The Role of Outcomes Registries in Blood and Marrow Transplantation

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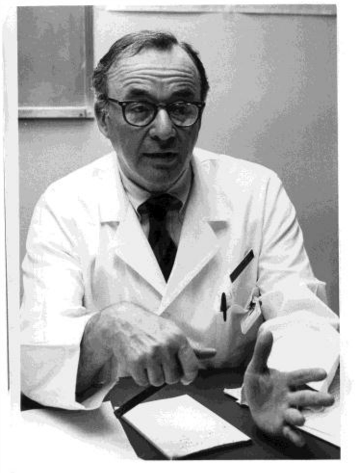
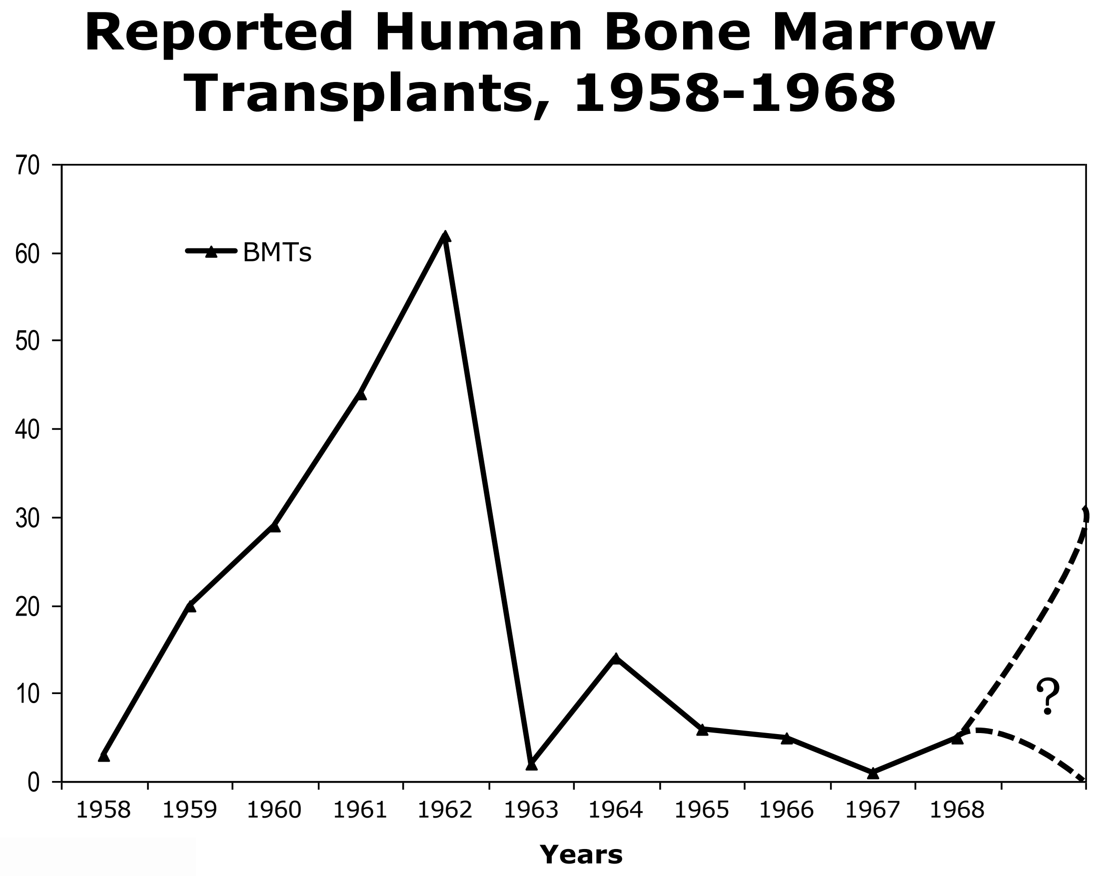
Cape Town, South Africa
November 2014

A Little History…….

