

# HLA Match Likelihoods For Hematopoietic Stem-Cell Grafts in the US Registry

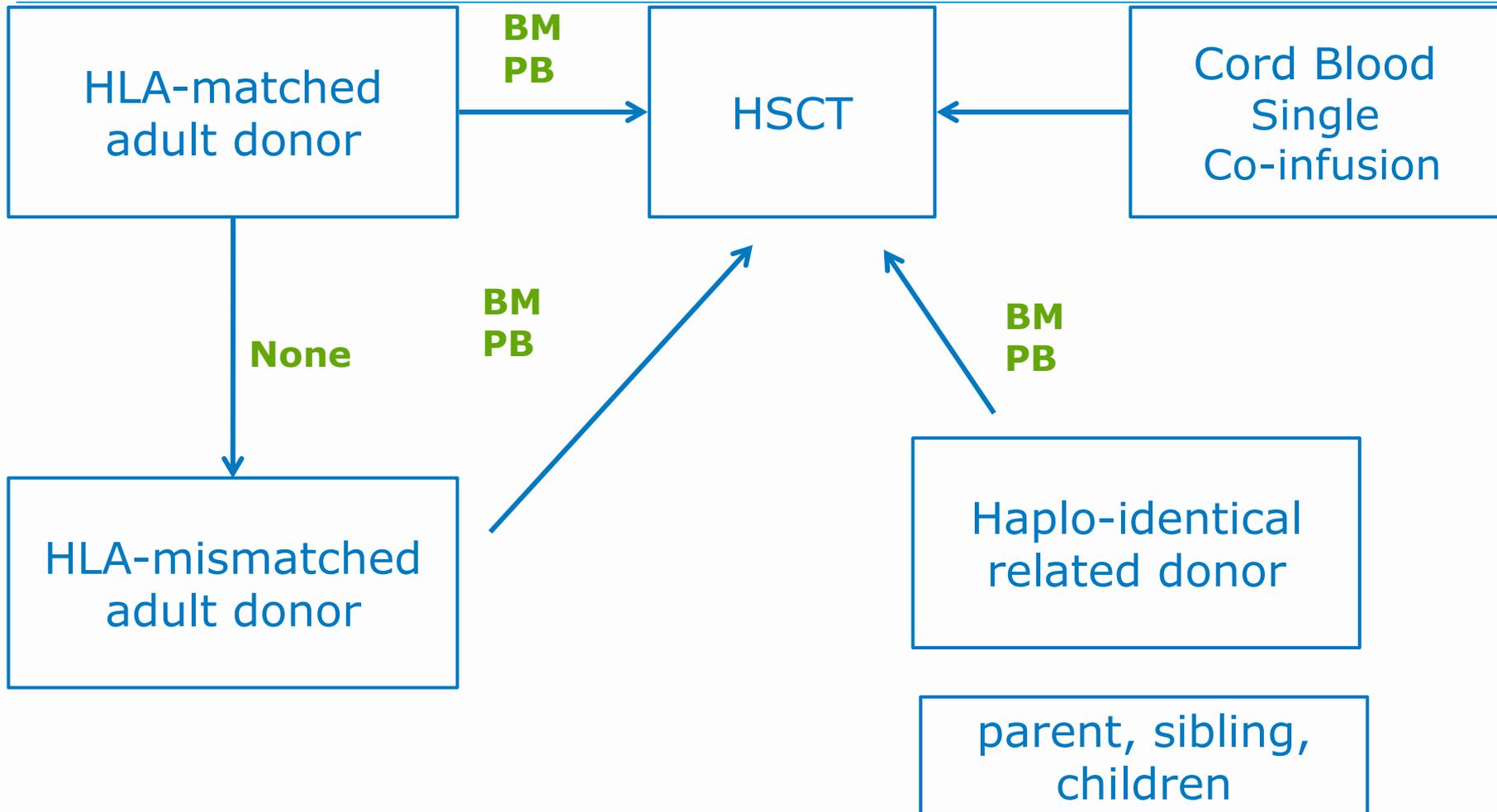
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# Introduction

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- Hematopoietic stem-cell transplant (HSCT) is a potentially life saving therapy for blood cancer and other diseases
- HSCT is infusion of graft (marrow [BM], peripheral blood [PB] or cord blood [CB]) collected from a donor into a patient
- Donor choices
  - Siblings, other relatives, unrelated adult or banked cord blood

# DONOR SELECTION WHEN A MATCHED SIBLING IS NOT AVAILABLE



## So what is the likelihood that a suitably matched unrelated donor is available in the US Registry?

- Unrelated Donor Registry in the US is maintained by the National Marrow Donor Program (NMDP)
- NMDP Donor Registry lists
  - More than 10.5 million adult volunteers
  - 200,000 cord blood units
- We know the success of unrelated donor HSCT is influenced by the degree of HLA matching between donor and recipient

# Optimal HLA Matching Between Adult Unrelated Donor and Recipient

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- We aim to match the donor and recipient at HLA-A, -B, -C and –DRB1 (8/8 HLA-match)
- Also acceptable is mismatching at a single HLA-locus (7/8 HLA-match)
- This lowers the patient's chance of being alive by 8 – 10% but this is considered clinically acceptable for someone who otherwise would die from his or her blood cancer.

