Considerations of Donor Search Strategies on Timing and Treatment Algorithms

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Conflict of Interest Disclosure

I attest that I have no relevant financial, professional, or personal relationship with a commercial interest producing health care goods/services related to this educational activity

I will not discuss off-label use of commercial products.

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Overview

- Disease status correlates with outcomes
- Certain donor characteristics
  - Are viewed as desirable by transplant centers
  - Can help predict donor availability
- Patient ethnicity can help predict the likelihood of finding a suitable donor
- Recognizing key donor and patient characteristics can help optimize the donor search
- Recommendations

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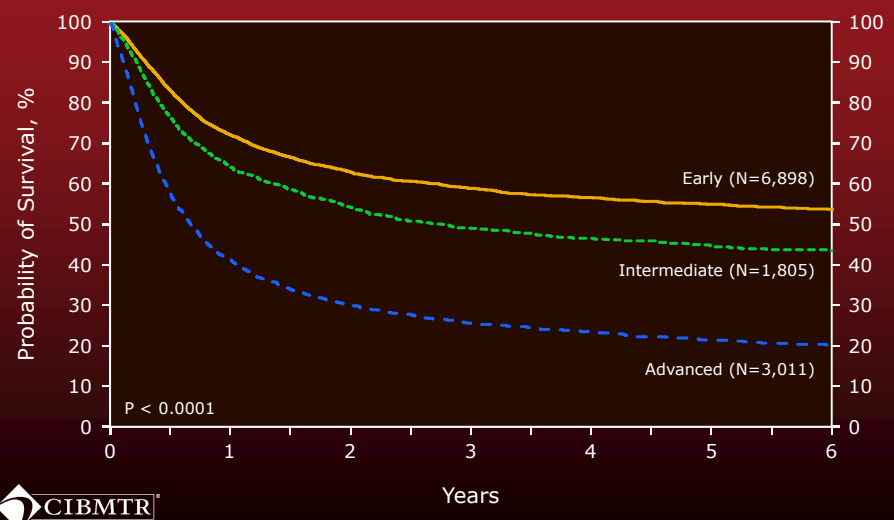
Probability of survival after HLA-matched sibling donor transplant for AML, by disease status, 1998-2008



