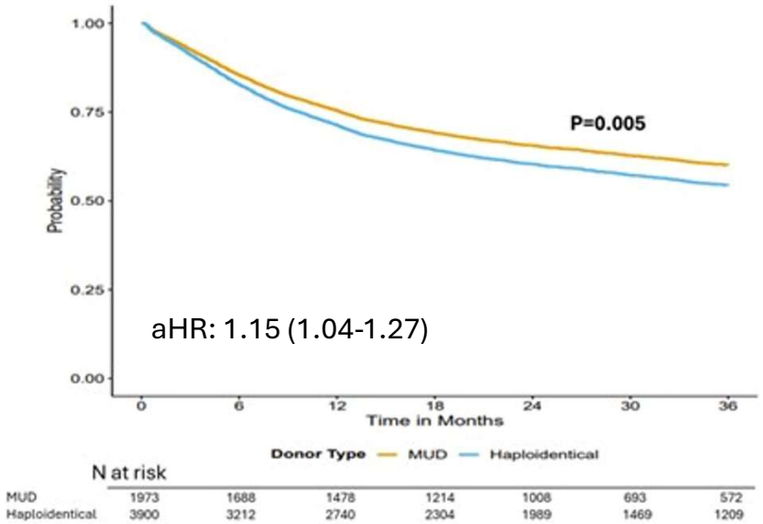
Spellman Blood Adv 2024



Dezern Blood Adv 2021

Unrelated Donors and Haploidentical Donors: Age and Outcomes

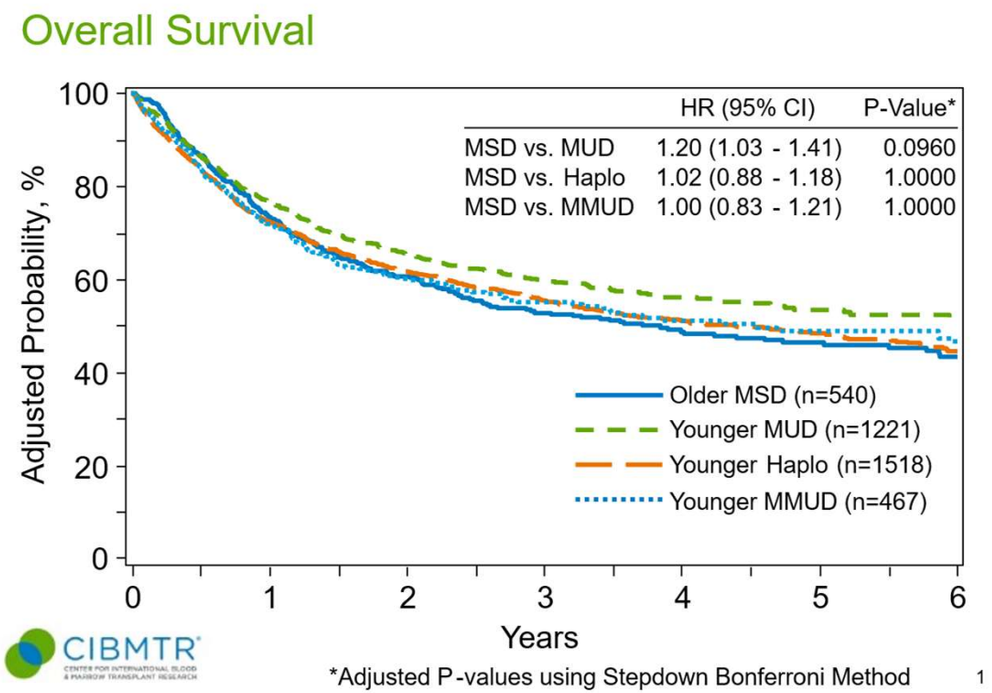




Graft	N	HR	P-value
MUD	1279	1.0	
Haplo	1217	1.12 (0.97-1.30)	0.13

Im et al TCT 2020
Shaffer et al JCO 2024

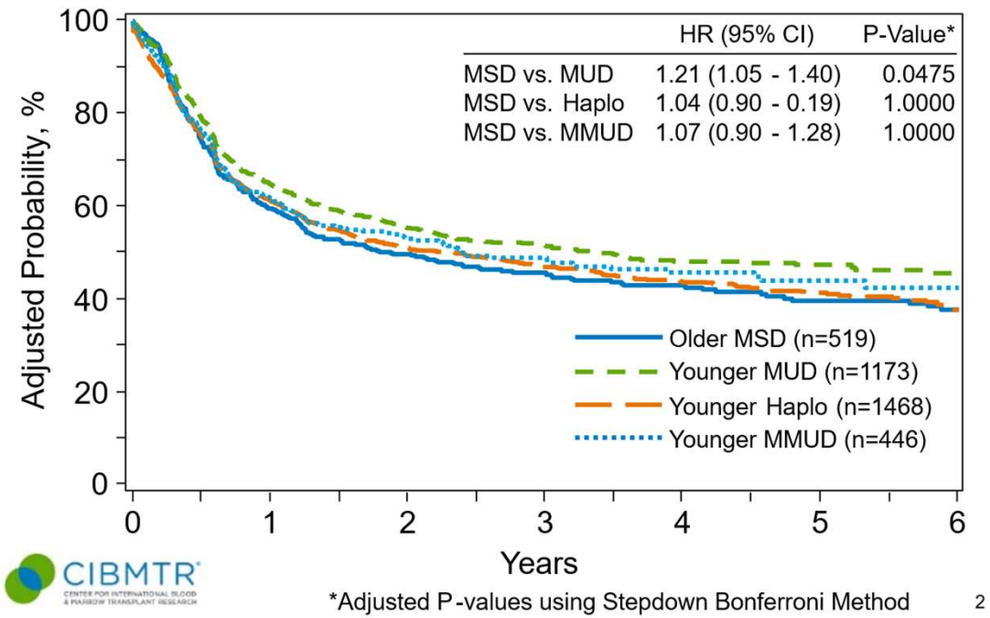
Older Sibling Donors vs. Younger Alt Donors



	MSD	MUD	Haplo	MMUD
5-yr OS	44%	52%	45%	46%

Donor Type	Patient Age	Donor Age
Older MSD N = 540	62 (5.9)	60 (5.7)
Young MUD N = 1221	65 (6.3)	26 (4.1)
Young Haplo N = 1518	61 (5.8)	28 (4.5)
Young MMUD N = 467	63 (6.5)	27 (4.0)