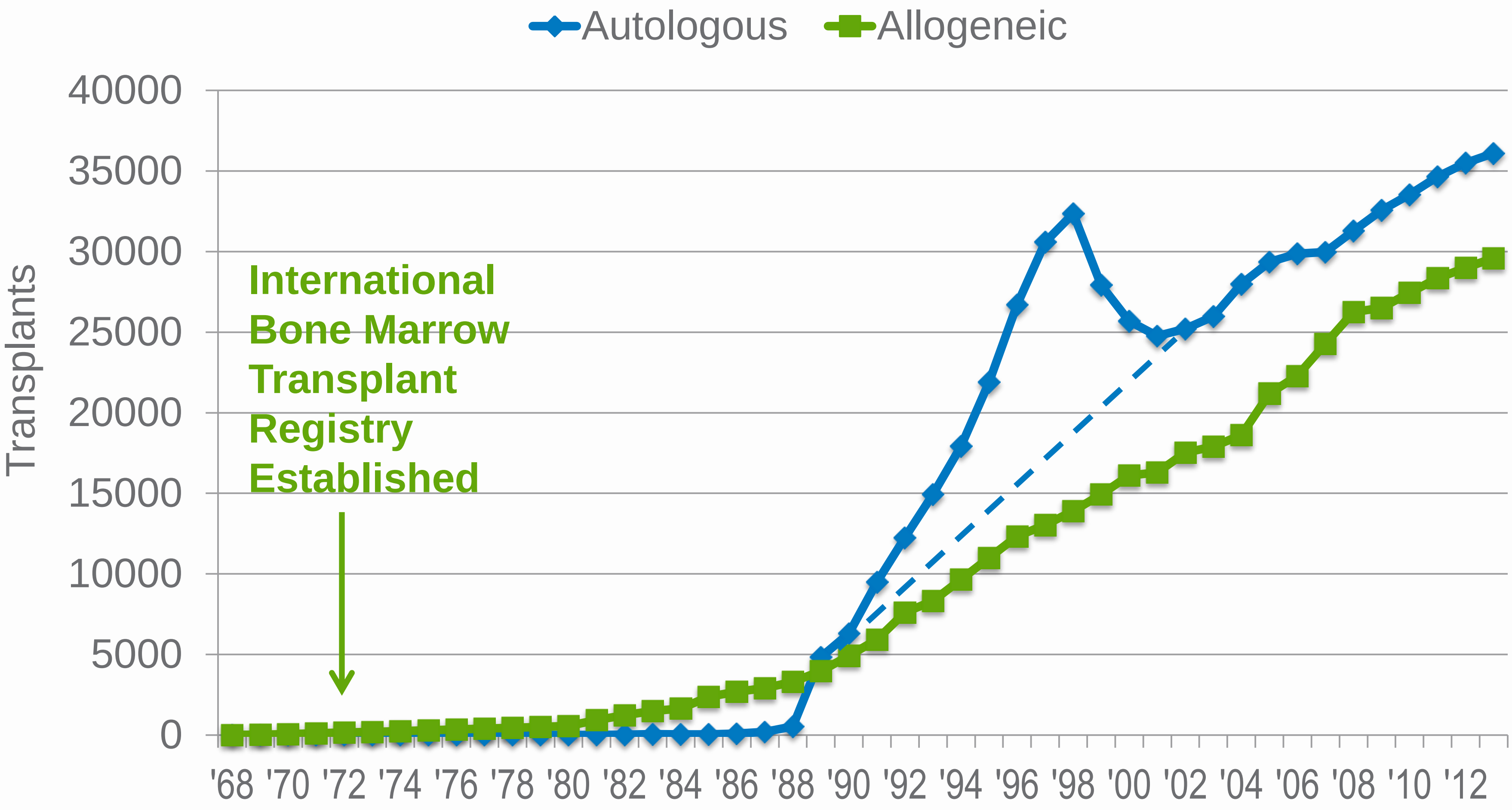




Reported Human Bone Marrow Transplants, 1958-1968

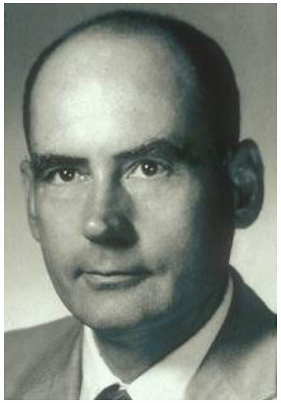
Bortin, Transplantation, 1970

Transplant Activity Worldwide
1968-2014



In the Beginning……

First Advisory Committee of the International Bone Marrow Transplant Registry

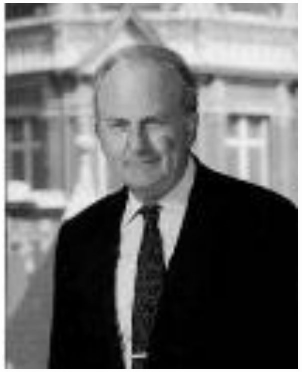

Don Thomas


Dirk van Bekkum


George Mathe


Bob Good

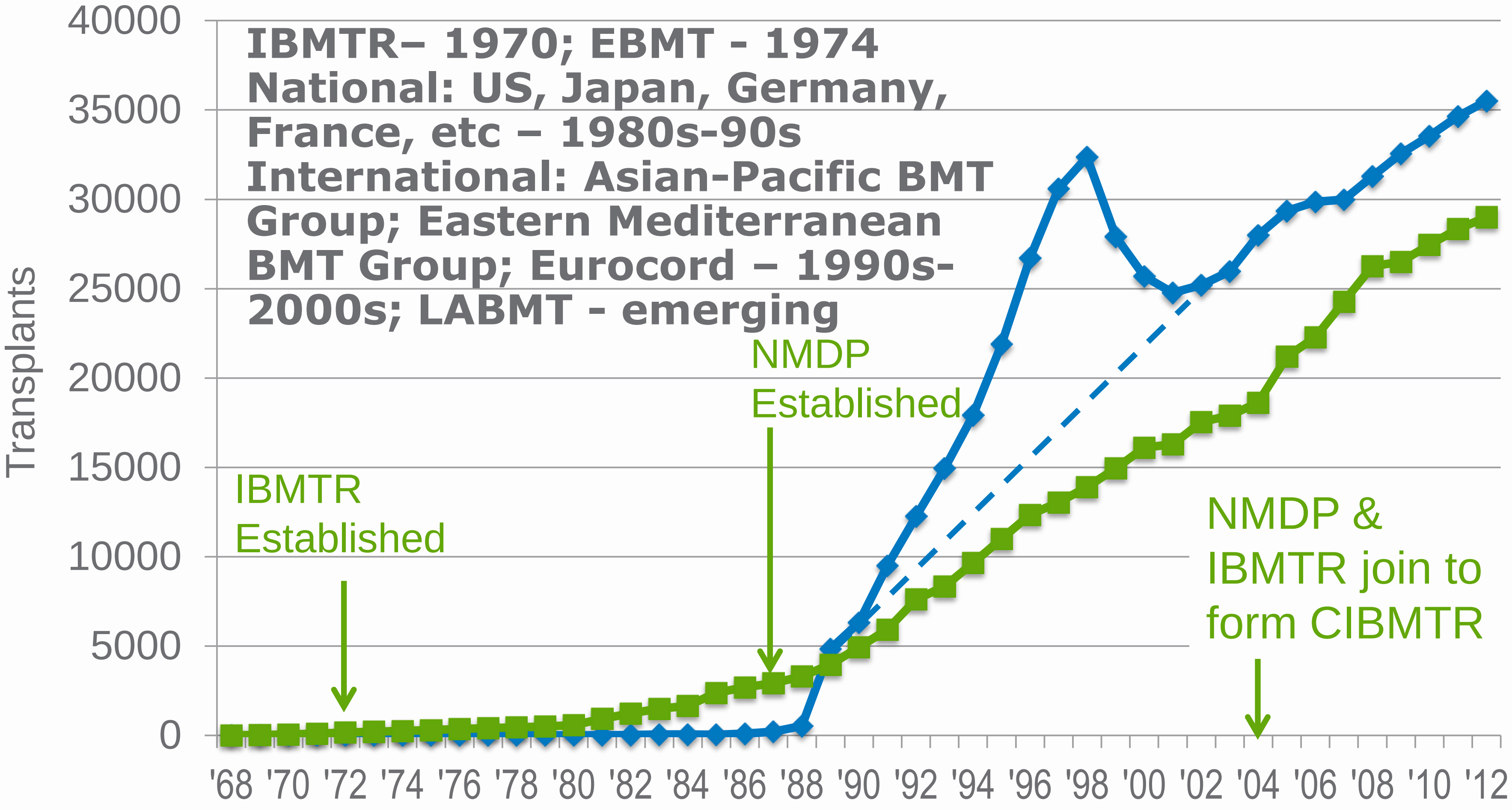