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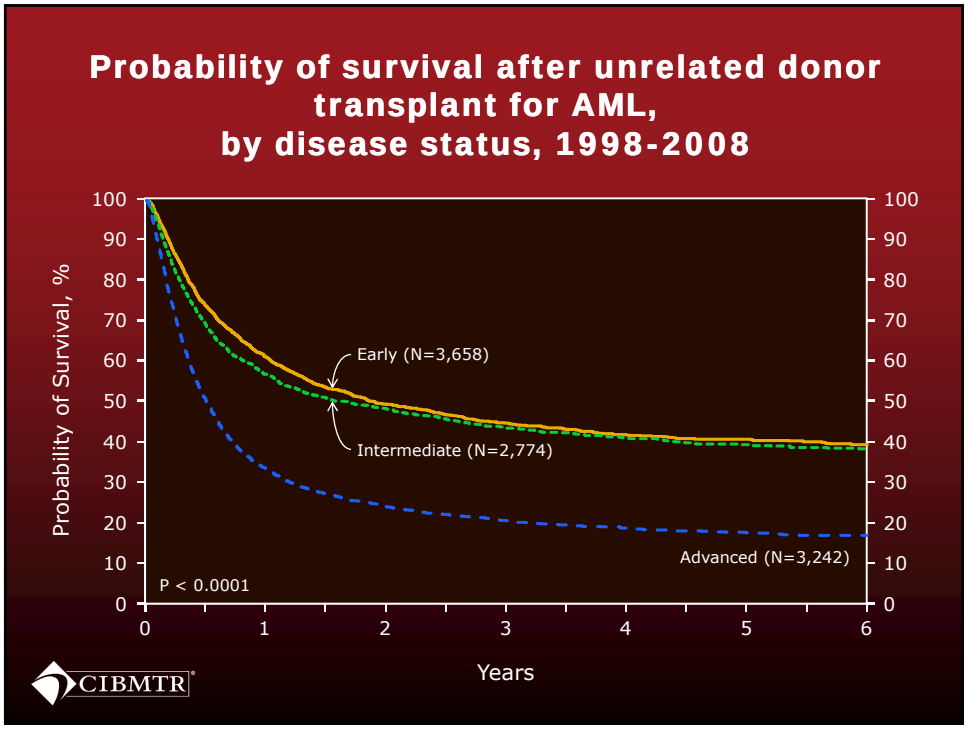
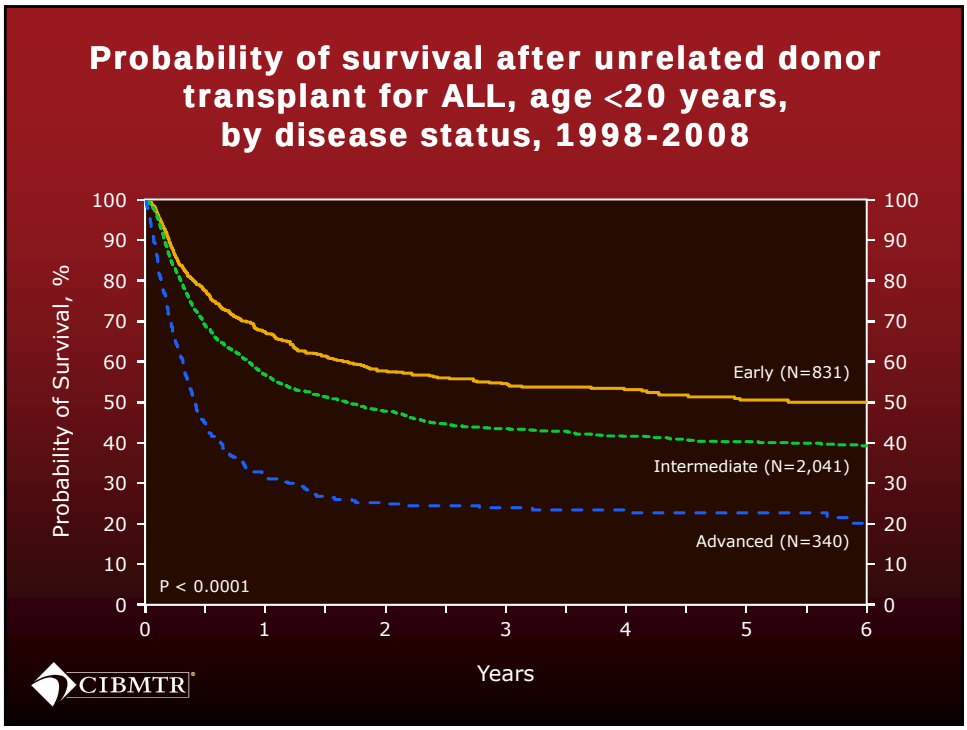
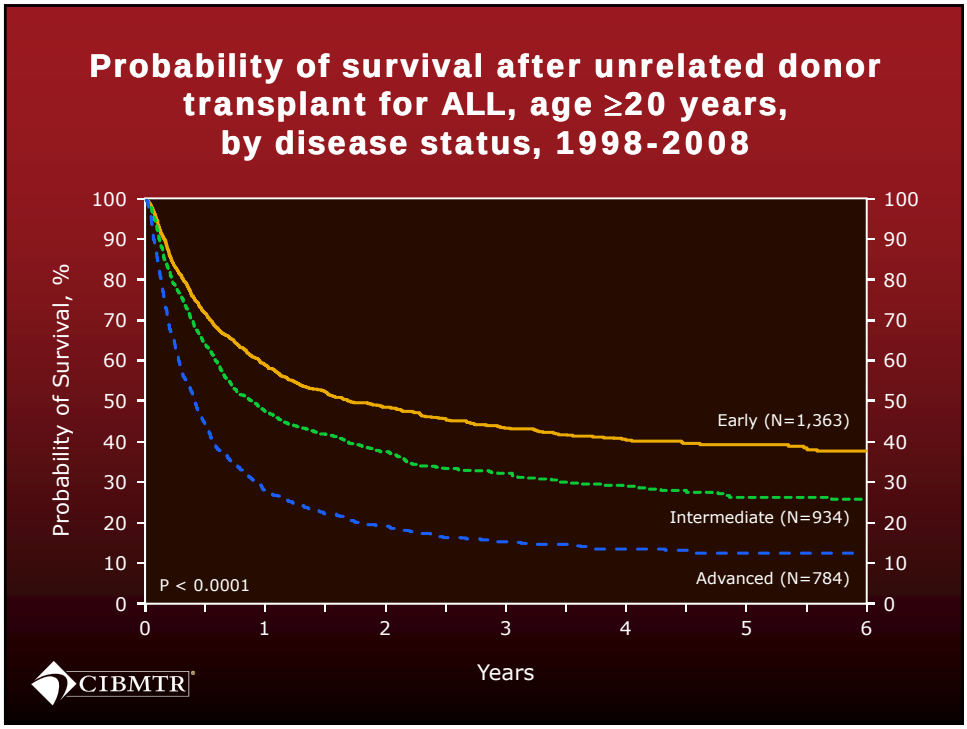

