# NIH Support of Research in Hematopoietic Stem Cell Transplantation

National Cancer Advisory Board Meeting
February 4, 2009

Roy S. Wu, Ph.D.
Chief
CGCB/CTEP/DCTD/NCI



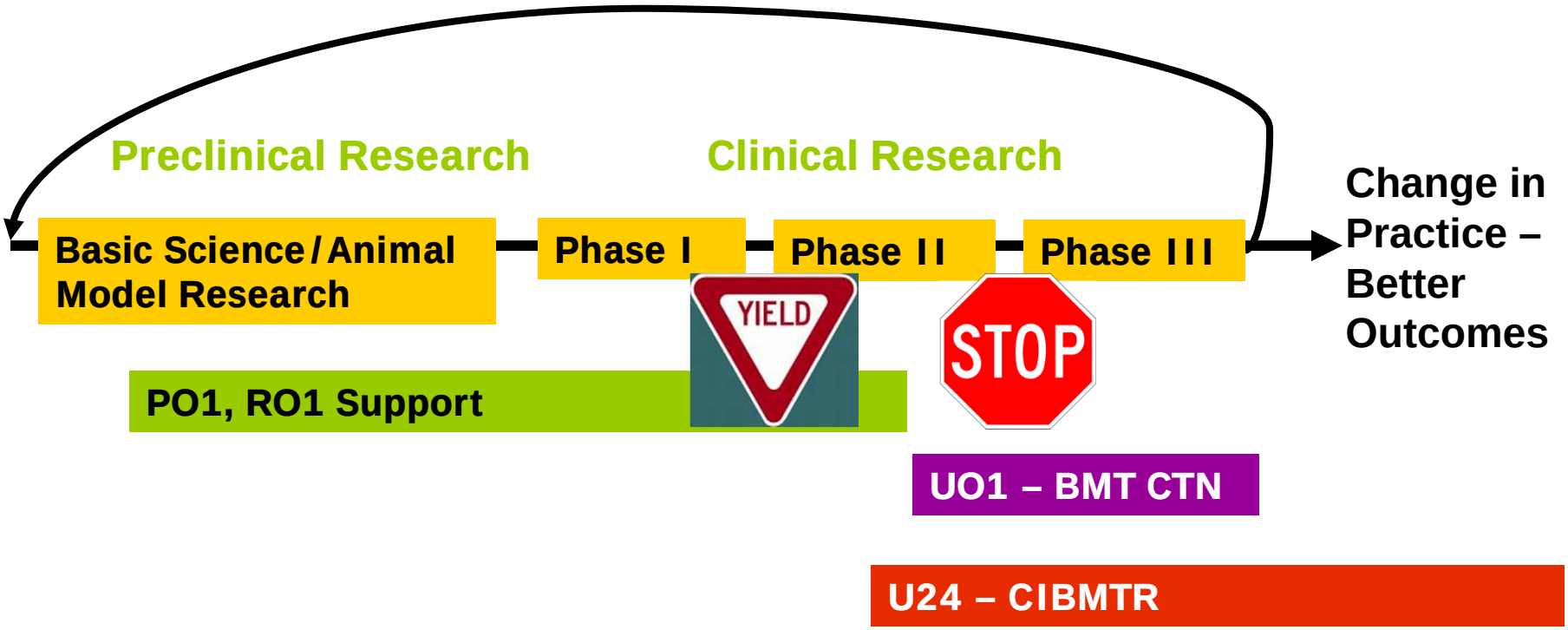
# Background

- **HCT – Curative therapy for malignant and non-malignant hematological diseases: many are rare**
- **No equivalent of big pharma HCT in the private sector**
- **Large federal investment to make HCT available through the C. W. Bill Young Cell Transplantation Program and the National Cord Blood Inventory (Public Law 109-219)**
- **NCI has supported BMT research successfully**
  - **Nobel Prize for Dr. Donnell Thomas**
  - **GM Prize for Dr. George Santos**

# Clinical BMT Funding by NIH
## (2008)

| **MECHANISM** | **NCI** Total dollars (#) | **NHLBI** Total dollars (#) | **NCI + NHLBI (+NIAID +NCMHD)** |
|---|---|---|---|
| R grants | 3,134,000 (9) | 4,332,000 (10) | 0 |
| P01/U19/U54 | 37,401,000 (14) | 11,363,000 (6) | 0 |
| U01 (BMT CTN) | 0 | 0 | 10,031,000 |
| U24 (CIBMTR) | 0 | 0 | 3,083,000 |

# From the bench to the bedside



# Presentations

- **Current use and outcomes of HCT** - *Dennis Confer, Chief Medical Officer, National Marrow Donor Program*
- **Health Resources and Services Administration (HRSA) support of HCT** – *Robert Baitty, Director, Blood Stem Cell Transplantation Program, Division of Transplantation, HRSA*
- **BMT CTN and CIBMTR: National networks for multicenter HCT research** – *Mary Horowitz, Scientific Director, Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin*