# HLA Matching Between CB Unit and Recipient

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- HLA matching standards are lower
  - Tolerate up to two mismatches
  - Lower resolution of HLA matching
  - HLA-A, -B and –DRB1
  - Matching at HLA-C locus is usually ignored
- Several studies have shown that survival after mismatched cord blood transplants are similar to that after mismatched adult donor transplants for patients with blood cancer

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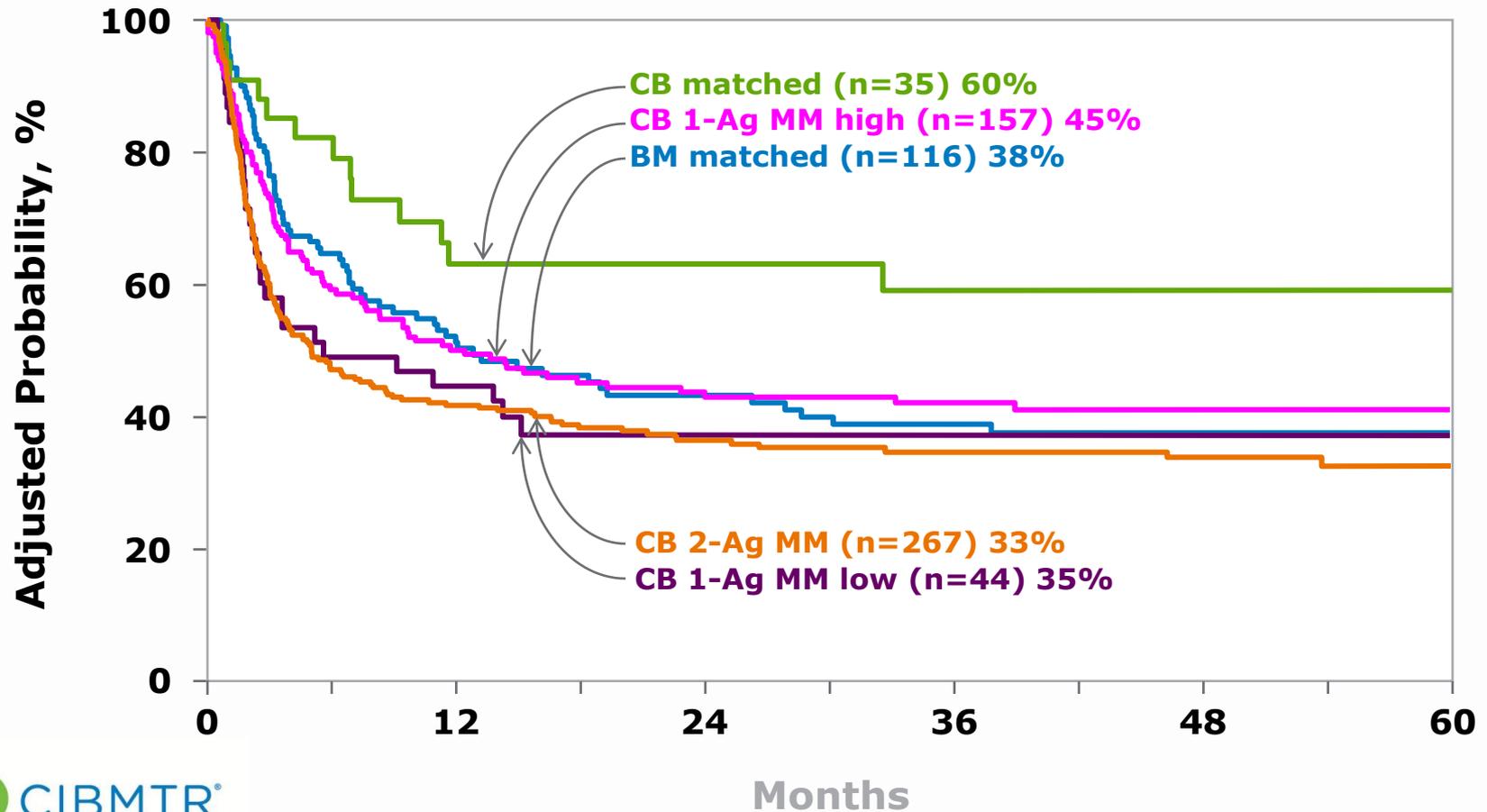
# *The Lancet, 2007*

Vol. 369 No. 9577 pp 1947-1954

## Outcomes of transplantation of unrelated donor umbilical cord blood and bone marrow in children with acute leukaemia: a comparison study

Mary Eapen, Pablo Rubinstein, Mei-Jie Zhang, Cladd Stevens, Joanne Kurtzberg, Andromachi Scaradavou, Fausto R Loberiza, Richard E Champlin, John P Klein, Mary M Horowitz, John E Wagner

# Leukemia-free Survival



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# *The Lancet Oncology*, 2010