Probability of survival after unrelated donor transplant for AML, by disease status, 1998-2008
Probability of Survival, %
Years
Early (N=3,658)
Intermediate (N=2,774)
Advanced (N=3,242)
P < 0.0001
CIBMTR


Probability of survival after unrelated donor transplant for ALL, age <20 years, by disease status, 1998-2008
Probability of Survival, %
Years
Early (N=831)
Intermediate (N=2,041)
Advanced (N=340)
P < 0.0001
CIBMTR



Earlier Disease Status at Transplant is Associated with Better Outcomes

- Caveats:
  - Those transplanted in more advanced stage in some cases have biologically distinct disease
  - Delays in proceeding to transplant earlier may reflect other factors which impact outcomes
    - Co-morbidities
    - Social factors
- Nevertheless, waiting until advanced disease to initiate HCT appears undesirable in many settings

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Efforts to improve donor search process

To help more patients in need of unrelated donor transplantation:

- Increasing "desirable" donors on registry
- Improving availability of donors
- Speeding the process from referral to transplant

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Be The Match Registry®: Adult Donor Facts and Trends

- Expanded diversity, younger donors targeted
  - 9.5+ million on Be The Match Registry
  - NMDP recruits over 400,000 donors per year; >80% <age 45
  - 41% new recruits of U.S. donors are minority
  - Over a third of the Registry is < 35 years
  - Over 50% of US donors giving confirmatory typing (CT) are < 35 years of age
- High quality HLA typing
  - All new recruits receive high-quality HLA typing from first-class ASHI accredited laboratories
  - Over 50% (including all male and female donors < age 30) receive C and DQ typing at recruitment
- Comparative analysis shows that 80% of non-U.S. donors selected have potentially matched HLA types in the Be The Match Registry.