NATIONAL MARROW DONOR PROGRAM®

# Worldwide Growth and Development of Hematopoietic Cell Transplantation

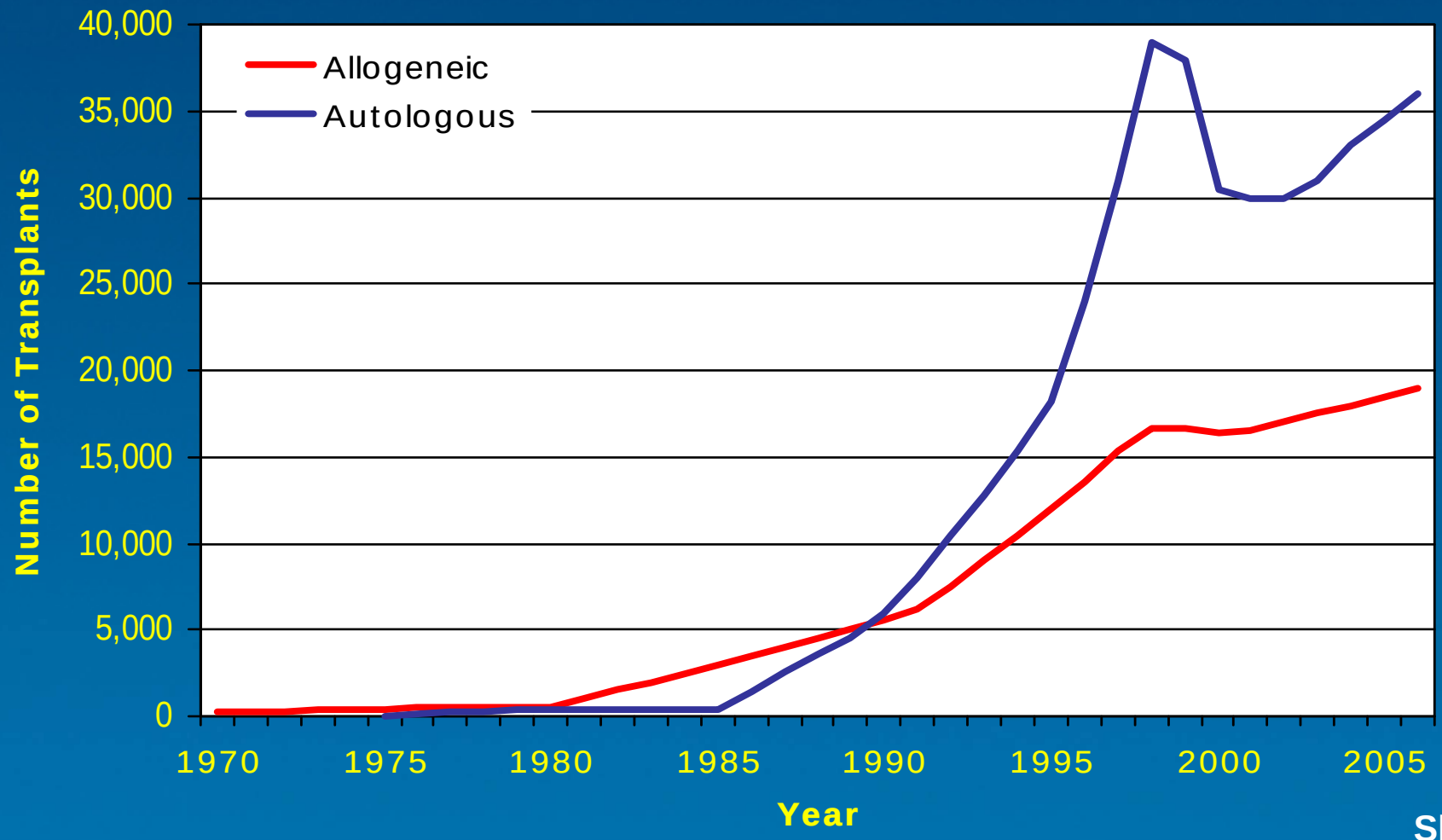
**Dennis L. Confer, M.D.**

**Chief Medical Officer, NMDP**

February 4, 2009

# Annual Numbers of Blood and Marrow Transplantations, 1970-2006 - Worldwide -

NATIONAL MARROW DONOR PROGRAM®



# Indications for Hematopoietic Stem Cell Transplantation in North America

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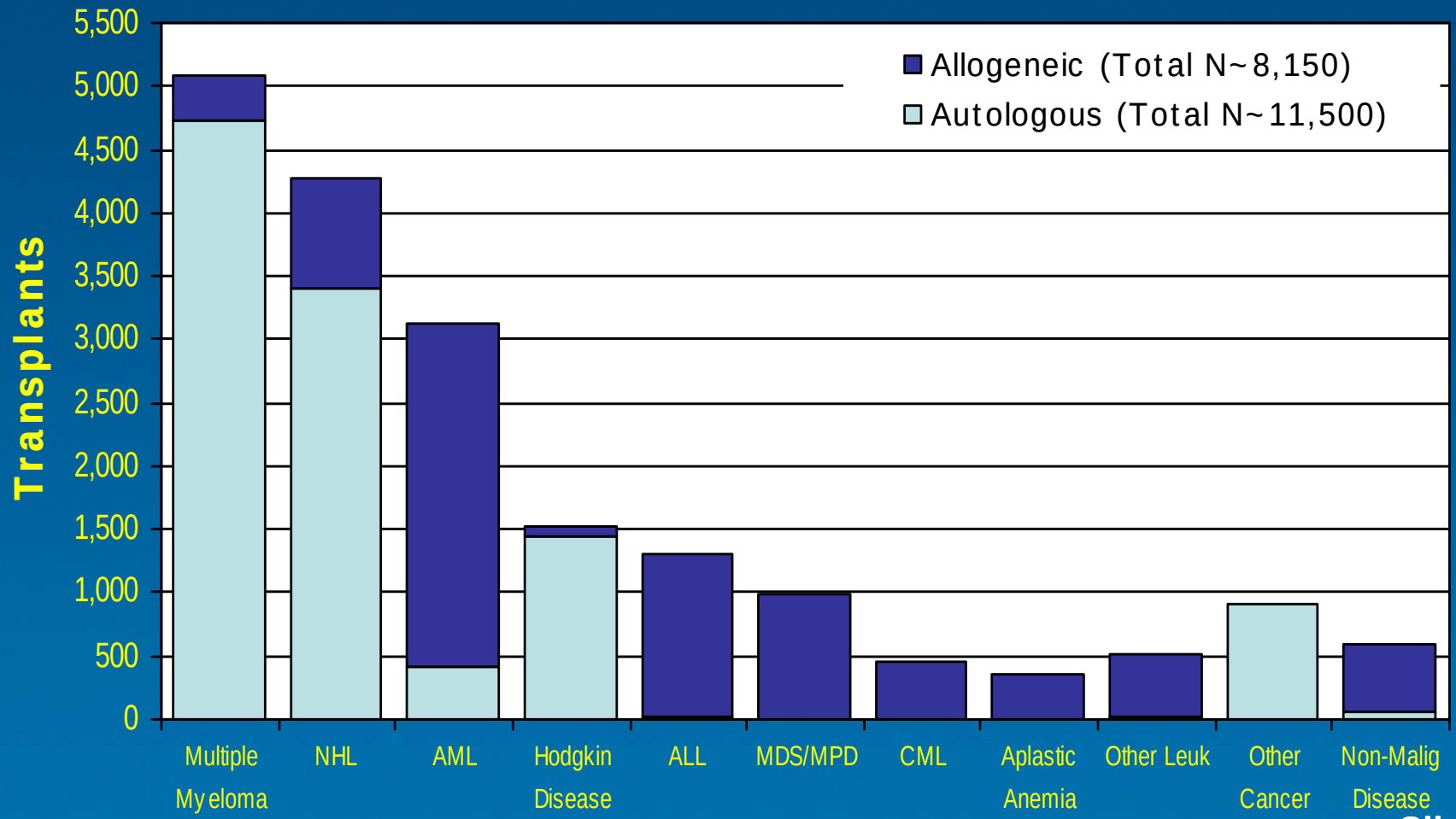
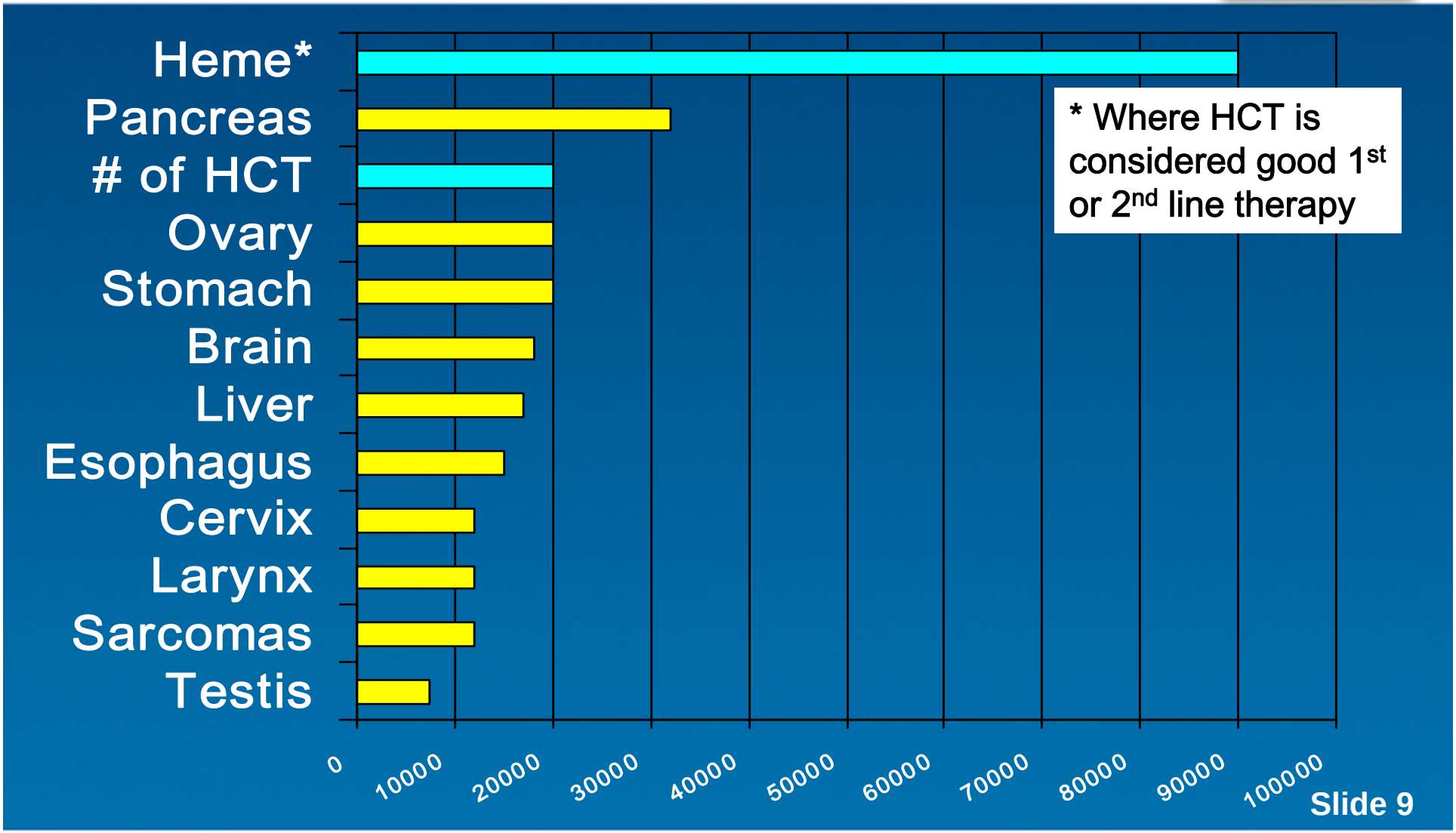


# Annual Numbers of HCTs vs Numbers of Other Selected Malignancies

NATIONAL MARROW DONOR PROGRAM®



# Current Annual Activity Estimates – Worldwide –

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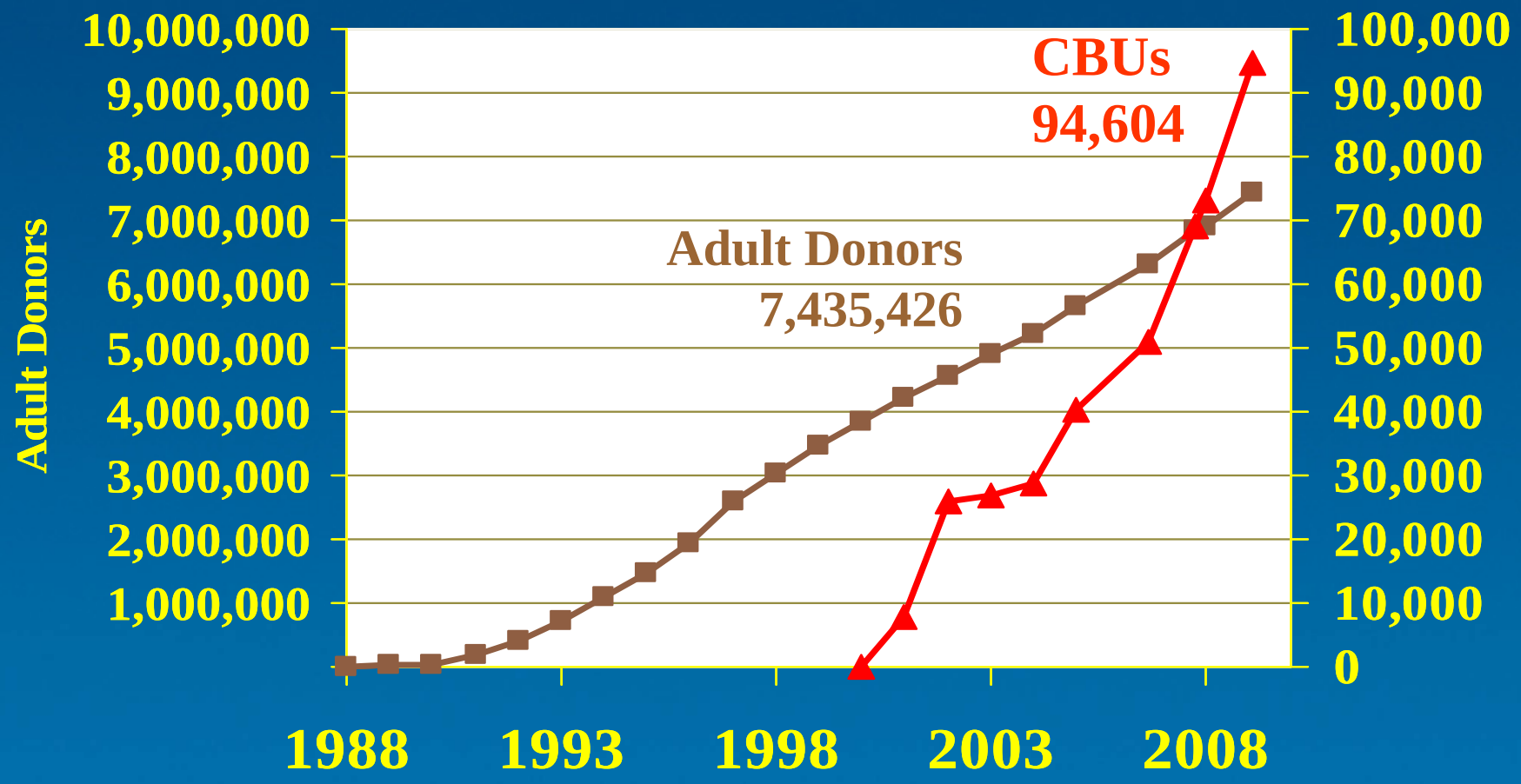
- Autologous transplants exceed 27,000
- Allogeneic transplants exceed 22,000
  - More than half of allogeneic transplants use unrelated donor products
  - More than 14 million adult donors are registered worldwide
  - The world's inventory of unrelated donor (i.e., public) umbilical cord blood units exceeds 400,000

