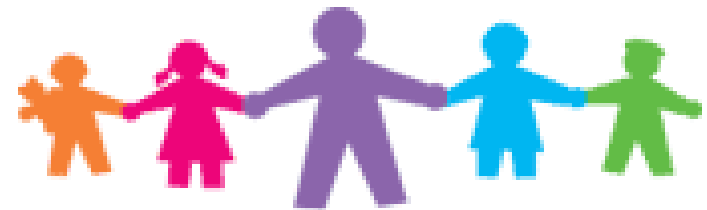




Umbilical Cord Blood Transplantation for Hemoglobinopathies

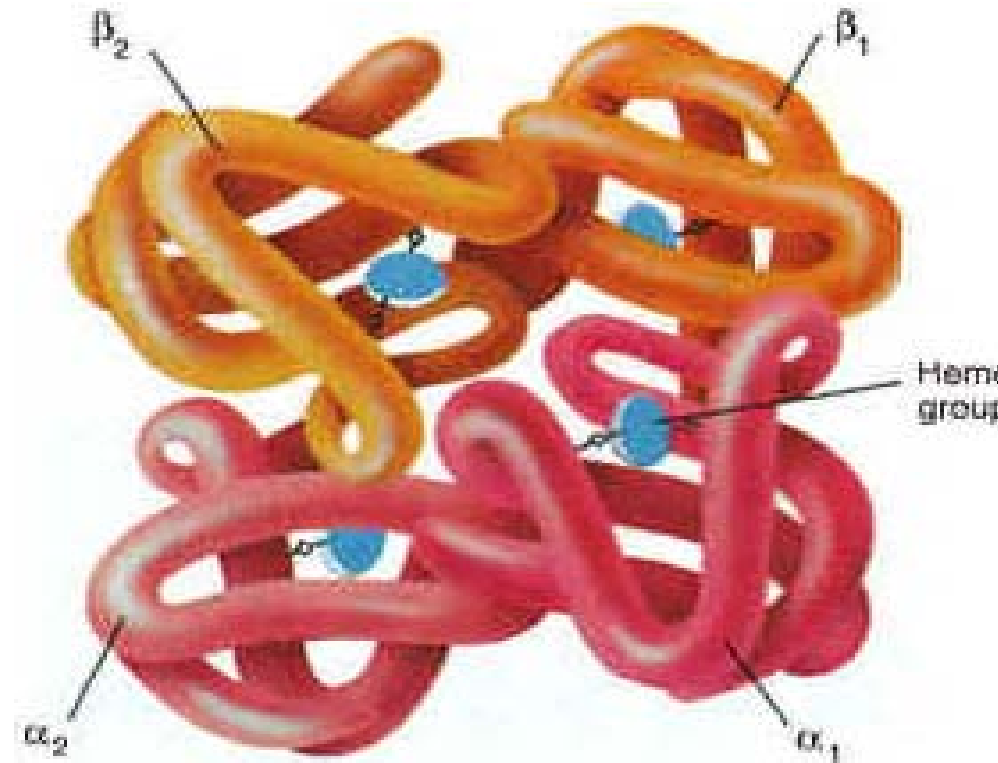
Mark Walters, MD
Director
Blood and Marrow
Transplantation Program



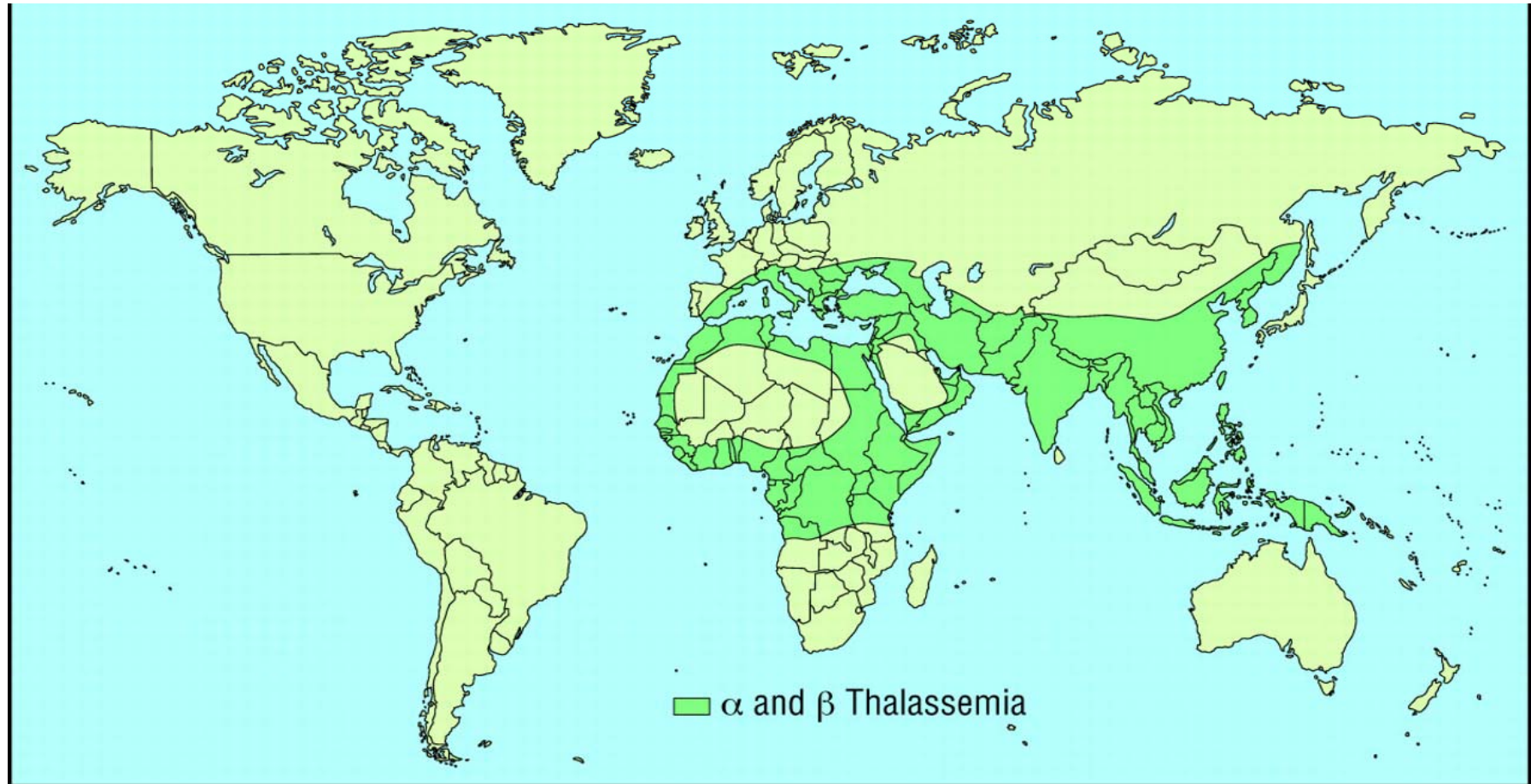
CHILDREN'S HOSPITAL
& RESEARCH CENTER OAKLAND

What are Hemoglobin disorders?

- **Alterations in the hemoglobin molecule that alter its abundance and/or function and stability**
- **Account for the most common human genetic disorders world-wide**
- **Associated with anemia, reliance on RBC transfusions, chronic illness**



Regions Where Thalassemia Is Endemic¹



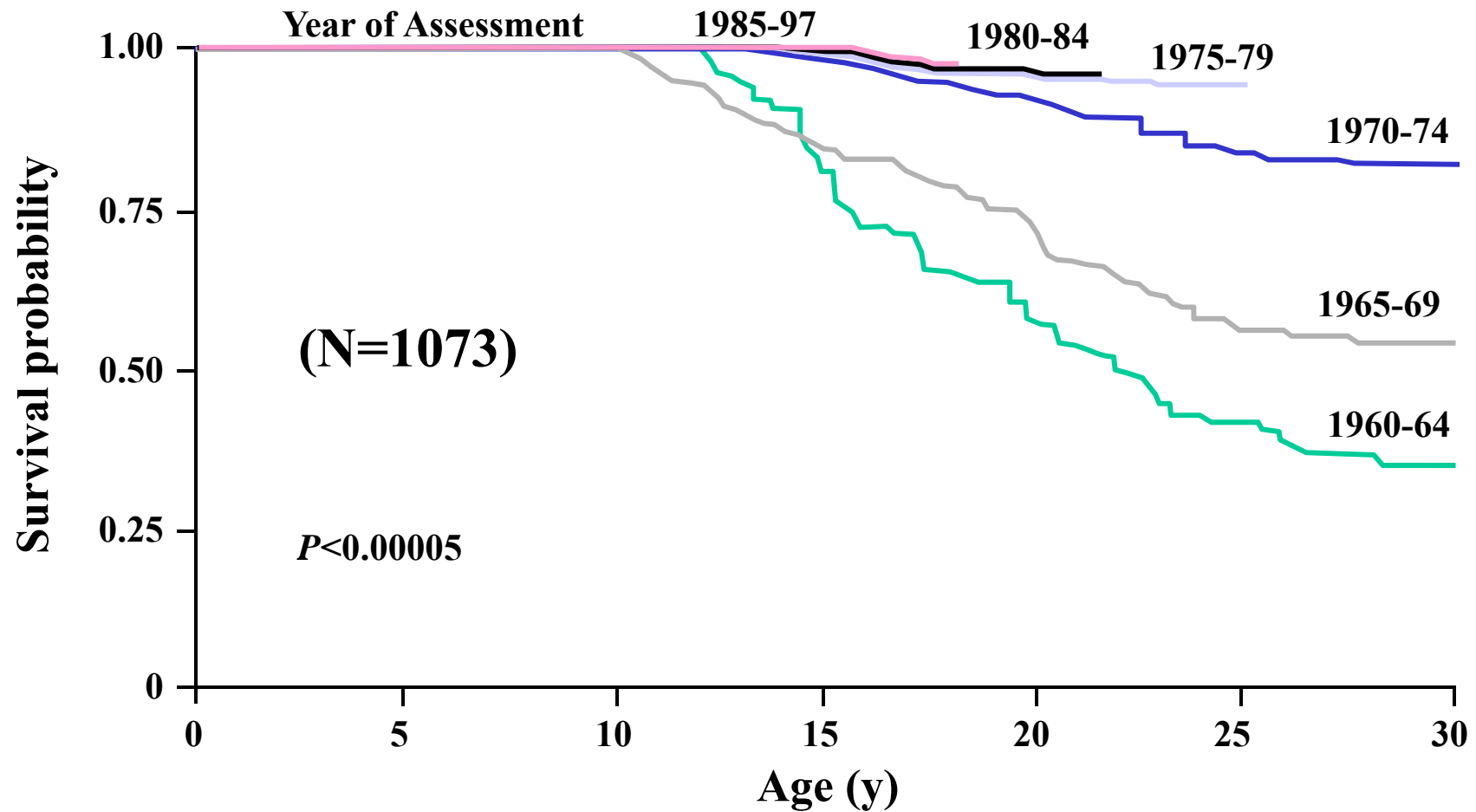
**75% of immigrants to the United States are from areas
where thalassemias are prevalent²**