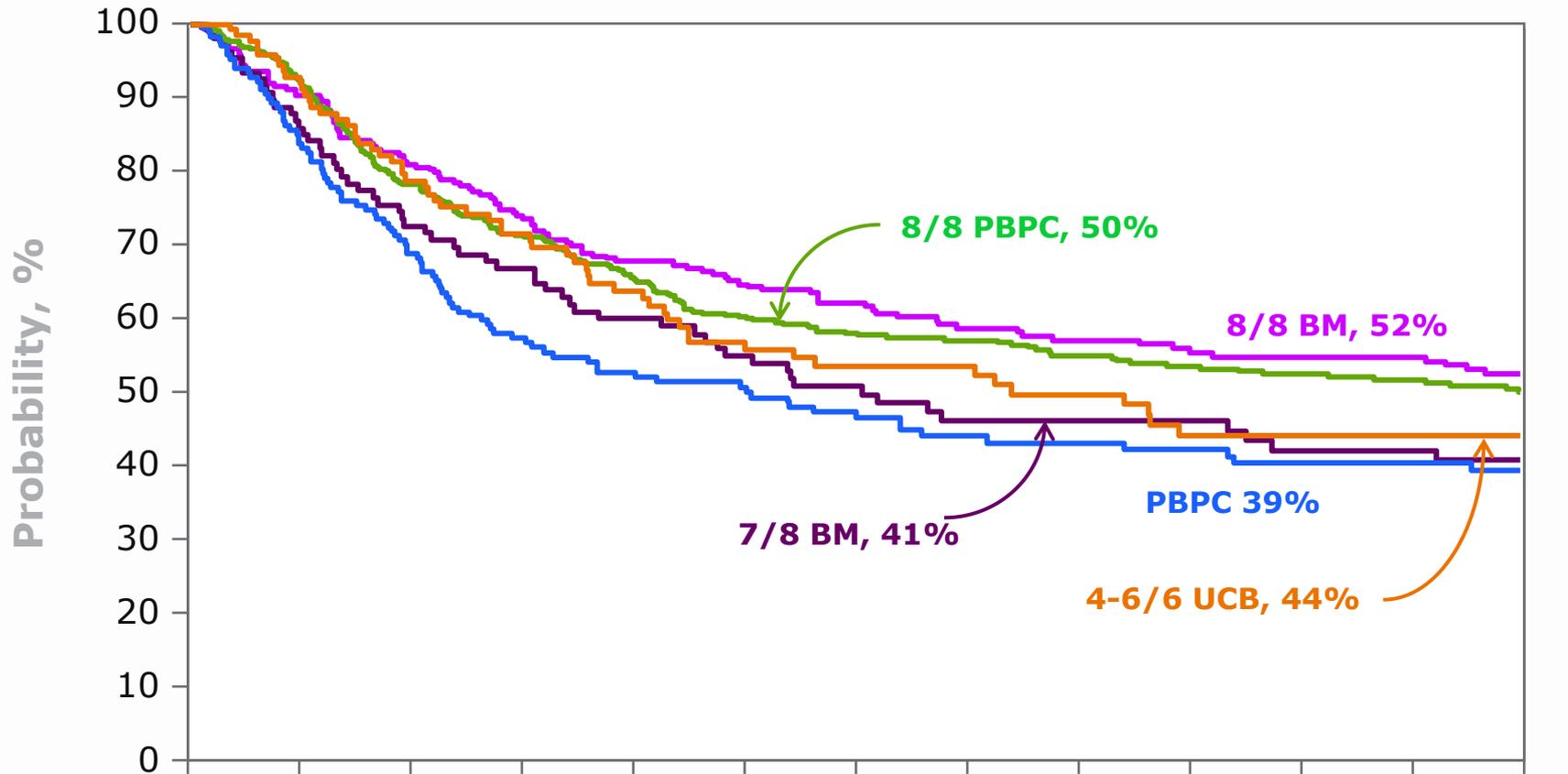
Vol. 11 No. 7 pp 653-660

## **Effect of graft source on unrelated donor haemopoietic stem-cell transplantation in adults with acute leukaemia: a retrospective analysis**

Mary Eapen, Vanderson Rocha, Guillermo Sanz, Andromachi Scaradavou, Mei-Jie Zhang, William Arcese and others

# Leukemia-free Survival

## - Transplantation in Remission -



Months **0**

**6**

**12**

**18**

**24**

8/8 matched BM 246

177

139

99

82

7/8 matched BM 106

69

46

35

31

8/8 matched PBPC 452

316

220

143

112

7/8 matched PBPC 166

89

66

45

36

4/6-6/6 matched UCB 123

77

47

30

24

## So what is the likelihood that a suitably matched unrelated donor is available in the US Registry?

- Unfortunately NOT everyone who might benefit from HSCT will have a suitably matched donor
- This is because
  - Levels of polymorphism of HLA genes are very high
  - Allelic variation is population specific
- So what is the likelihood of finding a suitably matched adult donor or cord-blood unit in the US registry?

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## HLA Match Likelihoods for Hematopoietic Stem-Cell Grafts in the U.S. Registry

Loren Gragert, B.S., B.A., Mary Eapen, M.B., B.S., Eric Williams, Ph.D., John Freeman, B.S., Stephen Spellman, M.B.S., Robert Baitty, M.P.P., Robert Hartzman, M.D., J. Douglas Rizzo, M.D., Mary Horowitz, M.D., Dennis Confer, M.D., and Martin Maiers, B.A.

