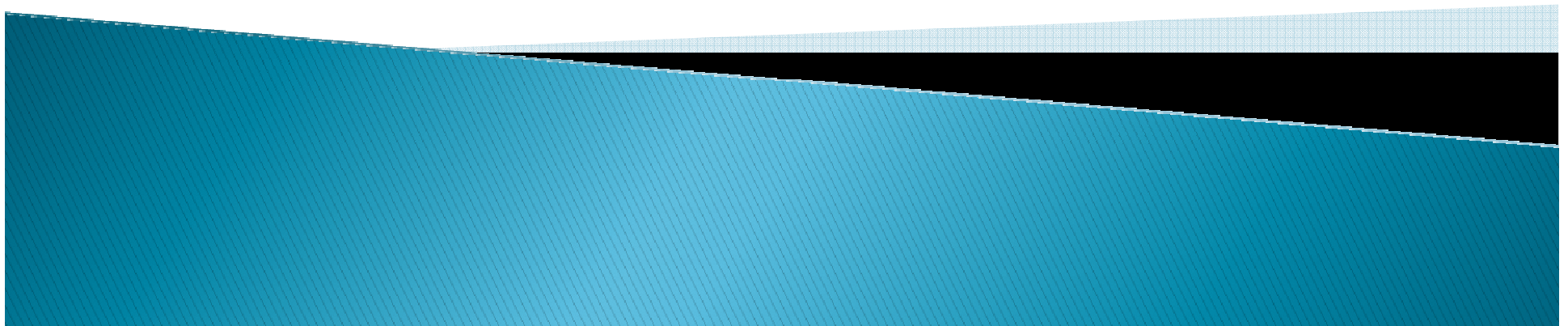


BM and PBSC Donor Outcomes and Recommended Follow Up

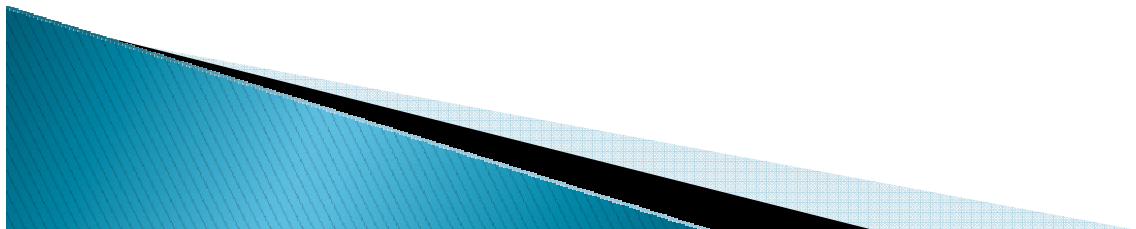
Michael A. Pulsipher, MD
Associate Professor
University of Utah School of Medicine



Donor Toxicity: Early and Late Follow Up

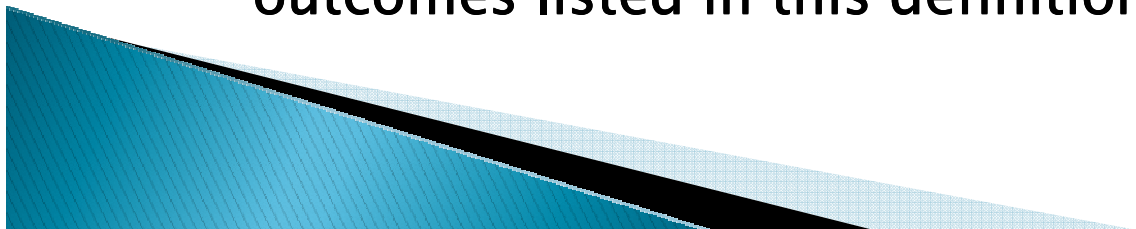
▶ Short Term Toxicities

- Standardized Follow up tools for Common Events
 - Pain Scales—mild, moderate, severe, intolerable
 - CTC scale is the best for common toxicities
 - Fatigue, insomnia, anorexia, nausea, dizziness, vomiting, site reaction, skin rash, fever, syncope
 - Apheresis issues
 - Symptoms of hypocalcemia, line issues, bleeding
 - Anesthesia issues
 - Blood products
 - Autologous vs. Allogeneic
 - Severe Adverse Events—FDA Definition



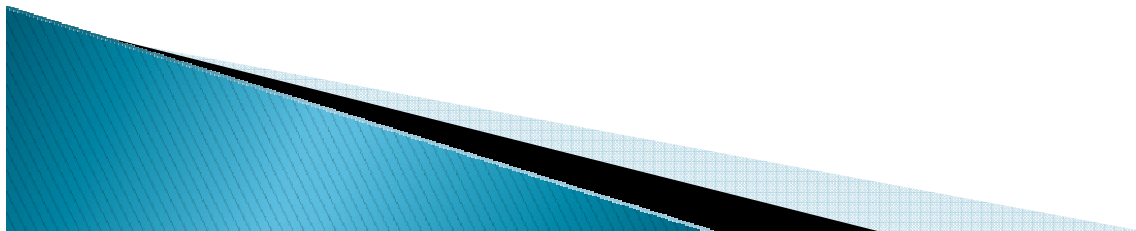
FDA Definition: Severe Adverse Events

- ▶ 1) Death
- ▶ 2) Life-threatening event (results in an immediate risk of death from the reaction as it occurred)
- ▶ 3) Unexpected inpatient hospitalization or prolongation of existing hospitalization
- ▶ 4) Persistent or significant disability / incapacity.
- ▶ 5) Congenital anomaly / birth defect
- ▶ 6) Other
 - Important medical events not listed above may be considered serious when they jeopardize the subject and/or may require intervention to prevent one of the outcomes listed in this definition.



Long-term Follow Up

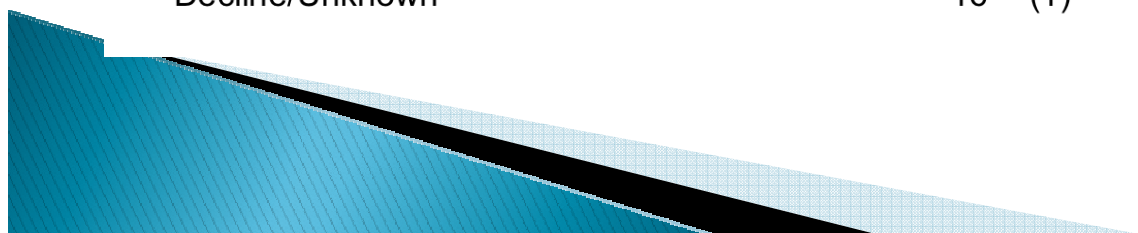
- ▶ Proven Long-term Complications
 - Chronic pain after BM donation
 - Long-term consequences of rare SAEs
- ▶ Possible Long-term Complications
 - G-CSF
 - Flare or activation of autoimmune illness
 - Thromboembolic event (stroke, MI)
 - Development of AML/MDS (or any cancer)
 - Psychological issues (especially in RD)