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Be The Match Registry: Cord Blood Facts and Trends

- Number of units accessible
  - Nearly 145,000 on Be The Match Registry
  - Real-time access to >185,000
  - Facilitating worldwide access to >550,000
  - More than 36,000 cord blood units added each year
- Expanded diversity and use
  - 40% minority units
  - More than 35% of NMDP-facilitated use more than one cord
  - Transplants for minority patients increased 42% 2010 vs 2008.
- Improved timing to meet Transplant Center needs
  - Domestic: 94% met 2-day request-to-ship requirement
  - International: Median 11 days request-to-CT

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Likelihood of a Match by Patient Ethnicity on the Be The Match Registry

66-93% likelihood depending on patient race/ethnicity*
- At ≥ 7 of 8
- Donor available, willing, and able

Availability of a suitable donor by patient race/ethnicity:
- 66% Black/African American
- 73% Asian/Pacific Islander
- 72% Hispanic/Latino
- 82% American Indian/Alaska Native
- 93% Caucasian

**Cord blood improves likelihood of finding an appropriate cell source for some patients*

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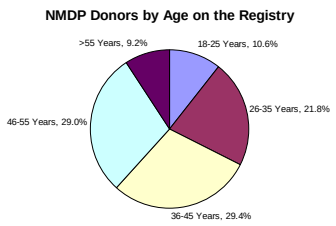
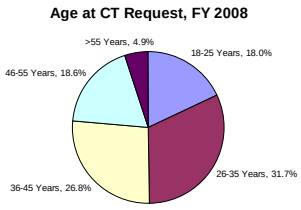
Donor Age is a Key Factor in Selection





≤ 35 years = 32.4%

≤ 35 years = 49.7%

Donors under the age of 35 are more likely to be selected for CT requests

Donor Selection and Availability

- Transplant Center preferences are clear – young, male, newly recruited (better typed) donors.
- Availability trends suggest challenges with this same group of donors when activated for a patient search
- Donor availability varies with recruitment venue

Understanding Donor Factors: Deferral Categories

- Four deferral categories were evaluated:
  - DD – Permanent Medical Deferral
  - TU – Temporarily Unavailable
  - UC – Unable to Contact
  - NI – Not Interested
- Deviation from the average is depicted in the graphs

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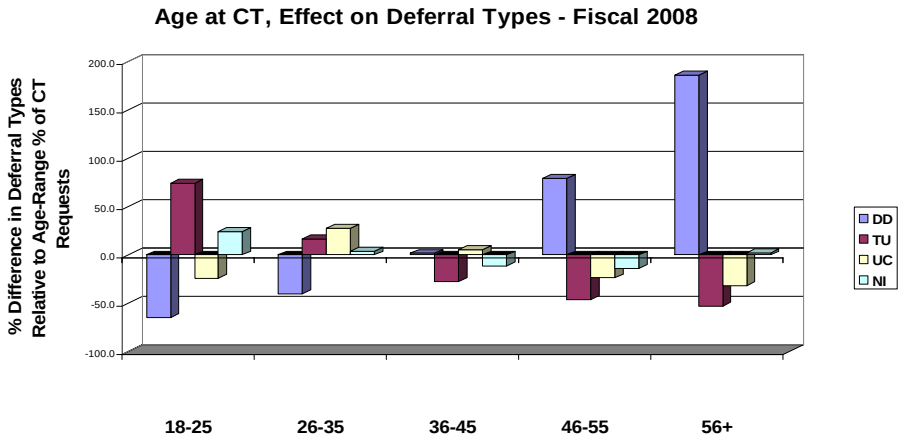

Age at CT Request	18-25	26-35	36-45	46-55	56+	Total
Count	4,958	8,718	7,388	5,106	1,351	27,521
Percent of Total	18.0	31.7	26.8	18.6	4.9	100