Mort Bortin


George Santos


Fritz Bach

JJ Bergan, JL Fahey,
Bob Levey, GN Rogentine

OUTCOMES REGISTRIES – A Part of the HCT Community Since the "Beginning" and Continuing to Grow



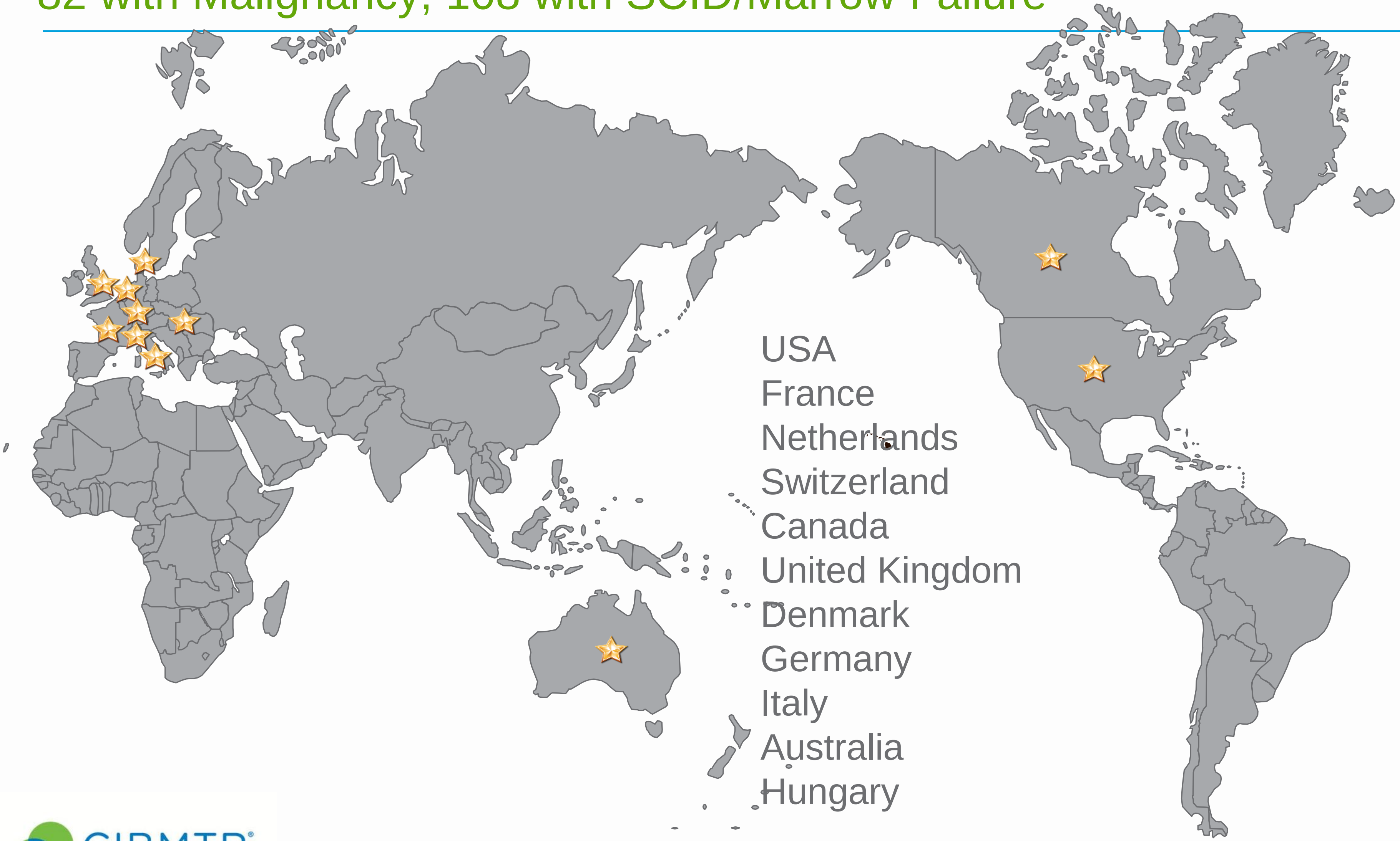
IBMTR– 1970; EBMT - 1974
National: US, Japan, Germany, France, etc – 1980s-90s
International: Asian-Pacific BMT Group; Eastern Mediterranean BMT Group; Eurocord – 1990s-2000s; LABMT - emerging