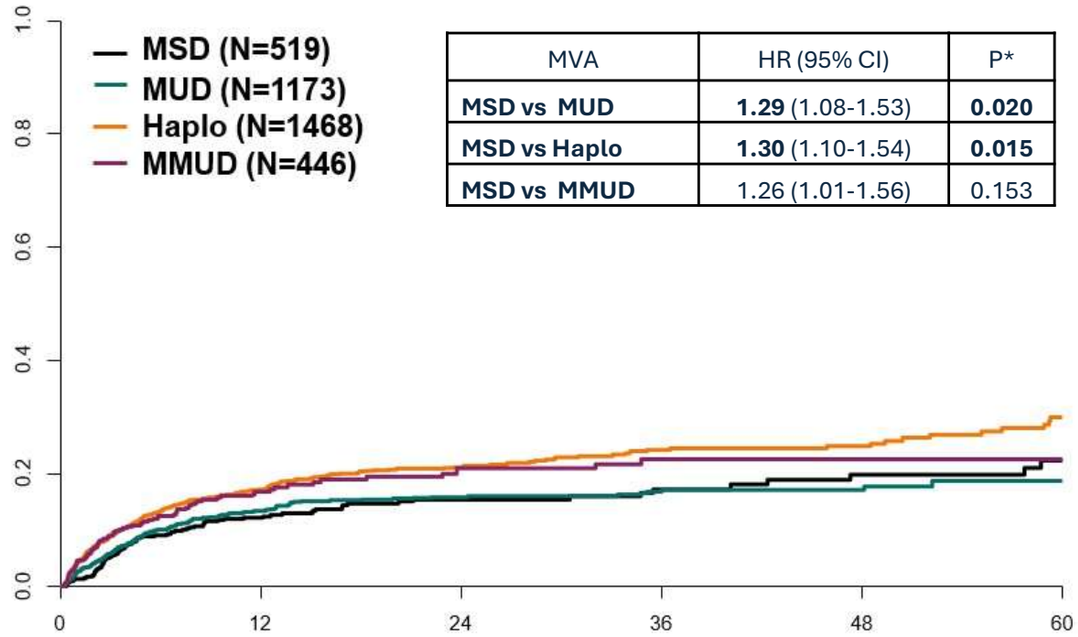
Disease-Free Survival



*Adjusted P-values using Stepdown Bonferroni Method

	MSD	MUD	Haplo	MMUD
5-yr DFS	38%	45%	38%	43%

Non-Relapse Mortality

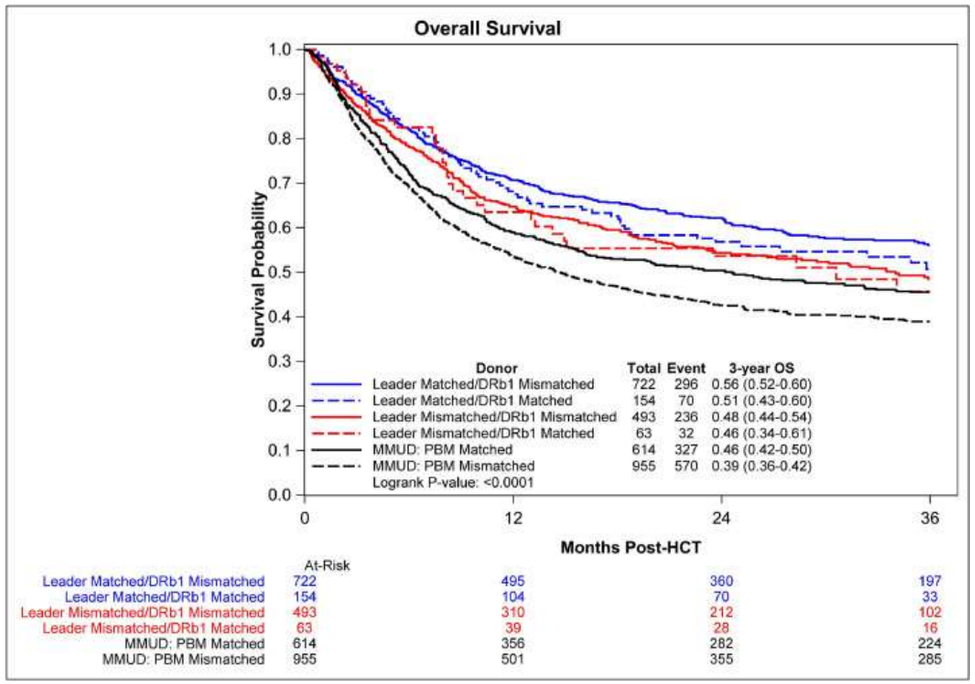


MVA	HR (95% CI)	P*
MSD vs MUD	**1.29** (1.08-1.53)	**0.020**
MSD vs Haplo	**1.30** (1.10-1.54)	**0.015**
MSD vs MMUD	1.26 (1.01-1.56)	0.153