Unrelated Donor Experience: NMDP 2004–2009

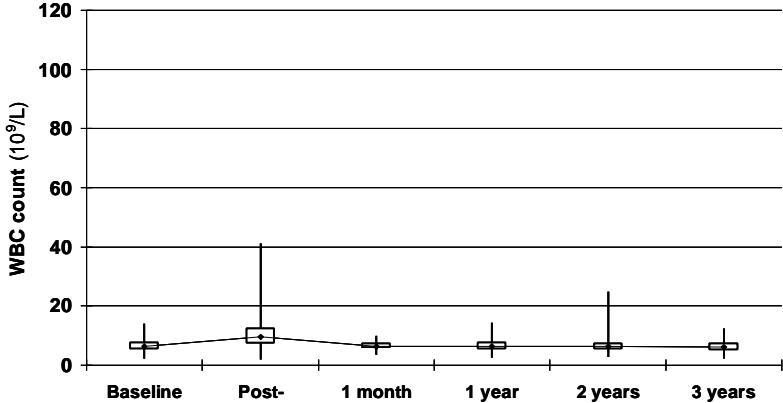
Pulsipher, unpublished data

Characteristic	Bone Marrow		PBSC		p-value
	N	(%)	N	(%)	
Number of donors	2726		6768		
Number of donor centers	81		76		
Number of collection centers	83		N/A		
Number of apheresis centers	N/A		98		
<i>Donor-related</i>					
Donor sex					0.168
Male	1638	(60)	4170	(62)	
Female	1088	(40)	2598	(38)	
Donor race/ethnicity					<0.001
Caucasian	1935	(71)	5083	(75)	
Hispanic	294	(11)	582	(9)	
Black/African American	165	(6)	320	(5)	
Asian/Pacific Islander	144	(5)	294	(4)	
American Indian/Alaska Native	42	(2)	77	(1)	
Other/Multiple Race	130	(5)	351	(5)	
Decline/Unknown	16	(1)	61	(1)	