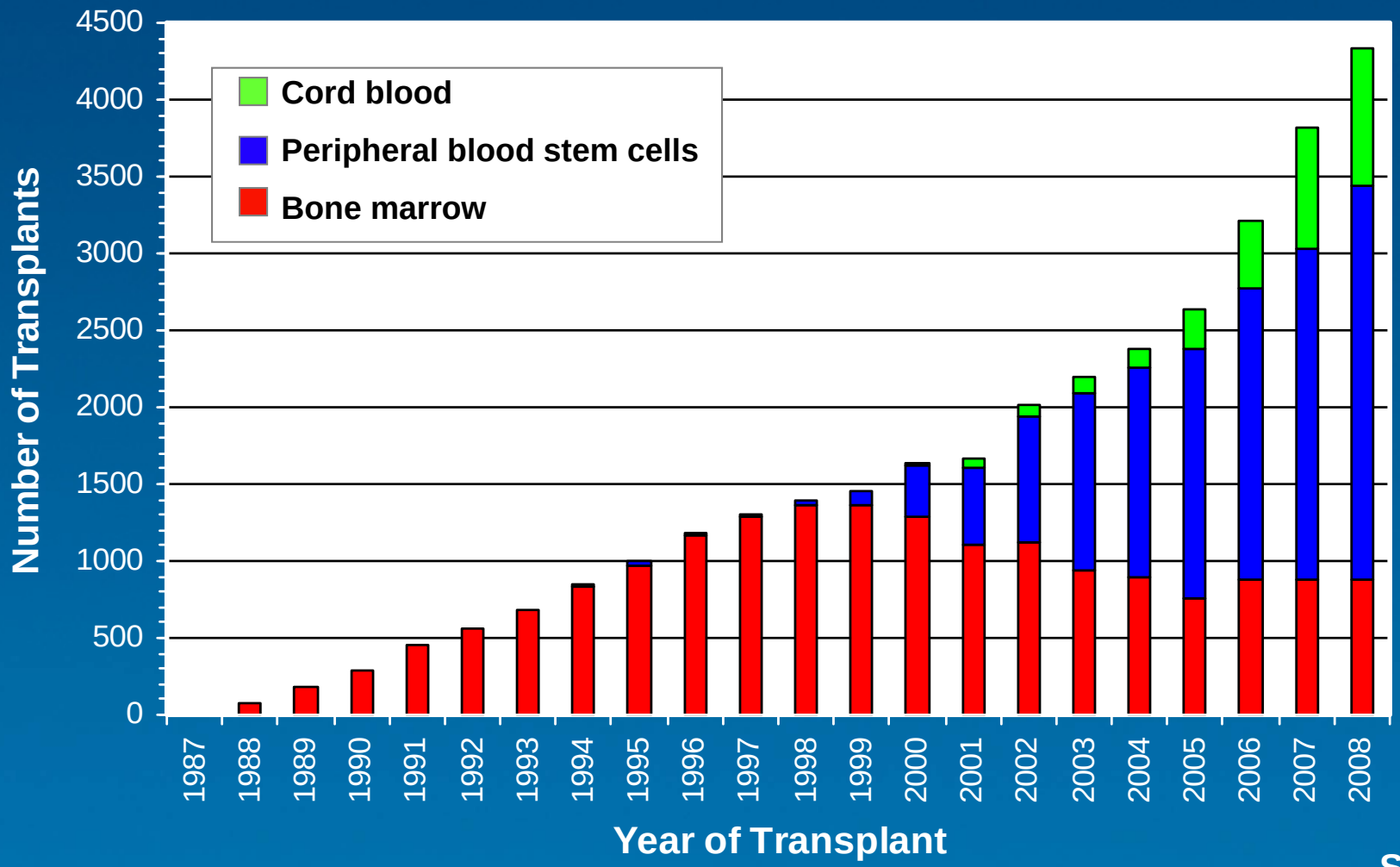
# National Marrow Donor Program Adult Donors & Cord Blood Units – Jan, 2009