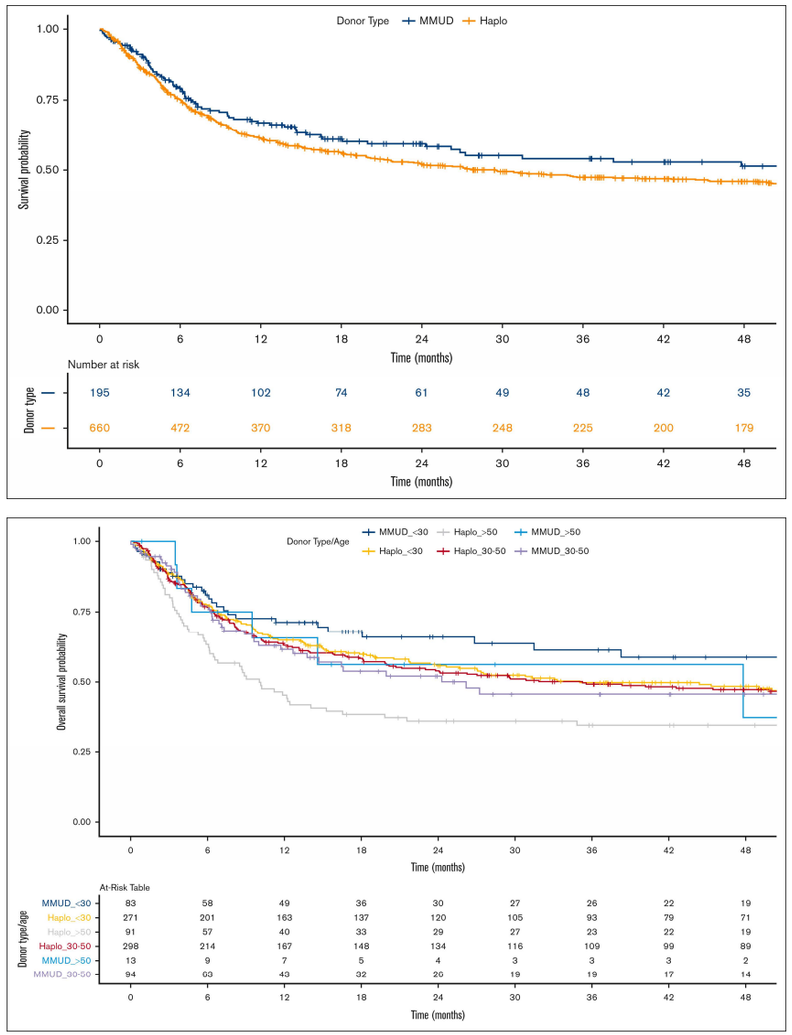
	MSD	MUD	Haplo	MMUD
5yr NRM	22%	19%	30%	23%