1. Weatherall. *BMJ*. 1997;314:1675.

2. Cohen et al. *Hematology (Am Soc Hematol Educ Program)*. 2004:14.

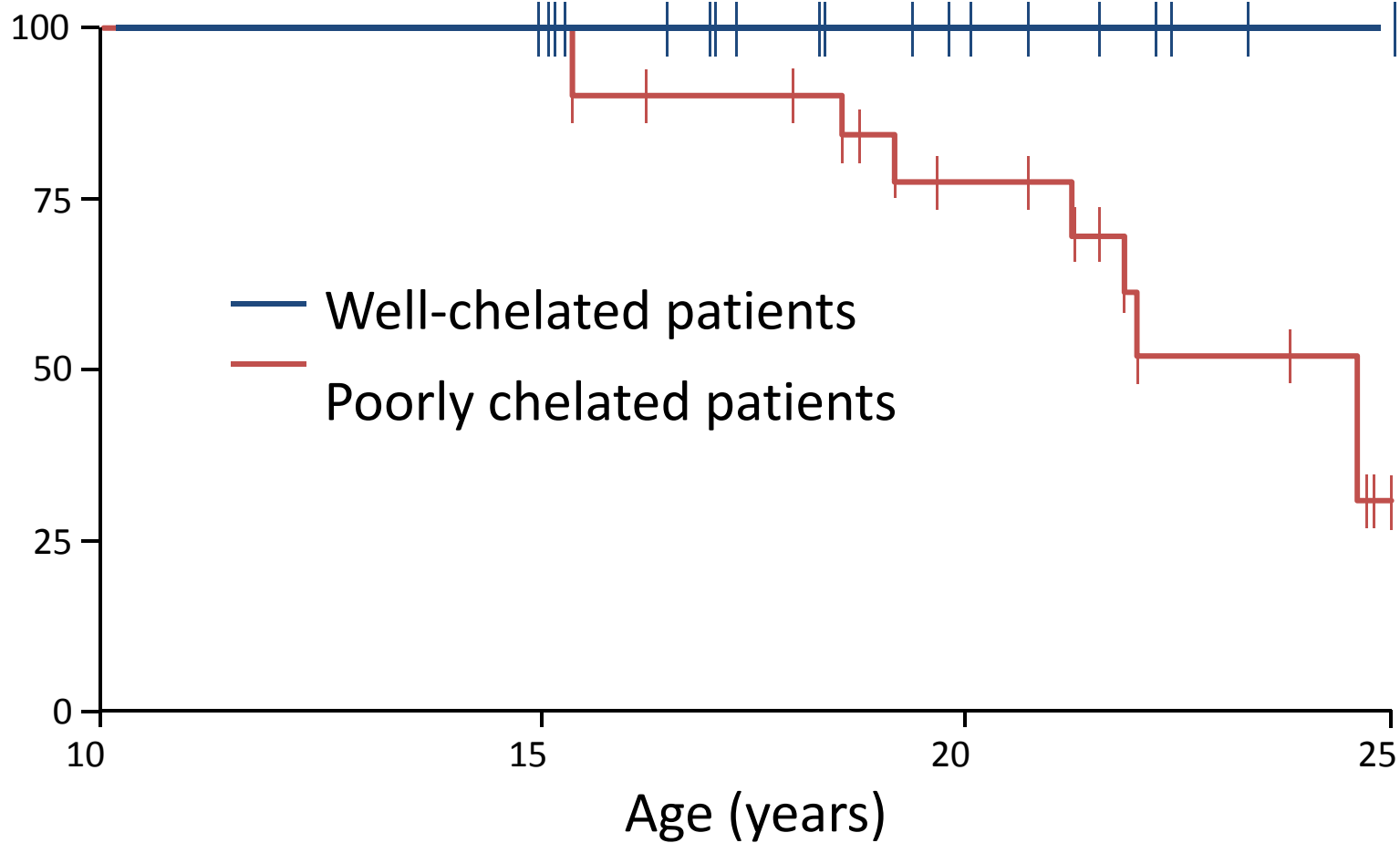
Survival by Availability of Chelation Therapy

Transfusion-Dependent Patients With Thalassemia Major



Benefit of Iron Chelation Therapy

Probability of Survival Among 38 Thalassemia Major Patients



Clinical Pathology of Sickle Cell Disease

1. **Anemia**
2. **Vaso-occlusion**
3. **Chronic organ damage**

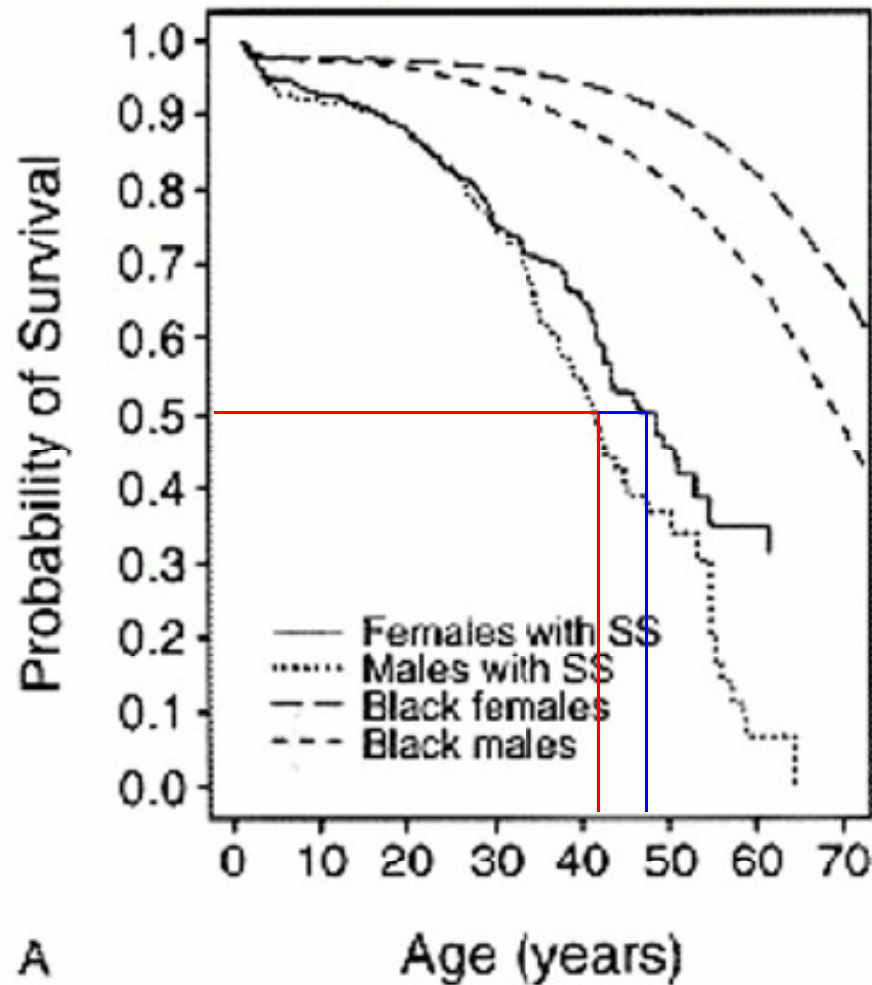


Wide variability in clinical expression

Claster and Vichinsky. *BMJ*. 2003;327:1151.