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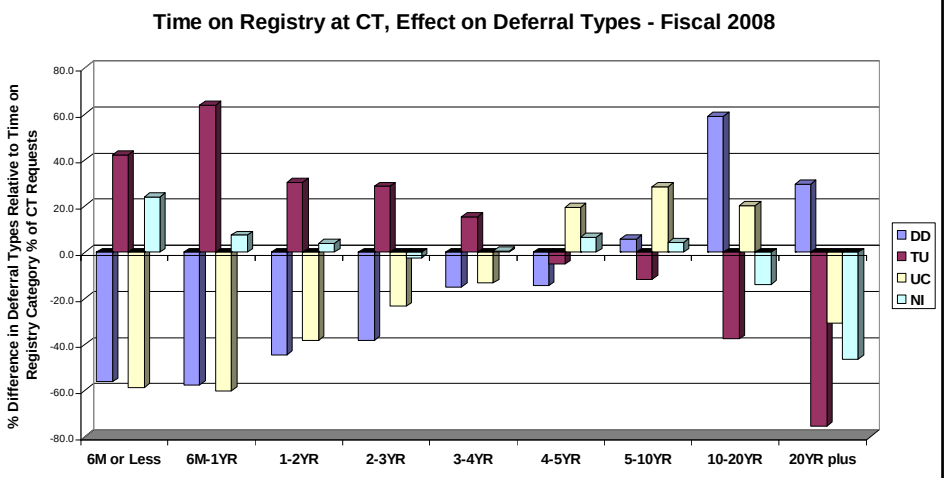

Time on Registry to CT	6M or Less	6M – 1YR	1YR – 2YR	2YR – 3YR	3YR- 4YR	4YR – 5YR	5YR – 10YR	10YR – 20YR	20YR plus	Total
Count	1,479	1,937	3,089	2,266	2,017	1,598	7,863	7,218	54	27,521
Percent of Total	5.4	7.0	11.2	8.2	7.3	5.8	28.6	26.2	0.2	100

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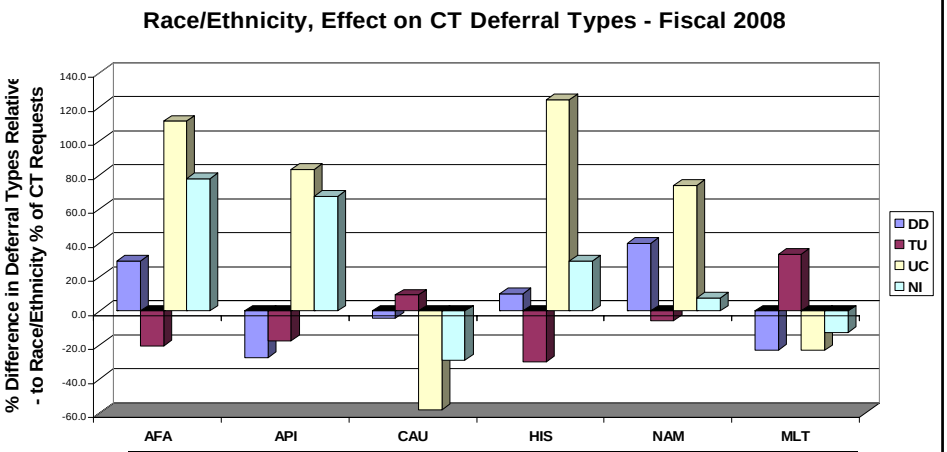

Race / Ethnicity	AFA	API	CAU	HIS	NAM	MLT
Count	2,813	2,268	16,351	3,749	438	1,496
Percent of Total	10.2	8.2	59.4	13.6	1.6	5.4

