

National Marrow Donor Program: Unrelated Donor Experiences

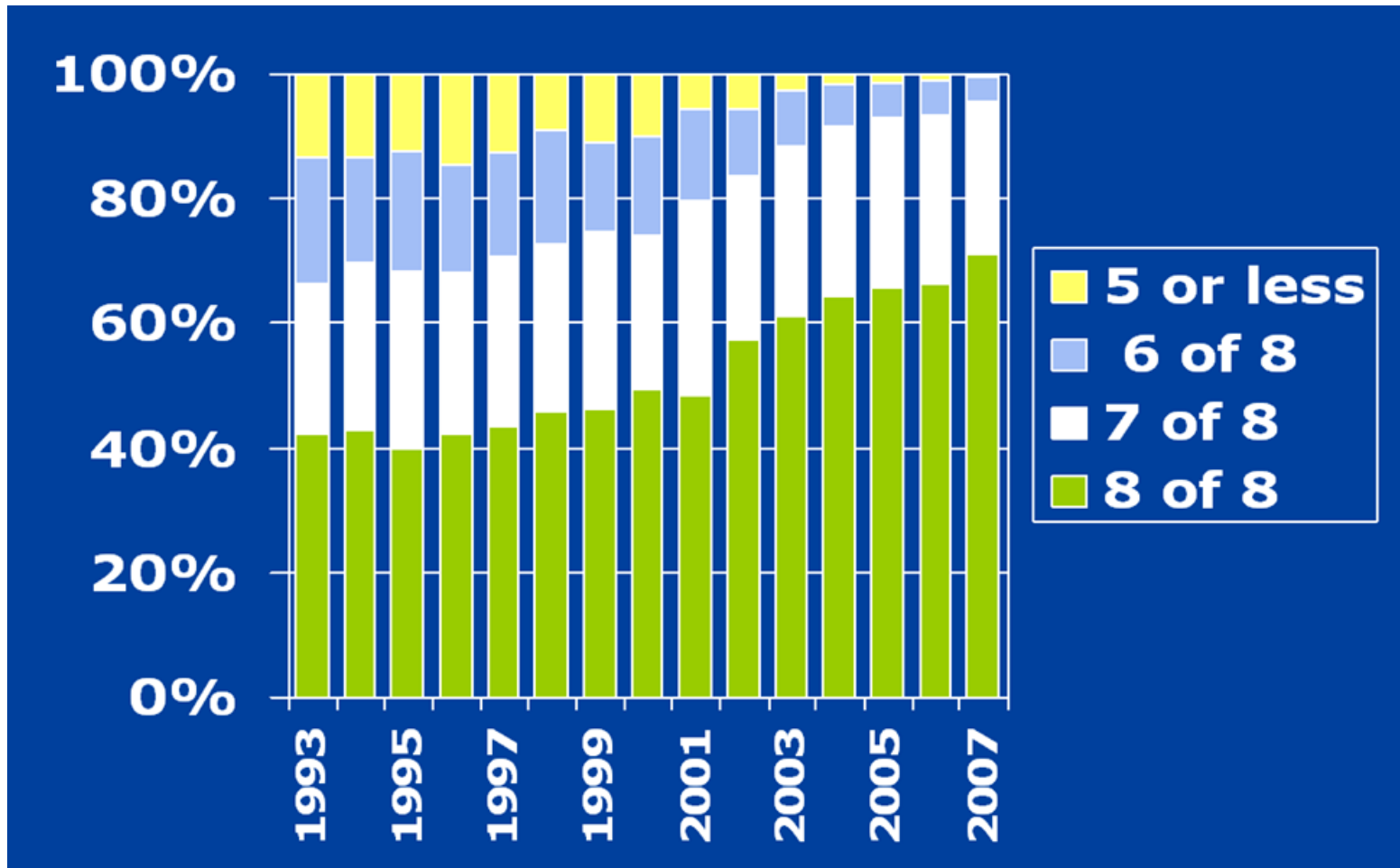
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Cellular Therapy Liaison Meeting
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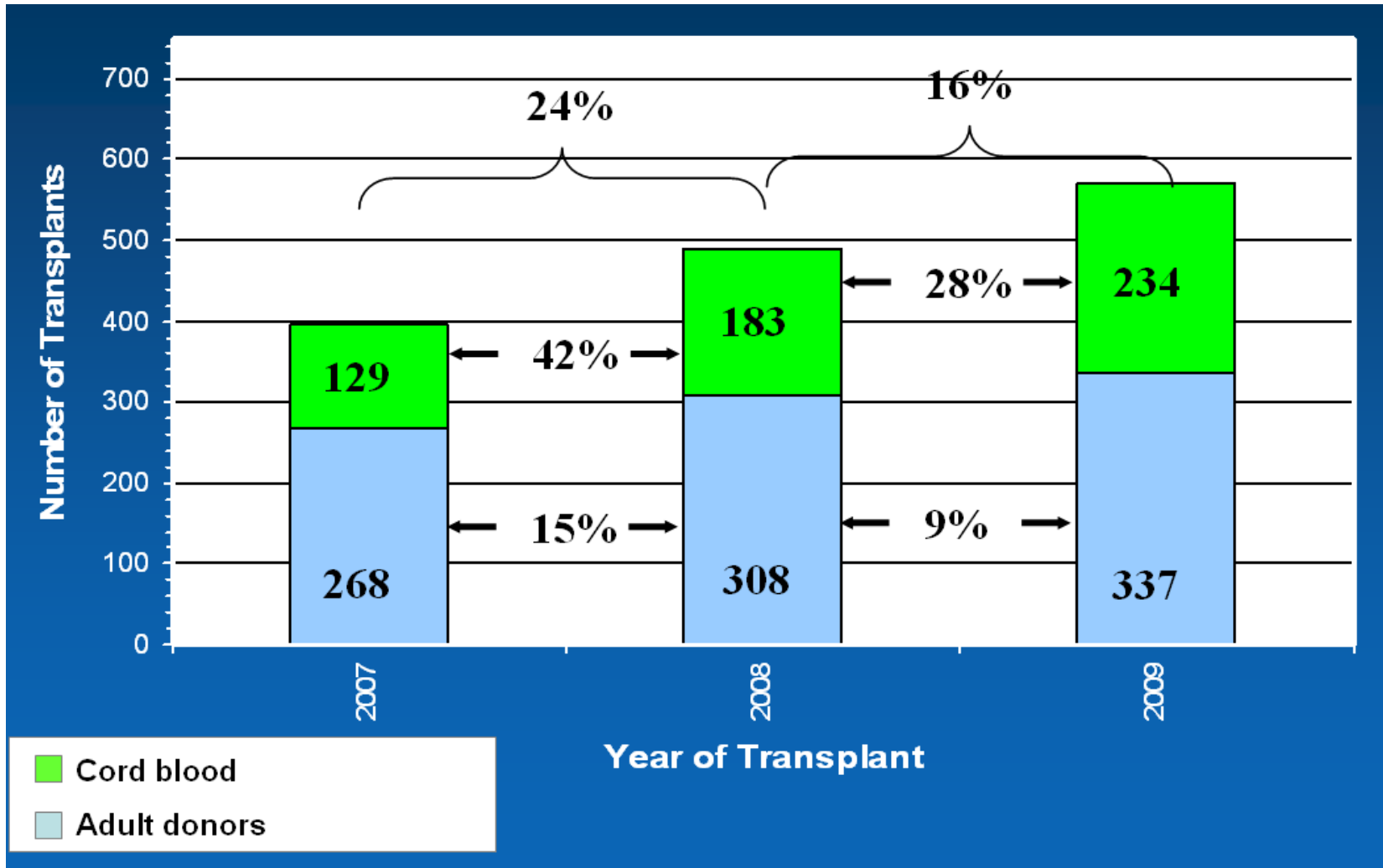
Background

- Donors of PBSC are providing an increasing number and percentage of stem cells for hematopoietic transplantation
- Questions remain which stem cell sources (PBSC, bone marrow or cord blood) provides the best clinical outcomes for transplant recipients
- From a donor's perspective, donation of bone marrow and PBSC have different safety profiles
- This presentation will outline the NMDP experience with unrelated bone marrow and PBSC donation and will discuss plans for further studies assessing the unrelated donor experience

Transplants Today Are Using Better Matched Donors



NMDP Minority Transplants FY Ending June 30



A Report on Marrow and PBSC Donors

Biology of Blood and Marrow Transplantation 14:29-36 (2008)
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1083-8791/08/1409-0001\$32.00/0
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Recovery and Safety Profiles of Marrow and PBSC Donors: Experience of the National Marrow Donor Program

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Miller JP, et al., Biol Blood Marrow Transplant, Sept 2008
Free online: www.bbmt.org/issues