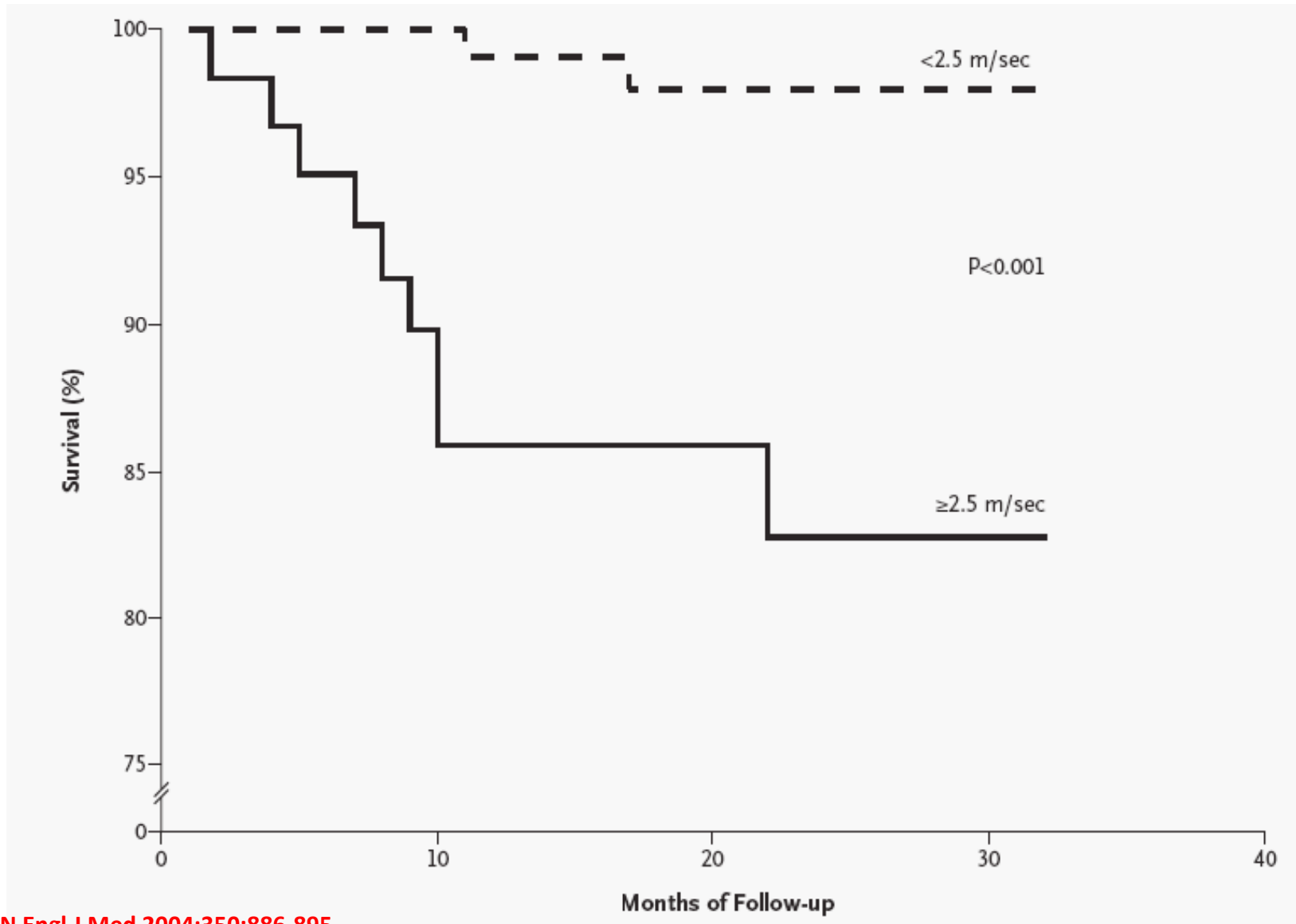
Schnog et al. *Neth J Med*. 2004;62:364.

Survival of Patients in the Cooperative Study of Sickle Cell Disease



A

Kaplan-Meier Survival Curves According to the Tricuspid Regurgitant Jet Velocity.



HCT for Hemoglobinopathies

- **First case report β -thalassemia in 1982, Seattle; first case for SCA in 1984, SJCRH**
- **subsequently >2500 transplants for thal performed worldwide with >1000 in Pesaro, Italy**
- **Most have received HLA-identical sibling marrow allografts after myeloablative preparation with Busulfan/Cyclophosphamide**
- **Similar results in children with sickle cell anemia, but many fewer treated by HCT**
- **Graft-versus host disease is leading cause of death**

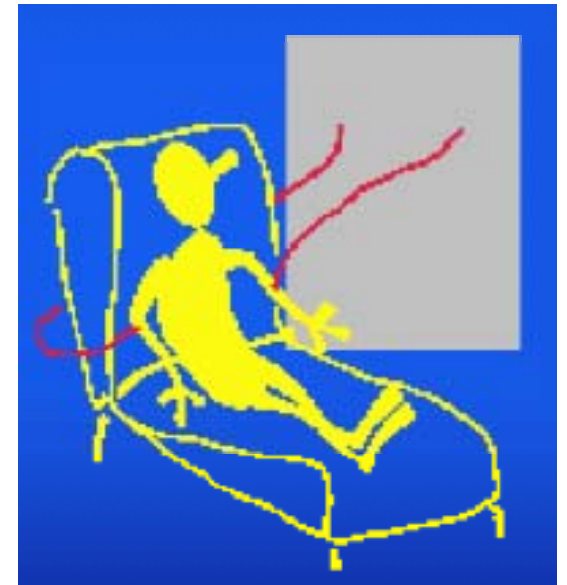
Sources of Hematopoietic Stem Cells

Marrow



Cord Blood

**Mobilized Peripheral
Blood Stem Cells**



Umbilical cord blood immunology

- **Compared to adult blood, cord blood has more abundant naïve T cells, fewer suppressor T cells, and similar NK and LAK activity**
- **Cord blood T cells:**
 - **proliferate in response to antigen**
 - **show *decreased* cytotoxicity**
- **Alloantigen priming induces state of unresponsiveness**
- **Reduced risk of Graft-versus-Host Disease**