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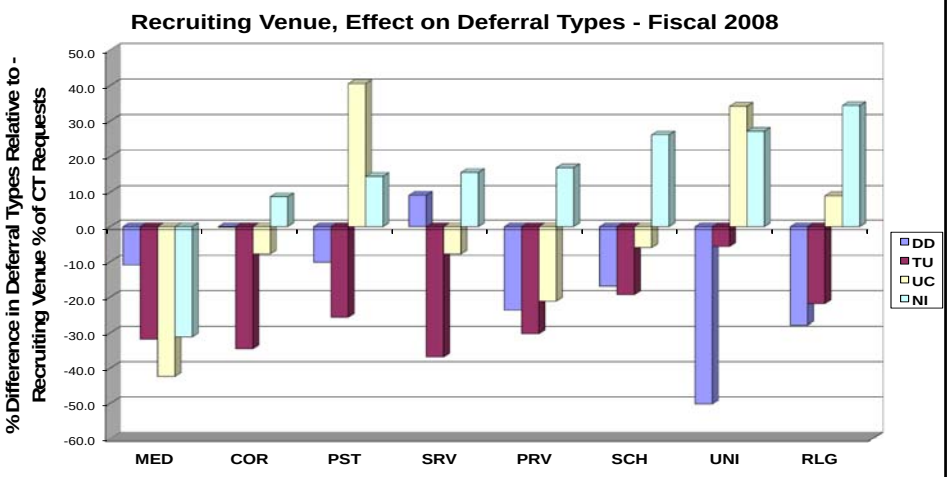

Recruiting Venue	MED	Not Recorded*	COR	PST	SRV	PRV	SCH	UNI	RLG	Total
Count	1,926	13,989	947	3,117	433	459	1,075	3,125	2,450	27,521
Percent of Total	7.0	50.8	3.4	11.3	1.6	1.7	3.9	11.4	8.9	100

*51% not recorded: Donors recruited before 1999 do not have recruitment venue assigned

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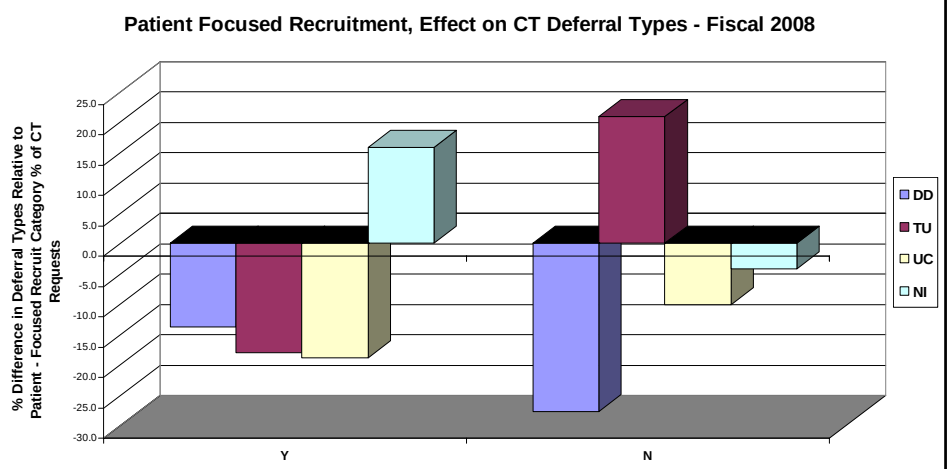

Patient Focused Recruitment	Y	N	Not Recorded*	Total
Count	4,994	15,391	7,136	27,521
Percent of Total	18.1	55.9	25.9	100

*26% of requests did not record whether patient focused (pre-1999 recruitment)

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Summary of Donor Factor Findings

Deferral Code	Found More Commonly Among:
Not Interested	• Younger (18-25 year old) donors • Recently recruited donors • Non-Caucasian donors • Donors recruited in Religious and Academic settings
Temporarily Unavailable	• Younger (18-25 year old) donors • Recently recruited donors • Over a third of DoD donors (military deployment)
Unable to Contact	• Non-Caucasian (especially young AFA and HIS) donors • Donors recruited in Public and Academic settings
Medical Deferral	• Donors on the registry longer • Older donors

+ Donors recruited via online recruitment (DIY) are more available then donors recruited through live drives.