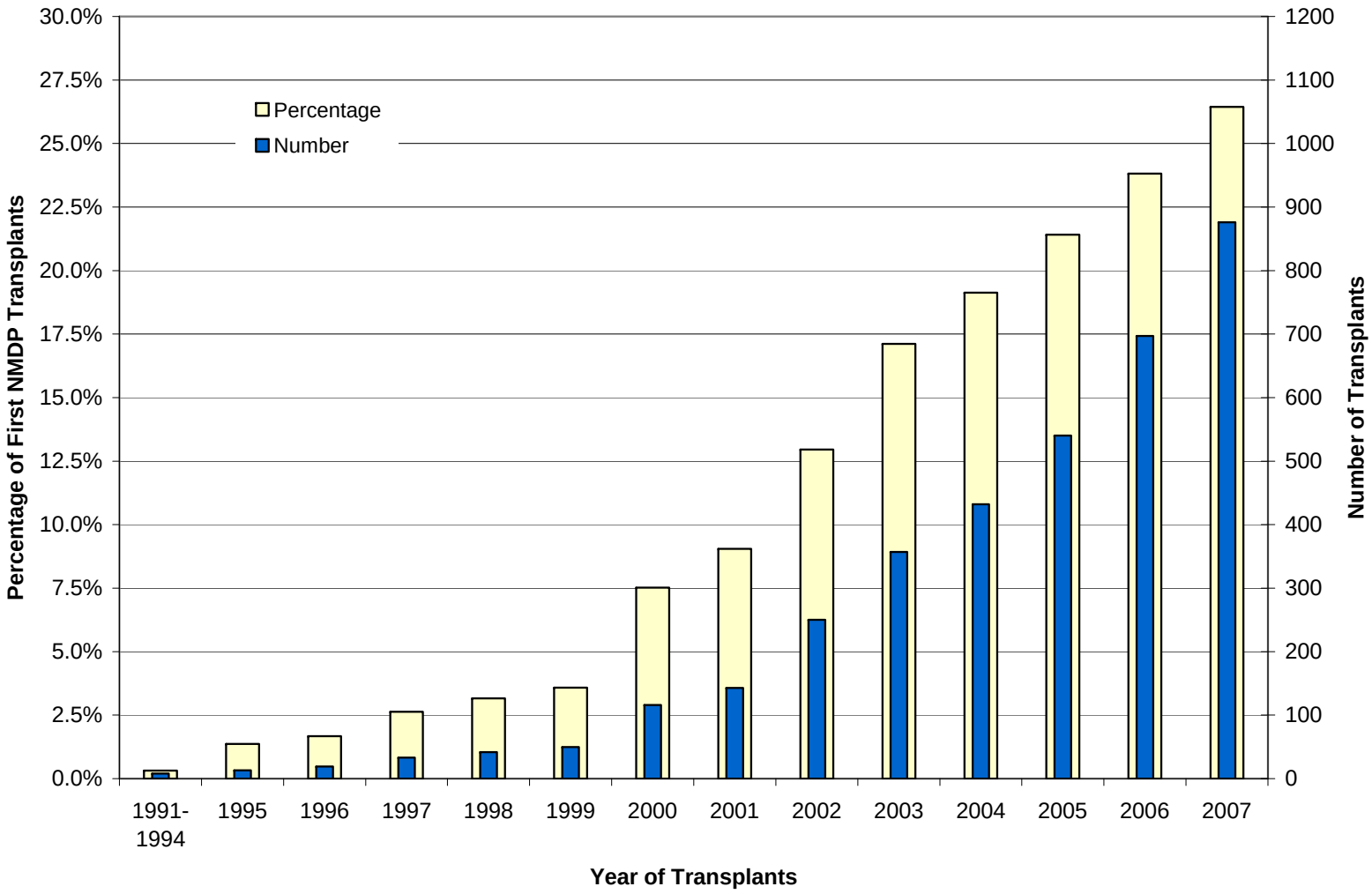
# NMDP Transplants Facilitated

## by Fiscal Year 1987–2008

NATIONAL MARROW DONOR PROGRAM®



# NMDP Recipients >55 Years of Age



# Is There Evidence of Improved Results?

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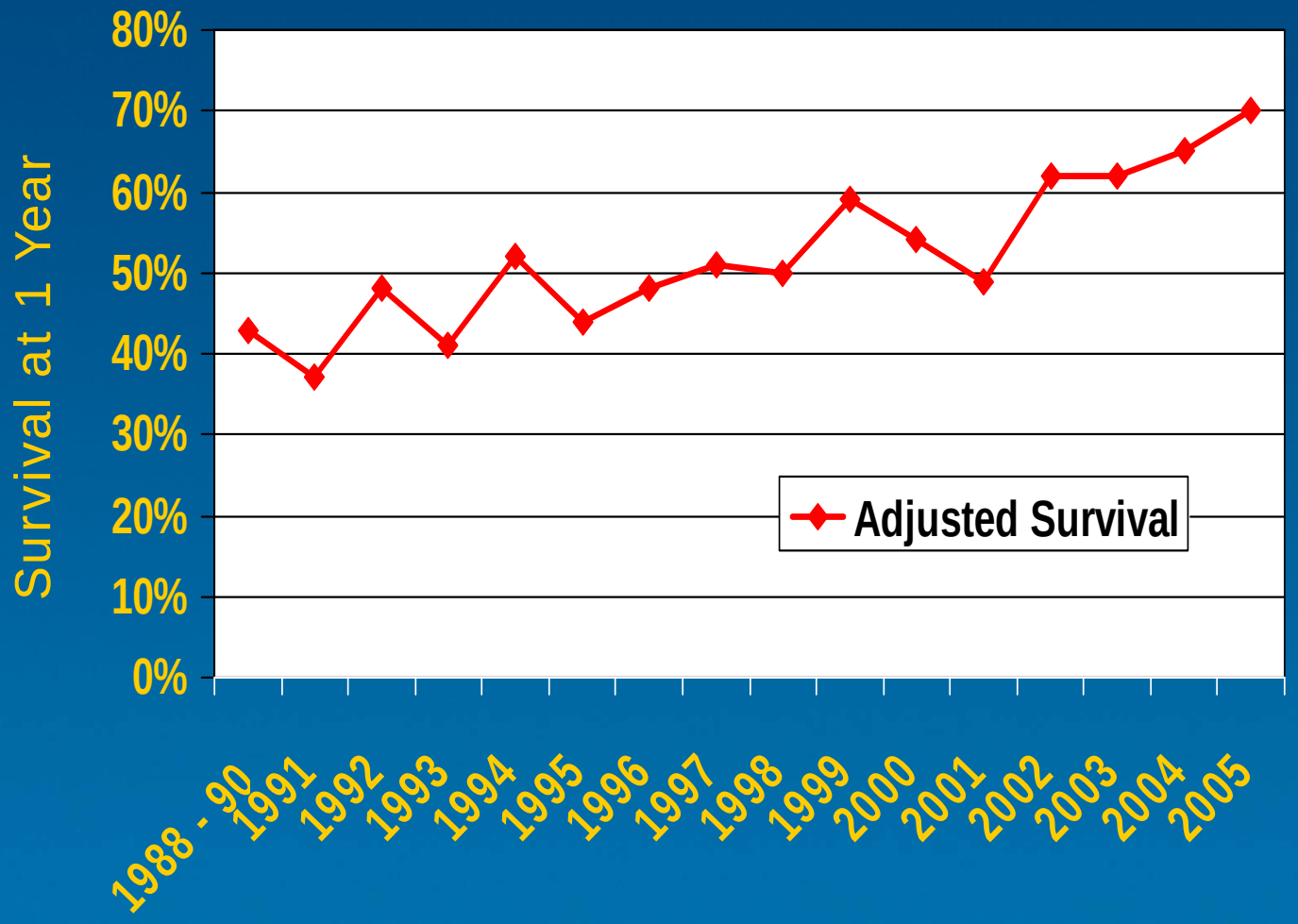
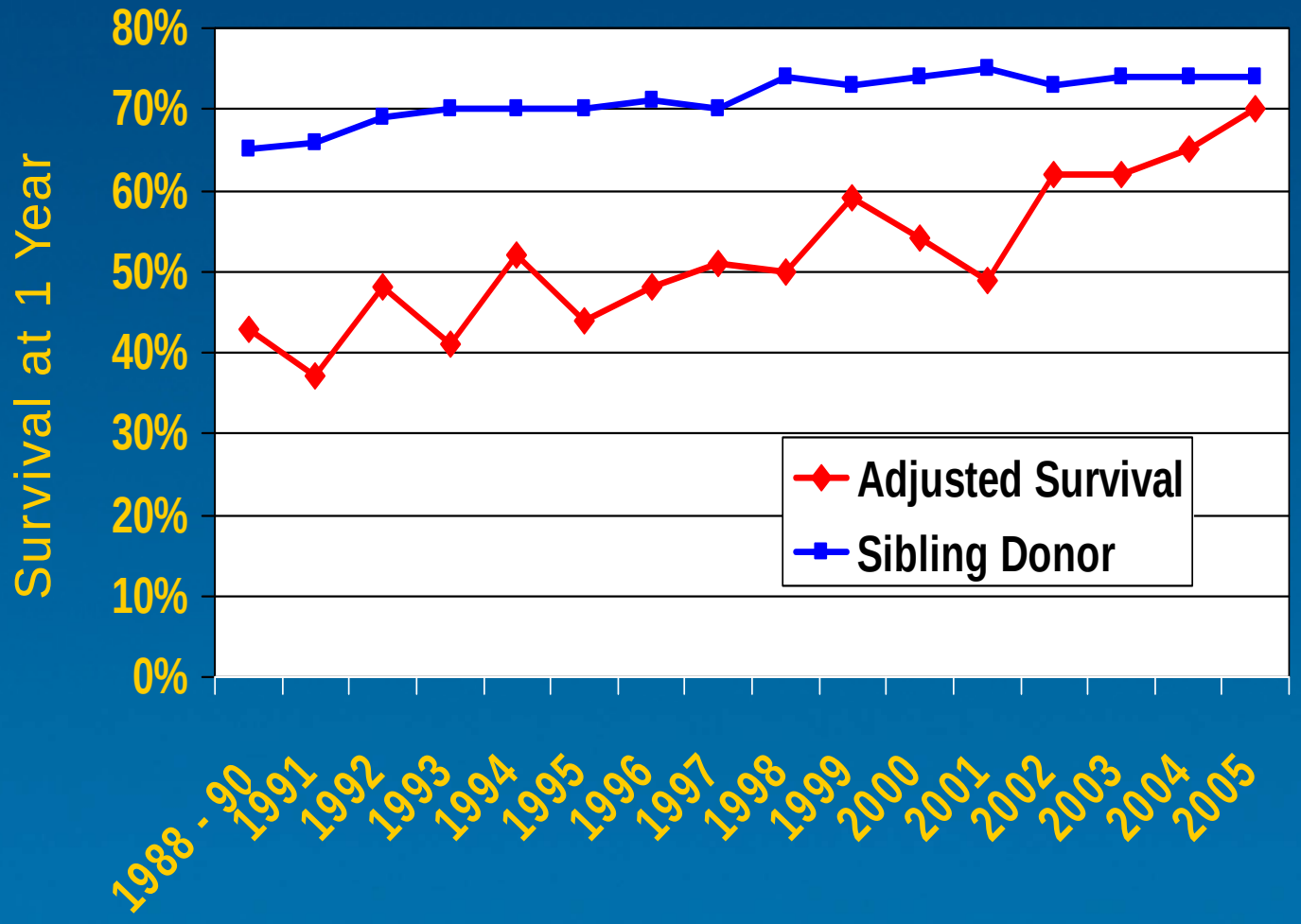
- 1-year survival for a defined subset of patients evaluated over time
  - Restricted to patients <50 years age
  - Myeloablative regimens only
  - Acute leukemias in any remission
  - Chronic Myelogenous Leukemia
  - Myelodysplastic Syndromes – RA or RARS only
- Analysis completed in mid-2007
  - 6,450 recipients through December 31, 2005
  - Adjusted for recipient age, sex, race, CMV status, BMI, disease type, stage, risk and duration, performance score, coexisting disease

# Adjusted 1-year Survivals over Time – 1988 through 2005 –



# Survivals over Time: Unrelated vs. Related Donors



# SUMMARY

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- Worldwide numbers of Autologous and Allogeneic HCTs continue to increase and the potential for further growth is high
- More than half of allogeneic transplants utilize unrelated donor products
- Outcomes with related donors and unrelated donors have improved over time and are comparable
- Continued clinical research is necessary to optimize outcomes

# HRSA's Role in Blood & Marrow Transplantation

# NCAB February 4, 2009

Robert L. Baitty, MPP

Director, Blood Stem Cell Transplantation Program, Division of Transplantation, Health Resources & Services Administration (HRSA)

# National Bone Marrow Donor Registry

- Purpose: Facilitate unrelated donor transplantation
- Preceded by National Organ Transplant Act-1984
- Registry established-1986
  - Navy grant (potential role in a marrow toxic event)
  - Oversight by NIH/NHLBI as a research activity
- Oversight transferred to HRSA-1994
- Operated by the National Marrow Donor Program since inception under HHS contracts
  - HHS and Navy have provided significant financial support to the Registry over 20+ years

# The Registry, cont'd

- Reauthorization Act of 1998:
  - Increase number of minorities in the Registry
  - Provide patient advocacy services
  - Quality standards and procedures
  - Collection of outcomes data on transplants facilitated by the Registry (unrelated-donor transplants)
  - Transplant center-specific survival analyses
    - Aid transplant center quality improvement
    - Provide patients and referring physicians with data to help guide choice of transplant center

# Stem Cell Therapeutics and Research Act of 2005 (Public Law 109-129)

- Exciting opportunity to expand access to HCT
- Aims to increase:
  - number of blood stem cell transplants using unrelated adult donor sources or umbilical cord blood grafts
  - Number of cord blood units available for research
- **Establishes National Cord Blood Inventory**
  - target of banking 150,000 new units of umbilical cord blood
  - Authorized at $15 million/year
  - FY 2009 Continuing Resolution funding ~$8.8 million
- **Establishes C.W. Bill Young Cell Transplantation Program**
  - Successor to the National Bone Marrow Donor Registry
  - Authorized at $38 million/year
  - FY 2009 Continuing Resolution funding ~$23.5 million