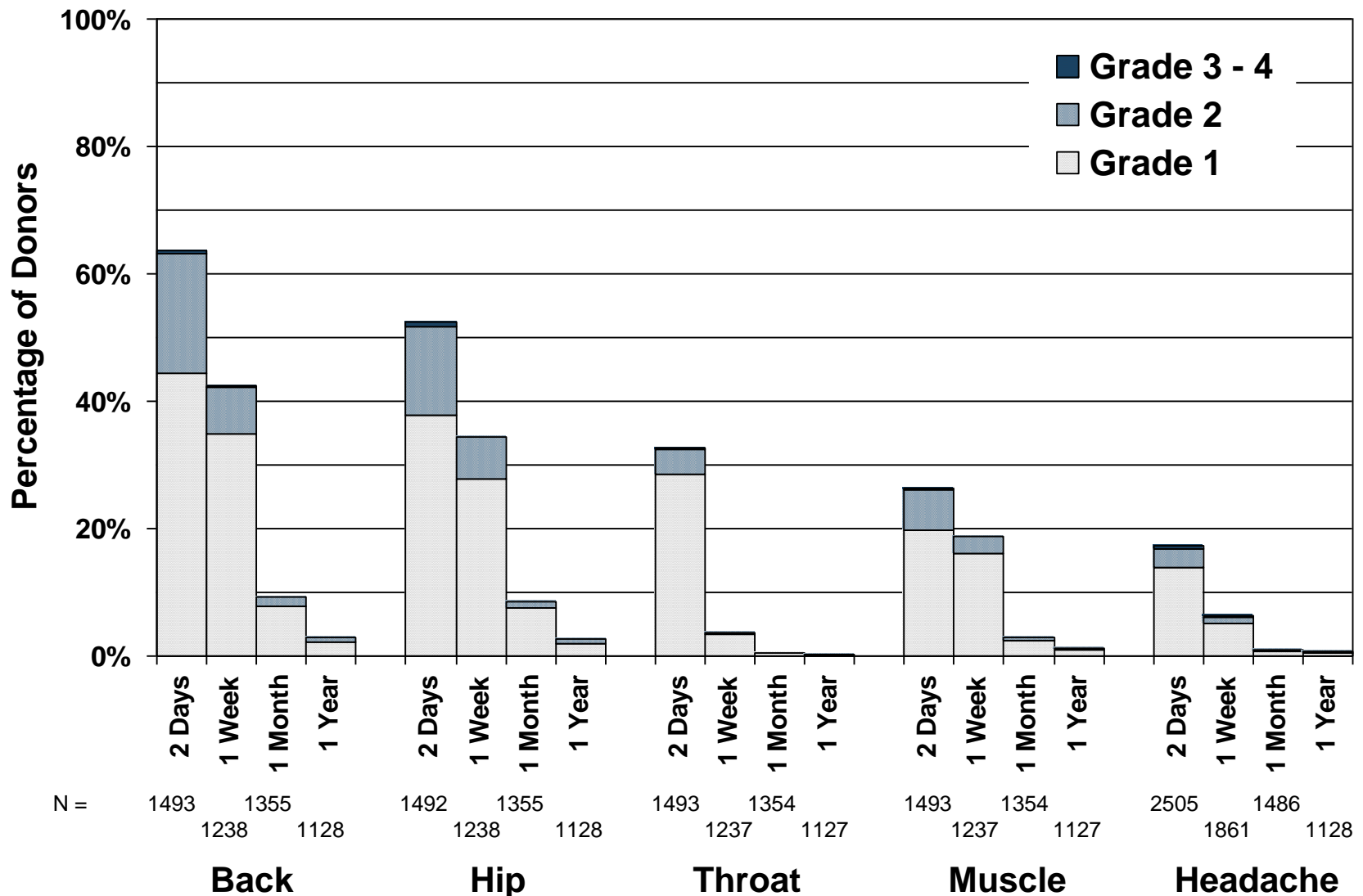
Unrelated Marrow Donor Outcomes

- From November 2001 through March 2006
- >2500 donations
- Donors provided 1 – 3 autologous blood units prior to donation
- 76% received at least 1 autologous blood unit transfusion

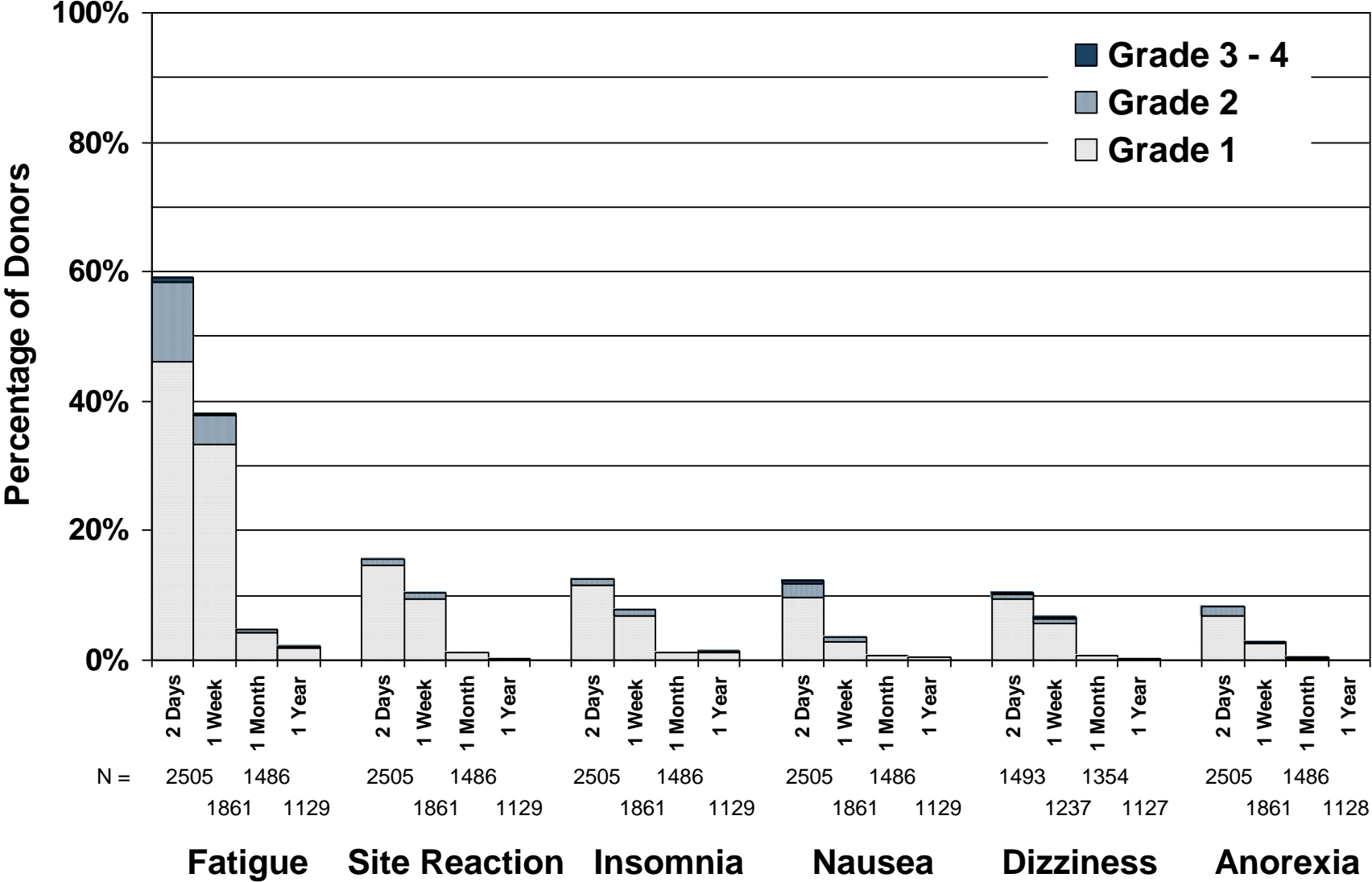
Donor Data Collection and Follow-up

- Similar data are collected on bone marrow and PBSC donors
- Time points for standardized data collection are:
 - Baseline
 - Daily during PBSC mobilization
 - Day(s) of collection
 - Two days post-donation
 - Weekly until fully recovered
 - 1 month, 6 months and annually
- Adverse events are reported upon occurrence