Nath et al. EBMT 2024

MMUD and Haploidentical Donor Outcomes

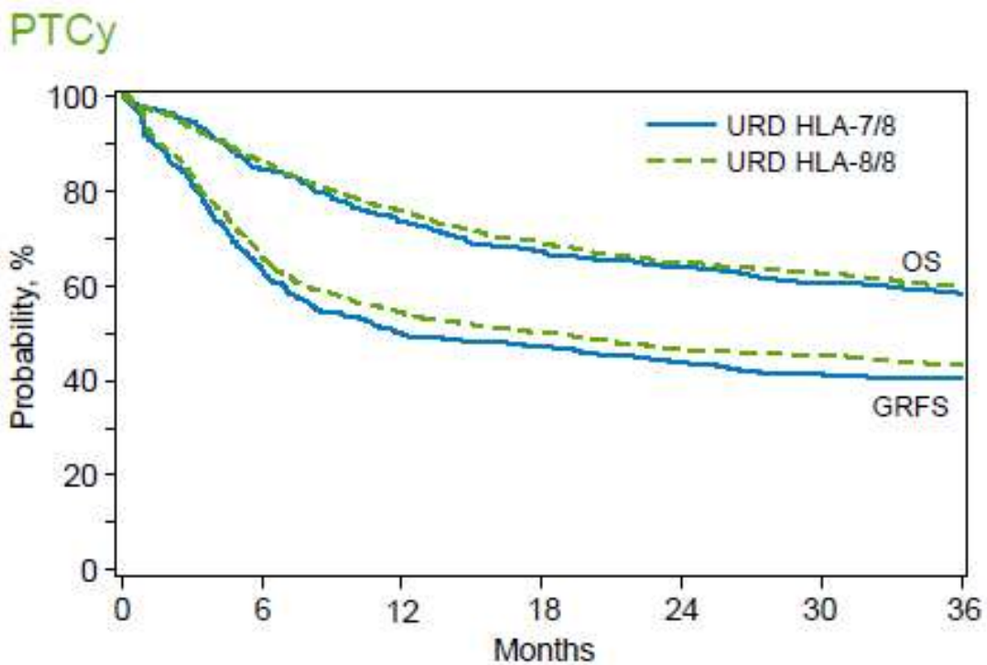


Mehta JTCT 2024

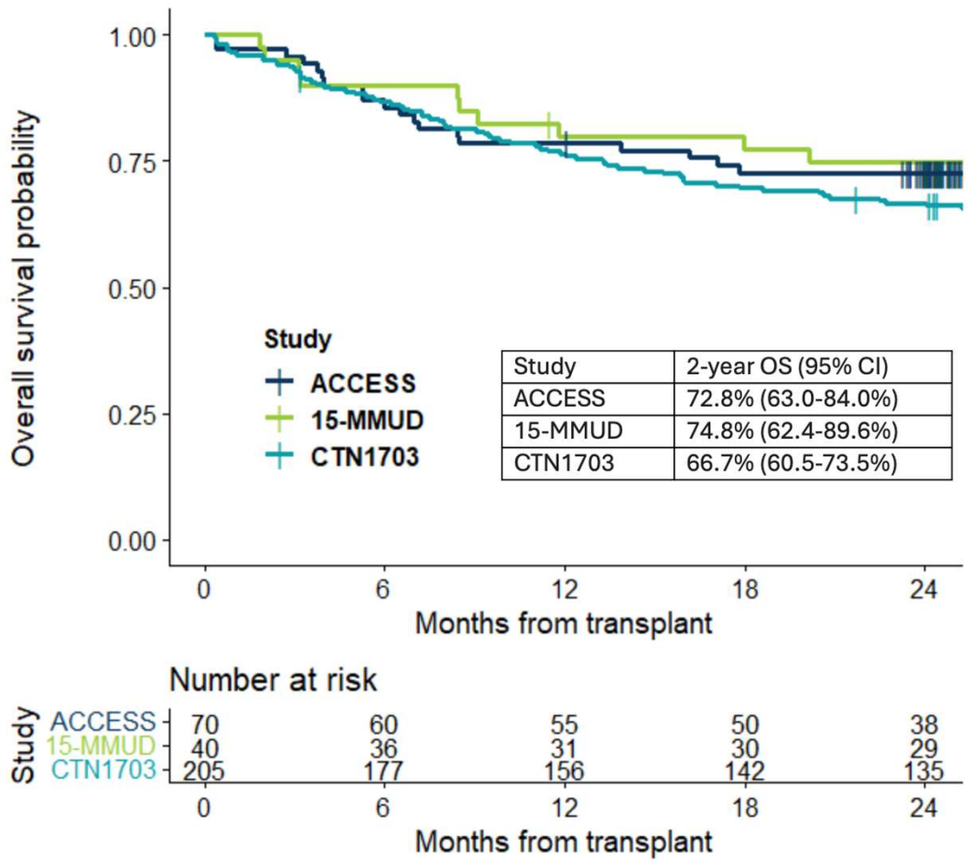