IBMTR Established

NMDP Established

NMDP & IBMTR join to form CIBMTR

First 200 Patients Reported to IBMTR
1968-73, 11 Countries, 35 Centers
82 with Malignancy; 108 with SCID/Marrow Failure



USA
France
Netherlands
Switzerland
Canada
United Kingdom
Denmark
Germany
Italy
Australia
Hungary

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD
& MARROW TRANSPLANT RESEARCH

International Bone Marrow Transplant Registry - 1985

1970 - 1985

- 200 centers
- 1,000 transplants
- 35 publications

Mortimer M. Bortin, MD
Scientific Director

Al Rimm, PhD
Statistician

D'Etta Waldoch
Sharon Nell
Diane Knudsen
Data Management

Karen Gurgul
Admin. Assistant

Key Contributions

Transplants Can Be Done Safely and Can Cure

- Bortin MM, Rimm AA. ACS-NIH organ transplant registry. 2nd scientific report. JAMA. 1972
- Bortin MM, Buckner CD. Major complications of marrow harvesting for transplantation. Experimental Hematology. 1983

Disease Specific Outcomes

- Bortin MM, Rimm AA. **Severe combined immunodeficiency disease**: characterization of the disease and results of transplantation. Transplantation Proceedings. 1977
- Bortin MM, Rimm AA. Bone marrow transplantation for **acute myeloblastic leukemia**. JAMA. 1978.
- Bortin MM, Rimm AA. Allogeneic bone marrow transplantation for of 144 patients with **severe aplastic anemia**. JAMA. 1981
- Gale RP, Kersey JH, Bortin MM, Dicke KA, Good RA, Zwaan FE, Rimm AA. Bone-marrow transplantation for **acute lymphoblastic leukaemia**. Lancet. 1983.
- Speck B, Bortin MM, Champlin RE, Goldman JM, et al. Allogeneic bone-marrow transplantation for **chronic myelogenous leukaemia**. Lancet. 1984

Key Contributions

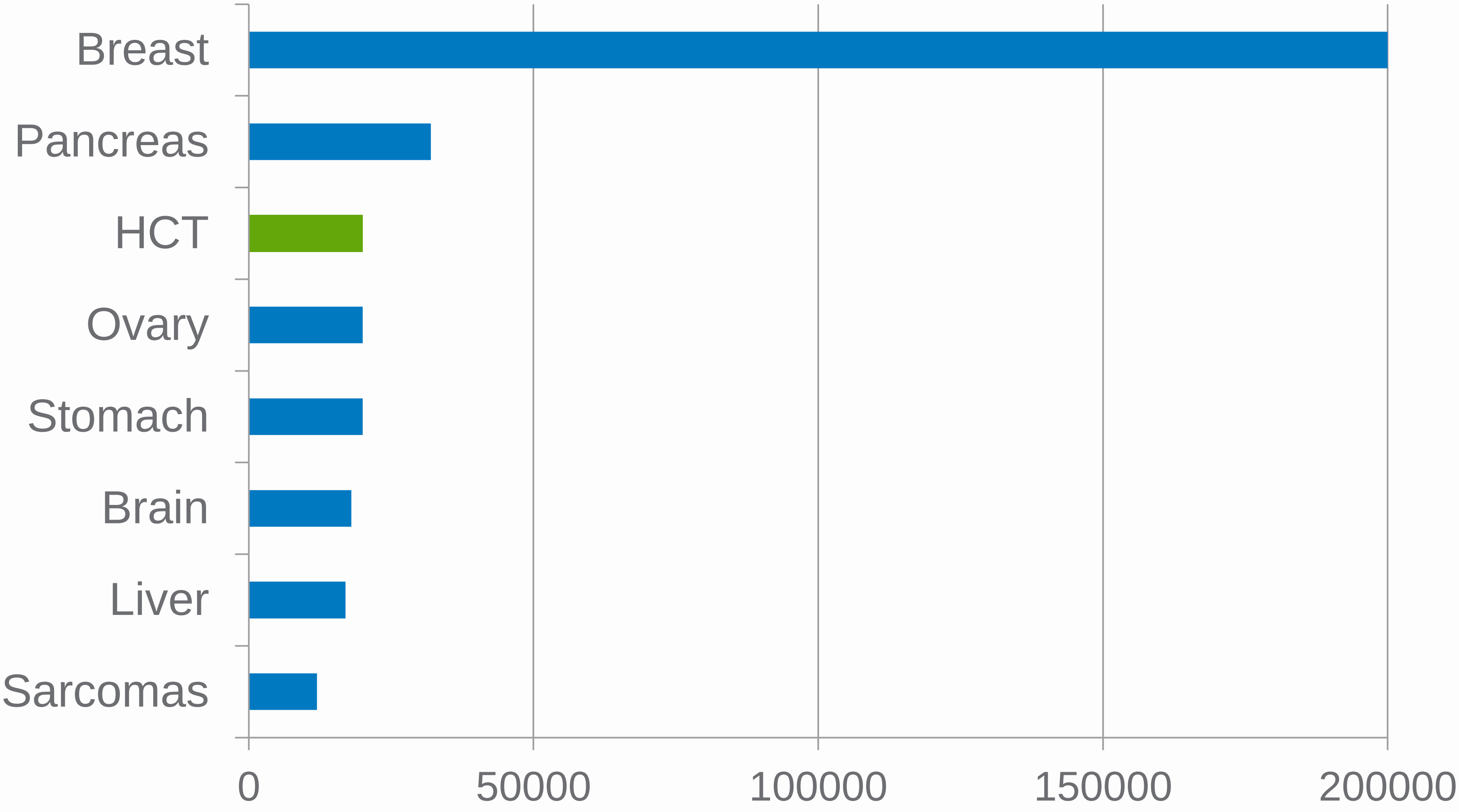
Risk Factors

- Bortin MM, Rimm AA. **Factors influencing success and failure** of human marrow transplantation: a review from the International Bone Marrow Transplant Registry. Experimental Hematology Today. 1979
- Bortin MM, Kay HEM, Gale RP, Rimm AA. **Factors associated with interstitial pneumonitis** after bone-marrow transplantation for acute leukaemia. Lancet. 1982
- Bortin MM, Gale RP, Kay HEM, Rimm AA. Bone marrow transplantation for acute myelogenous leukemia. **Factors associated with early mortality**. JAMA. 1983