Pain Post-Bone Marrow Donation

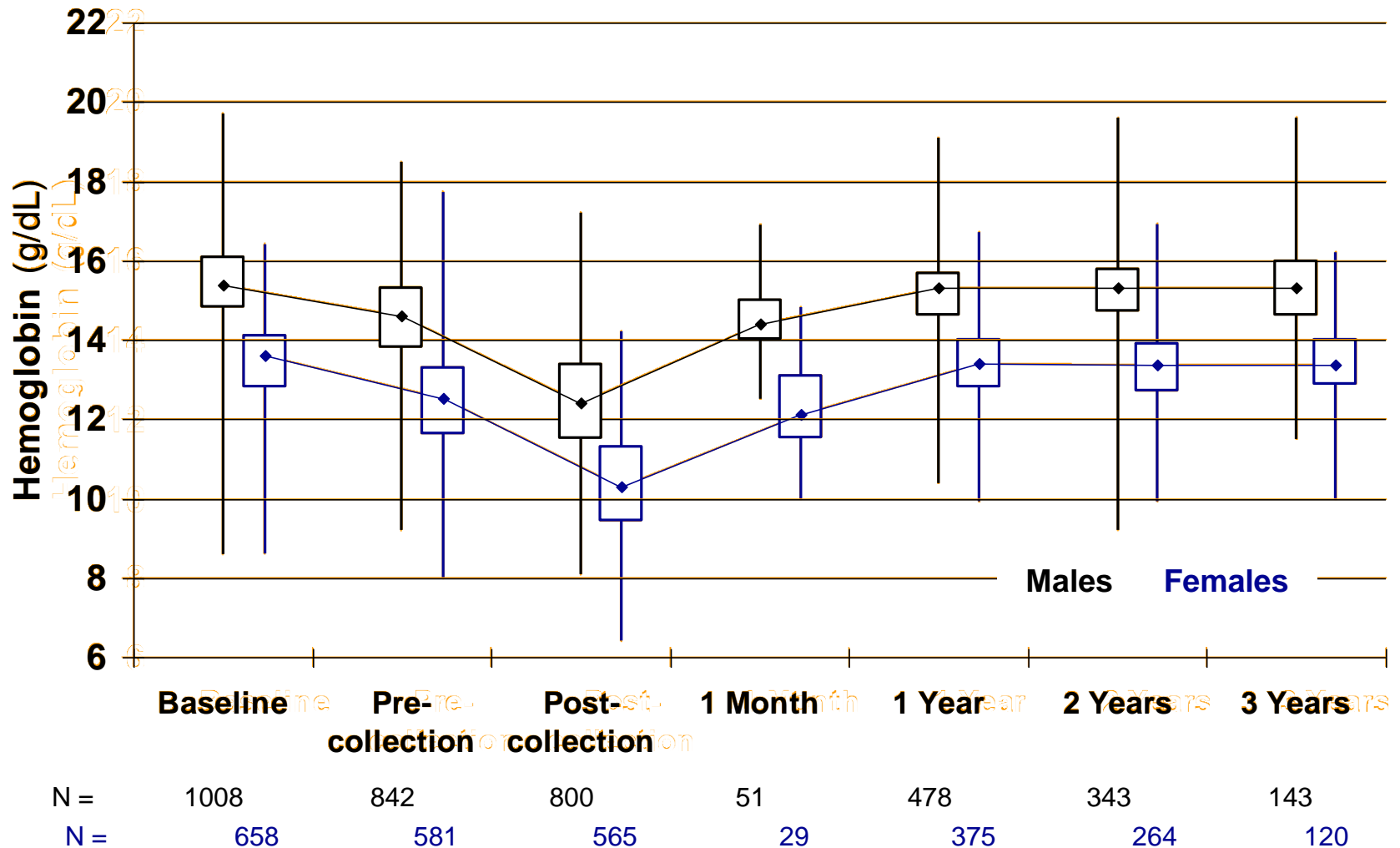


Non-Pain Symptoms Post Marrow Donation



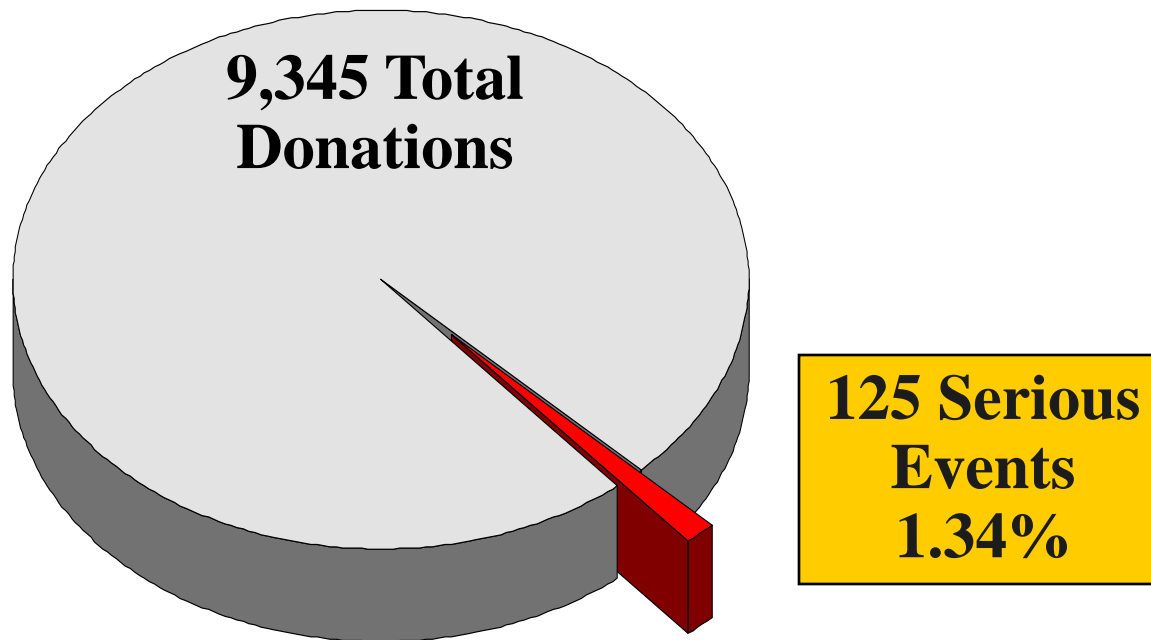
Bone Marrow Donor Hemoglobin Levels

(Maximum, Upper quartile, Median, Lower quartile, Minimum)



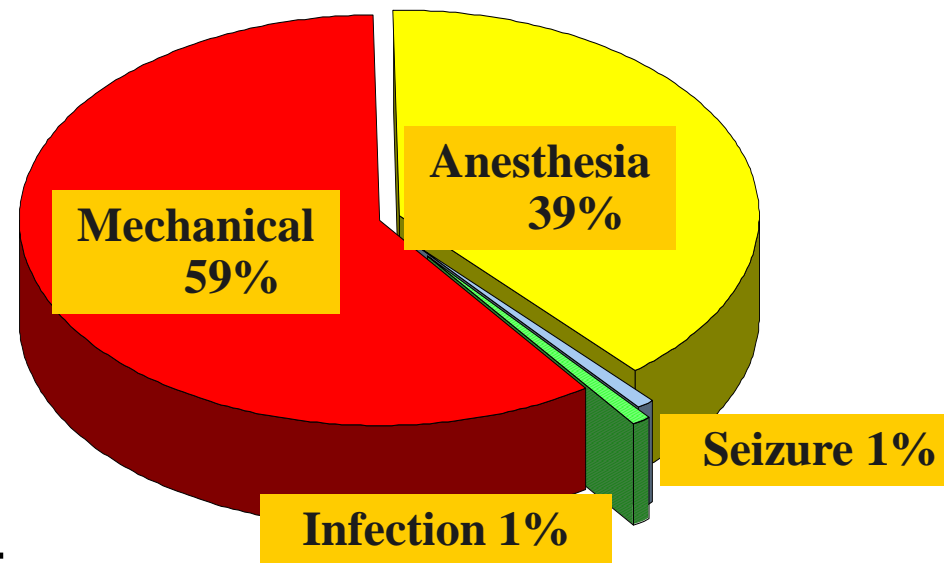
Serious Post-donation Events in NMDP Bone Marrow Donors

- 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



A Report on 2,408 PBSC Donors

blood

Prepublished online Feb 3, 2009;
doi:10.1182/blood-2008-08-175323

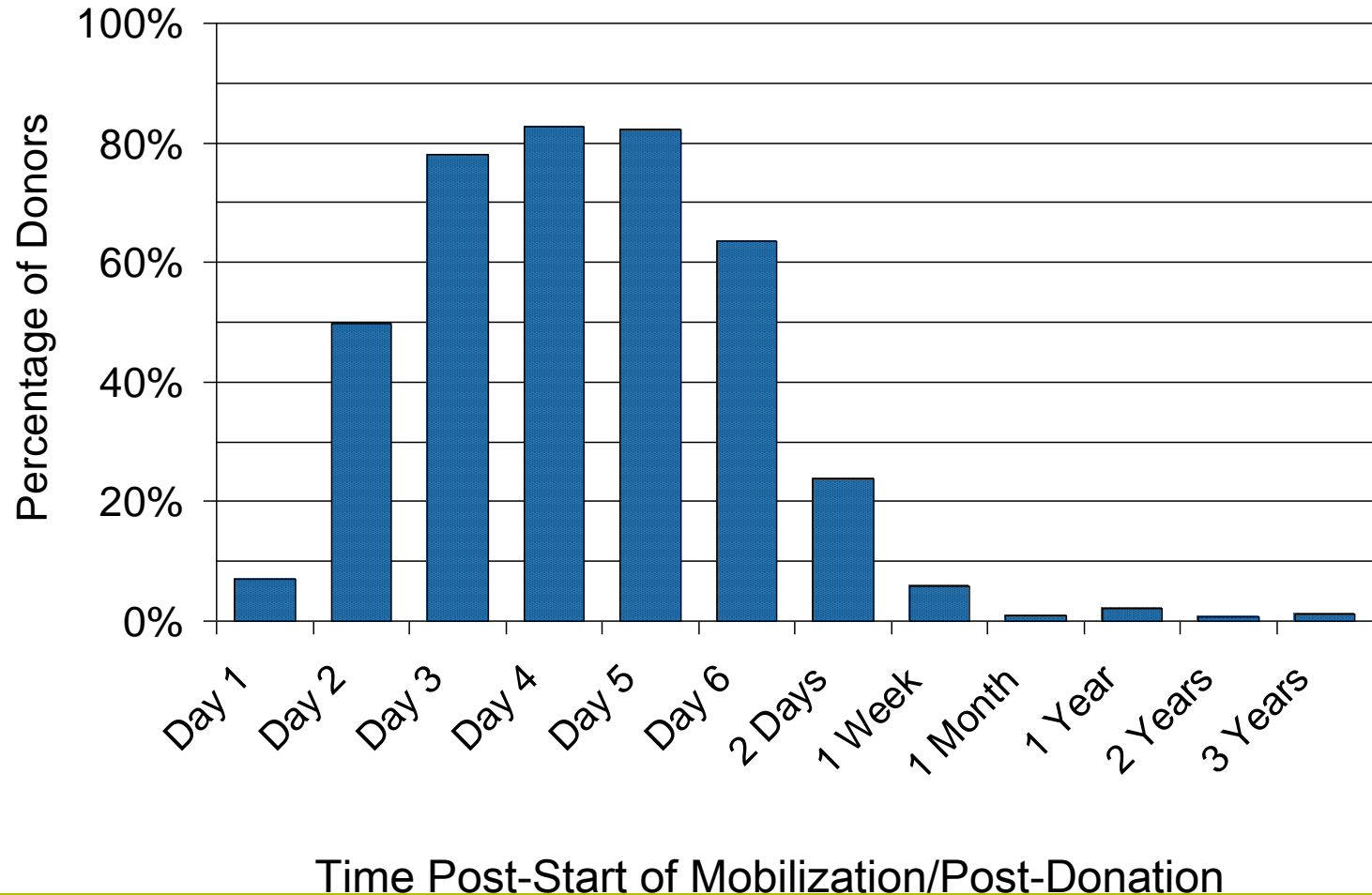
Adverse events among 2408 unrelated donors of peripheral blood stem cells: Results of a prospective trial from the National Marrow Donor Program