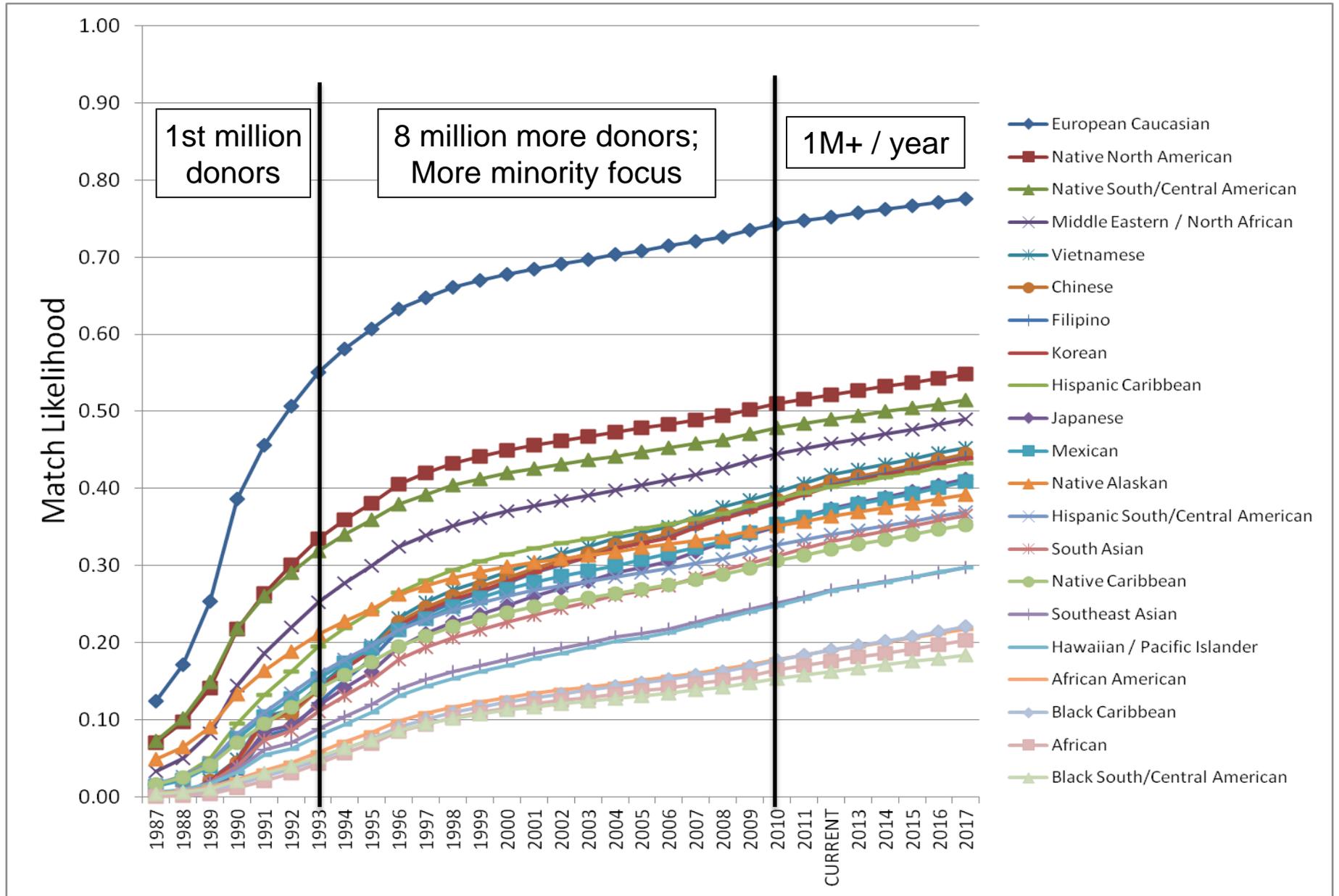
# Study Population

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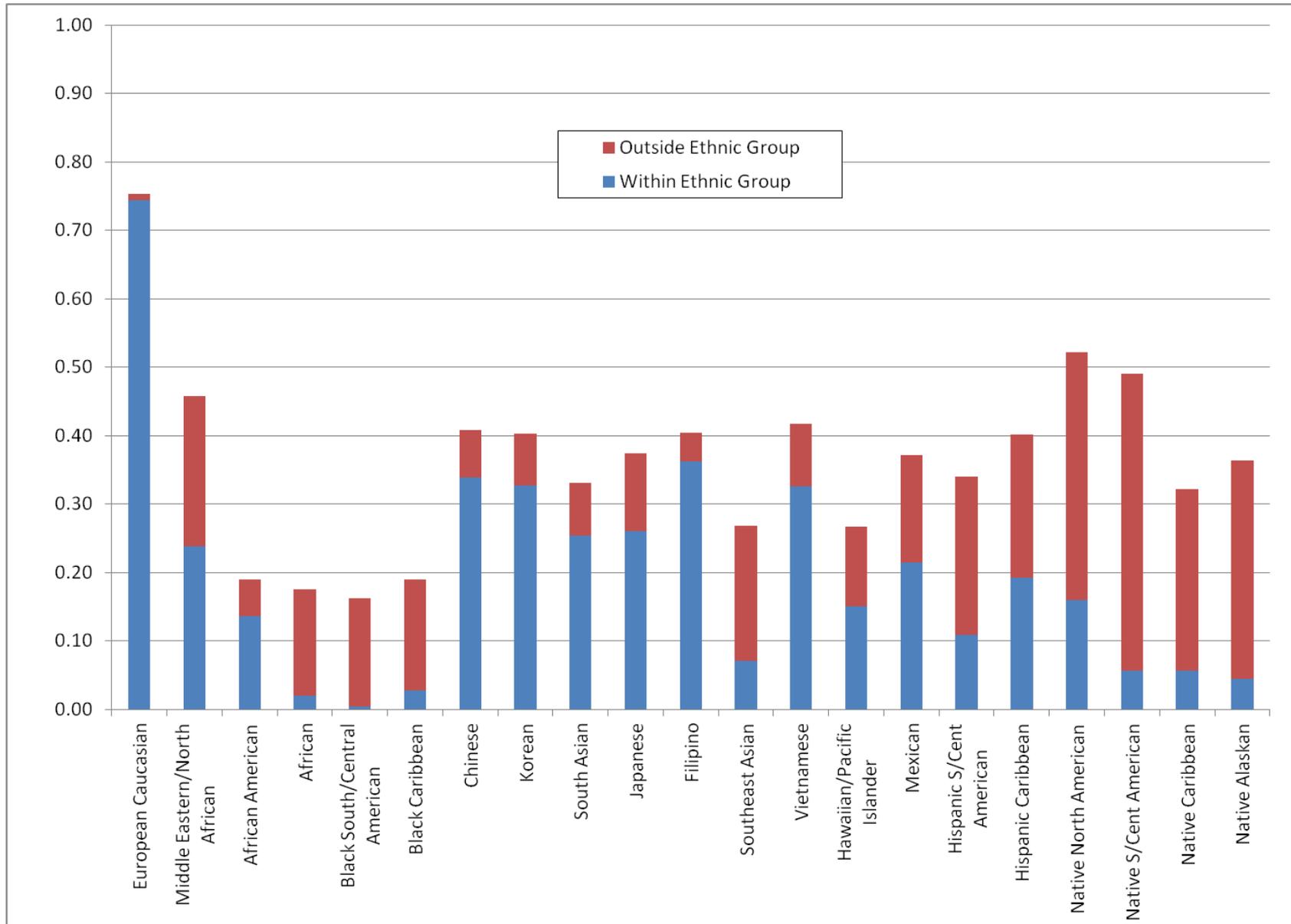
Donor Registry at the end of 2012