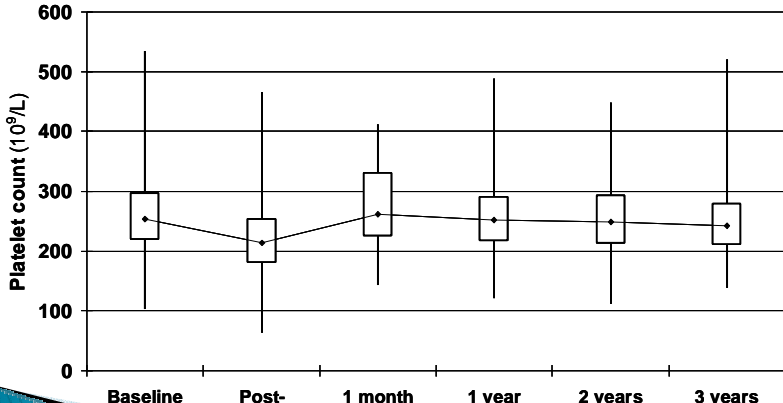


Donor WBC and Platelets peri-HCT: BM vs. PBSC

BM Donors

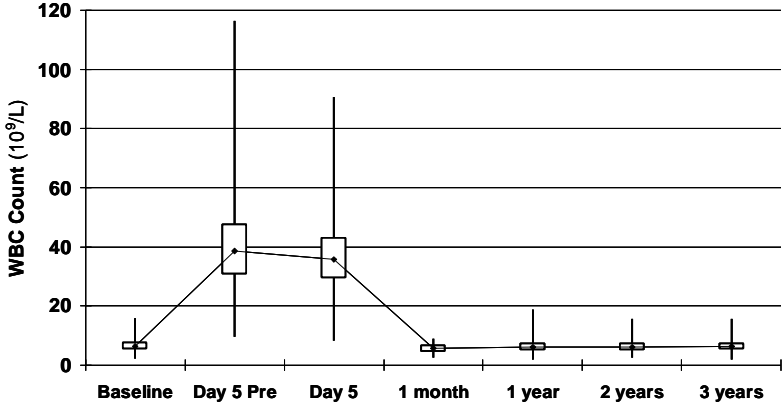


BM Donors
N = 2726 2624 20 935 541 274

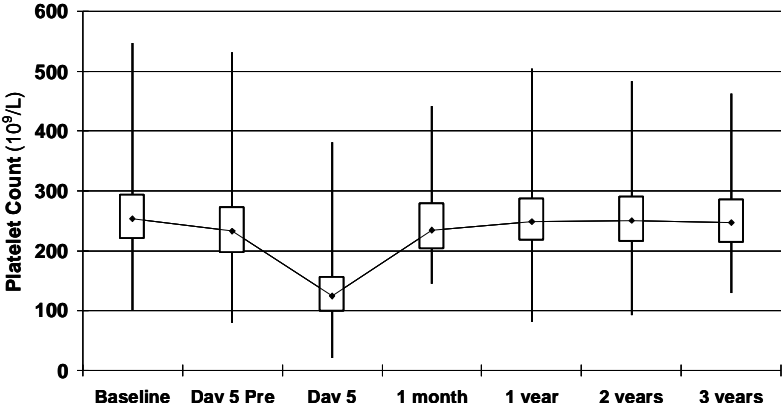


N = 2725 2623 20 935 541 274

PBSC Donors

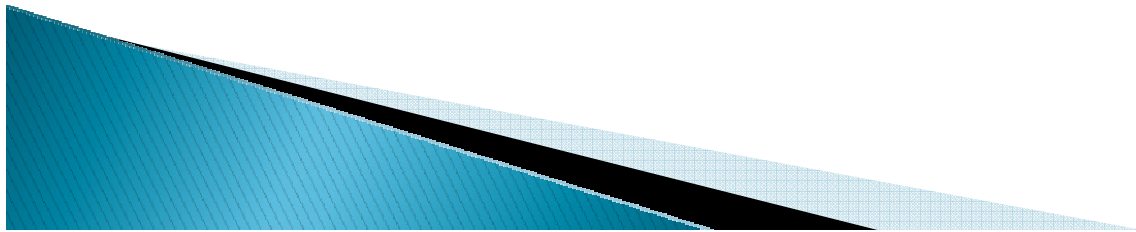
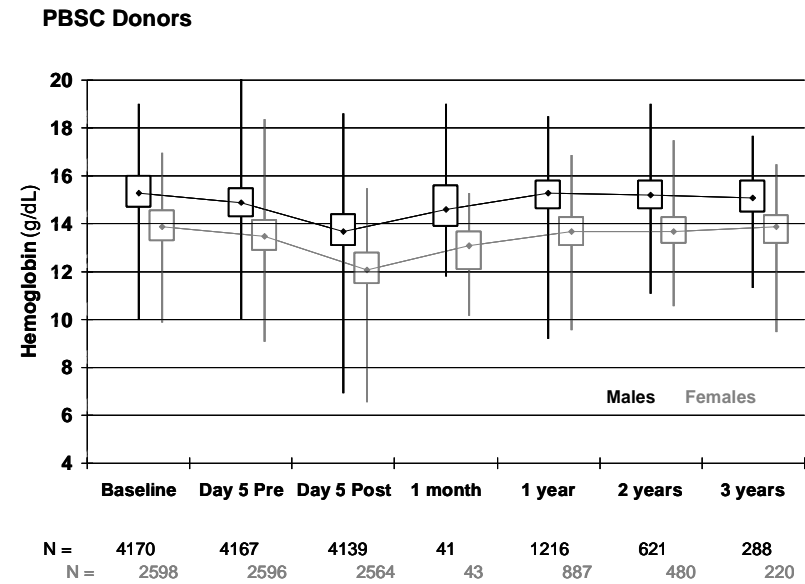
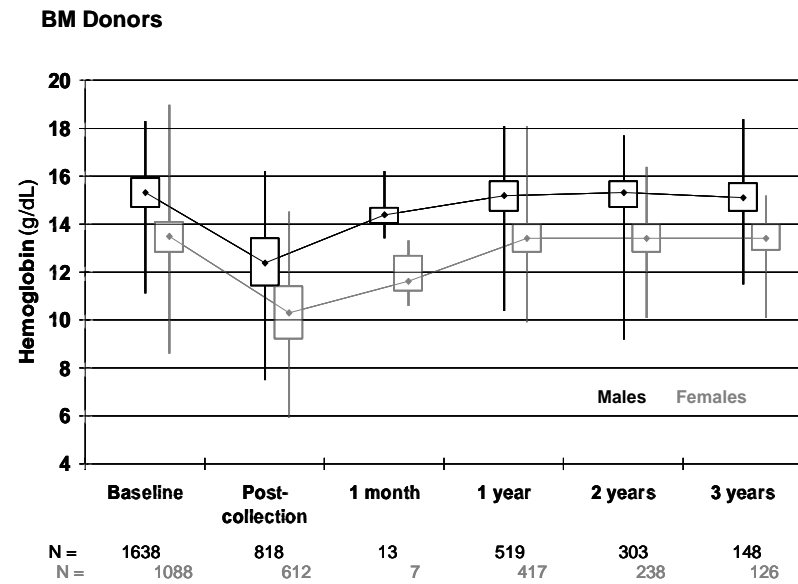


PBSC Donors
N = 6768 6767 6711 84 2104 1101 508



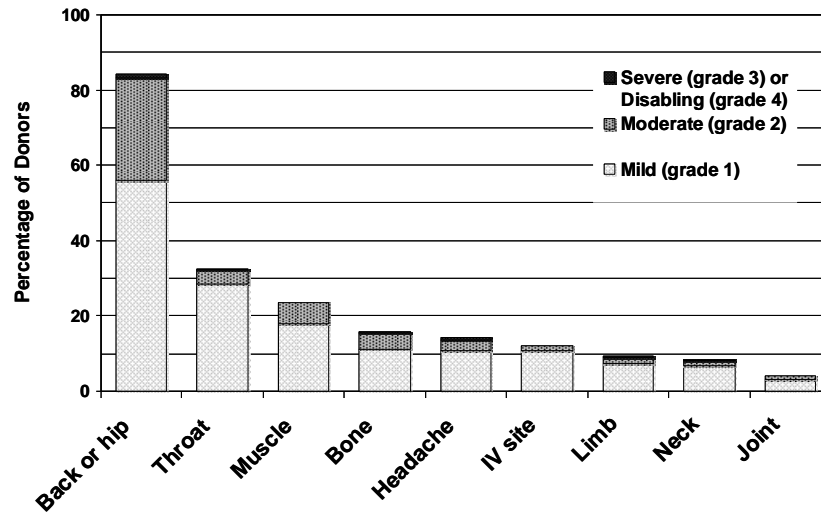
N = 6766 6767 6696 83 2095 1100 505

Donor Hemoglobin levels peri-HCT: BM vs. PBSC

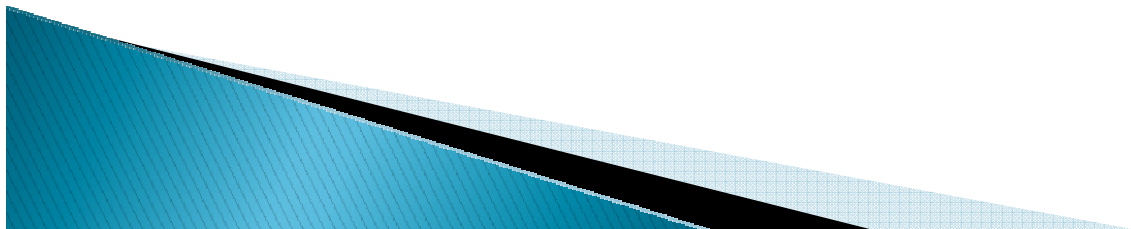
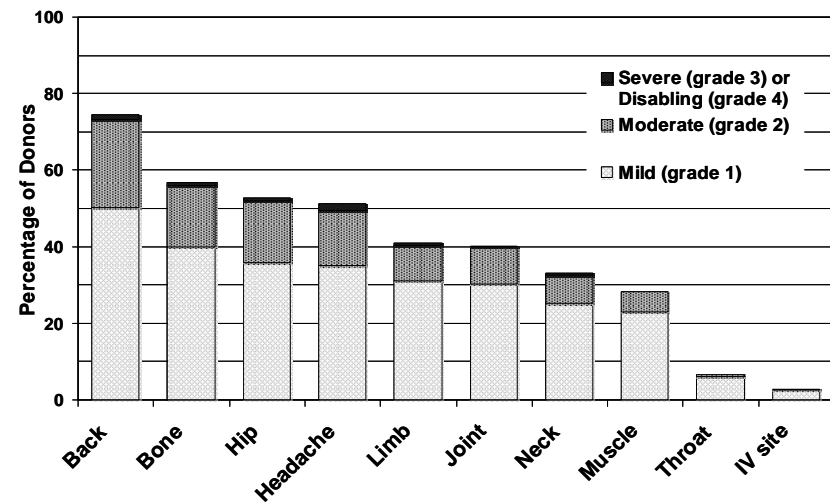