Michael A. Pulsipher, Pintip Chitphakdithai, John Miller, Brent R. Logan, Roberta J. King, J. Douglas Rizzo, Susan F. Leitman, Paolo Anderlini, Michael Haagenson, Seira Kurian, John P. Klein, Mary M. Horowitz and Dennis L. Confer

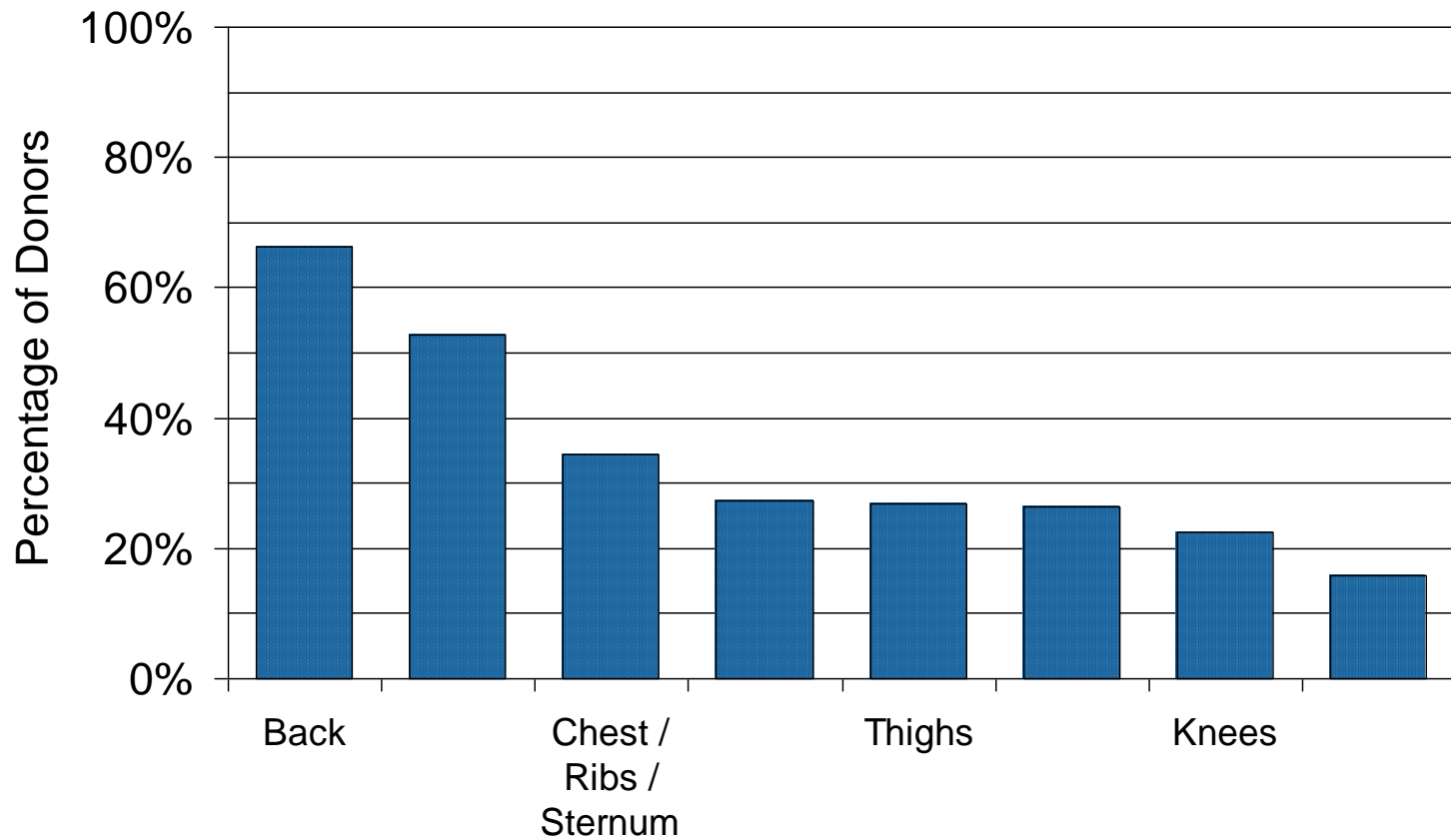
2,408 PBSC Donations – July 1999 through April 2004

- 60% males
- Received filgrastim ~ 10 mcg/kg-day x 5 days
- Data from 73 donor centers and 96 apheresis centers
- Two-thirds had 2 apheresis collections