- 10.8 million adult volunteers
- 186,000 cord blood units
- The likelihood of identifying donors (8/8 or 7/8 adult donor) or cord blood (6/6, 5/6 or 4/6) was calculated by racial and ethnic groups
- All cord blood units contained at least  $2.5 \times 10^7$ /kg recipient body weight
- Also considered “donor availability”

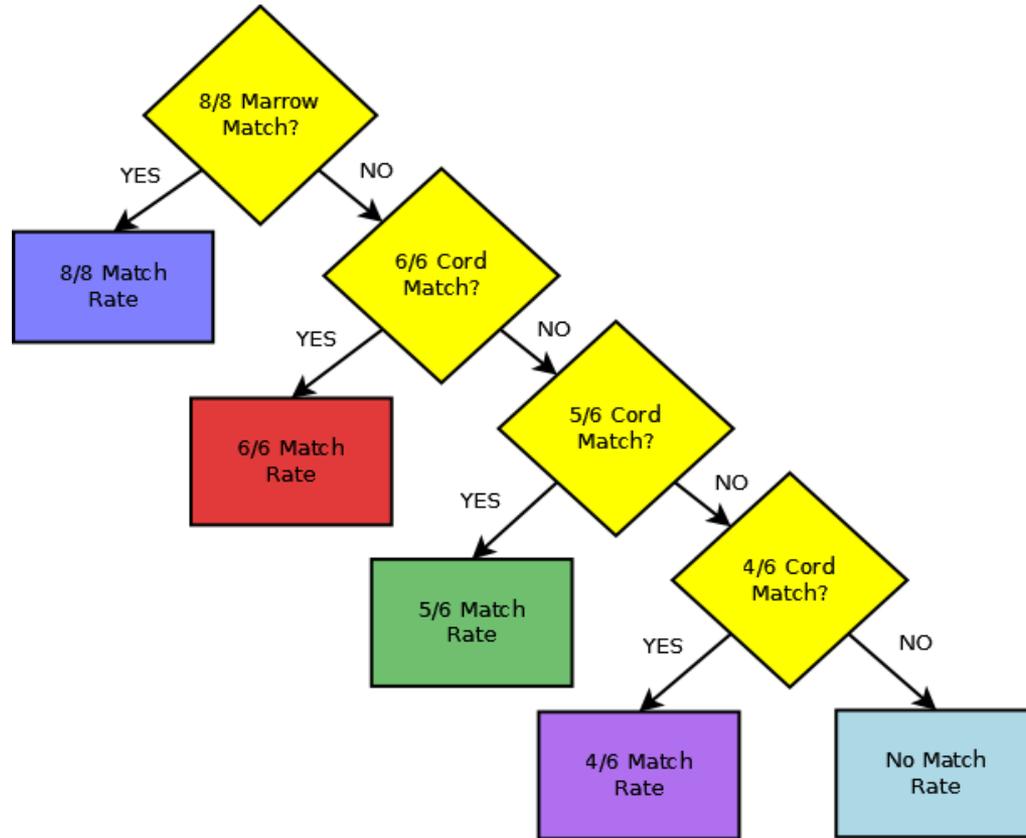
# 8/8 match likelihoods by year-end using current donor availability, extending recruitment trends to 2017



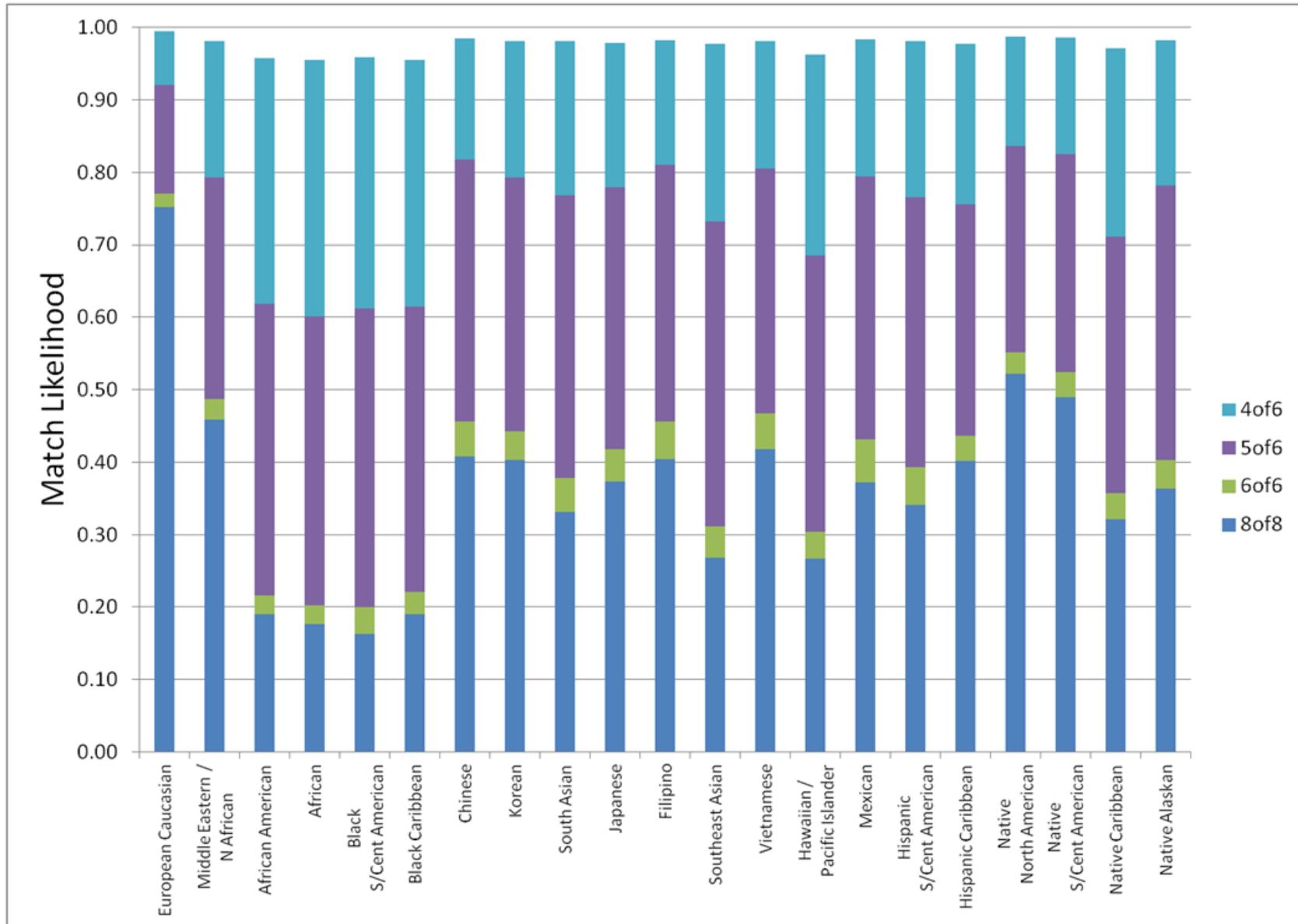
# 8/8 adult donor match rates within and between populations