Location and intensity of Pain after Donation: BM vs. PBSC

BM Donors

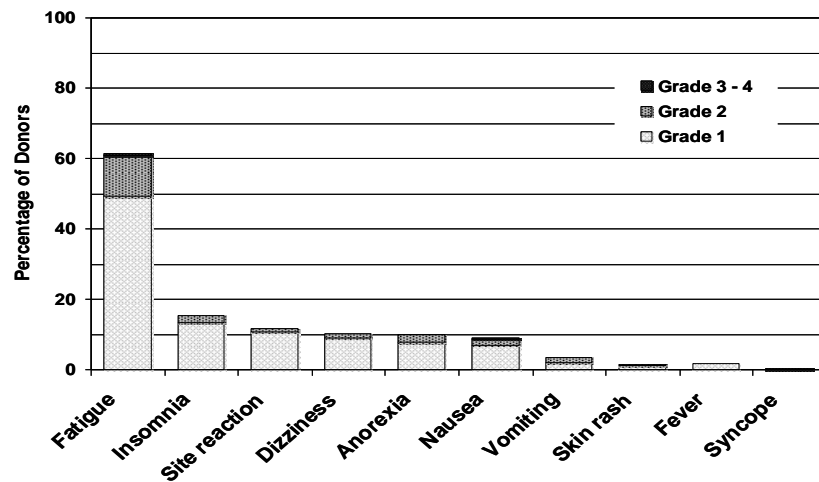


PBSC Donors

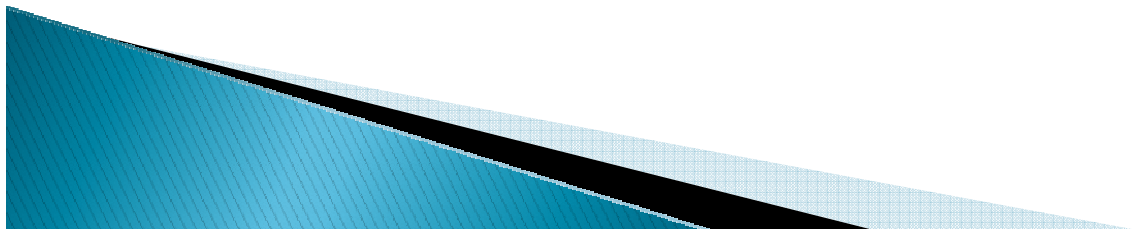
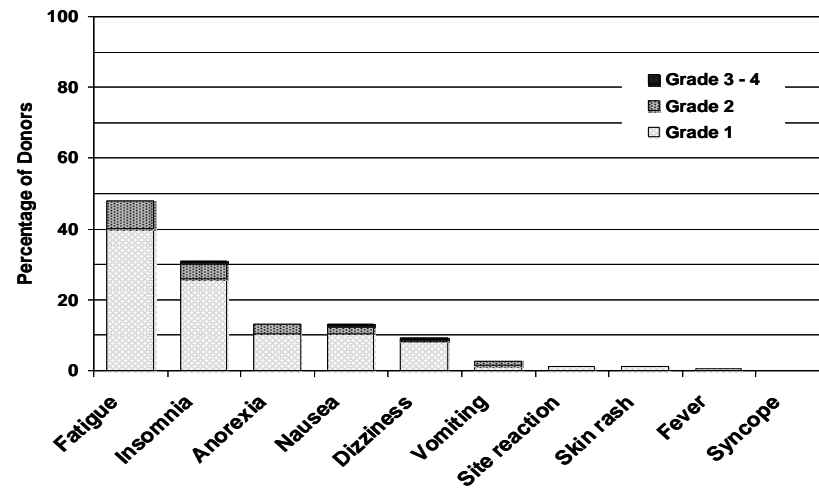