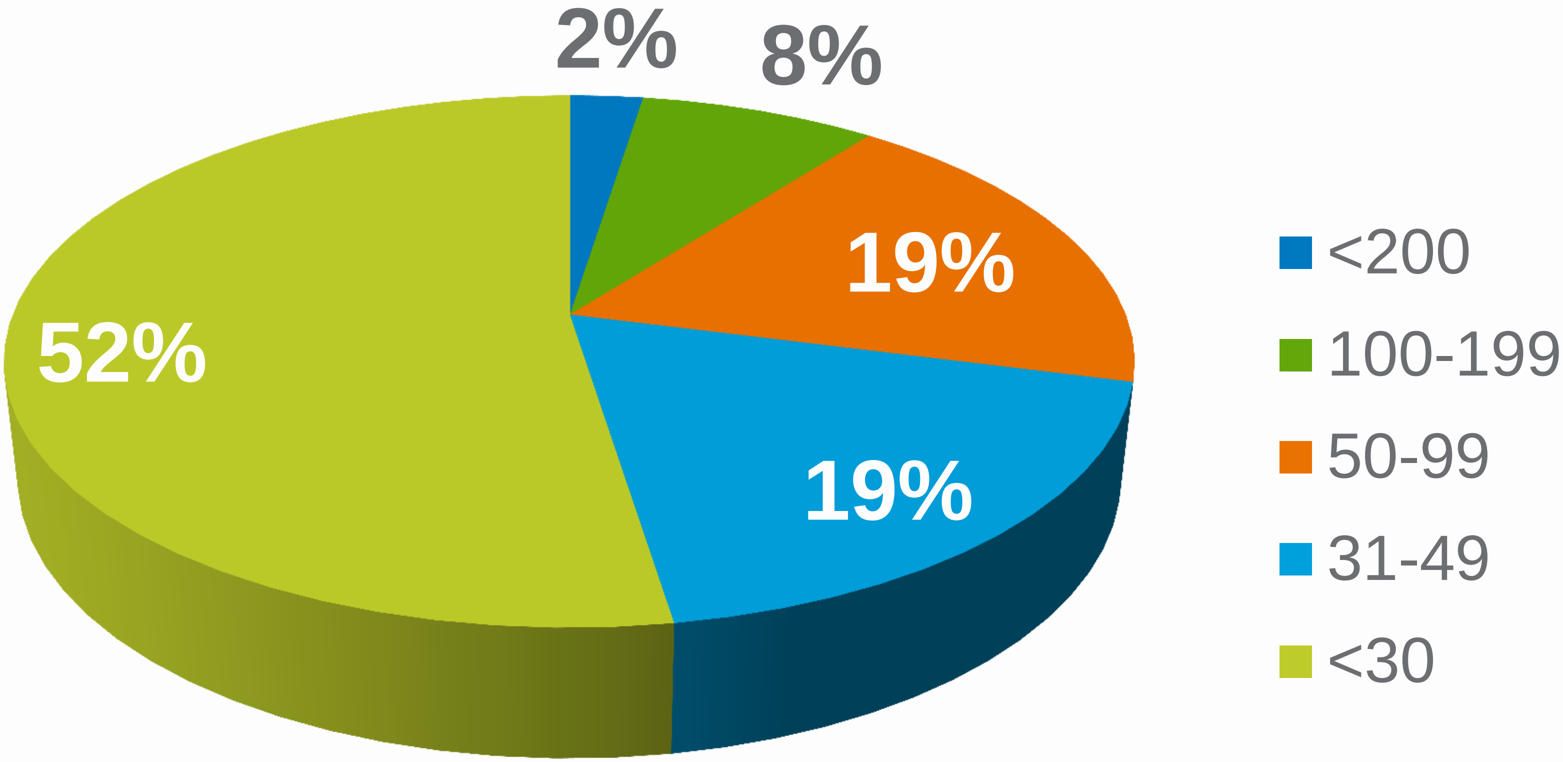
HLA Associations

- Rimm AA, Bortin MM. **HLA antigens and SCID**. Lancet. 1977
- D'Amaro JD, van Rood JJ, Rimm AA, Bortin MM. **HLA associations in Italian and non-Italian Caucasoid aplastic anaemia patients**. Tissue Antigens. 1983
- D'Amaro JD, van Rood JJ, Bach FH, Rimm AA, Bortin MM. **HLA C associations with acute leukaemia**. Lancet. 1984

Why are Large Registries Still Necessary? SMALL NUMBERS
Annual Numbers of HCTs vs Numbers of Selected Cancers in the US