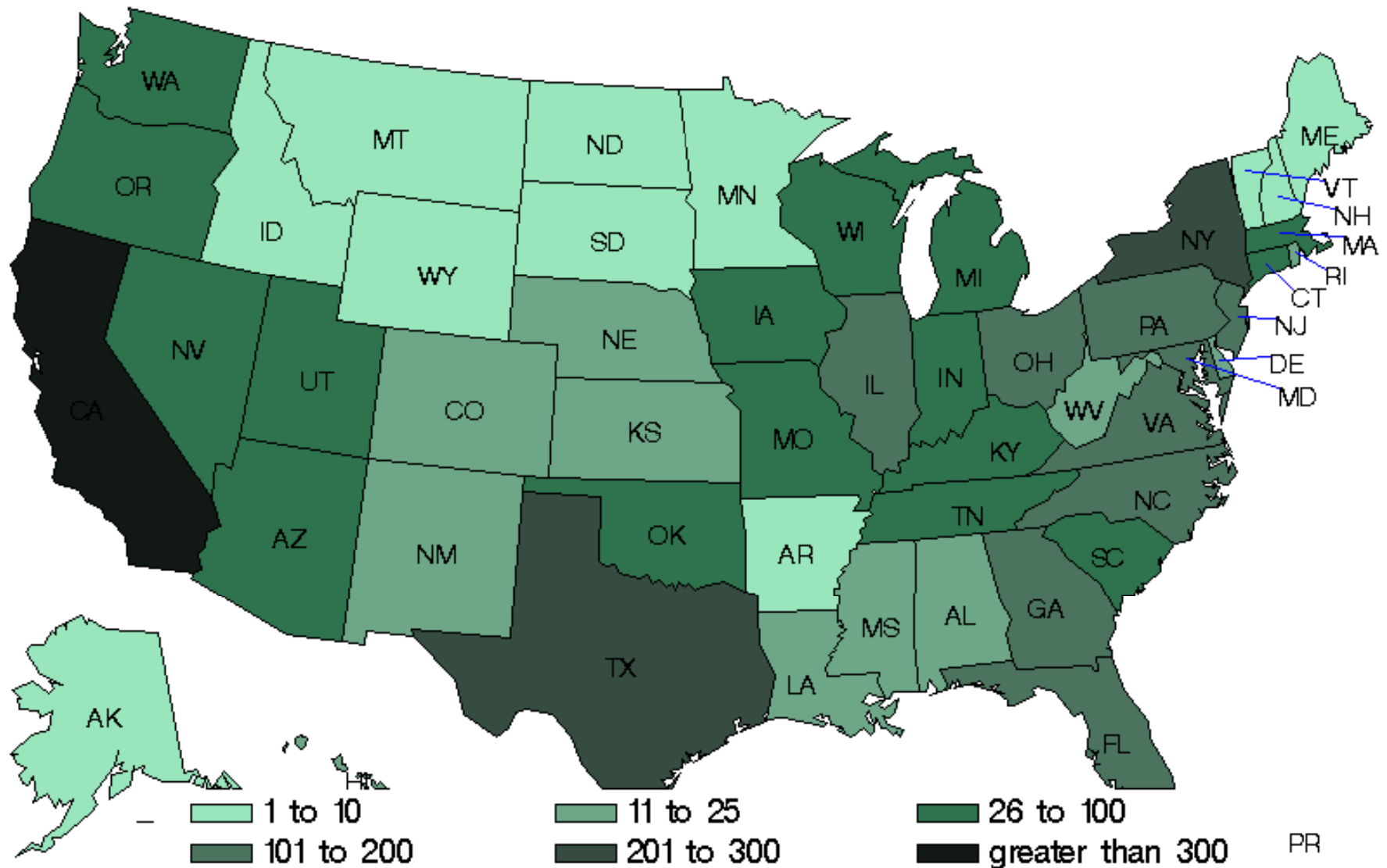
THE SIBLING CONNECTION

Sibling Donor Cord Blood Program from ViaCord – CHORI

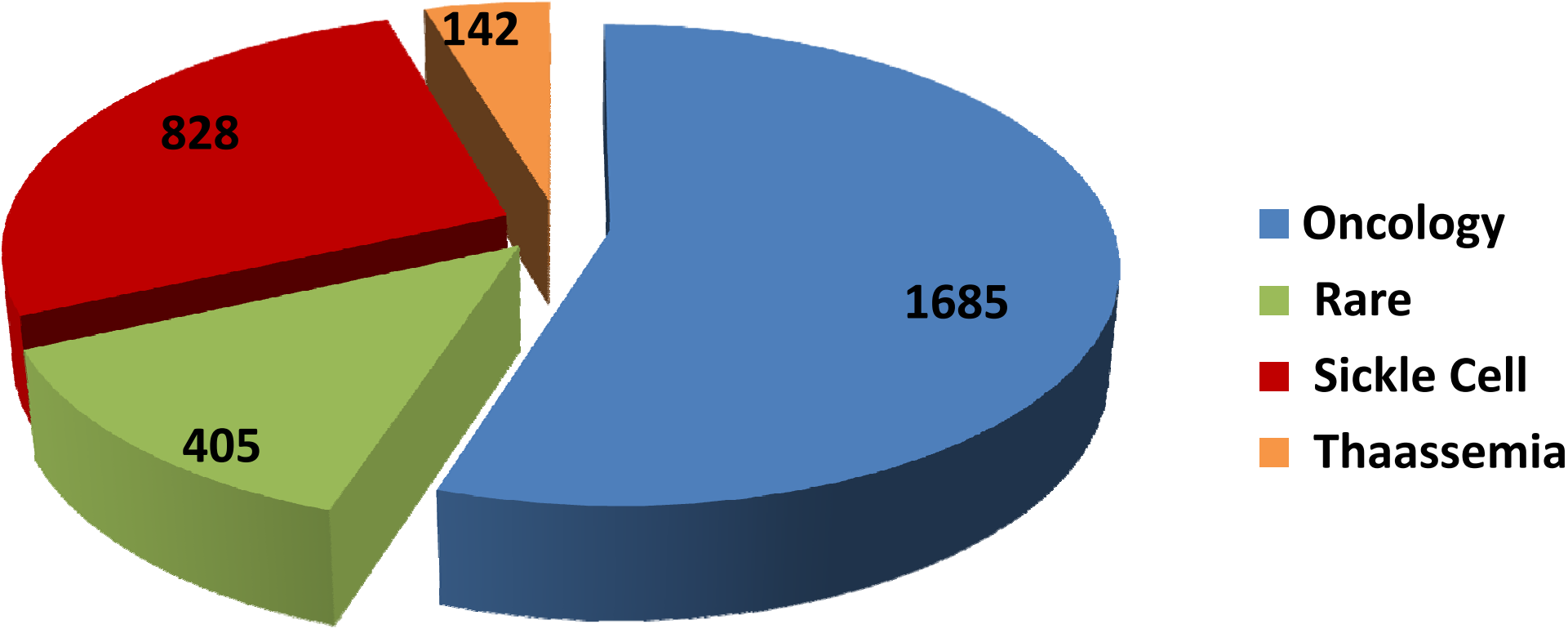
- ◆ **Families with children who have disorders treated by Hematopoietic Cell Transplantation**
- ◆ **Prospective, full sibling pregnancies**
- ◆ **Resource to collect, transport, characterize and cryopreserve sibling cord blood units in a central Umbilical Cord Blood Banking Facility**
- ◆ **Remote sites & community hospitals**

SDCB Program Collection by State

January 2010

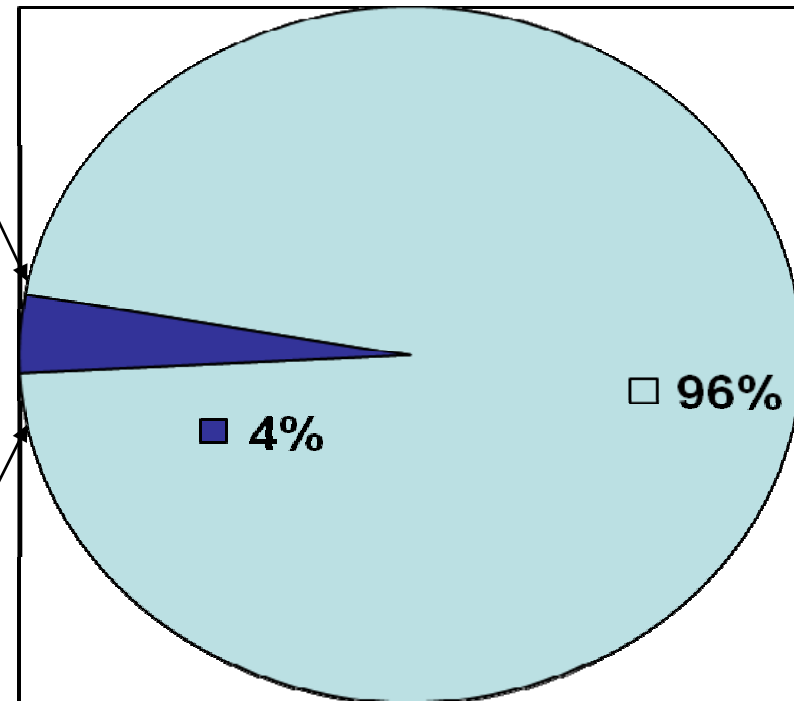


Collections by Diagnosis



Sibling Cord Blood Bank: Fraction of CBUs released for UCBT

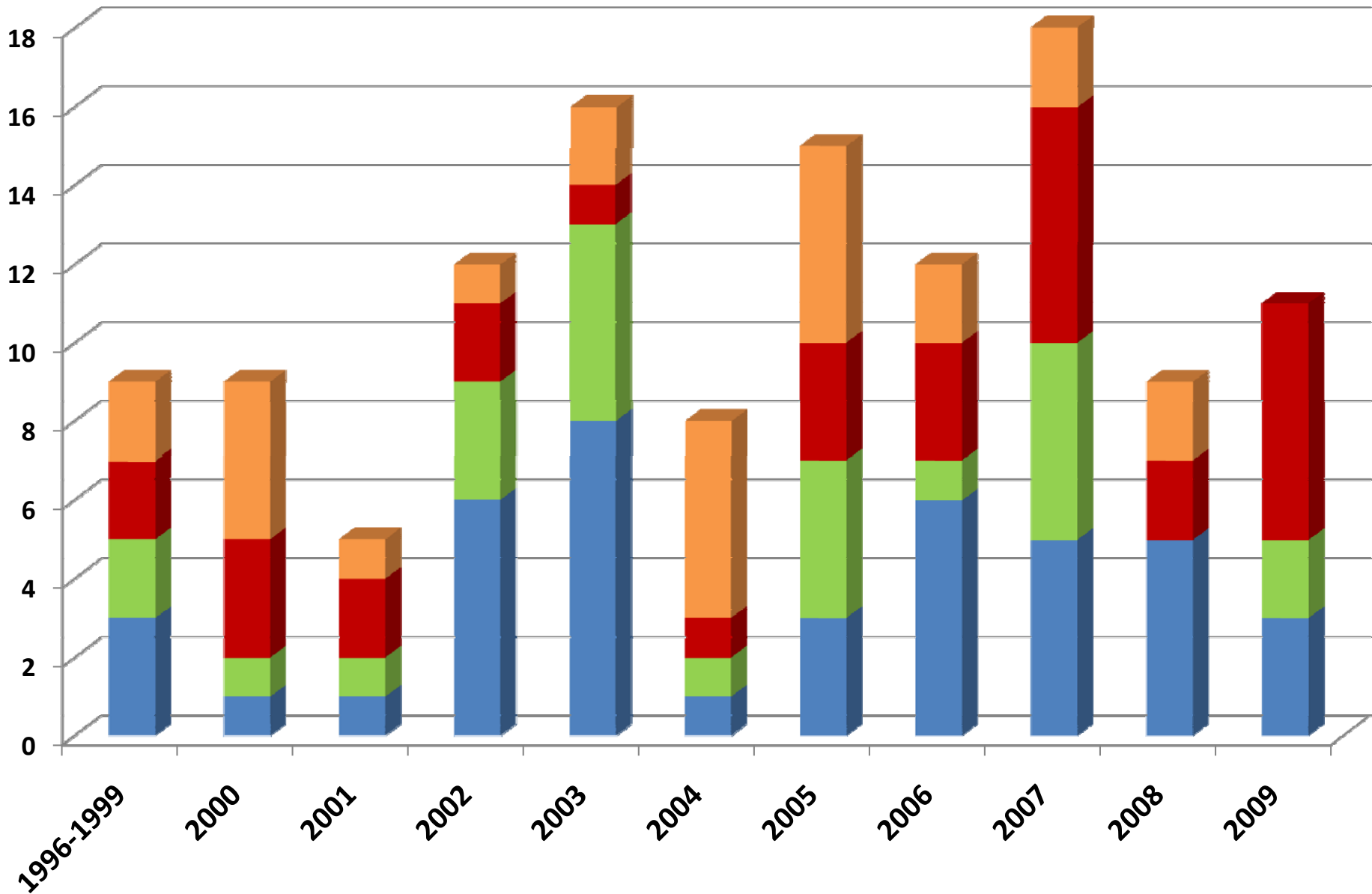
Malignant diseases	42
Sickle Cell	31
Other/Rare	25
Thalassemia	26