Aljawai Blood Adv 2025

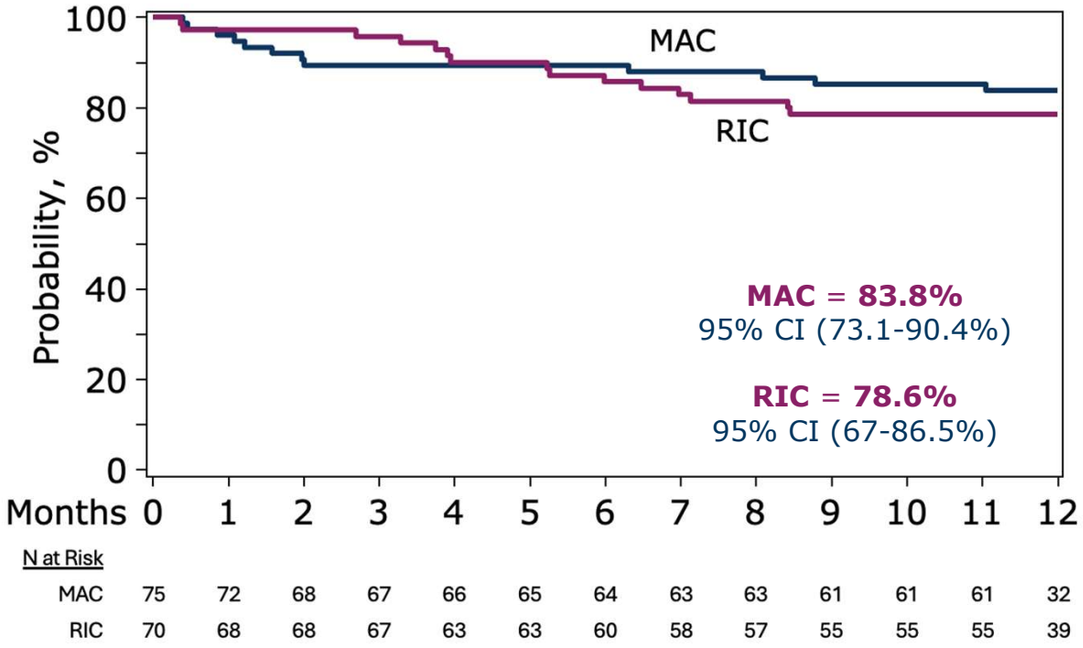
Survival in MMUD Patients Relative to MUD Patients in Real-World-Data and in BMT CTN 1703