# Stem Cell Therapeutics and Research Act of 2005, cont.

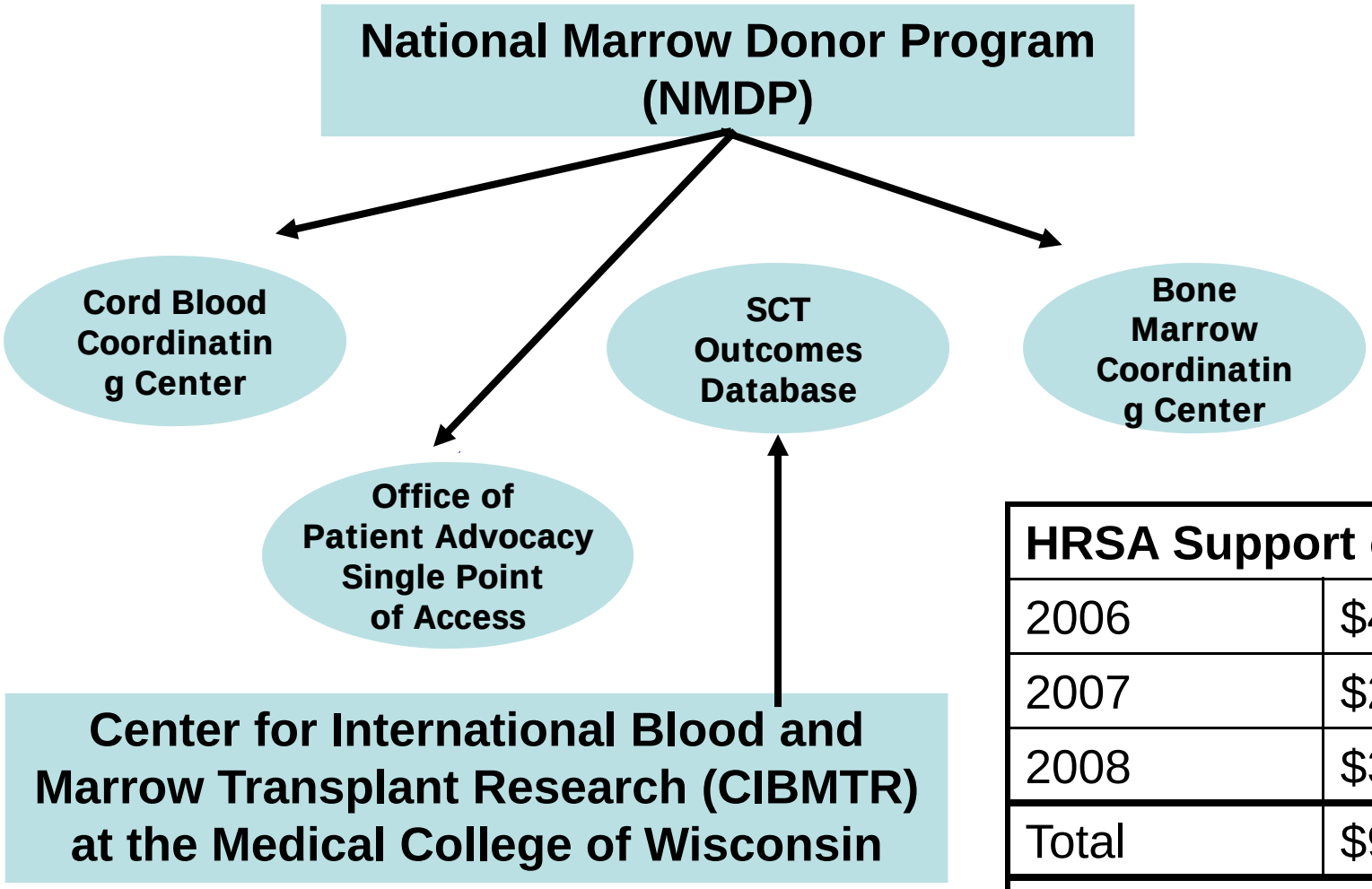
**Establishes:**

- **Secretary's Advisory Council on Blood Stem Cell Transplantation**
- **Bone Marrow Coordinating Center** to identify, match, and facilitate the distribution of adult blood stem cells to patients
- **Cord Blood Coordinating Center** to identify, match, and facilitate the distribution of umbilical cord blood to patients
- **Single Point of Access** through which patients and physicians can electronically search for and gain access to all blood stem cell graft sources
- **Patient Advocacy and Case Management** services independent of other services provided by the Program

## Stem Cell Therapeutics and Research Act of 2005, cont.

- **Stem Cell Therapeutic Outcomes Database** to collect basic scientific data on transplant recipients
  - Scope expanded to include both related and unrelated donor transplants
  - Limited data set for each patient
  - Operational research to evaluate Program
  - Annual center-specific outcomes analysis
- More comprehensive research data on HCT collected through other mechanisms
  - *Program depends on more comprehensive data and research to further the field of allogeneic transplantation and improve patient outcomes*

# C.W. Bill Young Cell Transplantation Program: *Contracting Structure*




| HRSA Support of SCTOD | |
|---|---|
| 2006 | $4.00 |
| 2007 | $2.24 |
| 2008 | $3.68 |
| Total | $9.92 |
| No $ for data submission | |

# Multicenter Networks for HCT Research: CIBMTR and BMT CTN

Mary M. Horowitz, MD, MS
Medical College of Wisconsin

CIBMTR™ CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

# The CIBMTR Grew Out of Two Important Collaborative Efforts in HCT

- An affiliation of
  - National Marrow Donor Program (NMDP)
  - International Bone Marrow Transplant Registry (IBMTR) at the Medical College of Wisconsin
    - Voluntary outcomes registry established in 1970 (2 years after the first successful HCTs) at a time when there were ~ 12 transplant centers, < 50 transplants a year worldwide
- Established CIBMTR in July 2004 to support clinical research in HCT & related fields

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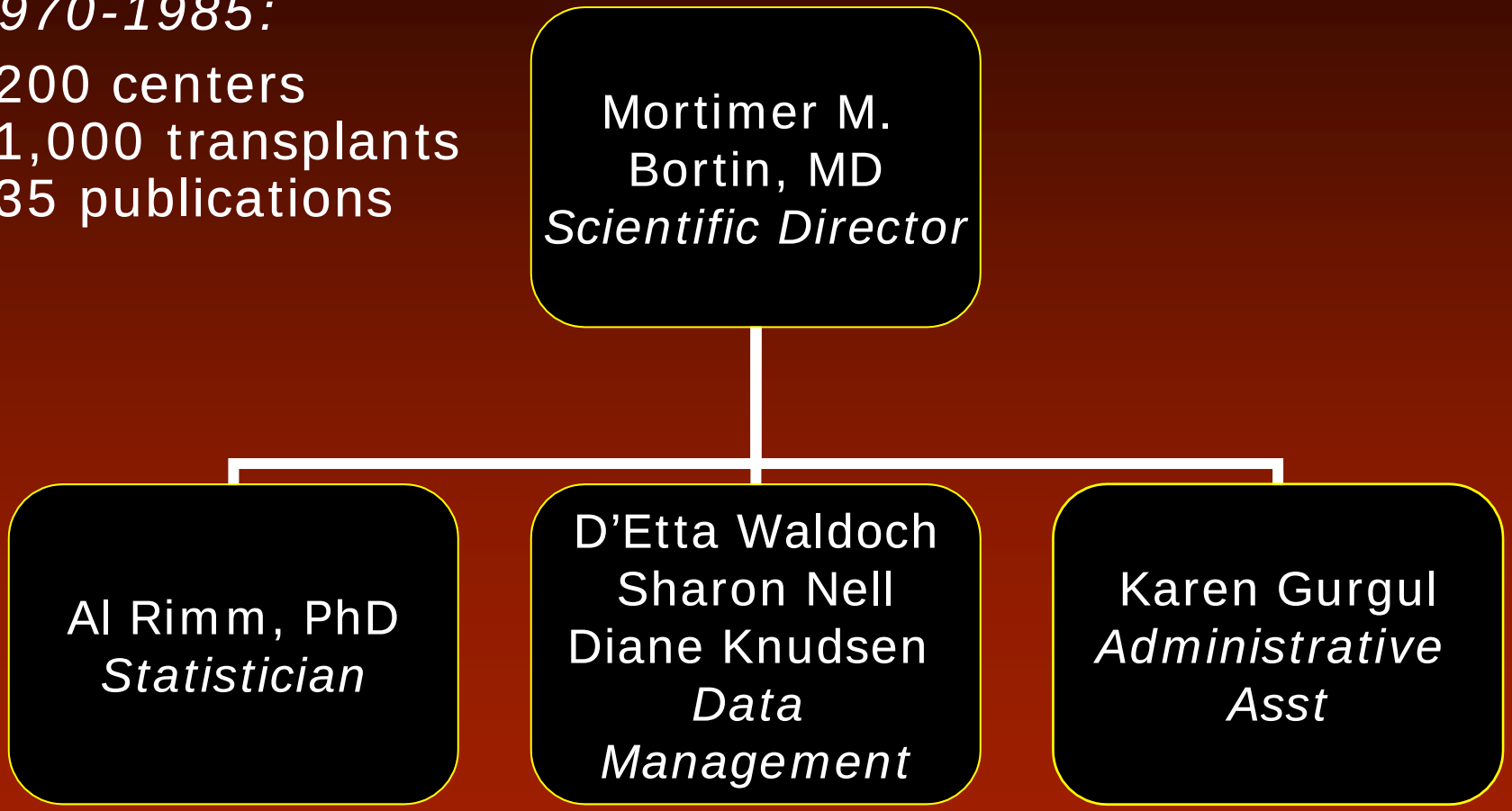
# IBMTR – 1985
# (year of first major NIH funding)