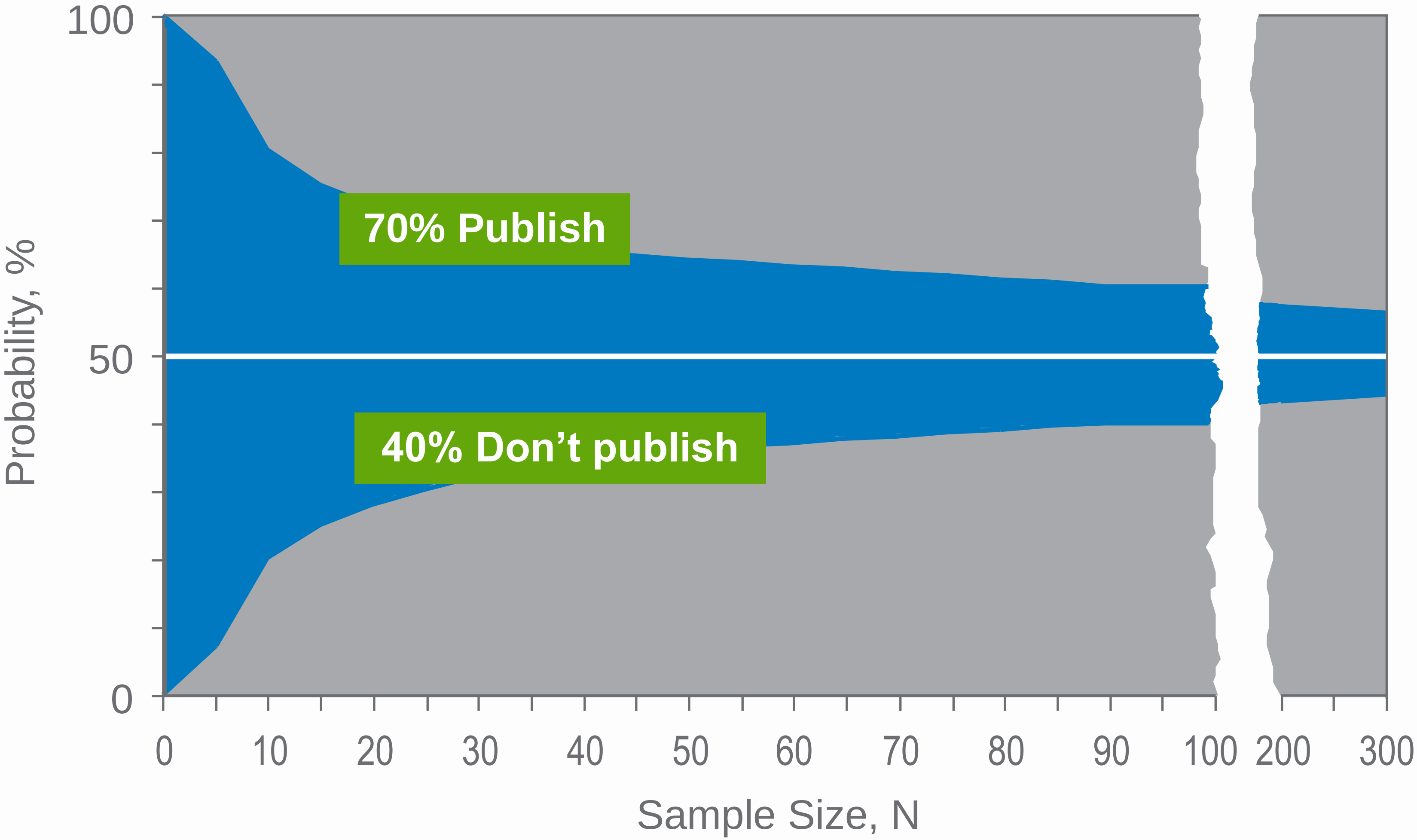


Distribution of Allotransplant Volumes Among 162 US Centers Reporting Data to CIBMTR in 2012



Individual transplant centers treat relatively few patients and these patients are heterogeneous in many factors that affect outcomes

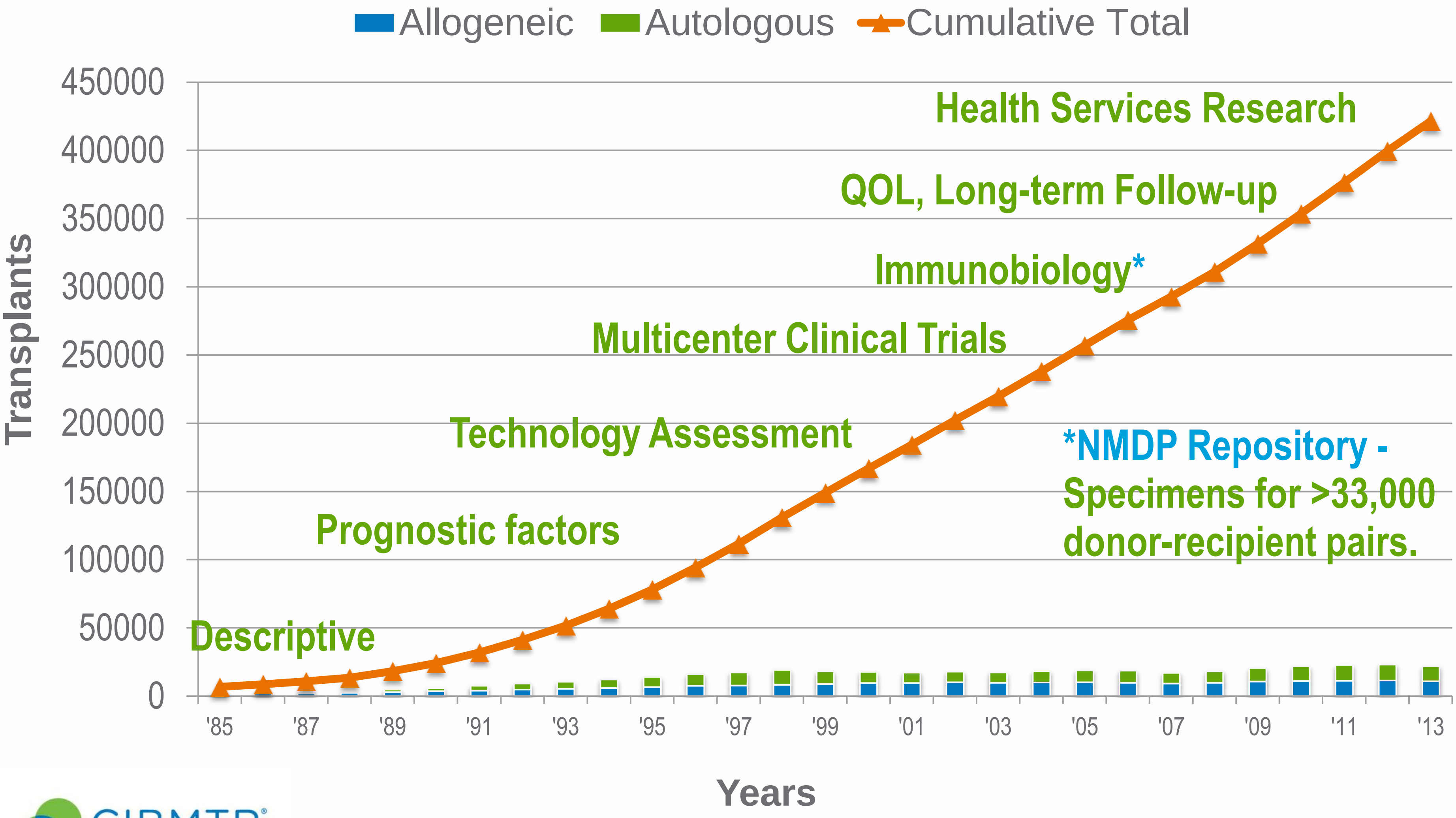
95% Confidence Intervals for Samples Drawn from a Population Receiving a Treatment Producing 50% Survival