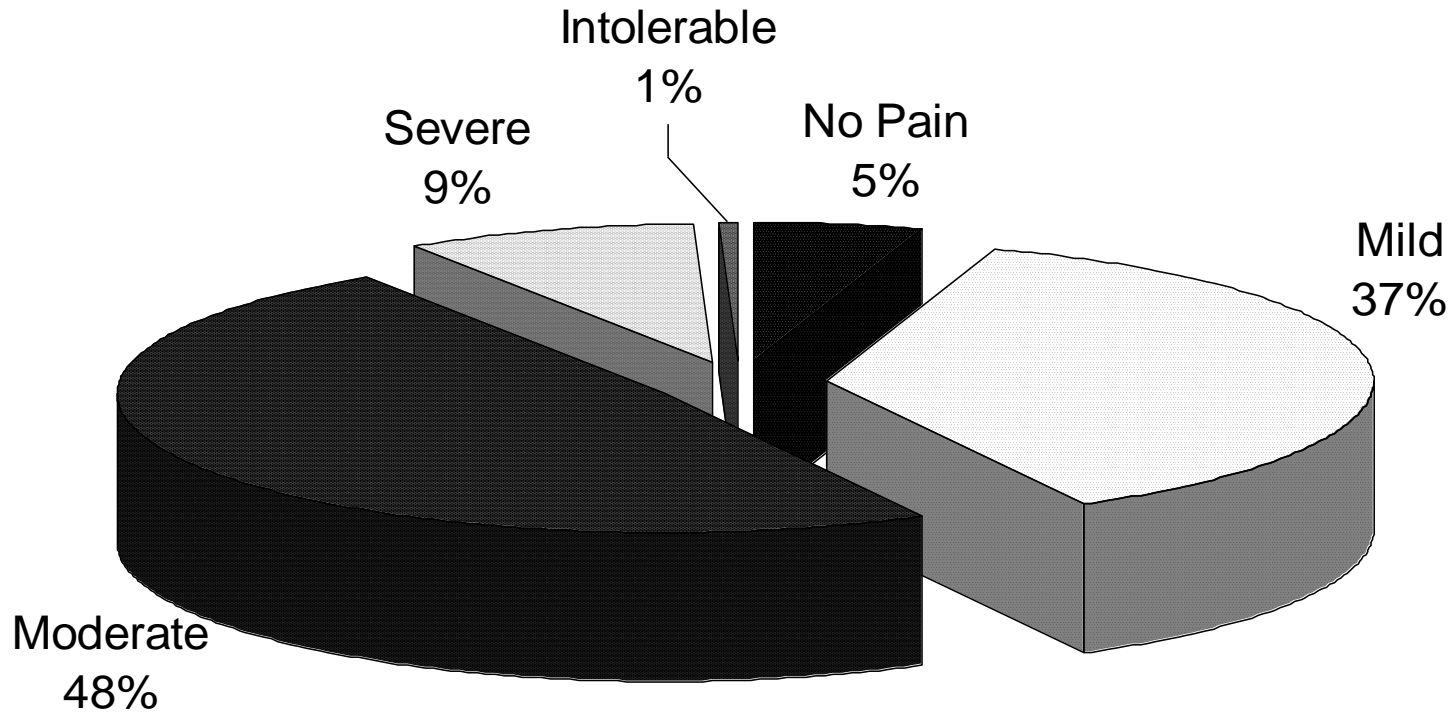
Frequency of Bone Pain in PBSC Donors



Sites of Bone Pain During Mobilization



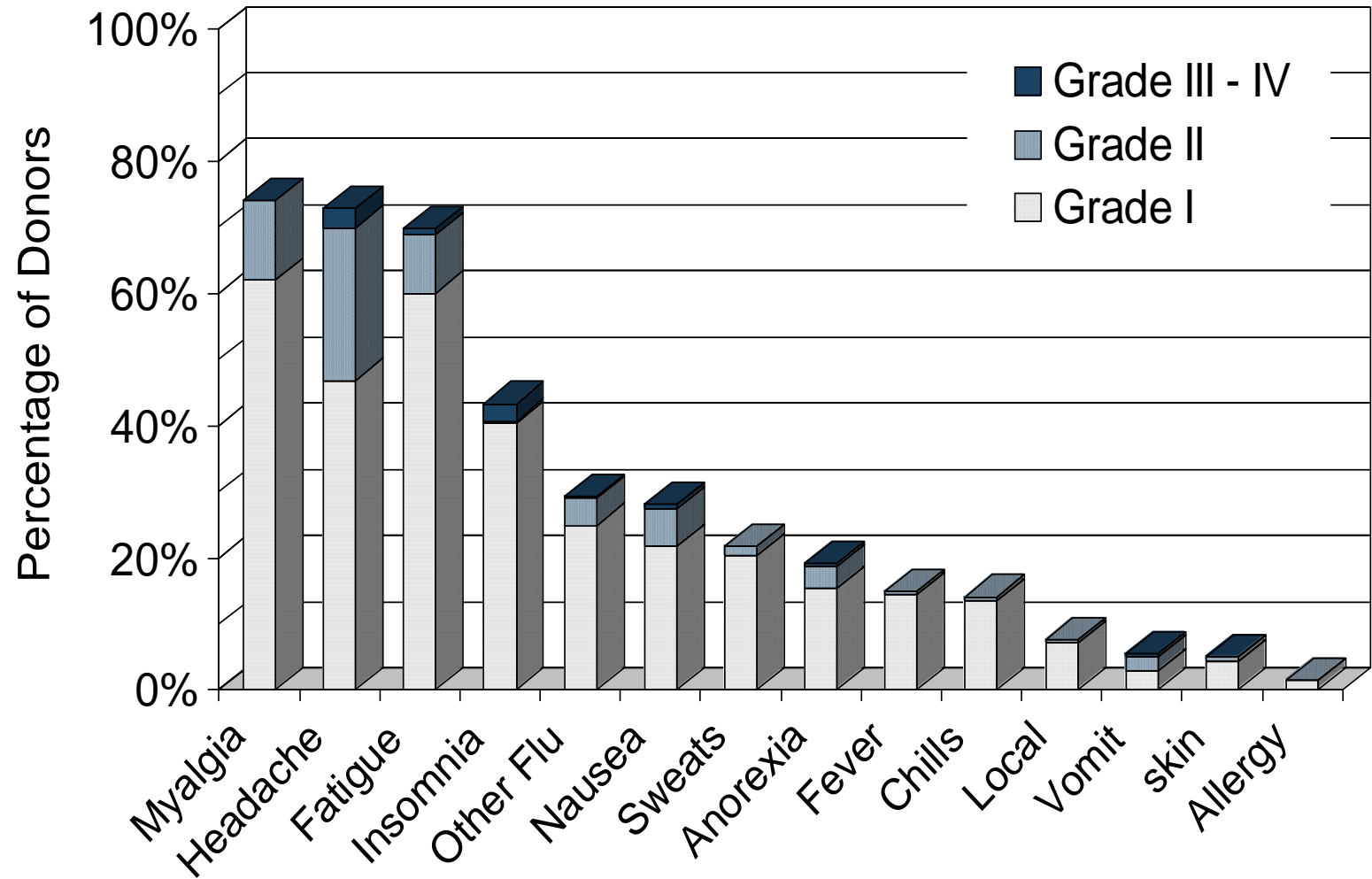
Maximum Bone Pain Severity for Donors



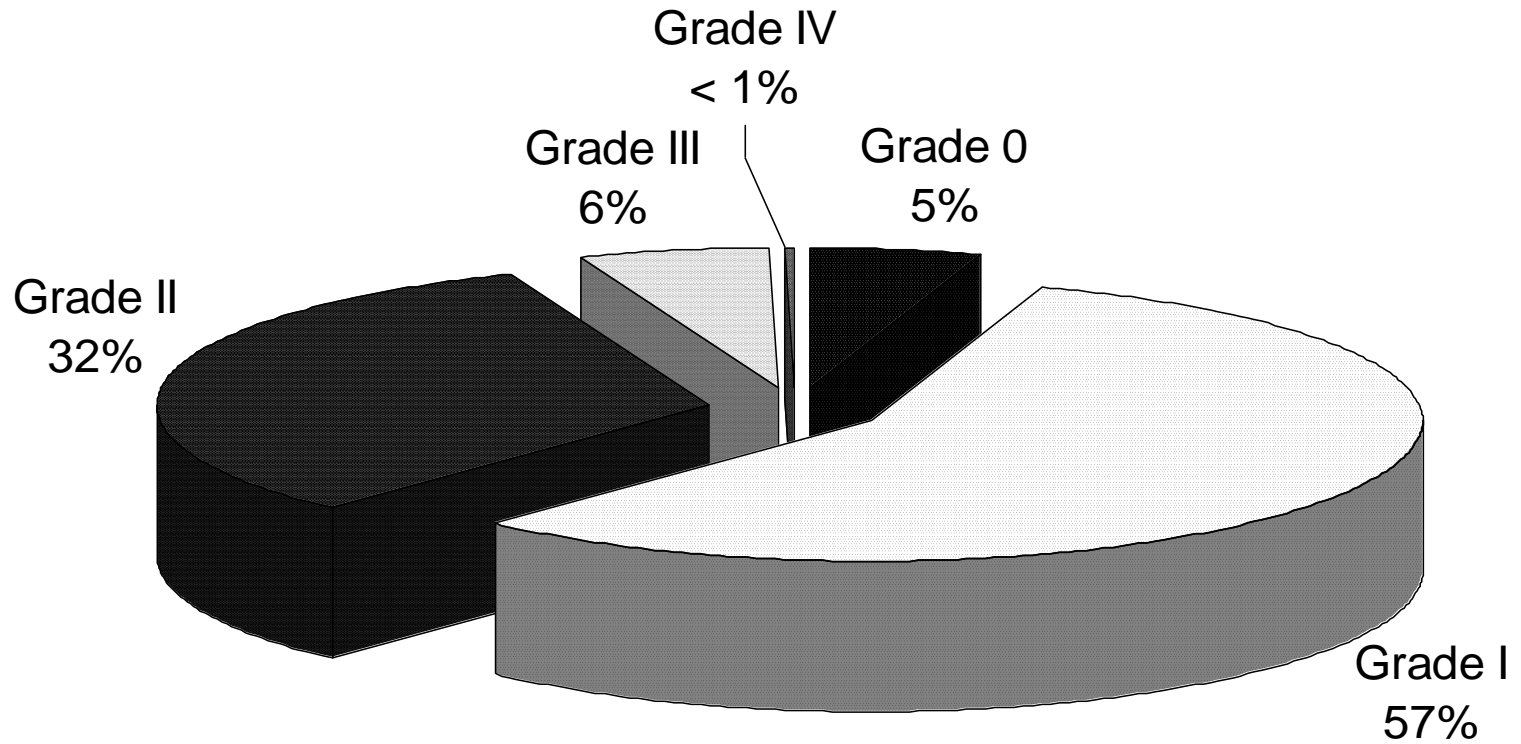
Pain Management

- With Pain medication (usually acetaminophen or ibuprofen):
 - 65% experienced some pain relief
 - 30% experienced complete relief