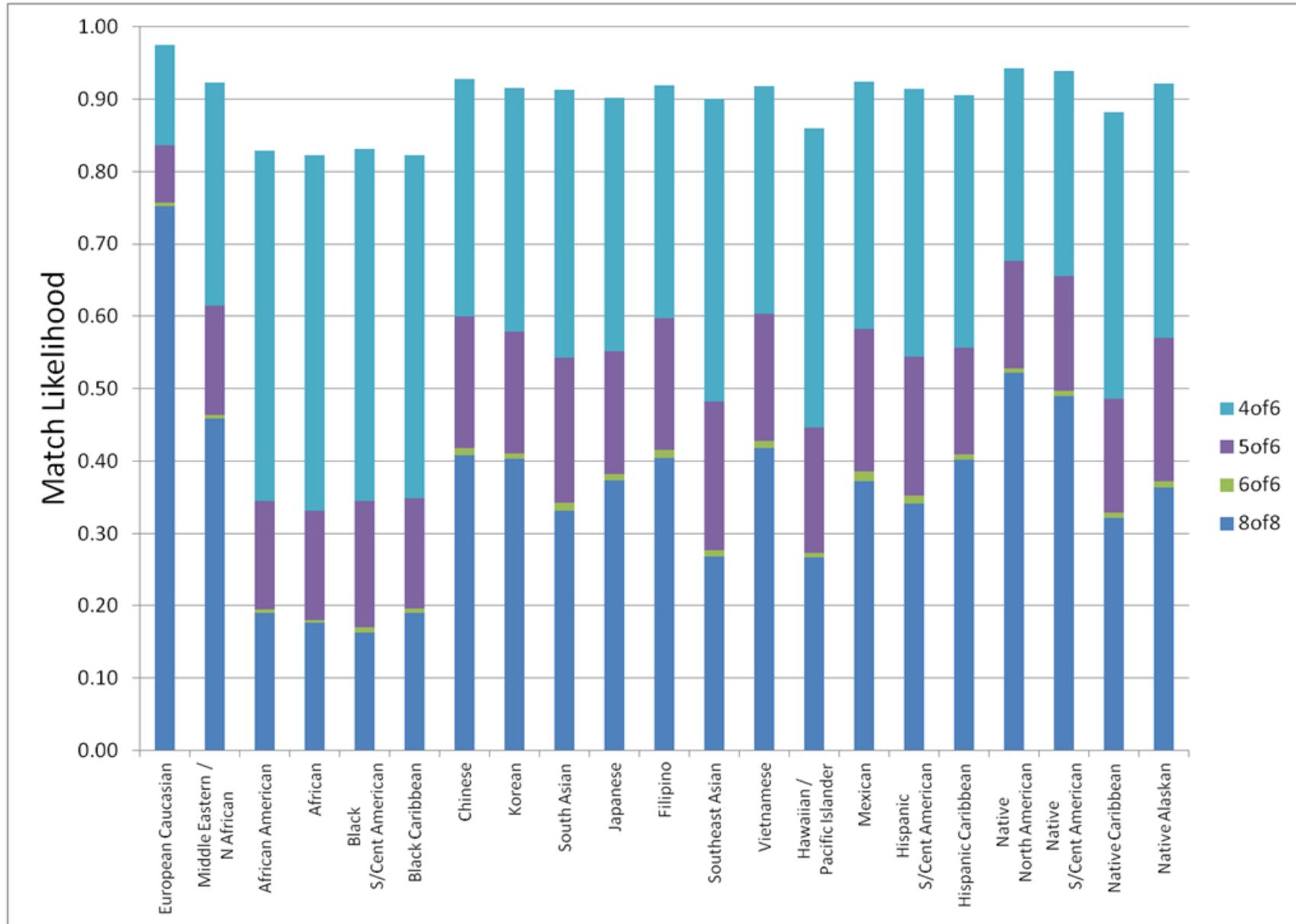
# 8/8 adult donor, then cord blood product search strategy