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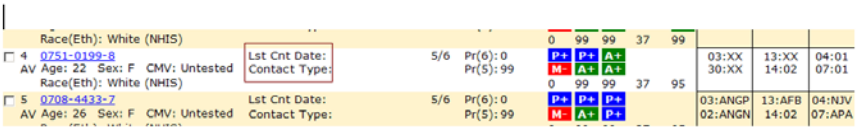
Traxis: last donor contact date added

Potential donor list screen:



Donor demographic screen:

Sex:	Female		
Weight (kg):	85	Weight Date:	
CMV:	Positive	CMV Date:	Mar 25 2011
Registry Status:	AC	Reg Date:	Jun 18 2008
Avail Date:		Last Contact Date:	Jul 20 2011
Ethnicity:	Hispanic or Latino	Contact Type:	Pre-Search HHQ
Race:	White - White Caribbean	Race Detail:	
Prev. Donations:	0		

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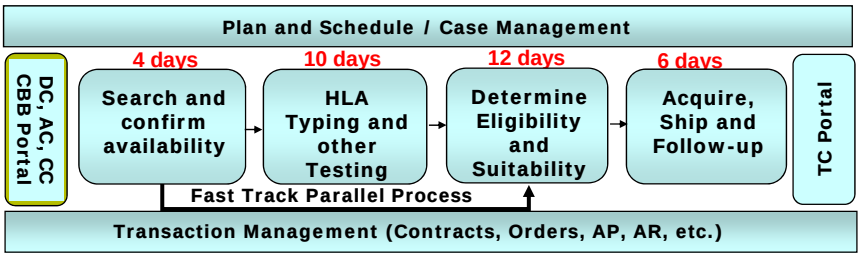
Speeding Internal NMDP Processes

FUTURE STATE PROCESS MODEL



Implications

- Faster – Search to Transplant in 35 – 45 days (vs. 96 days now)
- Less staff time per transplant
- Variability in donation process is purposeful
- Better balancing of demand and capacity

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Striving for Faster Searches: The Preliminary Search Project

- Plan
  - Proactively locate donors appearing on patient **preliminary** search reports before a request for confirmatory typing
  - update donor contact information
- Goals
  - Re-educate, screen, and remove donors who are deemed unavailable or medically unsuitable prior to formal activation
  - Reduce false hope for patients and their families
  - Expedite subsequent search processes for donor centers and searching patients

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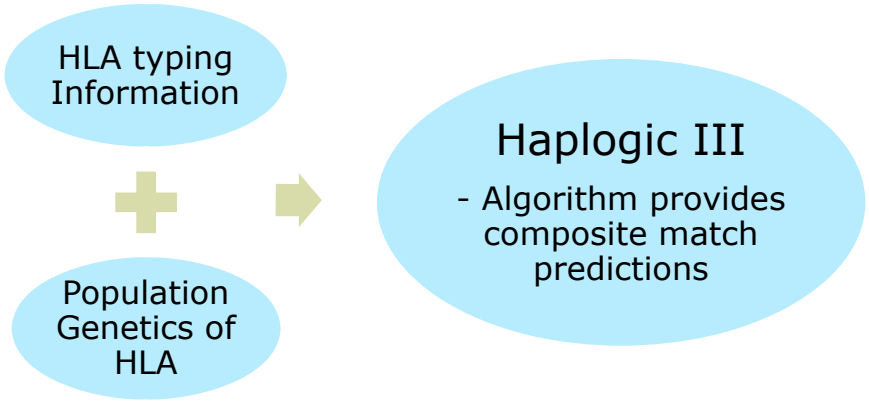
Haplotype Calculation



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Striving for More Efficient, Cost-Effective Searches

- Haplogic predictions reduce cost—can better predict which donors will match; less testing
  - Analysis on C and DQ: Predictions accurate
  - Transplant Centers now ordering fewer CTs, saving costs
- Customized typing service allows for fast and cost-effective HLA screening of donors to quickly identify the best-matched donors
  - Times for workup request to clearance superior
- NMDP proactively contacts selected donors at preliminary search; results now visible in Traxis
  - Improved availability for prescreened donors (only 8% of prescreened donors deferred at activation, versus 46.9% for all domestic requests in the first half of 2011).