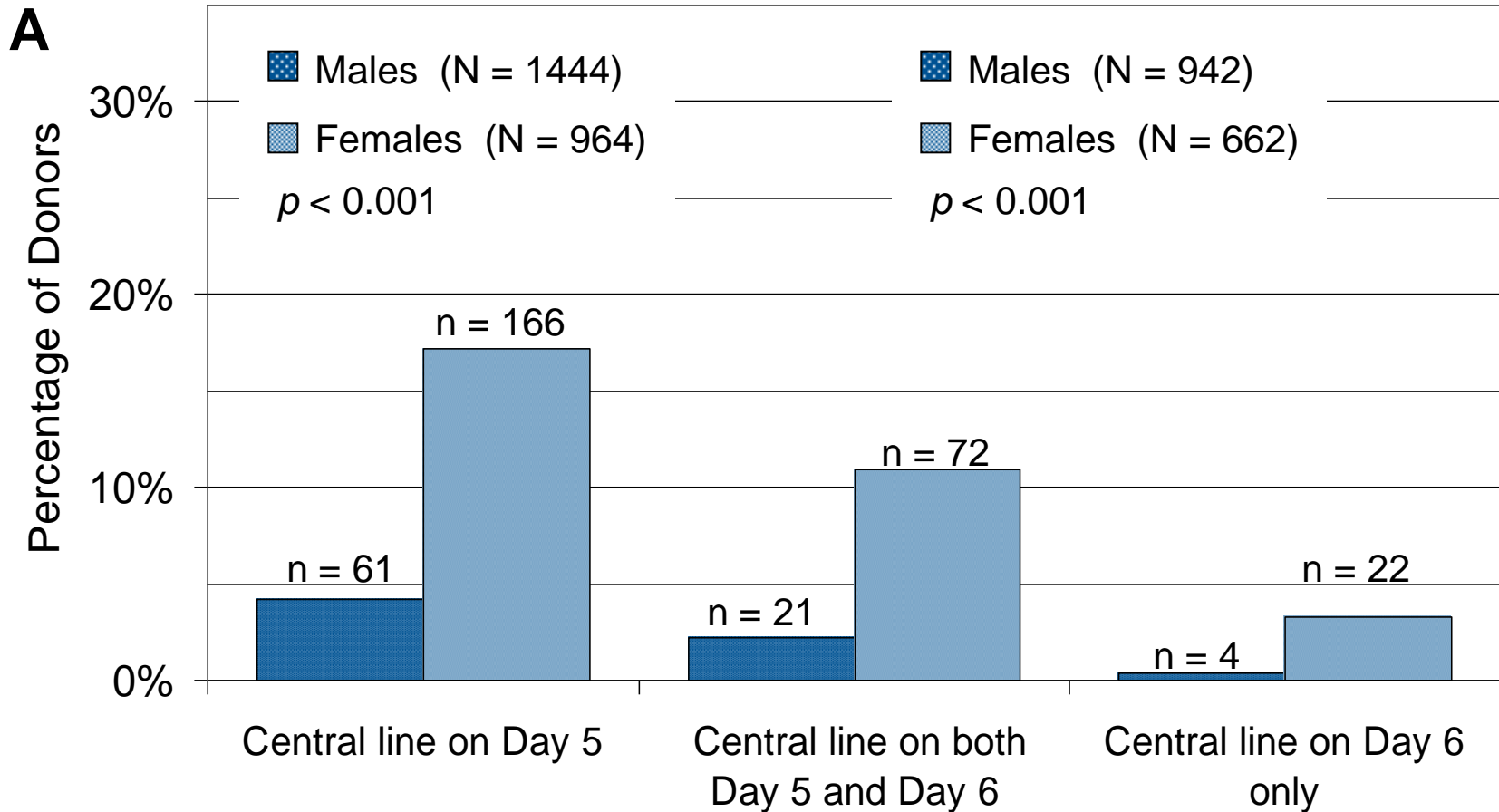
Symptom Score During Mobilization



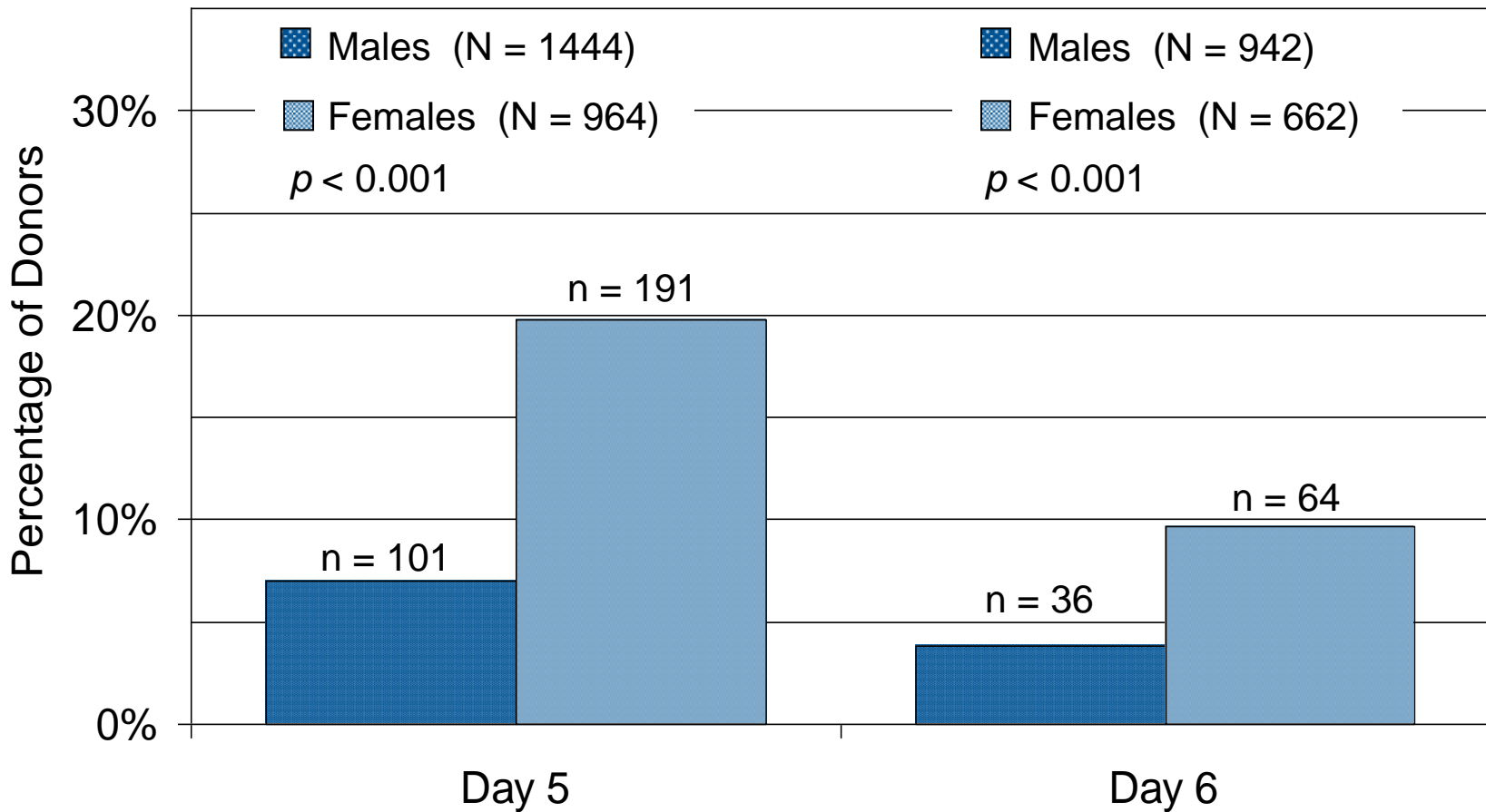
Maximum Grade of Any Symptom



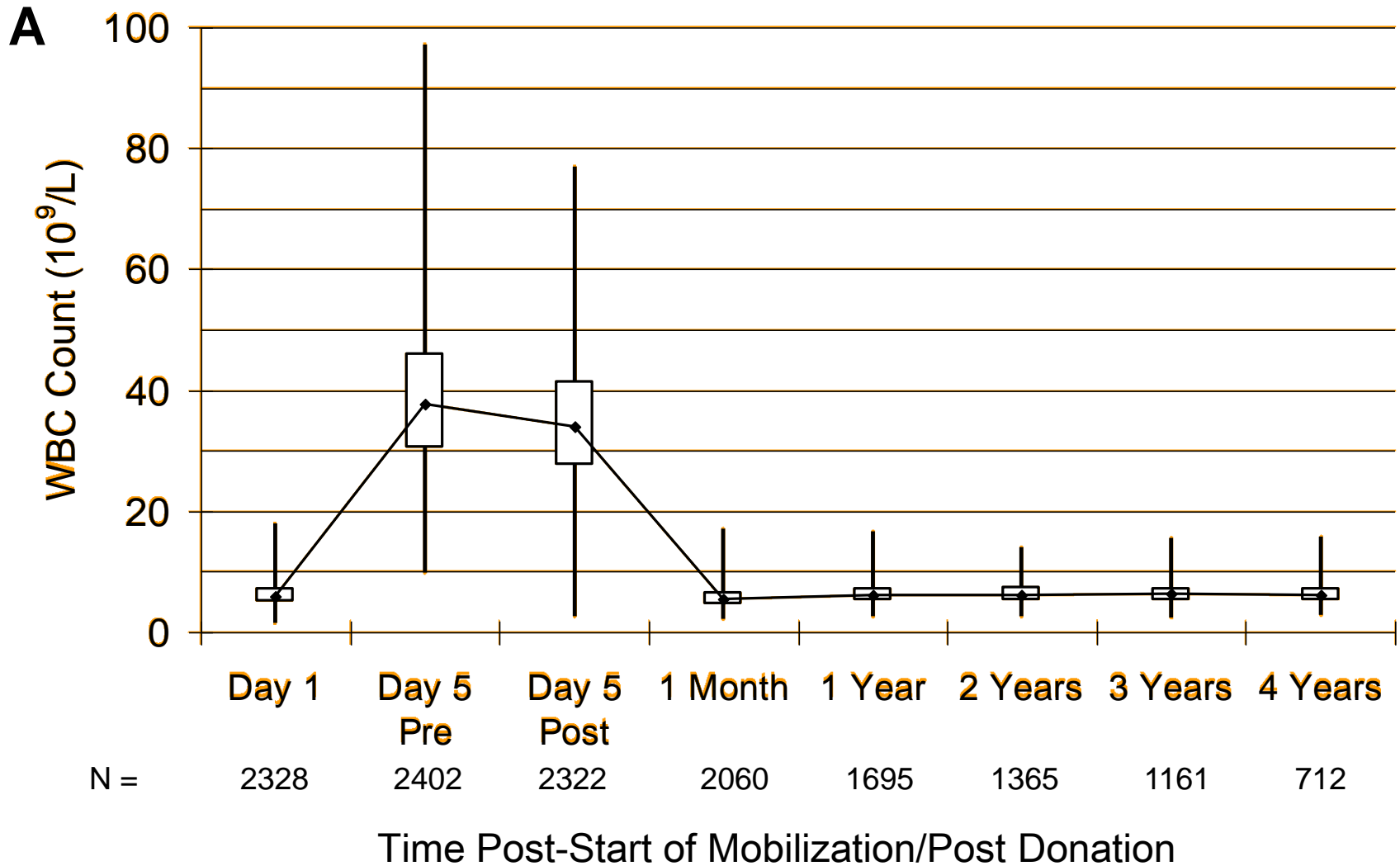
Frequency of Central Lines



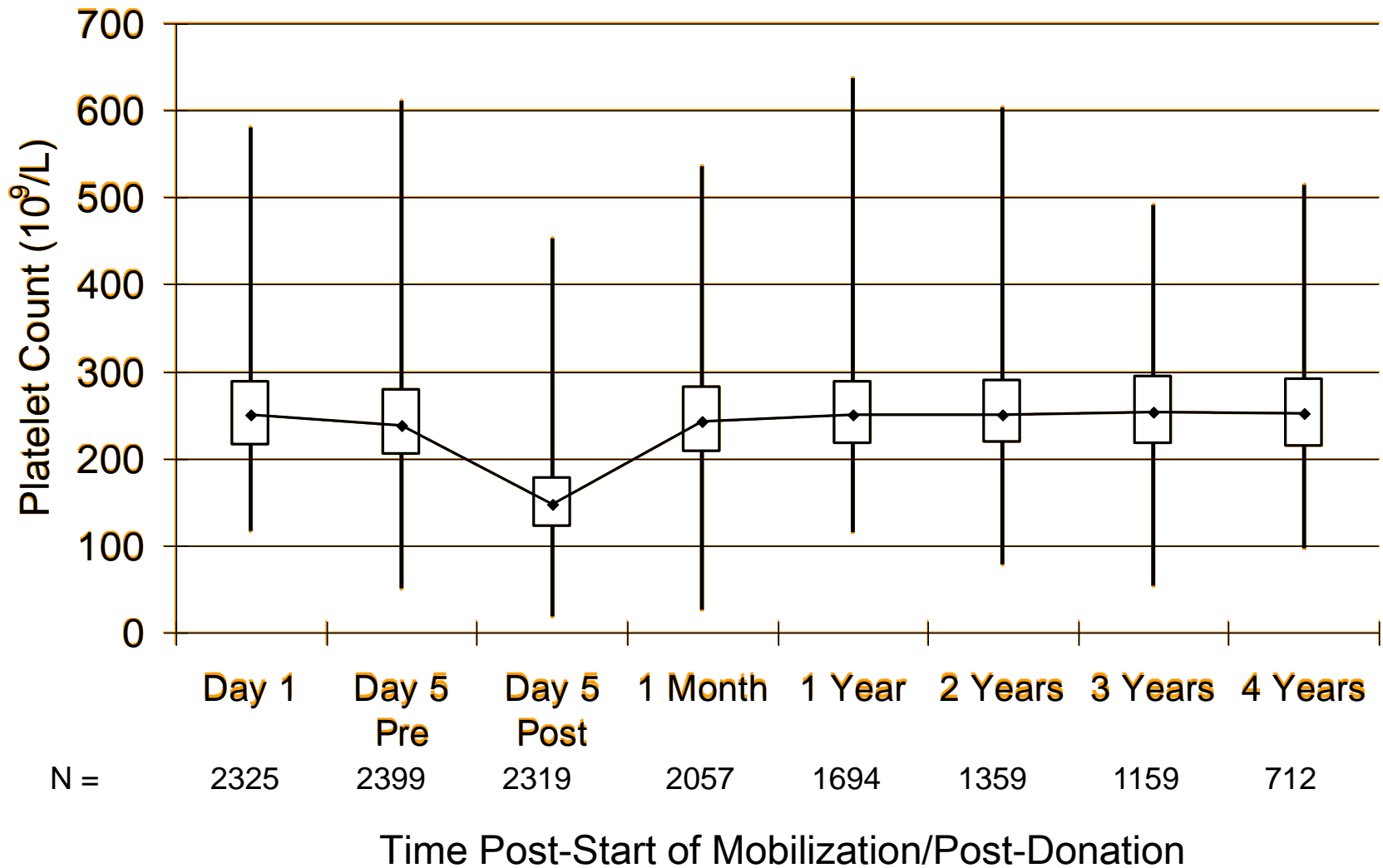
Frequency of Apheresis-Related AEs



Changes in WBC (range and quartiles)



Change in Platelets (range and quartiles)



SAEs in PBSC Donors: 1999-2010

- 50 Total SAEs in 18,029 donors (0.3%)
 - 23 Serious by virtue of hospitalization