70% Publish

40% Don’t publish

CIBMTR 420,000 Cases Registered, 1985-2013 > 900 Publications



Health Services Research

QOL, Long-term Follow-up

Immunobiology*

Multicenter Clinical Trials

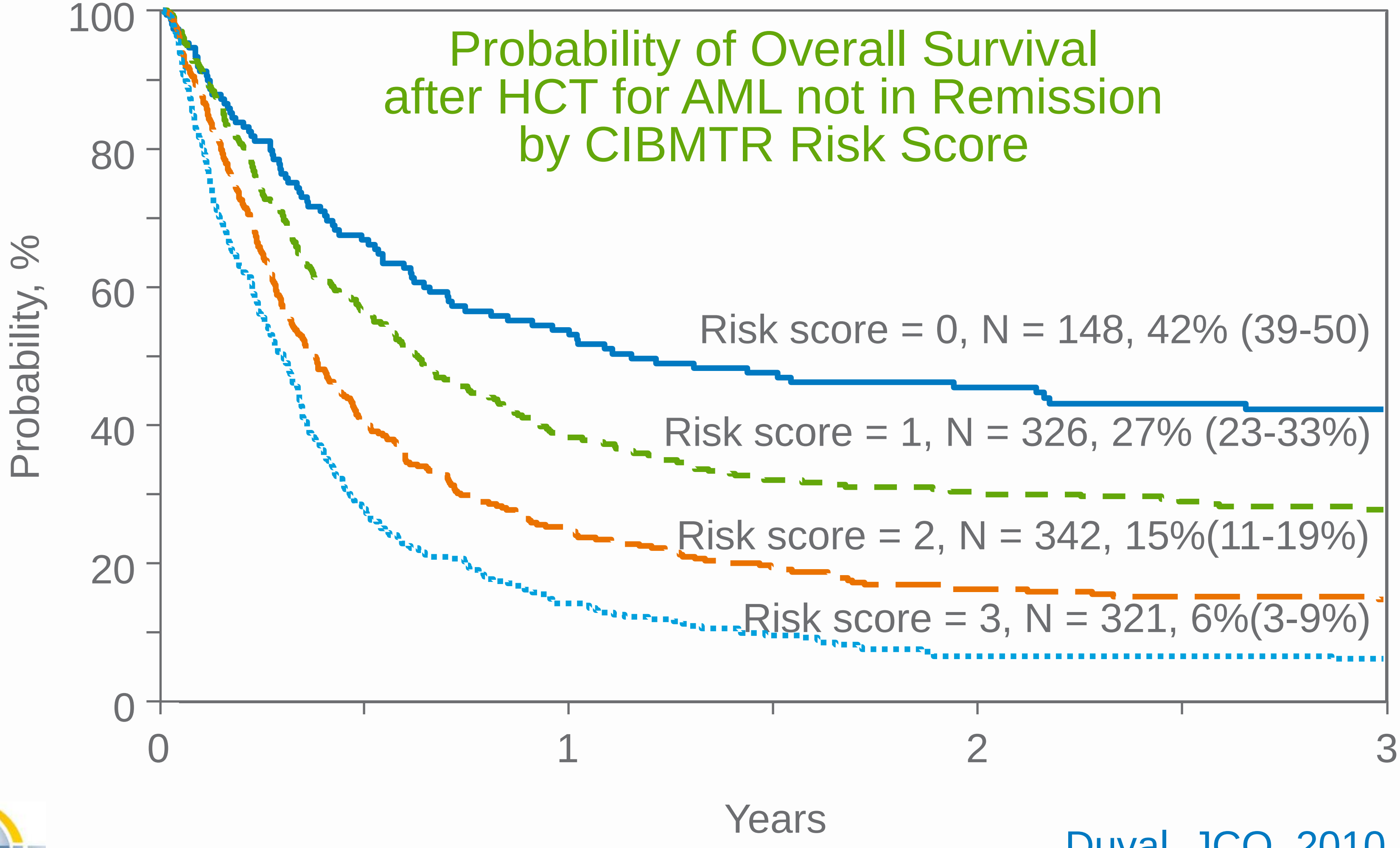
Technology Assessment

Prognostic factors

Descriptive

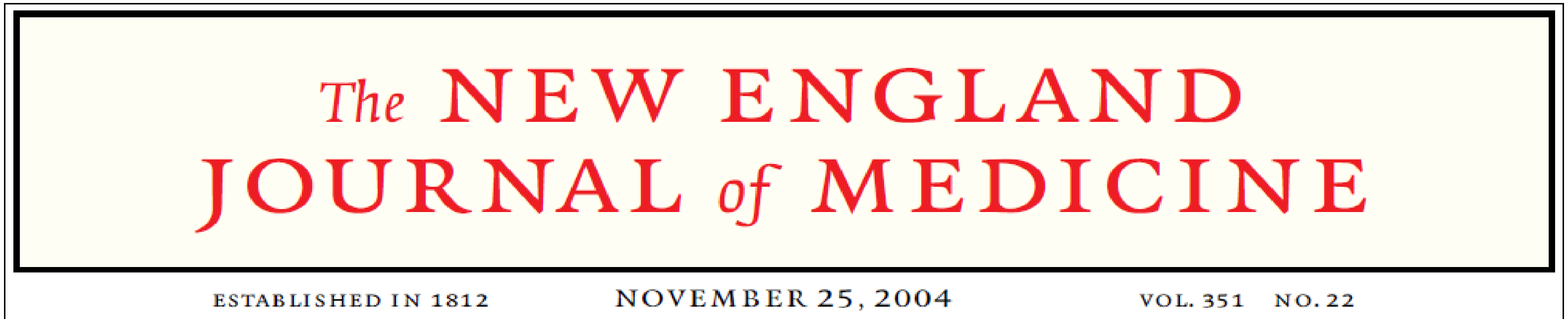
***NMDP Repository - Specimens for >33,000 donor-recipient pairs.**

The Value of Outcome Registries: Identifying patients most likely to benefit from BMT