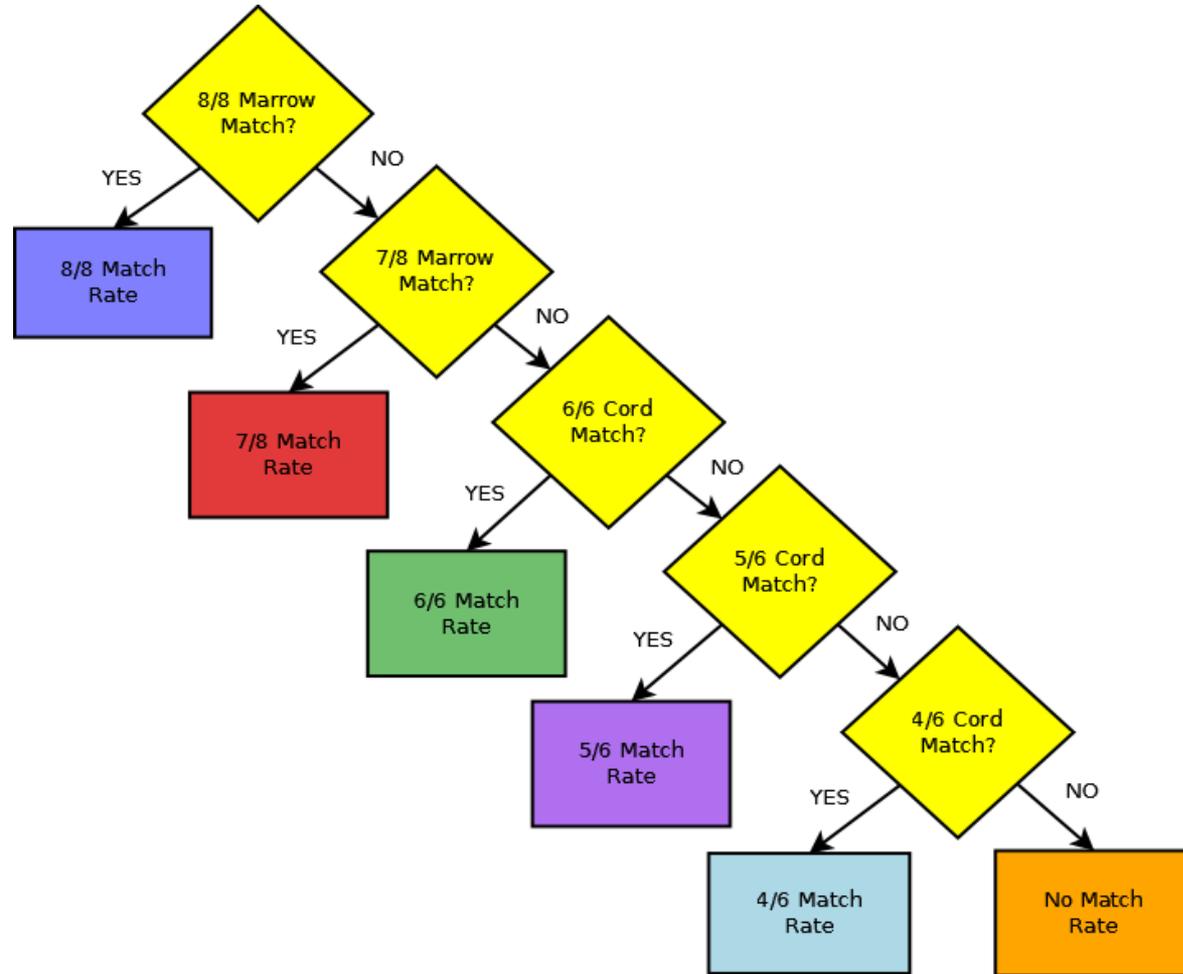
# 8/8 adult donor, then cord blood product search strategy for **pediatric** patients



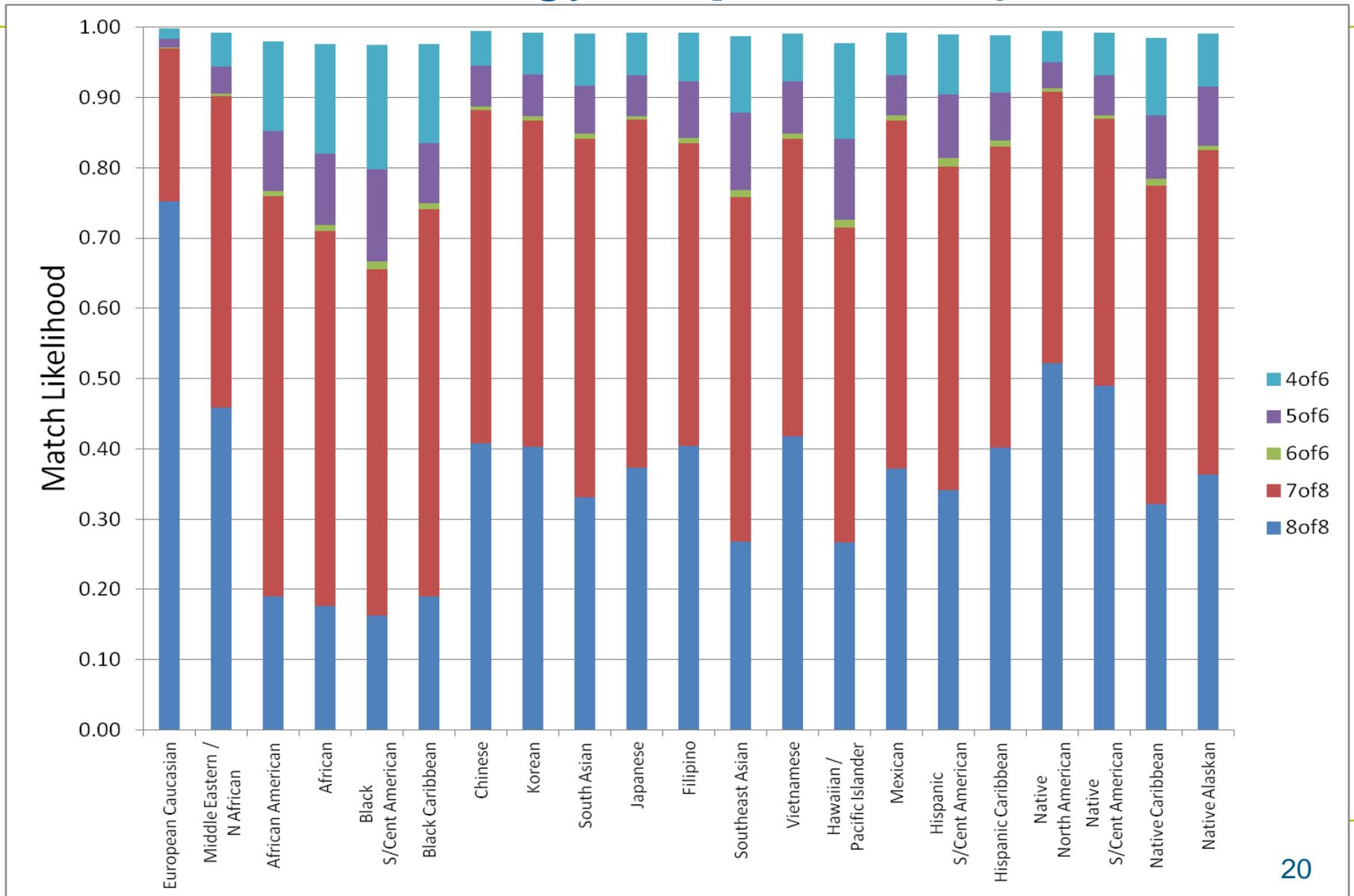
# 8/8 adult donor, then cord blood product search strategy for **adult** patients