Common CTC toxicities peri-HCT: BM vs. PBSC

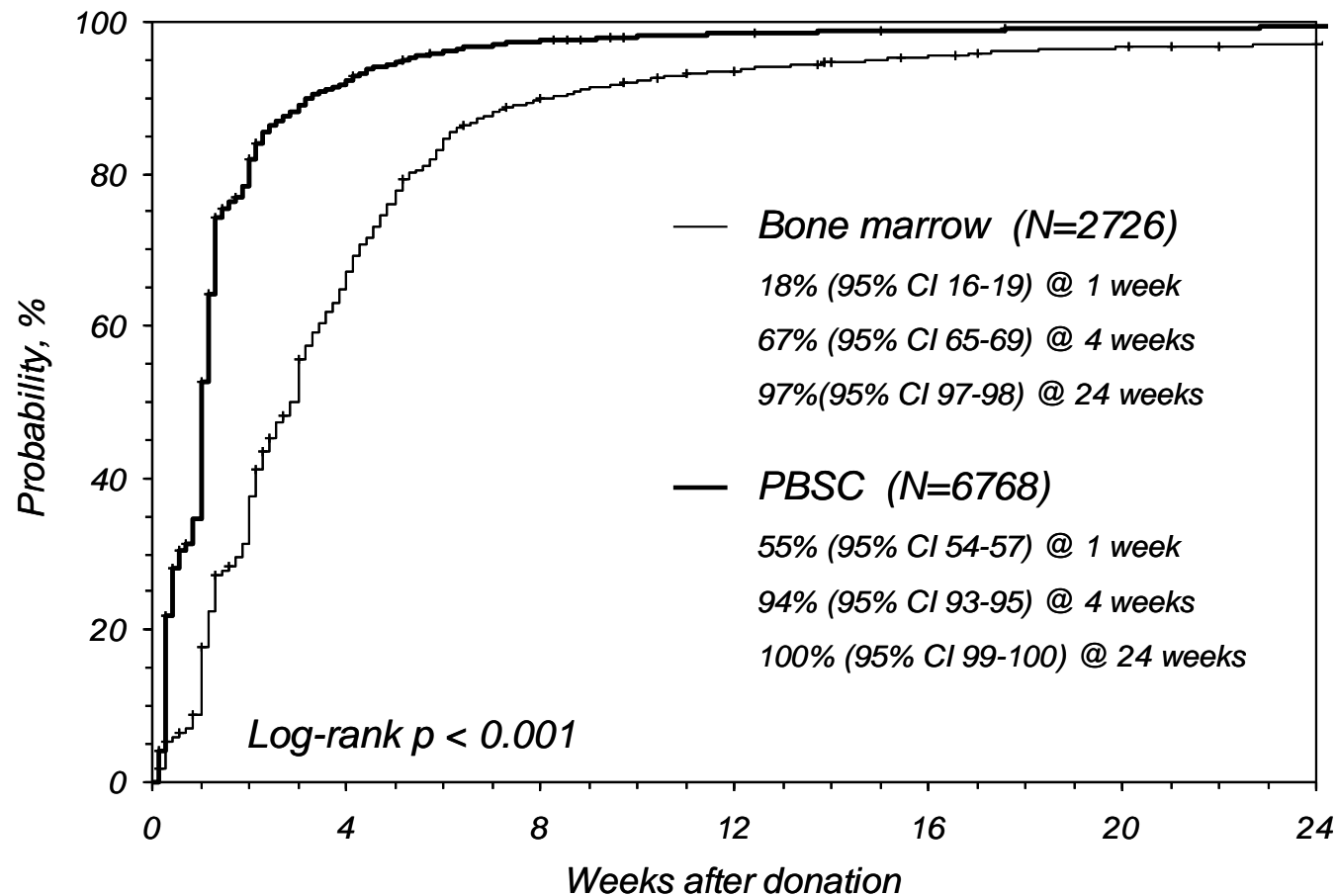
BM Donors



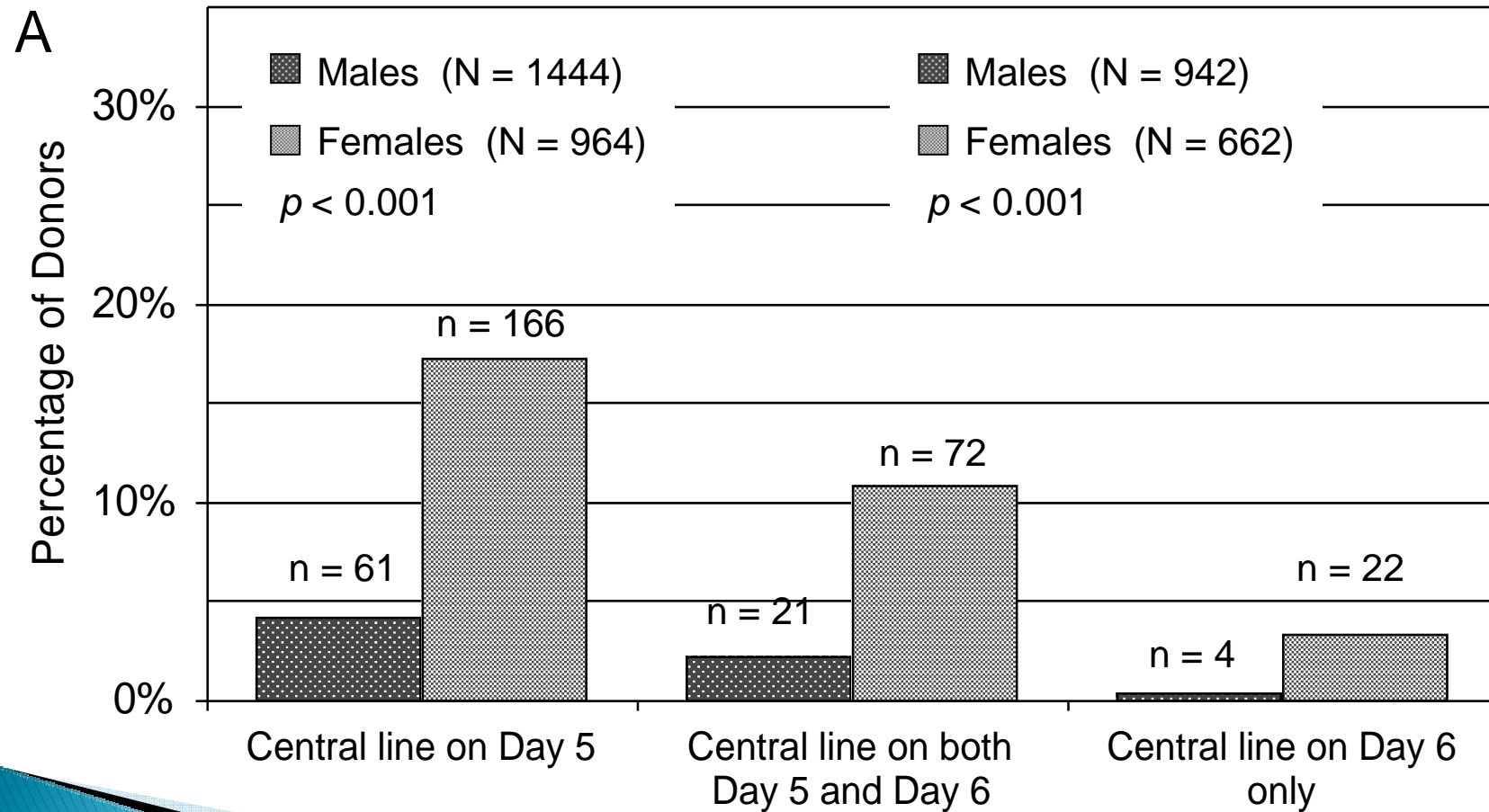
PBSC Donors



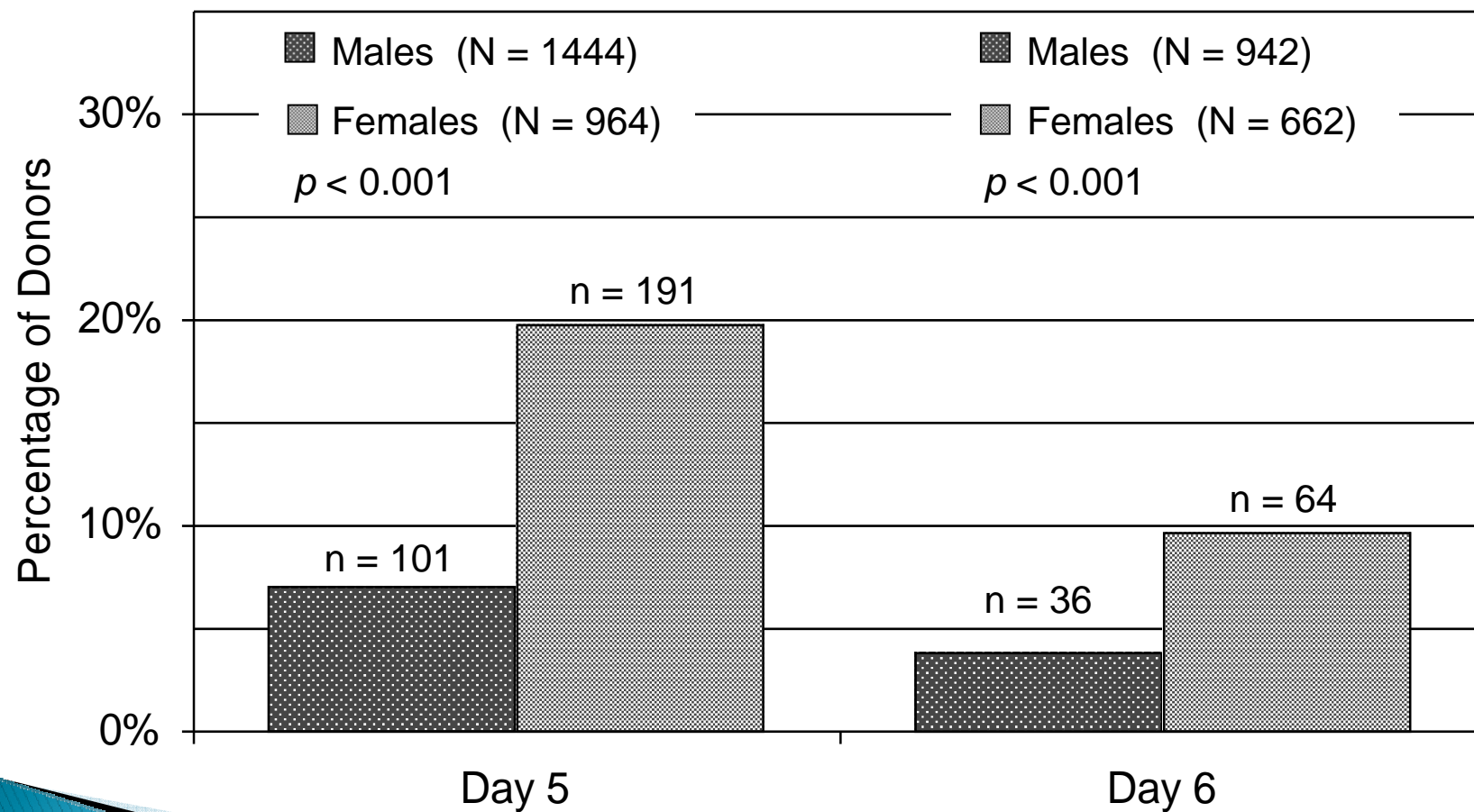
Recovery after HSC Donation: BM vs. PBSC