 - 8 Central line complications
 - 4 Low platelet counts
 - 1 ITP
 - 4 Cancer
 - 2 Pneumonia
 - 1 Cardiac (elevated troponin)
 - 1 Asthma
 - 1 DVT
 - 1 Hematuria
 - 1 Subdural hematoma
 - 1 ICH
 - 1 Ventricular Tachycardia (nonsustained)
 - 1 Vasculitis

Serious, But Not Unexpected AEs in PBSC Donors: 1999-2010

- 4 cases in 18,029 donors (0.02%)
 - 3 Splenic bleeding
 - 1 AML
- Total Serious Adverse events =

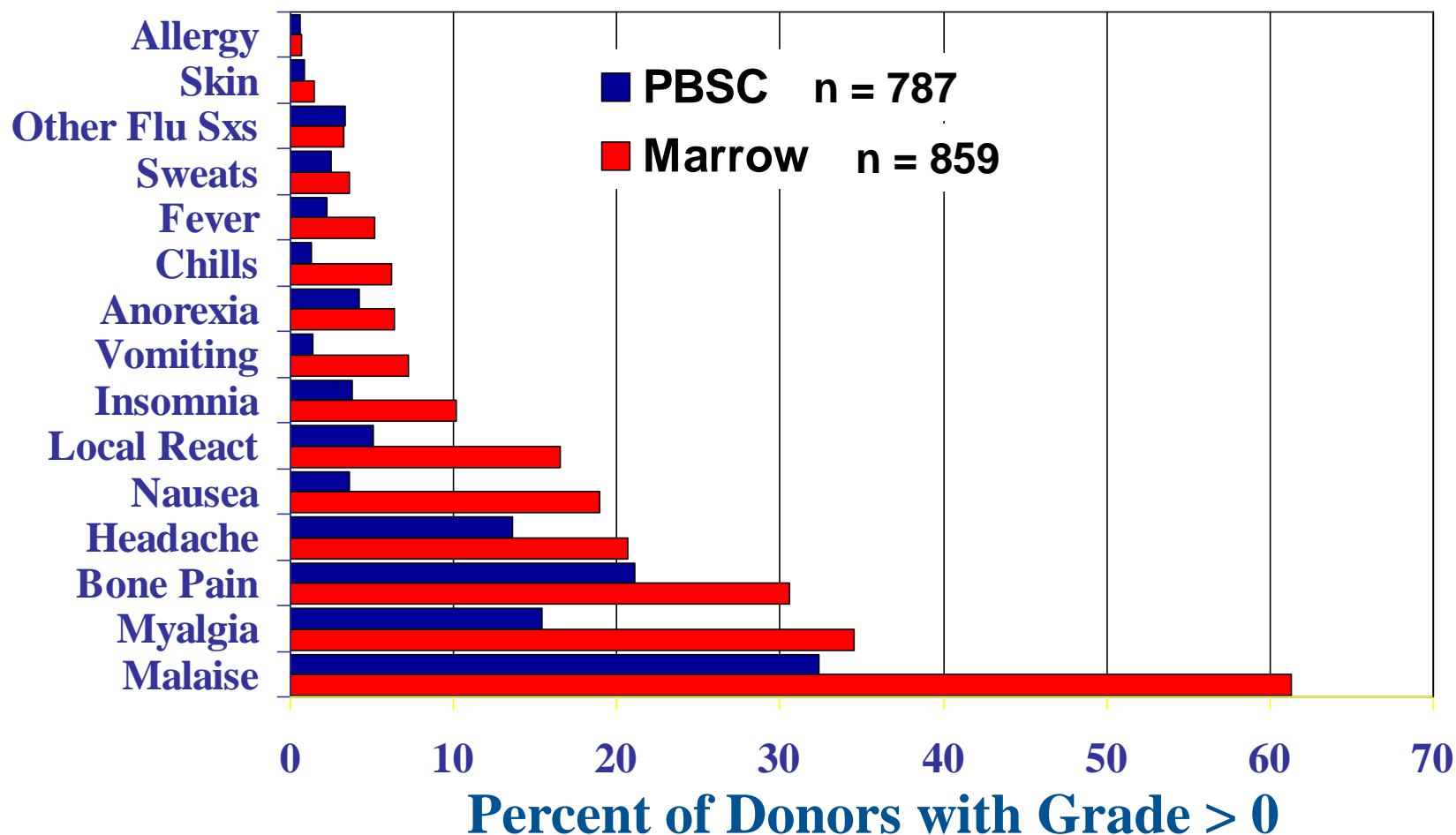
54/18,029 (0.3%)