Jan 2010



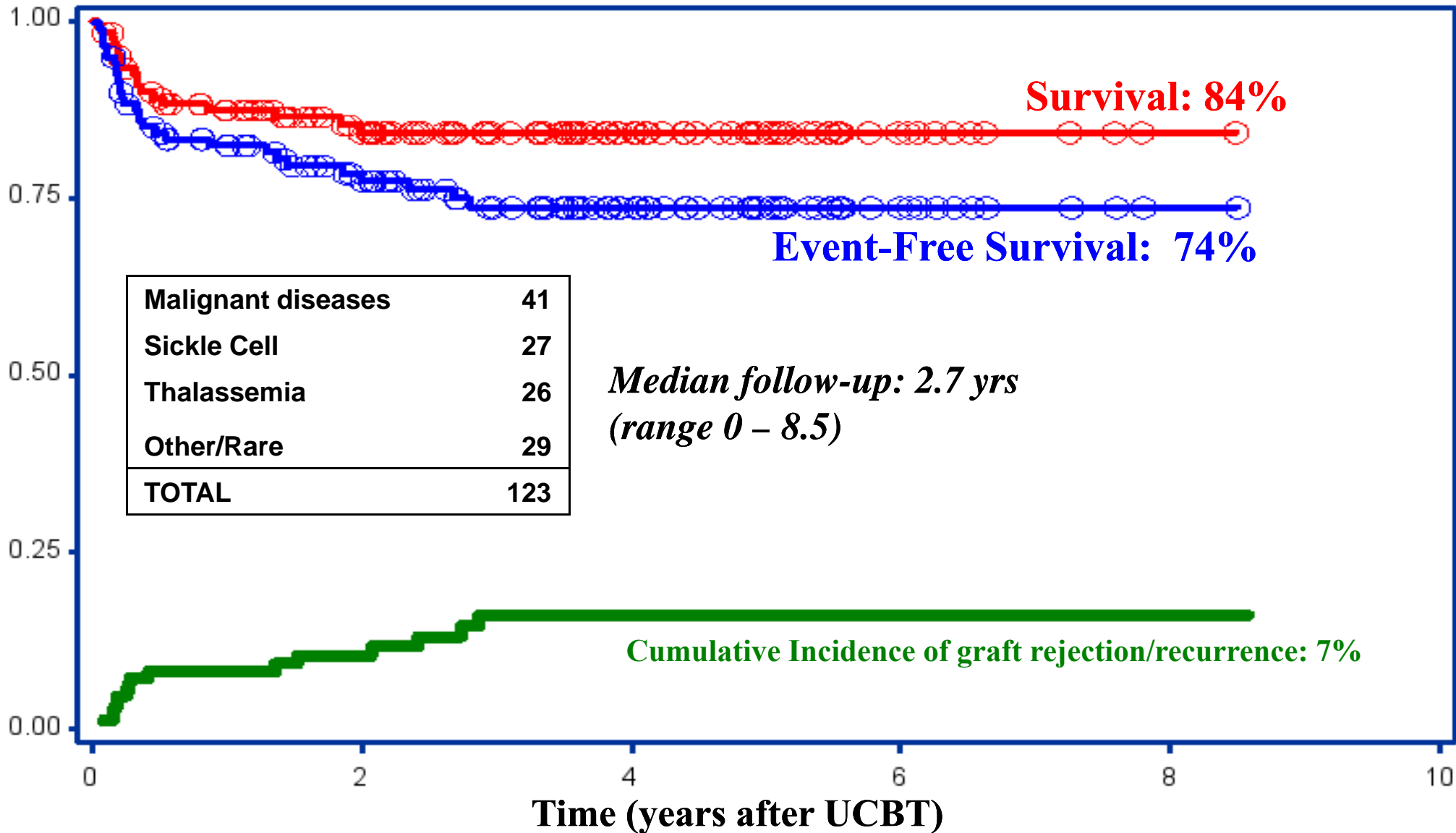
Sibling Donor Program units distributed



Outcome after SDCB Transplantation (N=123)

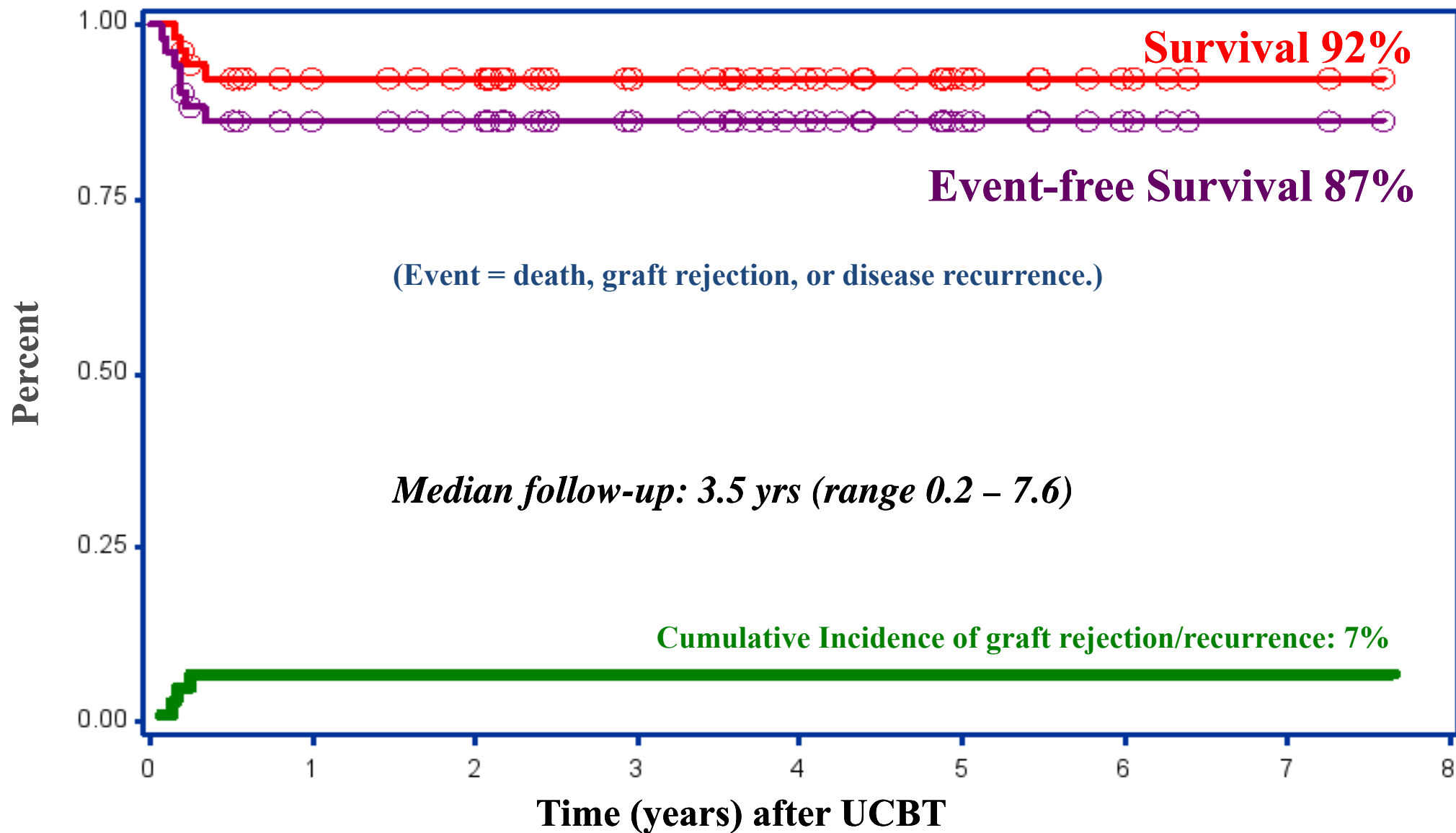
Event = death, graft rejection or disease recurrence