*1970-1985:*

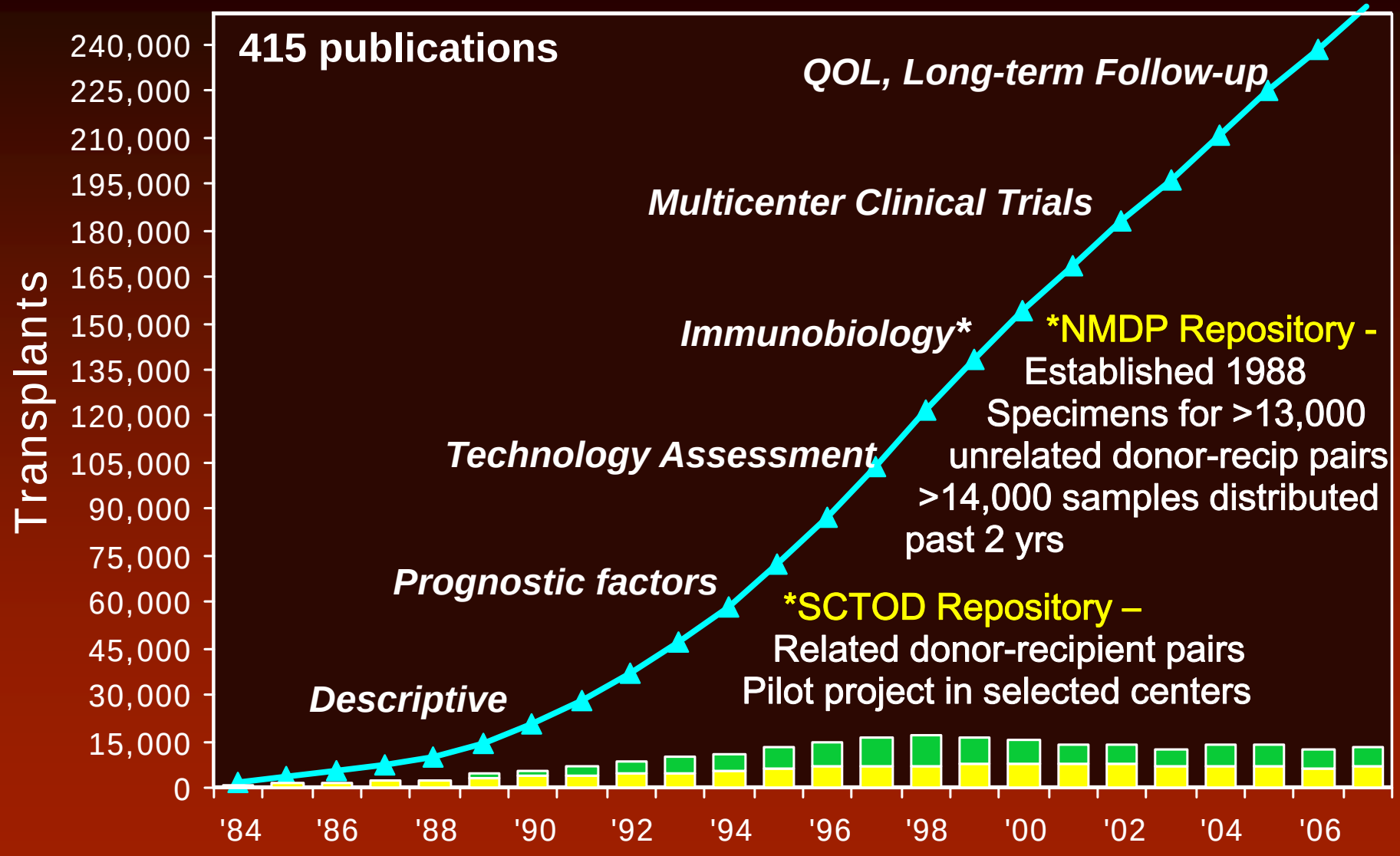
- 200 centers
- 1,000 transplants
- 35 publications



# Location of Centers Participating in the CIBMTR, 2009

135 staff including, 5 PhD statisticians, 11 MS statisticians, 10 MD-MS faculty; Active program of statistical methodology research specifically focused on transplant outcomes in addition to supporting clinical studies

# CIBMTR Observational Database (415 publications)

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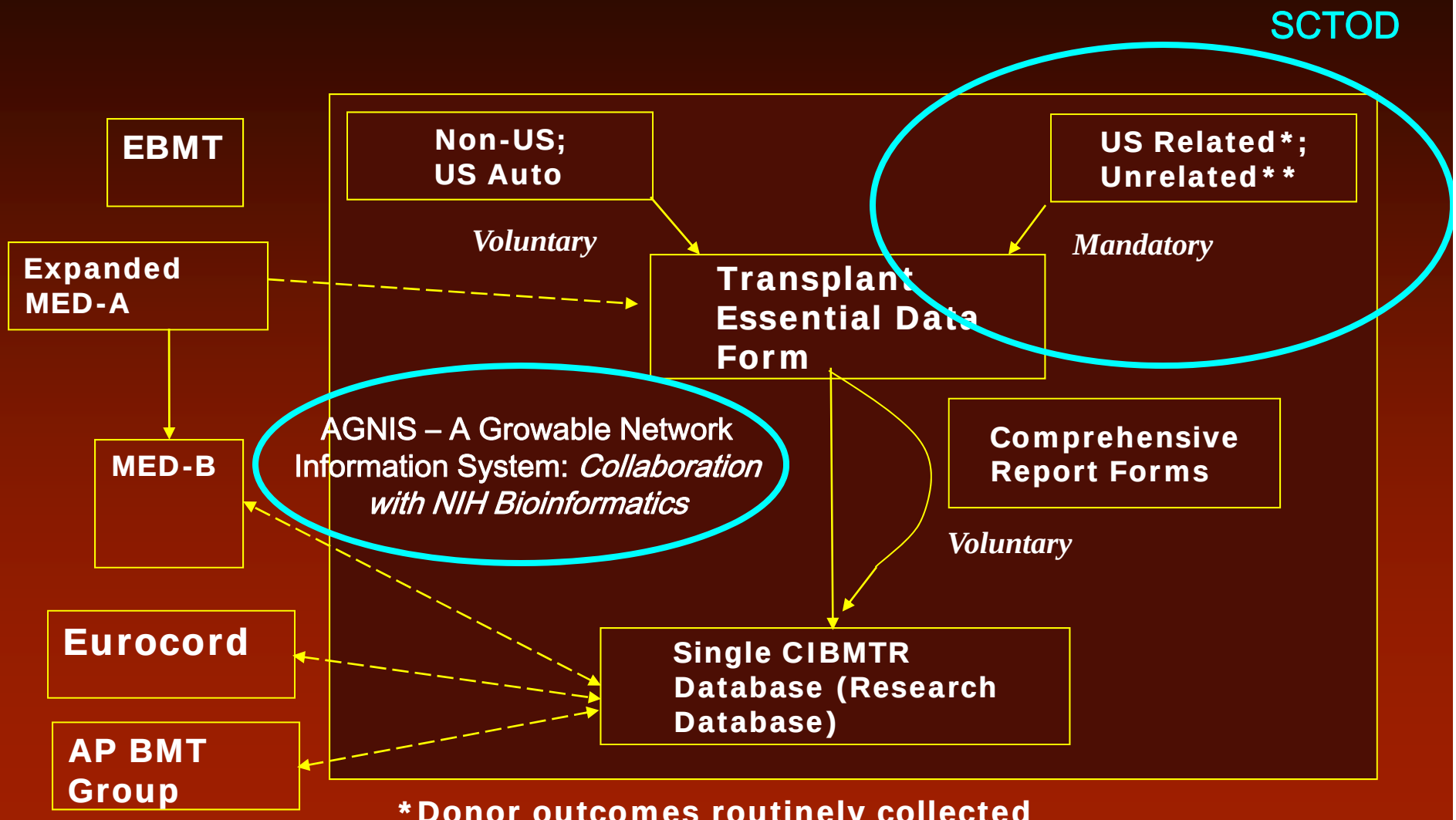
# Current/Future Data Flow




*Donor outcomes routinely collected

**Donor outcomes to be collected on subset

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# WORKING COMMITTEES

- Acute Leukemia
- Chronic Leukemia
- Lymphoma
- Plasma Cell Disorders
- Solid Tumors
- Pediatric Cancer
- Non-Malignant Marrow Disorders
- Immune Deficiencies / Inborn Errors
- Autoimmune Diseases
- Graft Sources/Manipulation
- GVHD
- Late Effects & QOL
- Immunobiology
- Infection / Immune Reconstitution
- Regimen-related Toxicity
- Emerging Cellular Therapies
- Health Services & Psychosocial Issues
- Donor Health & Safety
- International Studies

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# CIBMTR PUBLICATIONS

| | 1993-1997 | 1998-2002 | 2003-2007* |
|---|---|---|---|
| Peer-reviewed pubs | 34 | 66 | 115 |
| # Different authors | 177 | 295 | 403 |
| # Different Institutions | 98 | 158 | 216 |

*34 publications in 2008

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# ROLE OF OBSERVATIONAL DATABASE IN CLINICAL RESEARCH

- Analyze trends
- Descriptive studies
- Identify factors associated with outcome
  - Clinical
  - Center-specific
  - Socioeconomic
  - Biologic/genomic
- Assess treatments / strategies
  - Donor selection
- Study late effects
- Analyze access / utilization
- Design / Interpret / Facilitate clinical trials