Long Term Follow-up of PBSC Donors

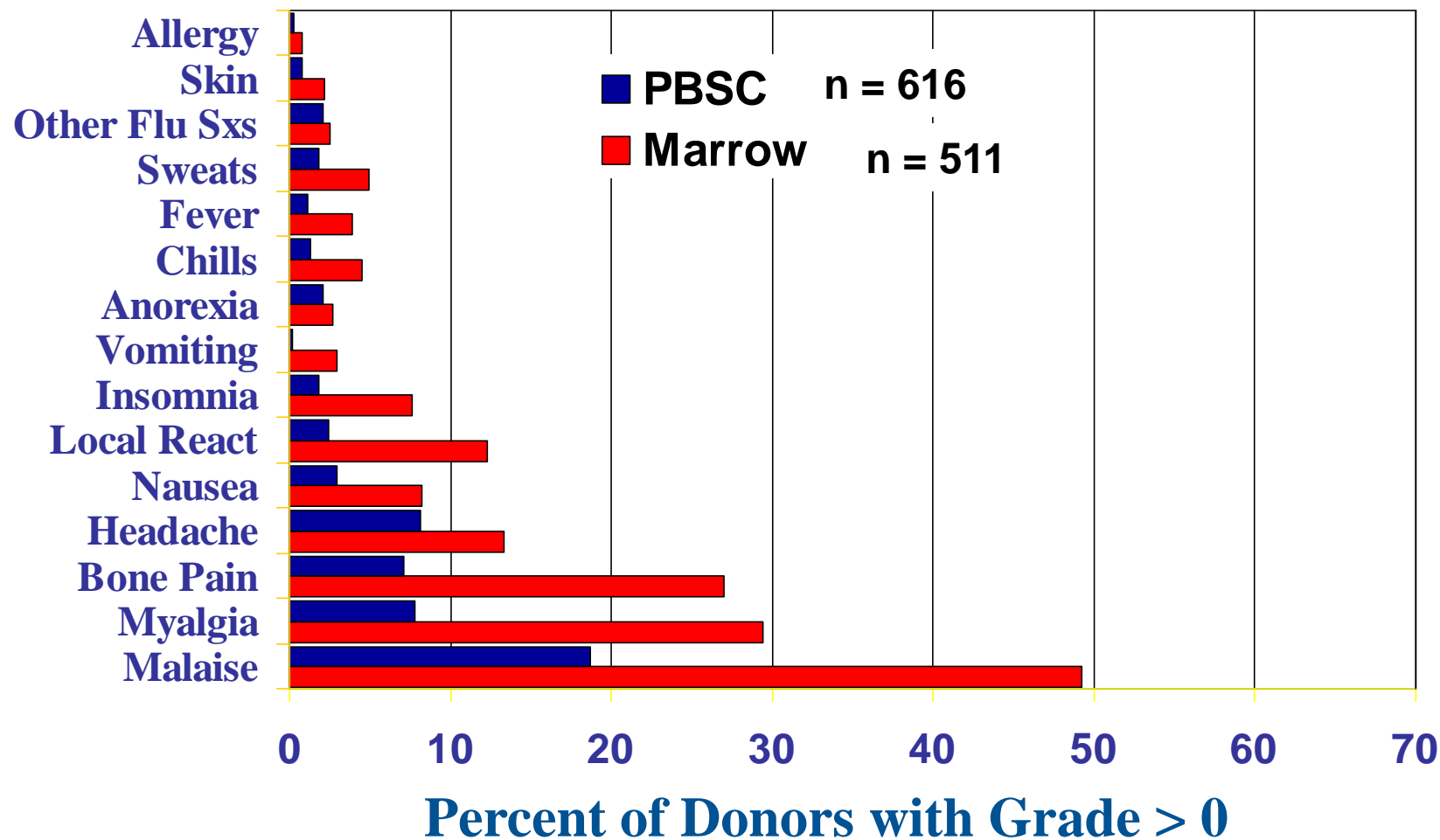
80 cases of cancer identified:

- 26 Skin (19 non-melanoma, 7 melanoma)
- 12 Breast
- 8 Prostate
- 7 Colorectal
- 3 Lung, testicular
- 2 NHL, myeloma, cervical, bladder, thyroid, uterine, pancreatic
- 1 CML, AML, CLL, esophageal, laryngeal, renal cell, vulvar

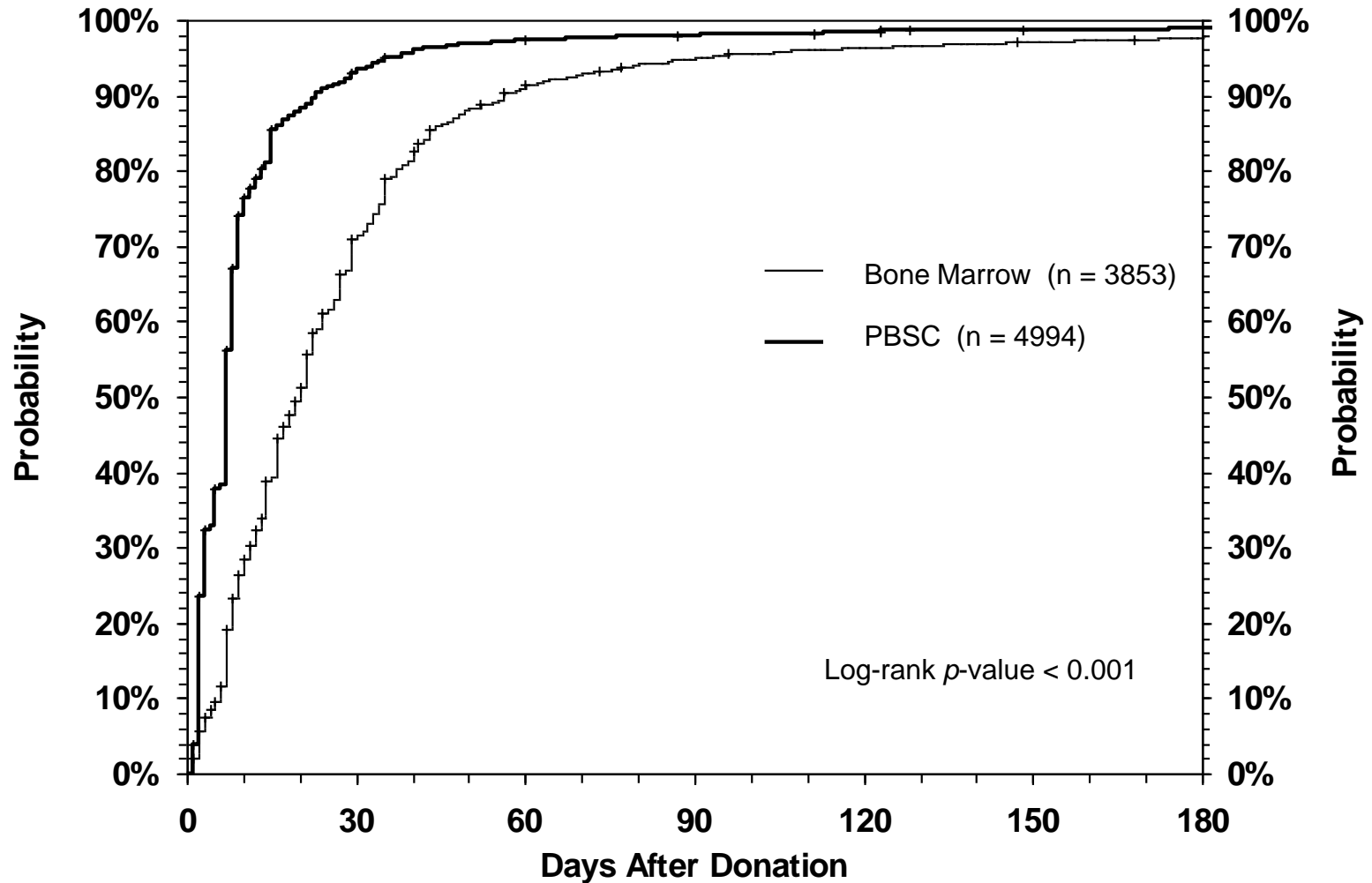
Donor Symptoms Following Donation: Two Days After



Donor Symptoms Following Donation: One Week After



Recovery from First Donation (November 2001 – March 2006)



What About Related Donors?

RDSafe Study

- Participants at the Donor Safety Conference in Arlington, VA, 2005, cited the lack of safety data from related HCT donors as a serious deficit
- RDSafe Study (Related Donor Safety)
 - CIBMTR Study funded by NHLBI
 - Michael Pulsipher, PI

RDSafe Adverse Event Study

Primary Objectives:

- Compare incidence of serious and severe AEs for donors age 18-40 and 41-60 vs URD
- Describe serious and severe AEs for donors age <18 and >60

2,300 related HCT donors

- 750 less than 18 y/o
- 1,300 18 – 60 y/o
- 250 greater than 60 y/o

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

Long Term Donor Follow-up Study



Incidence of Hematologic and Non-Hematologic Malignancies, Thrombotic Events, and Autoimmune Disorders in Unrelated Normal Donors Undergoing Bone Marrow Harvest Versus Peripheral Blood Stem Cell Mobilization with Recombinant Human Granulocyte Colony-Stimulating Factor (rhuG-CSF)

Long Term Donor Follow-up Study

- Hypothesis:

The incidence of malignant, thrombotic and autoimmune disorders after unrelated hematopoietic stem cell donation are similar between bone marrow and filgrastim mobilized PBSC donors.

- Primary Objective:

To describe the long-term incidence of malignant myeloid hematologic disorders in donors who received and in those who did not receive filgrastim.

Long Term Donor Follow-up Study

- Secondary objectives to describe the long-term incidence in donors receiving or not receiving filgrastim:
 - Malignant hematologic disorders
 - Non-hematologic malignant disorders
 - Thrombotic events
 - Autoimmune disorders

Long Term Donor Follow-up Study

- Retrospective and Prospective cohorts
 - 1999-2015
- Expected Enrollment:
 - 10,956 unstimulated marrow donors
 - 21,172 filgrastim mobilized PBSC donors
- Enrollment began Oct 2010

Summary

For PBSC and bone marrow unrelated donors –

- Pain and fatigue are the most common symptoms
- Symptoms are generally mild to moderate
- Serious AEs are seen more frequently with marrow donors
- Recovery from PBSC donation is more rapid than from bone marrow donation
- In long-term follow-up, blood counts (WBC, Hgb and platelets) return to baseline levels

Summary

For PBSC and bone marrow unrelated donors -

- Women who donate PBSC are more likely to require central venous access and they experience more apheresis-related adverse events
- Long-term follow-up of PBSC donors has failed to disclose any evidence of hematopoietic injury
- Studies are underway to evaluate the experiences of related donors in comparison to unrelated donors and to assess key rare events in filgrastim mobilized PBSC versus marrow donors



Questions?