Feb. 2010



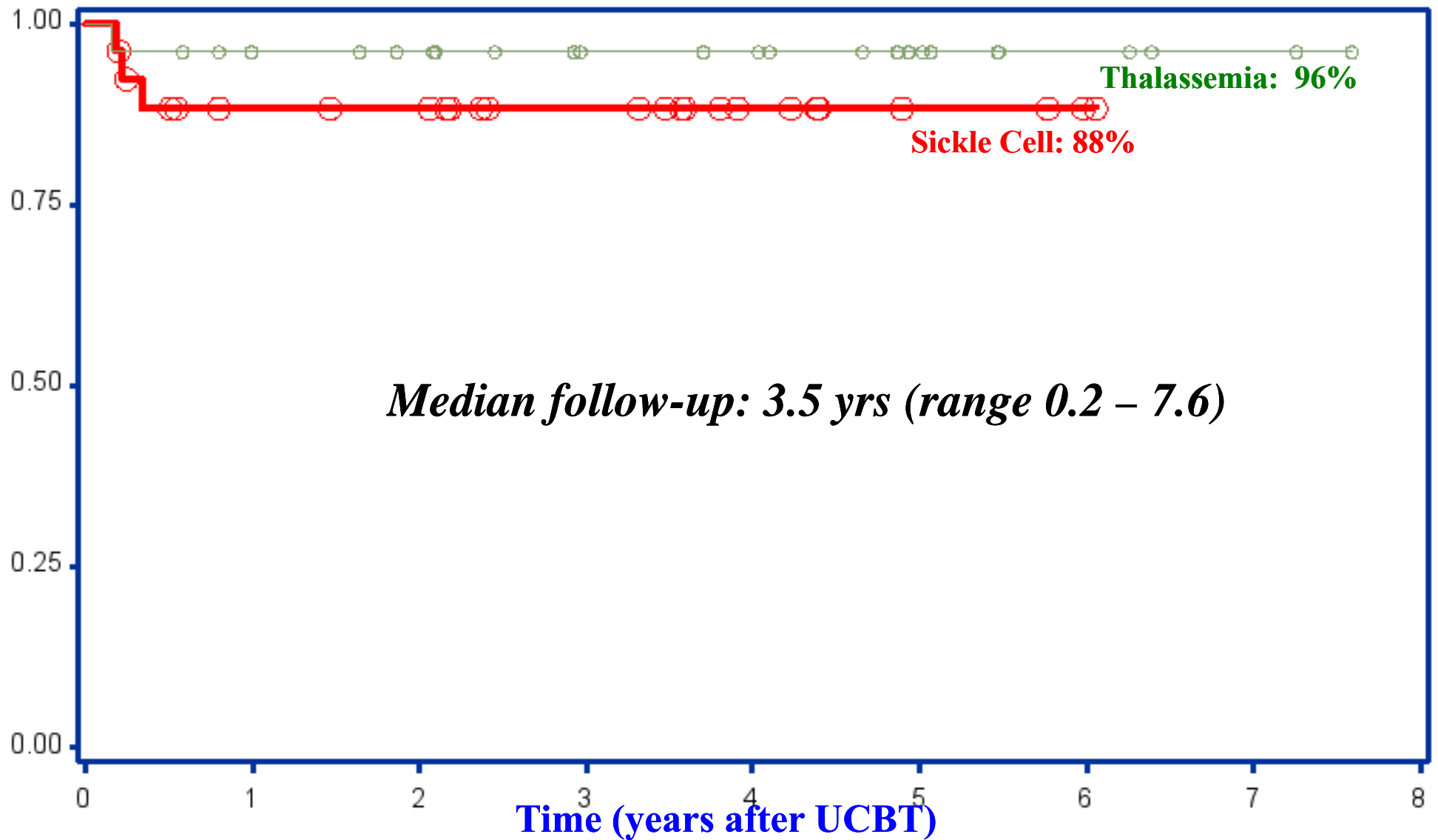
Sibling Donor Cord Blood Transplant for SCA/Thalassemia (N=53)

Feb. 2010

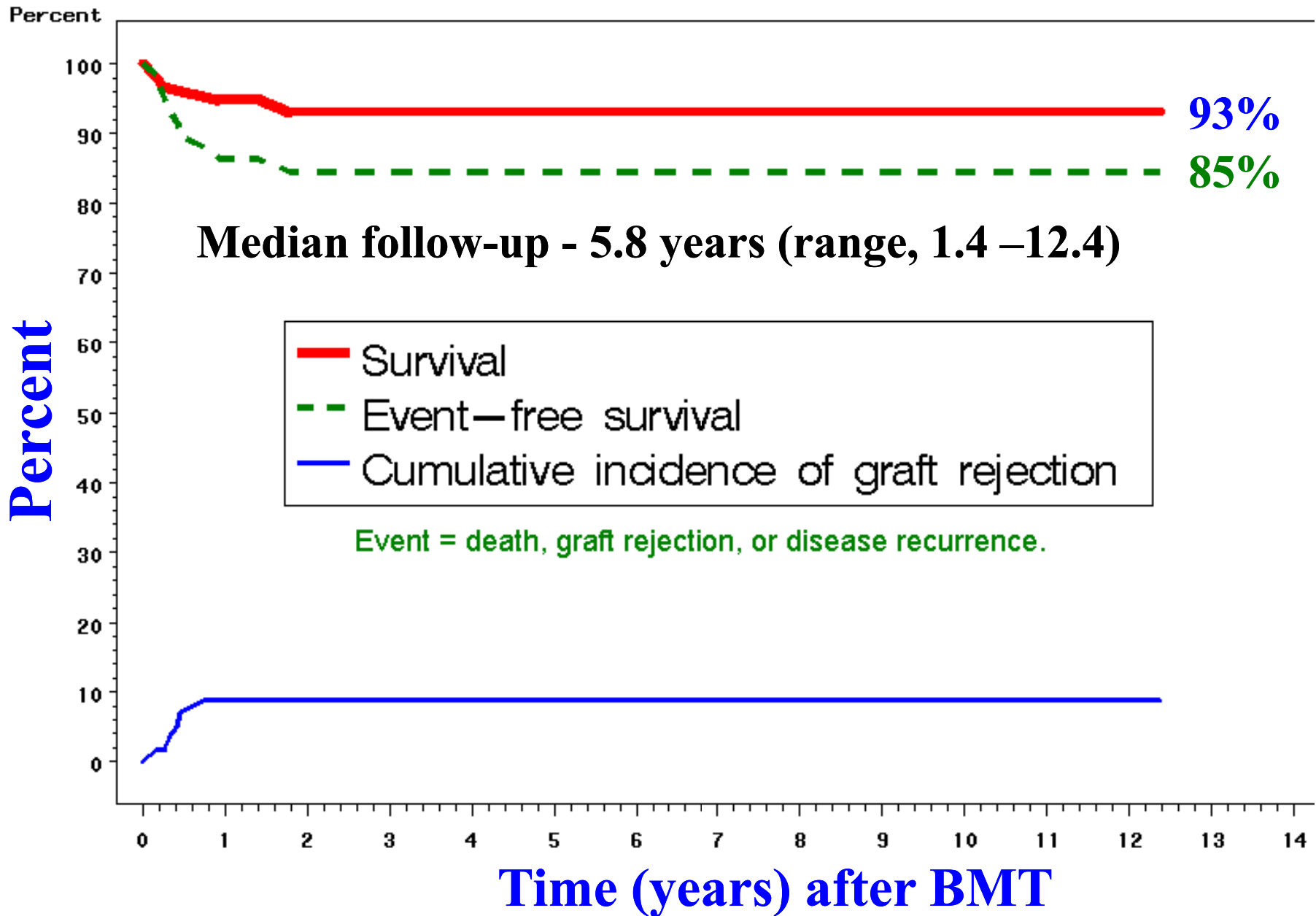


Survival after SDCB Transplantation (N=53) (Sickle Cell Disease and Thalassemia)