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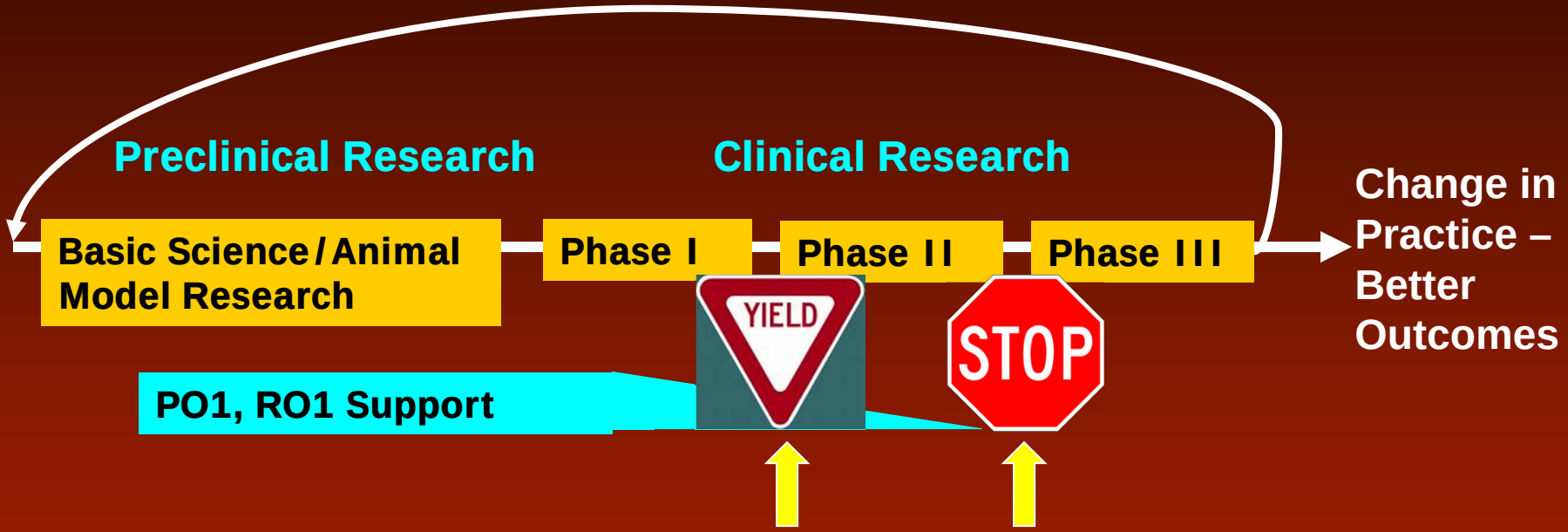
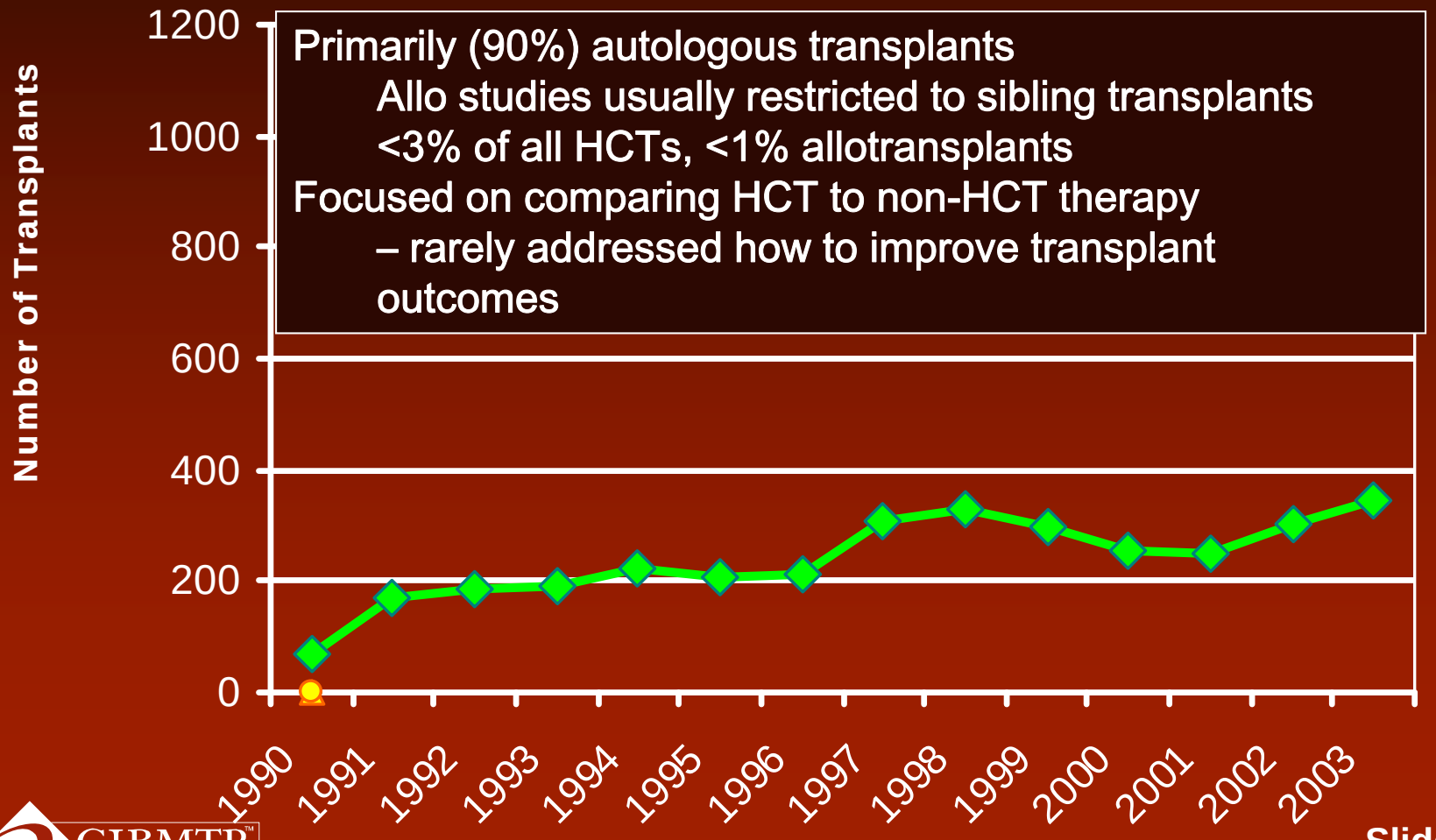
# From the bench to the bedside



# US Transplants on Cooperative Group Trials: Before the BMT CTN

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BLOOD AND MARROW
TRANSPLANT
CLINICAL TRIALS NETWORK

- Established: Sept. 2001; renewed Oct. 2006
  - 16 Core Center cooperative agreements
  - 1 DCC cooperative agreement:
    CIBMTR with subcontracts to NMDP & EMMES
- Goal of the Program:
  - Provide the infrastructure needed to allow promising HCT therapies to be developed/evaluated in high quality multicenter studies

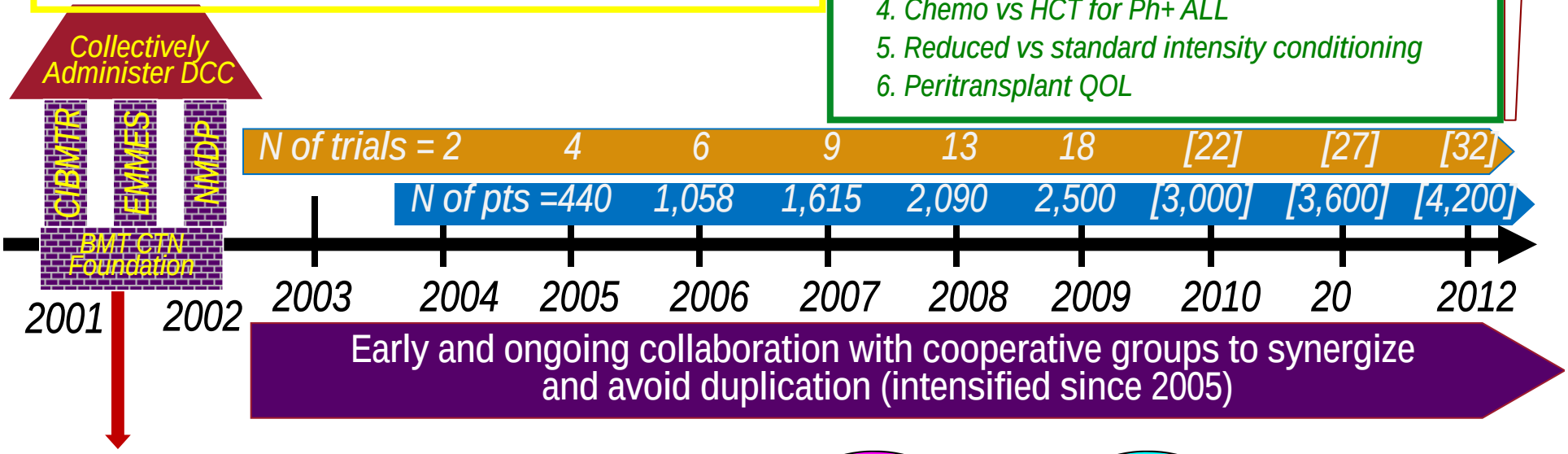
## 2000 State of Science Symposium #1 - Set scientific agenda for 2001-07 ⇨ 7 focus areas for HCT trials

1. Expanding donor/graft source
2. Reduce regimen related toxicity
3. GVHD prevention/therapy
4. Decrease relapse
5. Decrease infections
6. Late effects/QOL
7. Rare diseases

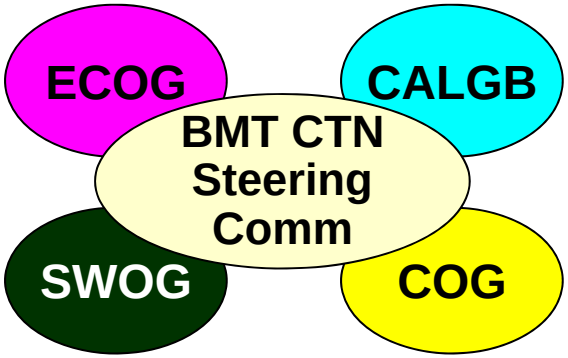
## 2007 State of Science Symposium #2 Sets scientific agenda for 2008-12+ ⇨ 12 Working Committees

*11 high priority trials – 6 in development:*

1. *Maint vs consol vs 2nd Tx for MM*
2. *Calcineurin-inhibitor-free Rx for CGVHD*
3. *Reduced intensity tx for CLL*
4. *Chemo vs HCT for Ph+ ALL*
5. *Reduced vs standard intensity conditioning*
6. *Peritransplant QOL*