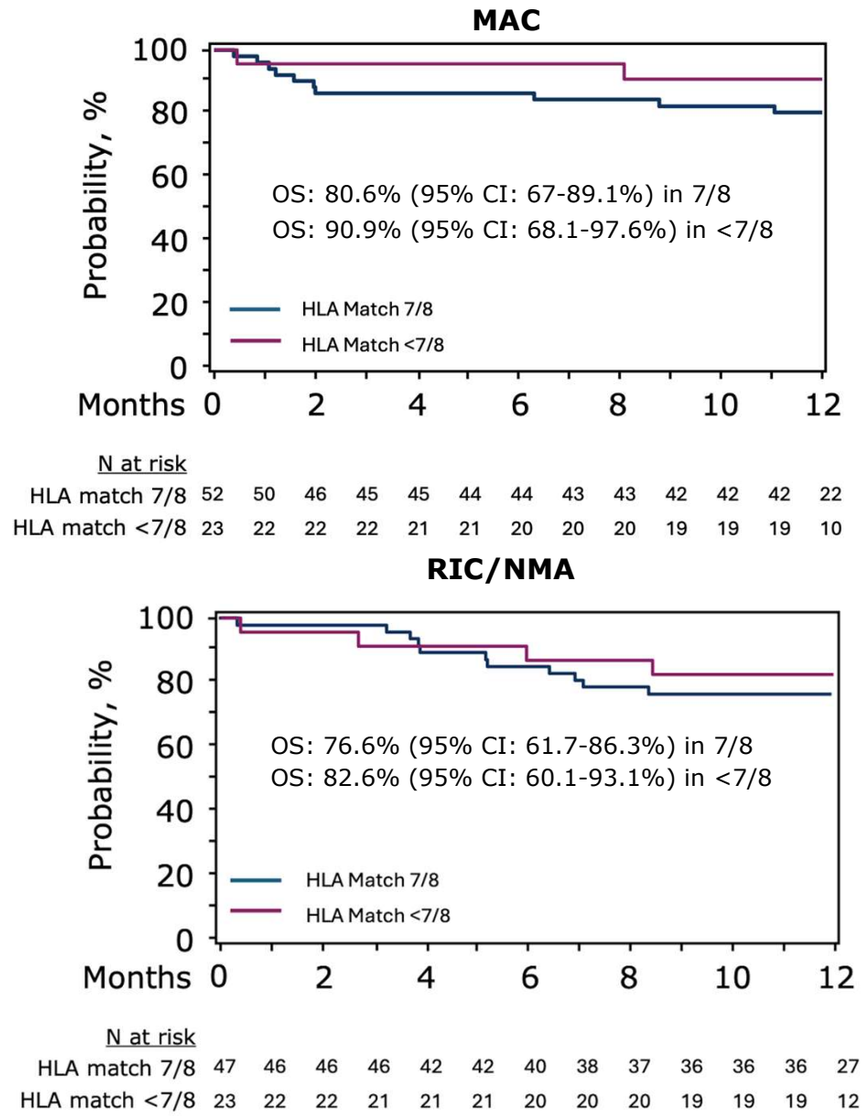


Shaffer JCO 2024



Outcomes in More Highly Mismatched URD Recipients in ACCESS Study





Al Malki JCO 2025

Comments on Umbilical Cord Blood

- Both randomized studies and registry data suggest decrement in OS.
- Center practice differs widely, and not all centers describe this trend.
- Use is generally declining and to what degree this is important as a national topic is debatable (<300 HCTs/year).

Summary

- Known parameters that influence outcome are limited to age, HLA matching, and to a lesser extent ABO.
- Inconsistent but potential synergy between HLA matching and donor age.
- Interaction between smaller disease subsets and donor parameters are not well described.
  - Very high-risk leukemia.
  - Traditionally immune sensitive disorders (MPN)