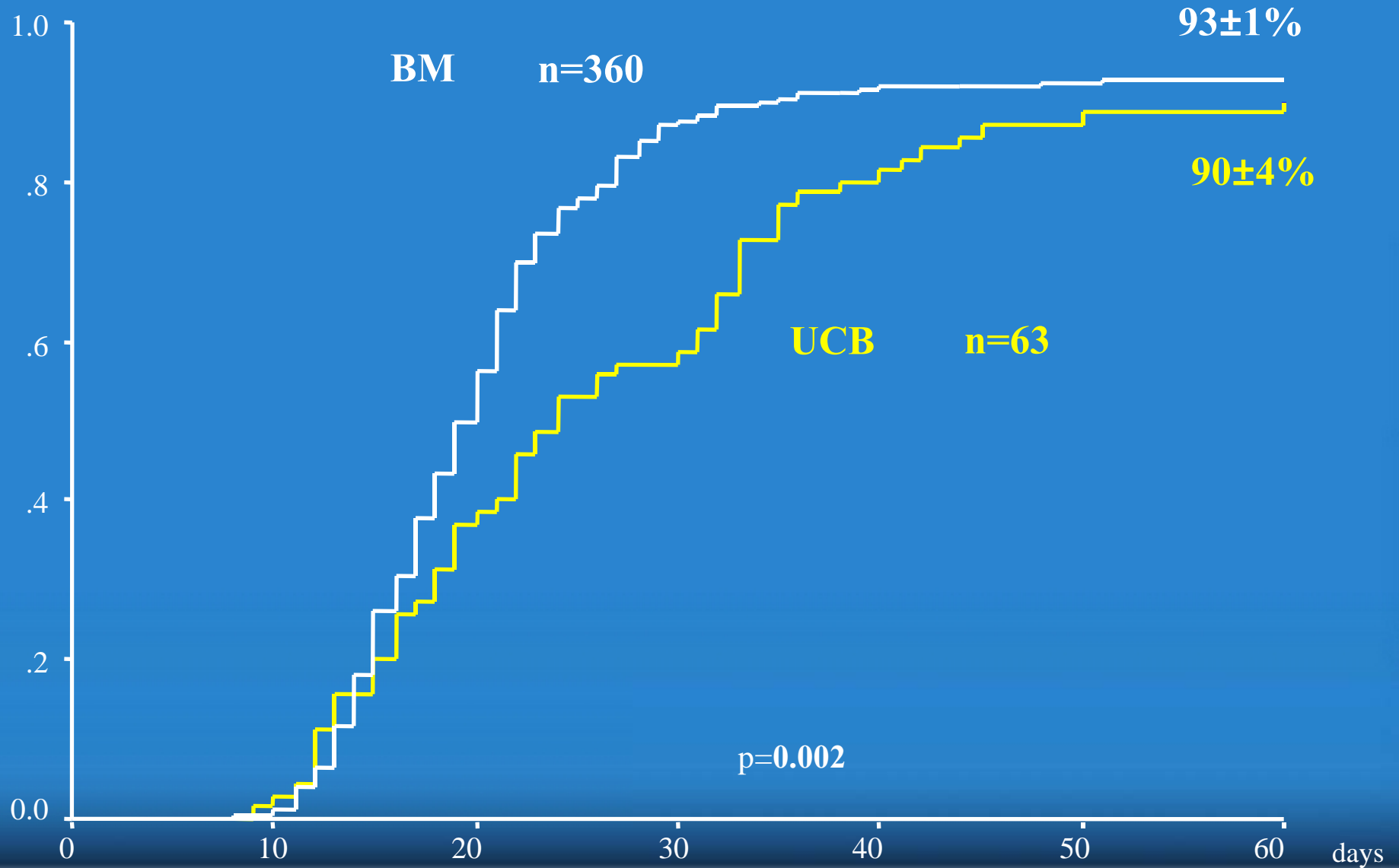
Feb 2010



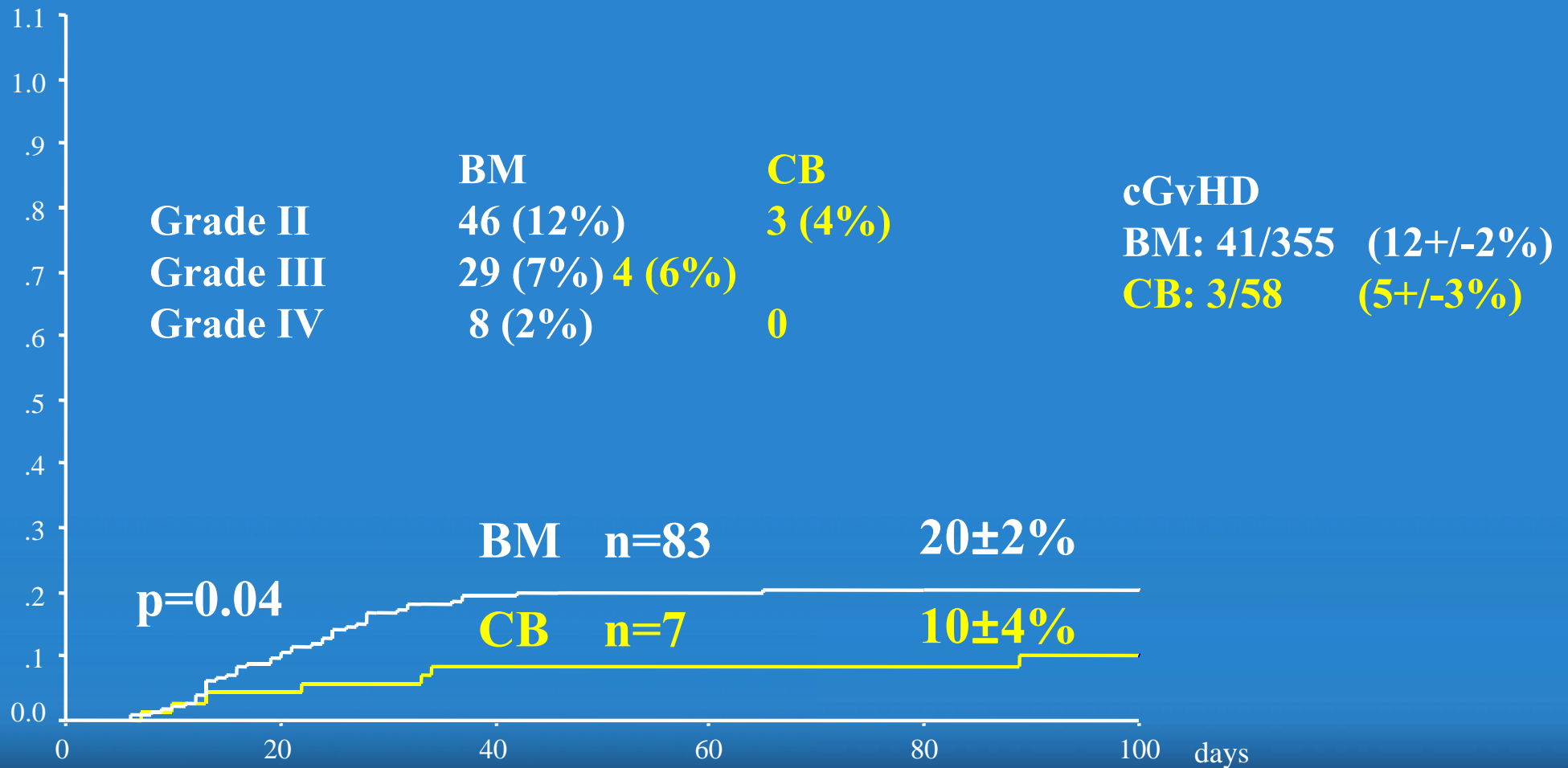
BMT for SCD (N=59)