Complications Specific to PBSC Collection: Frequency of Central Line Placements

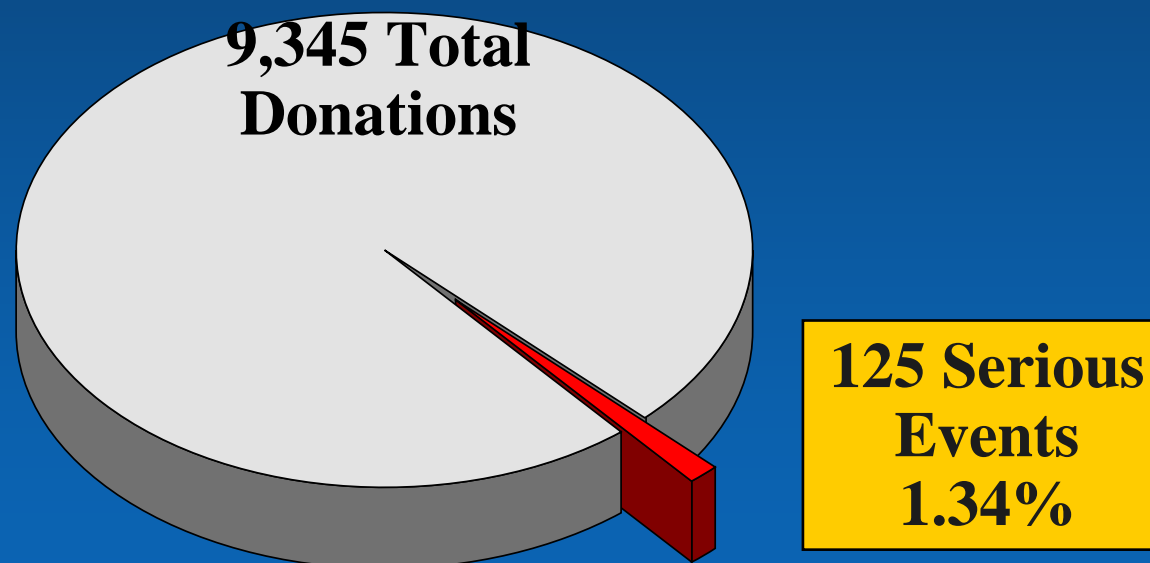


Frequency of Apheresis-Related AEs



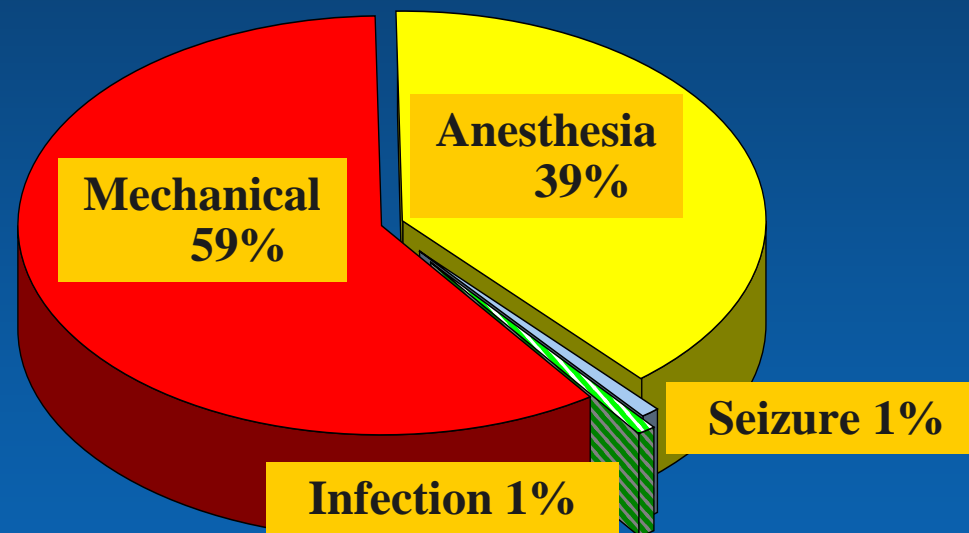
Serious Post-donation Events in NMDP Bone Marrow Donors

- Retrospective review of incident reports from 9,345 NMDP marrow collections performed between December, 1987 – December, 1999



116 Post-donation Events were Related to the Donation

- 69 cases of mechanical injury (median 10 months)
- 45 cases anesthesia related (all short lived)
 - Prolonged recovery
 - Spinal headache
 - Cardiac arrhythmia
 - Pulmonary edema



- 1 life-threatening infection
- 1 new-onset seizure disorder

Serious Adverse Events: NMDP PBSC Donors 1999-2006

- 42 Total SAEs in 5962 donors (0.7%)
 - 34 Serious by virtue of hospitalization
 - 25 with symptoms: headache, N & V, chest pain, bone pain, low calcium
 - 4 central line complications
 - 4 low platelet counts
 - 2 pneumonia
 - 1 asthma
 - 1 DVT
 - Other serious
 - 1 low platelet count without hospitalization

The burning question: Does GCSF increase the risk of leukemia in donors?

- Nagler: Asynchronous gene/chromosome replication timing and aneuploidy reported in recipients of GCSF (Exp Hemat 2004)
 - Hirsh Blood 2011: No findings of increased aneuploidy
- 2 cases of AML in 200 *sibling* donors (Bennett, BJH 2006)
- Hernandez: 9203 genes studied, some showed transient increased (374) or decreased (387) expression, but all returned to normal by 2 or 6 mos (Leukemia 2005)
- WMDA consensus on NMDP consent language on cancer risk
- Unpublished European and Japanese studies
 - No indication of increased cancer risk