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Enhancing Donor Center Performance

- Four–tiered performance ranking system is based on:
  - Percent of CT samples collected within 10 days
  - Caucasian donor CT availability
  - Minority donor CT availability
  - Donor satisfaction
  - Time from work-up request to clearance
- Benefits seen early
  - 2 day decrease in workup clearance times after announcement, even before implementation

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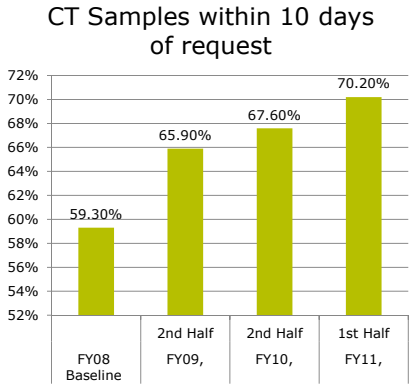
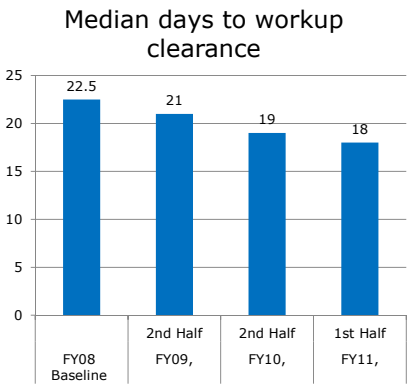
Reduced search times





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Initiatives Underway

Donor Contact Initiatives

- Preliminary Search Donor Contacts
  - Recently expanded to leverage Search Strategy service with prospective typing
- Temporarily Unavailable Re-contact Project
  - Implementation in Fall of 2011 as demonstration of Customer Relationship Management software

Last Donor Contact Date to Transplant Centers

- August 1, 2011 Traxis® Release

Tiered Donor Management Performance System

- Expanded to evaluate availability at work-up

Initiatives Underway

Expansion of Registry Communications

- Introduced **anniversary e-mail** (Feb. 2011)
- Introduced **welcome e-mail series** to newly recruited members (Mar. 2011)
- Targeting **engagement mailing to prospectively-typed donors**
  (n ≈ 180,000 in FY 2011)
- Planning **2-step recruitment pilot** for FY '12

NMDP/ASBMT Referral Consultation Guidelines

Example:

Adult leukemias and myelodysplasia

Acute myelogenous leukemia (AML)

- High-risk AML including:
- Antecedent hematological disease (e.g., myelodysplasia (MDS))
- Treatment-related leukemia
- Induction failure

- CR1 with poor-risk cytogenetics or molecular markers
- CR2 and beyond

Acute lymphoblastic leukemia (ALL)

- CR1 up to age 35
- High-risk over age 35 including:
- Poor-risk cytogenetics (e.g., Philadelphia chromosome (t(9;22)) or 11q23 rearrangements)
- High WBC (>30,000 - 50,000) at diagnosis
- CNS or testicular leukemia
- No CR within 4 weeks of initial treatment
- Induction failure

- CR2 and beyond

Online, print, mobile app: www.marrow.org/md-guidelines

Recommendations for Optimizing Unrelated Donor Searches

- Once allogeneic HCT is a consideration, determine as early as feasible whether an unrelated donor search will be needed
  - HLA typing of patient, family
- If an unrelated donor search is needed, consider a preliminary search at no cost to assess likelihood of a match
- Search support is available for more challenging cases

Summary

- NMDP, which operates Be The Match, has been working to improve processes to accelerate product procurement via:
  - Better understanding of predictive donor characteristics
  - Internal process improvements
  - IT enhancements (Phoenix, Traxis, Haplogic III)
  - Network partner performance feedback

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Acknowledgments

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- Dennis Confer, MD – Chief Medical Officer
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