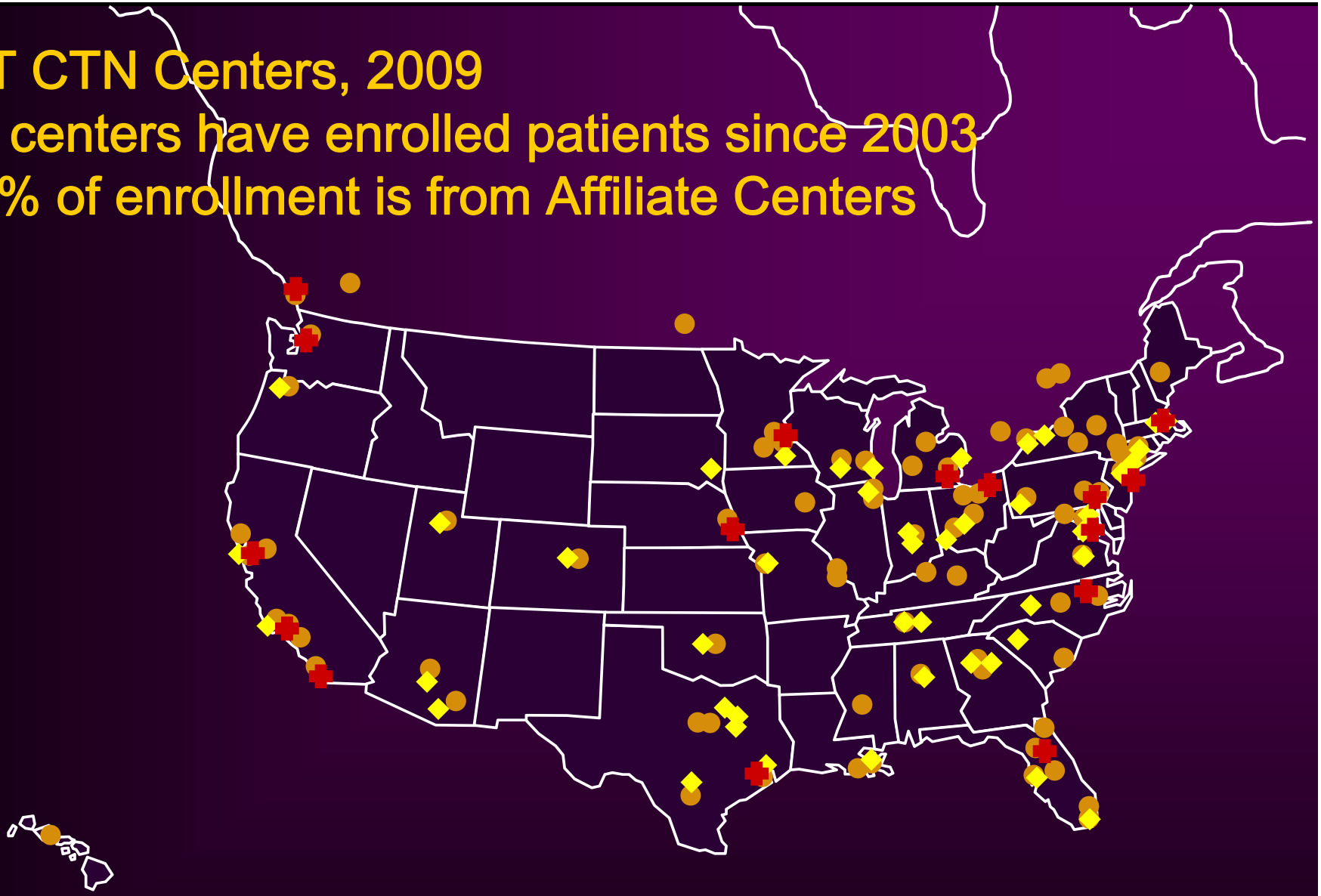

- Governance and leadership
- Established 16 Core Centers
- Manual of Policies/procedures
- Electronic data capture system
- Per patient reimbursement model
- Websites for members & public



# BMT CTN Centers, 2009

>70 centers have enrolled patients since 2003

~25% of enrollment is from Affiliate Centers

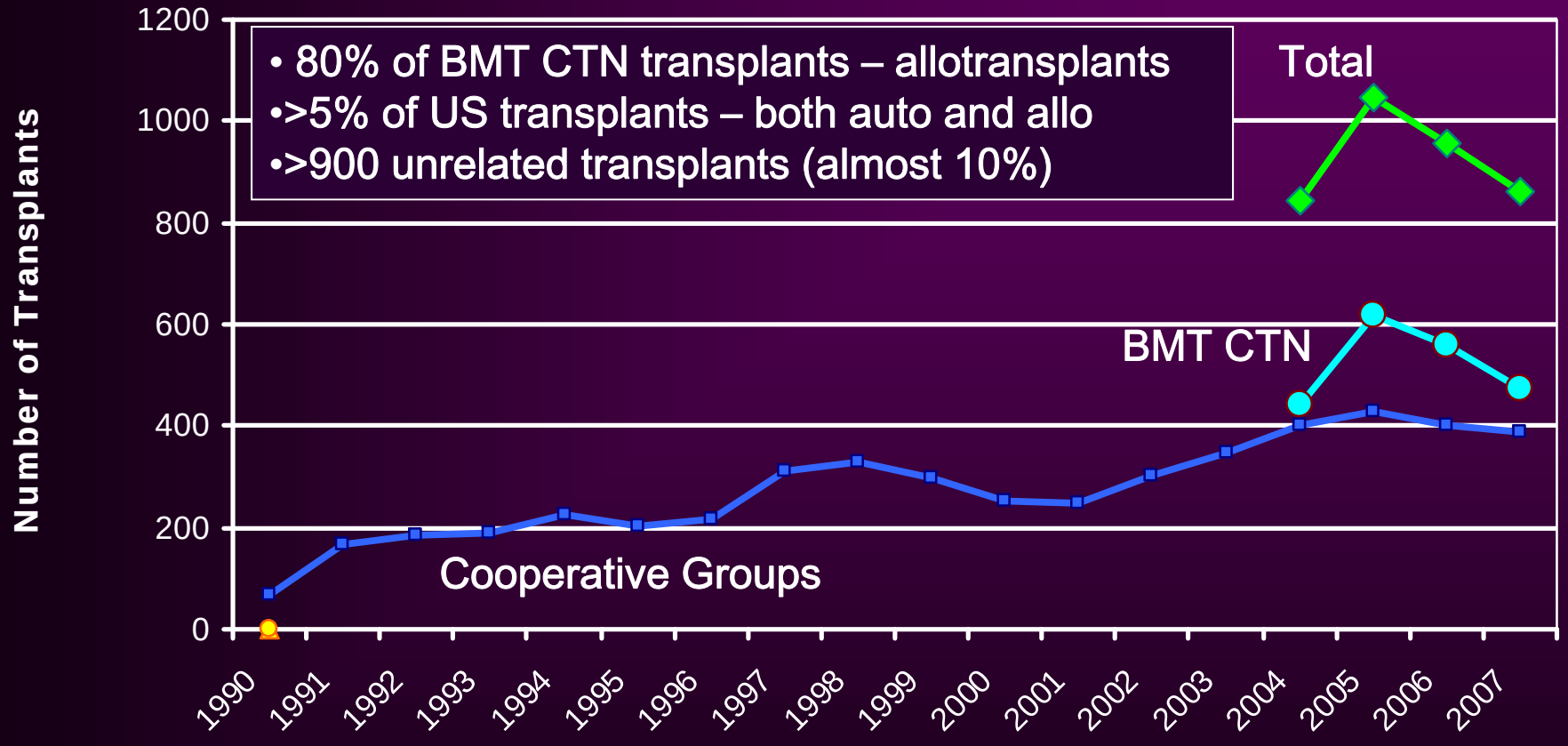


= Core Centers

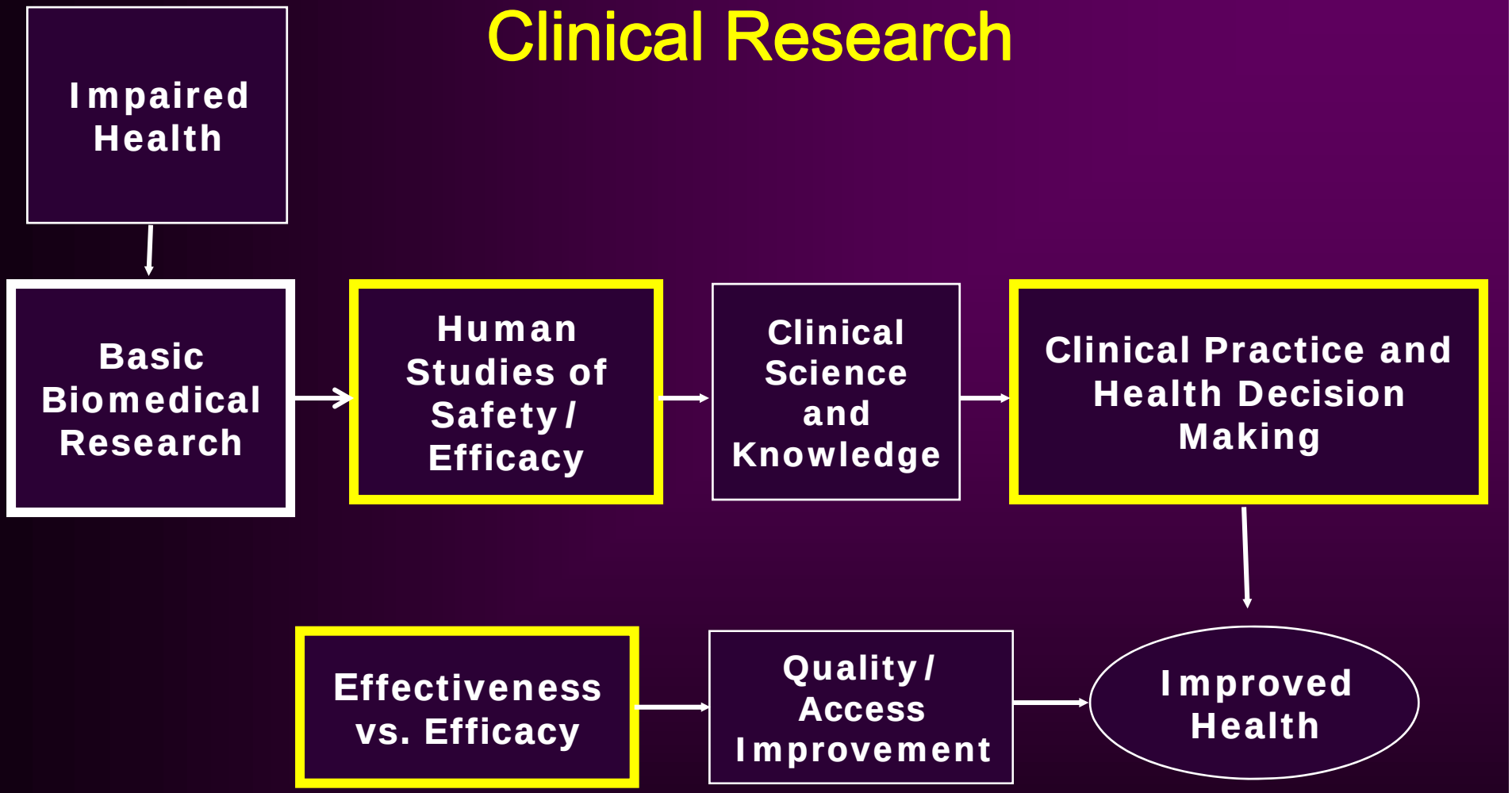
= Affiliate Centers

= PBMTC Centers

# US Transplants on Cooperative Group Trials: Impact of the BMT CTN



# Clinical Research




From: Sung et al. Central challenges facing the national clinical research enterprise. JAMA 2003;289:1278-87.

# DHHS Support for Clinical Research in HCT: Roles of BMT CTN and CIBMTR