Long Term Follow-up of PBSC Donors

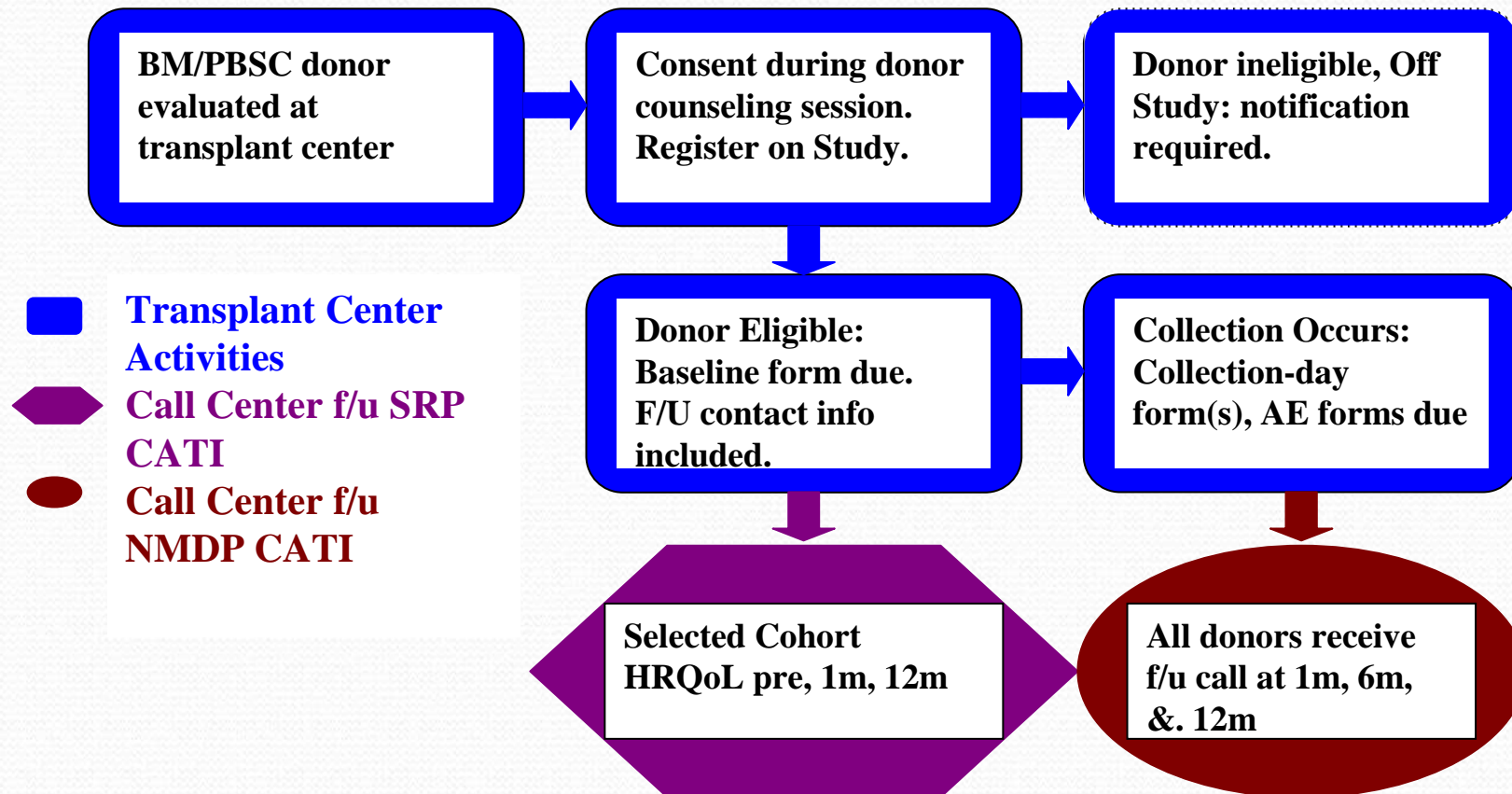
- Median follow-up 49 months (0.1 – 99)
- 26 cases of cancer identified
 - 5 Breast
 - 4 Prostate
 - 4 Basal Cell Carcinoma
 - 3 Melanoma + 2 Melanoma *in situ*
 - 1 each Larynx, Renal, Testicular, Lung, Esophageal, Uterine and Cervical
 - 1 case of CLL
- When compared with expected—no increased risk Pulsipher Blood 2009

RDSafe Health-Related QoL Study

Primary Objectives:

- Compare HRQoL for related vs URD donors age 18-60
- Compare HRQoL for related pediatric and adult (18-60, >60) donors with age-matched normative controls
- 300 related HCT donors
 - 100 less than 18 y/o
 - 100 18 – 60 y/o
 - 100 greater than 60 y/o
- 100 unrelated HCT donors

RDSafe Schema



Current Definition as Applied to HSC Donation

Nested HRQoL Indicators

Physical

- Pain
- Side Effects
- Recovery time

Psychological

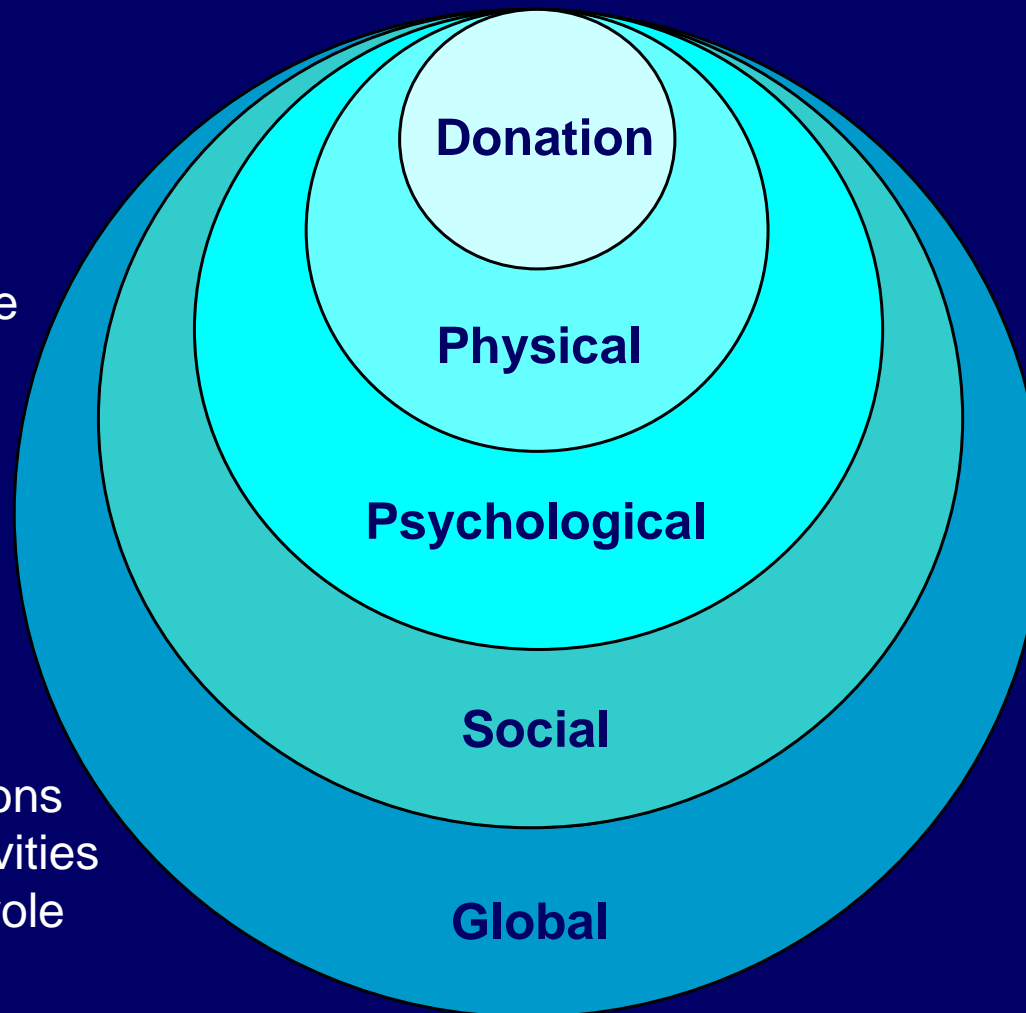
- Anxiety
- Depression
- Ambivalence
- Self-worth