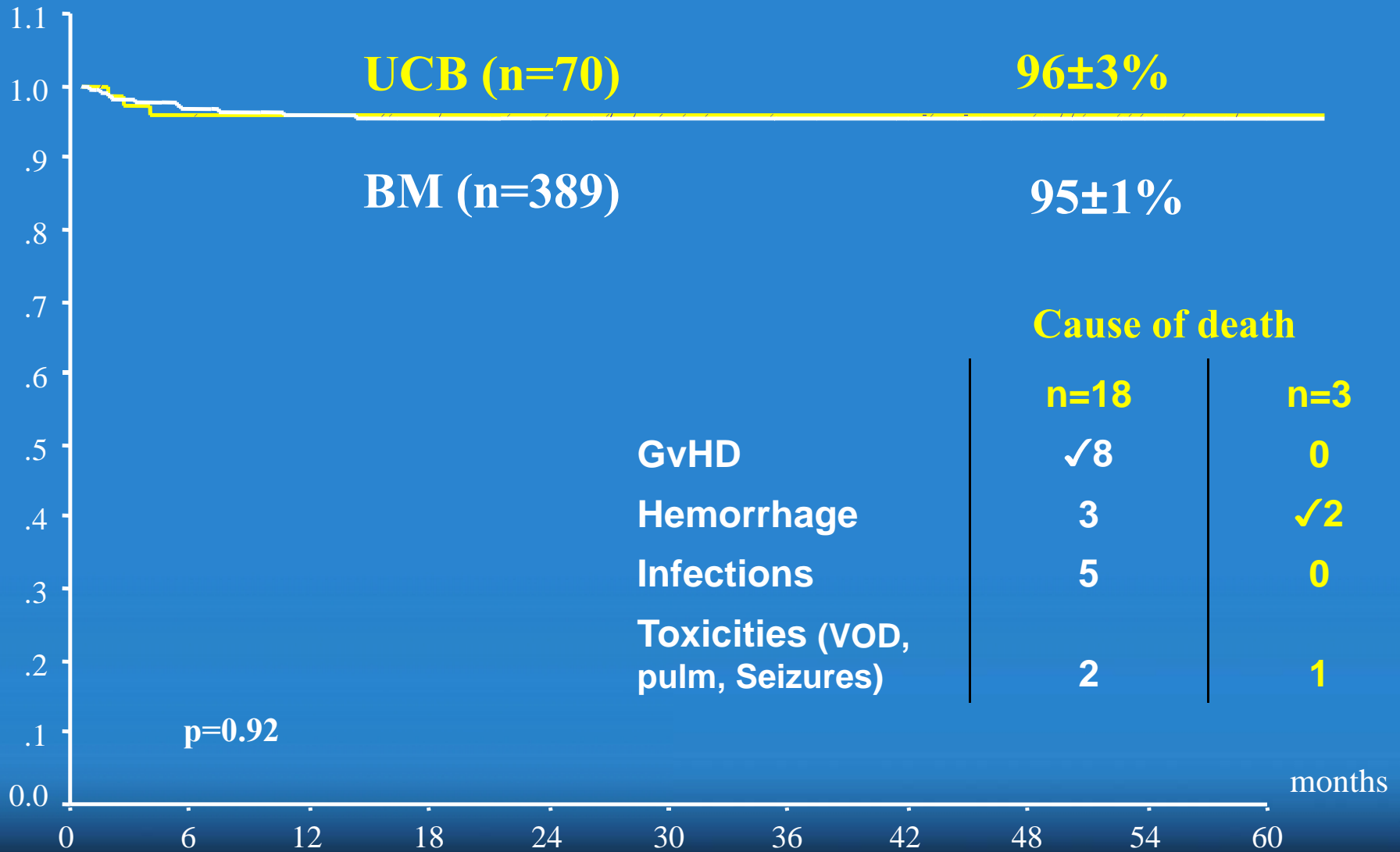
Probability of Neutrophil Recovery



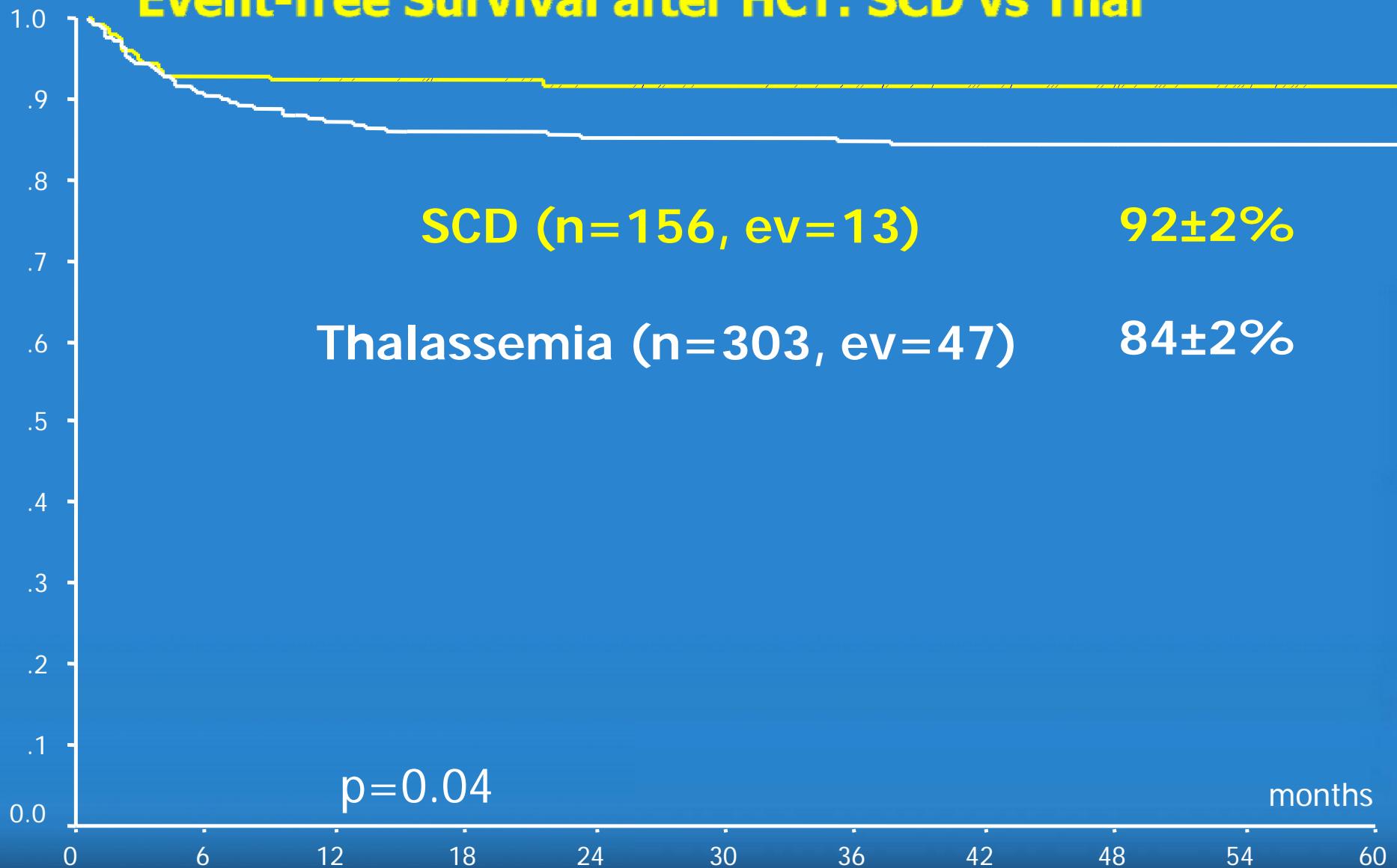
Cumulative Incidence of Acute GvHD (II-IV) and cGvHD



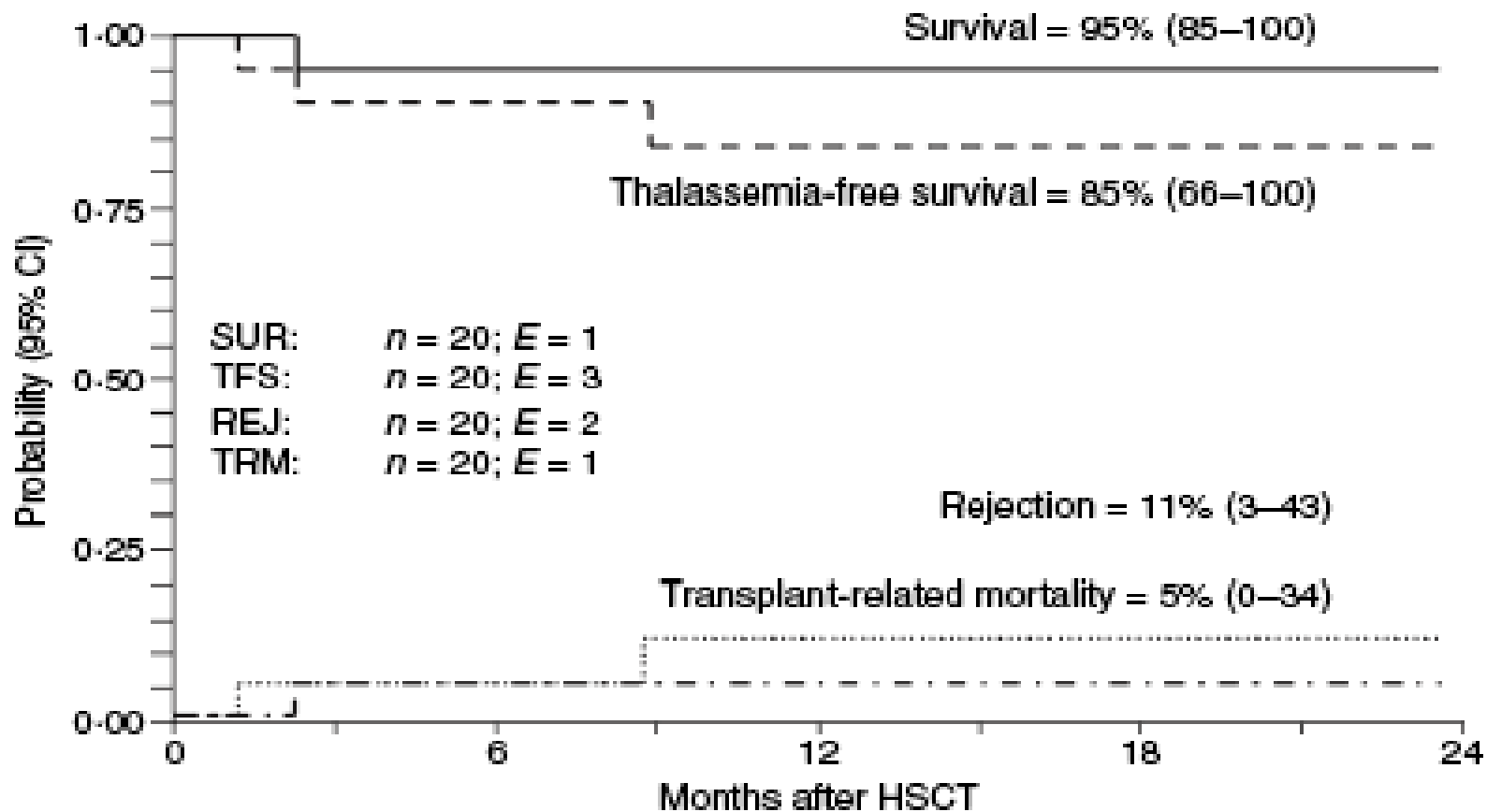
Overall Survival by graft type



Event-free Survival after HCT: SCD vs Thal



URD BMT for Thalassemia Major – 2005-2007 (N=20)



Treosulfan, Flu,
TT

Unrelated UCBT for thalassemia

- Between 7/01 and 9/06, 47 UCBT were performed 41 children at 14 transplant centers (6 received 'double' UCBT)
- Risk class 1 (19), class 2 (4), class 3 (1), and unknown (17). The median age was 5 (range 0.3-20) years
- median duration ANC>500, platelet>20K were **16** days (range 11-32) and **38** days (range 16-99)
- 32 of 41 patients survive (2 lost to follow-up), 27 survive (**66%**) free of thalassemia - TRM was 14.6%

Unrelated UCB Transplantation for SCD

- **Seven children had SCD and stroke**
- **HLA-mismatched CBUs (HLA 4/6, n=5, 5/6, n=2)**
- **Four treated by myeloablative regimens: 1 had GR, 1 died of GVHD, 2 survive free of SCD**
- **All 3 who received a non-myeloablative regimen had GR**
- **57% had viral infections (adeno, CMV, paraflu)**
- **Conclusion: Engraftment GVHD, and infections remain challenges**

Summary

- **Cord Blood Transplants can cure children with genetic and malignant diseases.**
- **Results after cord blood and marrow transplantation are similar**
- **There is a reduced risk of GVHD after cord blood transplantation, which is useful in hgb disorders**
- **Cord blood collection and storage should be encouraged for all families who currently have a child with a transplantable disease who are expecting another child.**