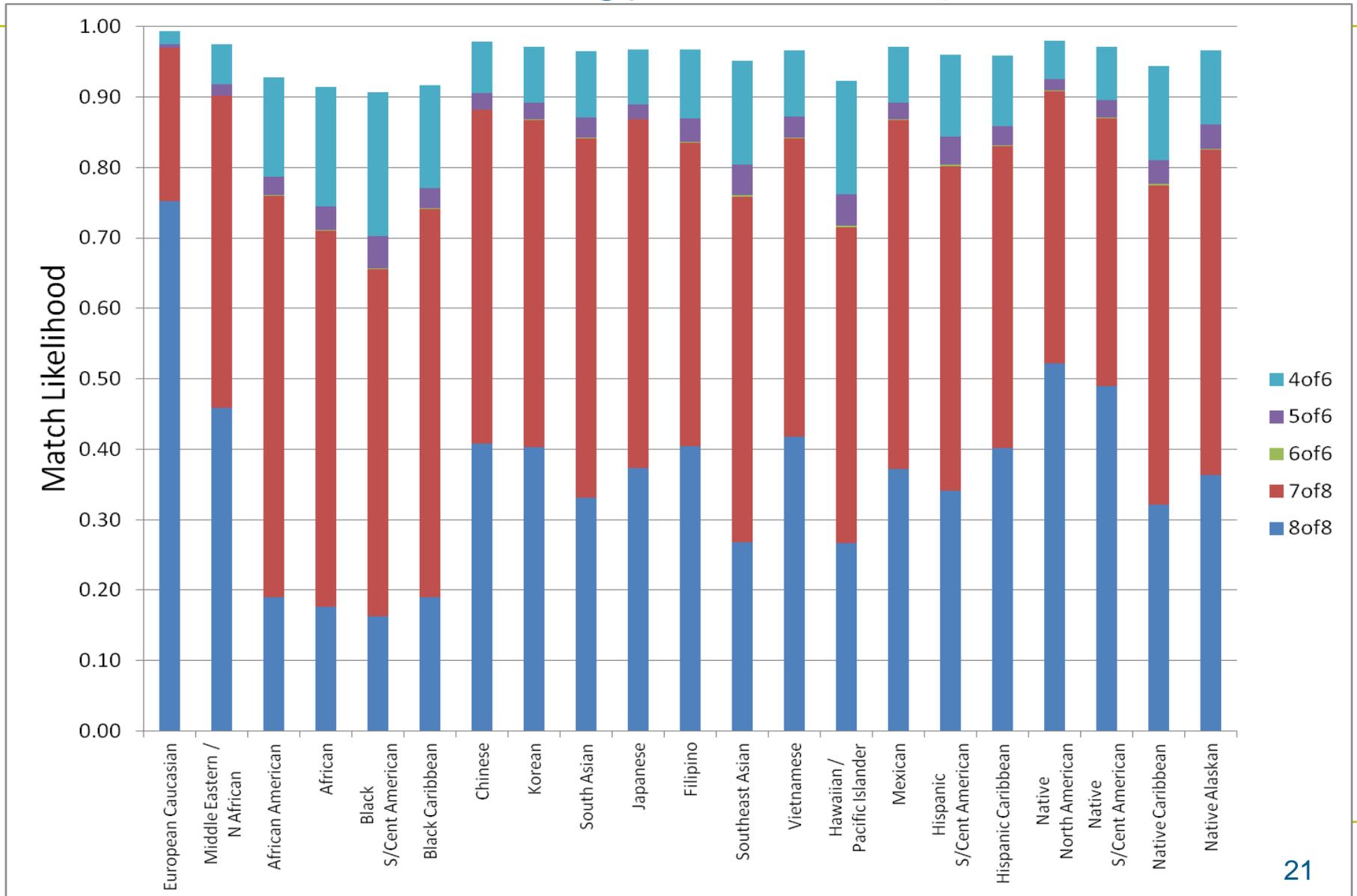
# 7/8+ adult donor, then cord blood product search strategy



# 7/8+ adult donor, then cord blood product search strategy for **pediatric** patients



# 7/8+ adult donor, then cord blood product search strategy for **adult** patients



# SUMMARY

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- Most patients likely to benefit from HSCT will have a donor
- Public investment in donor recruitment and cord blood banks has expanded access to HSCT
- If a match is NOT found on initial search, fewer than 5% of searches identified a suitably matched donor after 2 months from initial search
- Targeted donor recruitment are desirable

# ACKNOWLEDGEMENT

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  - L Garget, M Maiers, D Confer
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