Social

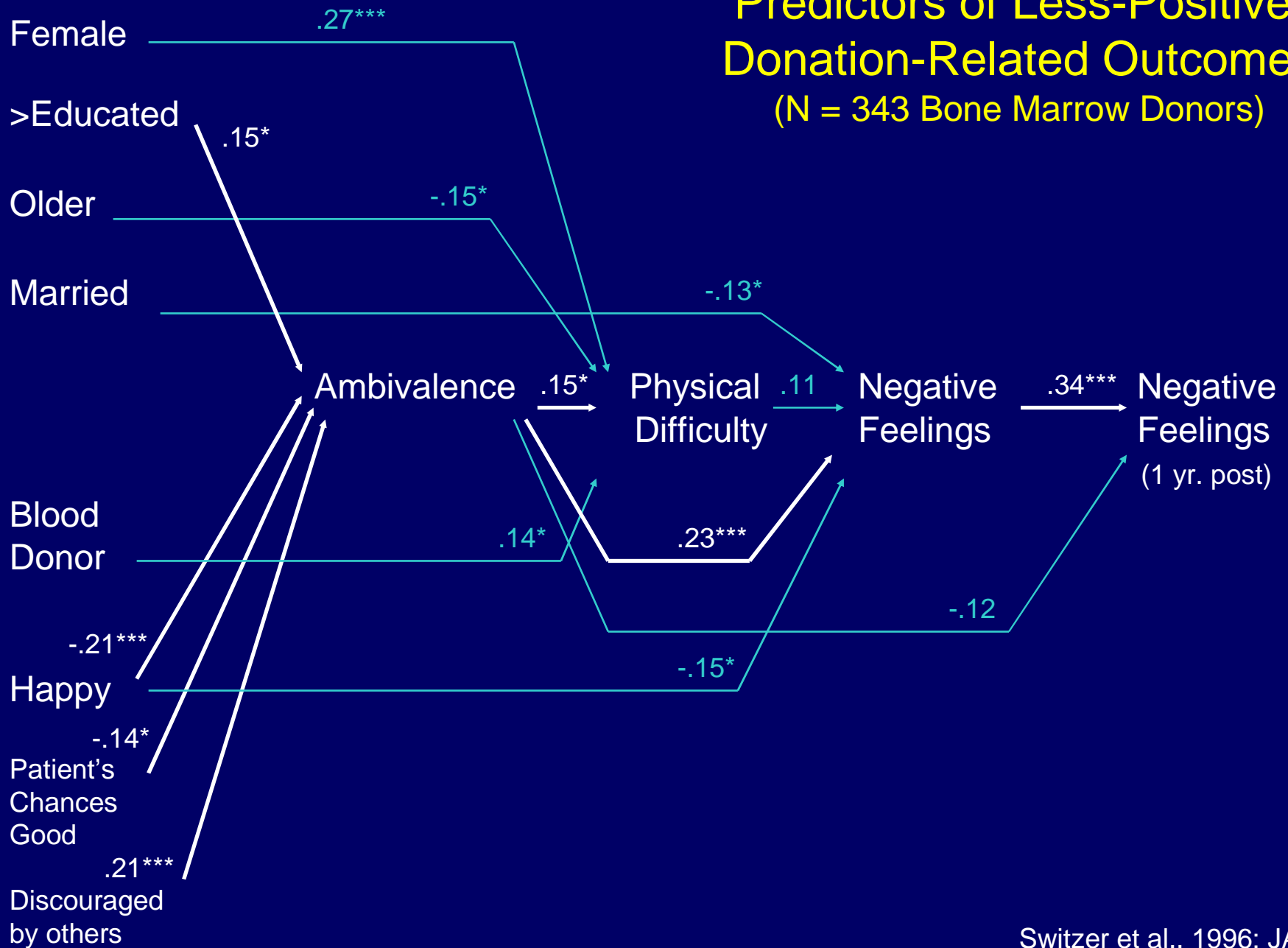
- Other's reactions
- Return to activities
- Donor social role

Global

- Perceived health
- Future concerns
- Satisfaction
- Well-being

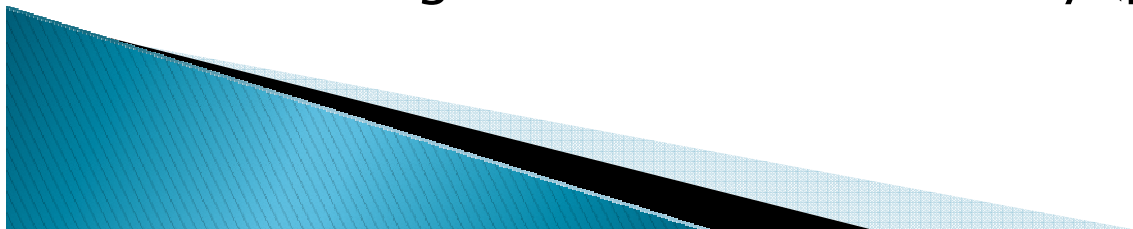


Predictors of Less-Positive Donation-Related Outcomes (N = 343 Bone Marrow Donors)



Conclusions

- ▶ We have a specific obligation to maximize donor safety
 - This means we need to measure donor outcomes to ensure that harvests/aphereses are safe
- ▶ We need to use the right tools to monitor
 - Standard toxicity scales allow comparison to literature
 - Psychological studies important, especially for RD
- ▶ Long-term Studies Important
 - G-CSF not shown to increase donor cancer risk
 - Larger related donor studies needed
 - Studies to date not large enough to show small risk increases
 - New agents need careful study (plerixafor)



Acknowledgements

- ▶ RDSafe Team:
 - Dennis Confer
 - Mary Horowitz
 - Galen Switzer
 - James Varni
 - Doug Rizzo
 - John Miller
 - Willis Navarro
 - Rebecca Drexler
 - Amy Hays
 - Brent Logan
 - Roberta King
 - Susan Leitman
 - Marci Tomblyn
- Amy Foley
- Kathleen Delaney
- Paolo Anderlini
- ▶ CIBMTR Donor Committee
 - Tanya Pederson
 - Paul O'Donnell
 - David Stroncek
- ▶ WMDA Donor Committee
 - Bronwen Shaw
 - Derwood Pamphilon
 - William Hwang
 - Ann-Marie Van Walraven
- ▶ Children's Oncology Group
SCT
 - Steve Grupp