Duval, JCO, 2010

The Value of Outcomes Registries: Evaluating Graft Sources



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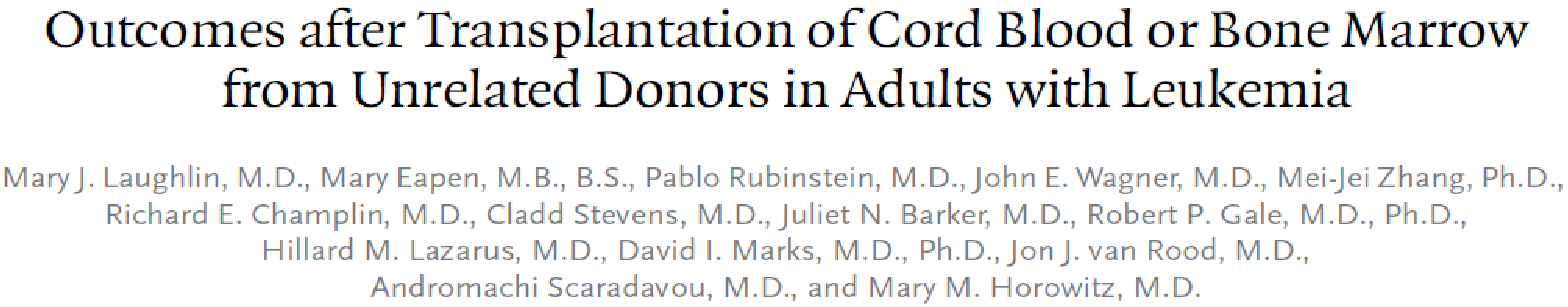
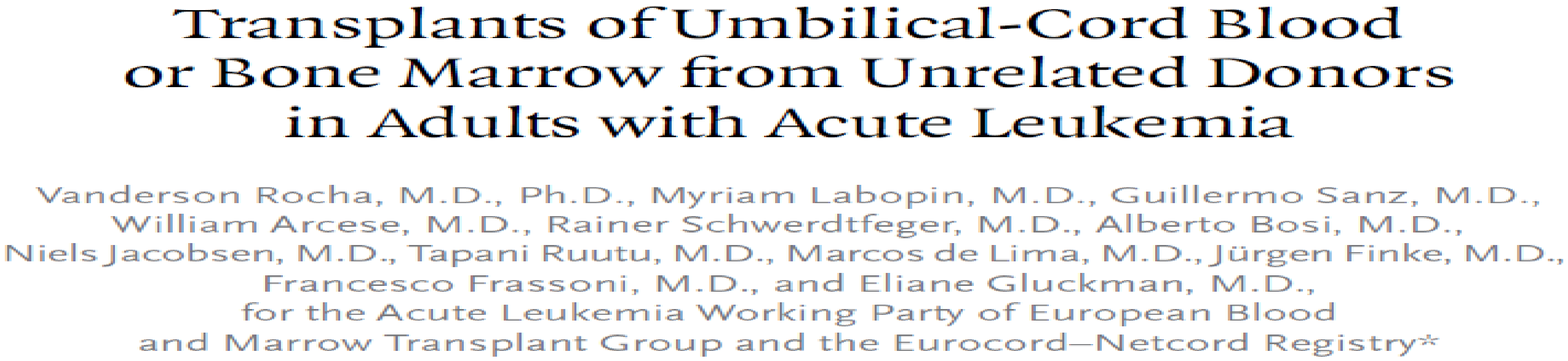
ESTABLISHED IN 1812 NOVEMBER 25, 2004 VOL. 351 NO. 22



Outcomes after Transplantation of Cord Blood or Bone Marrow from Unrelated Donors in Adults with Leukemia

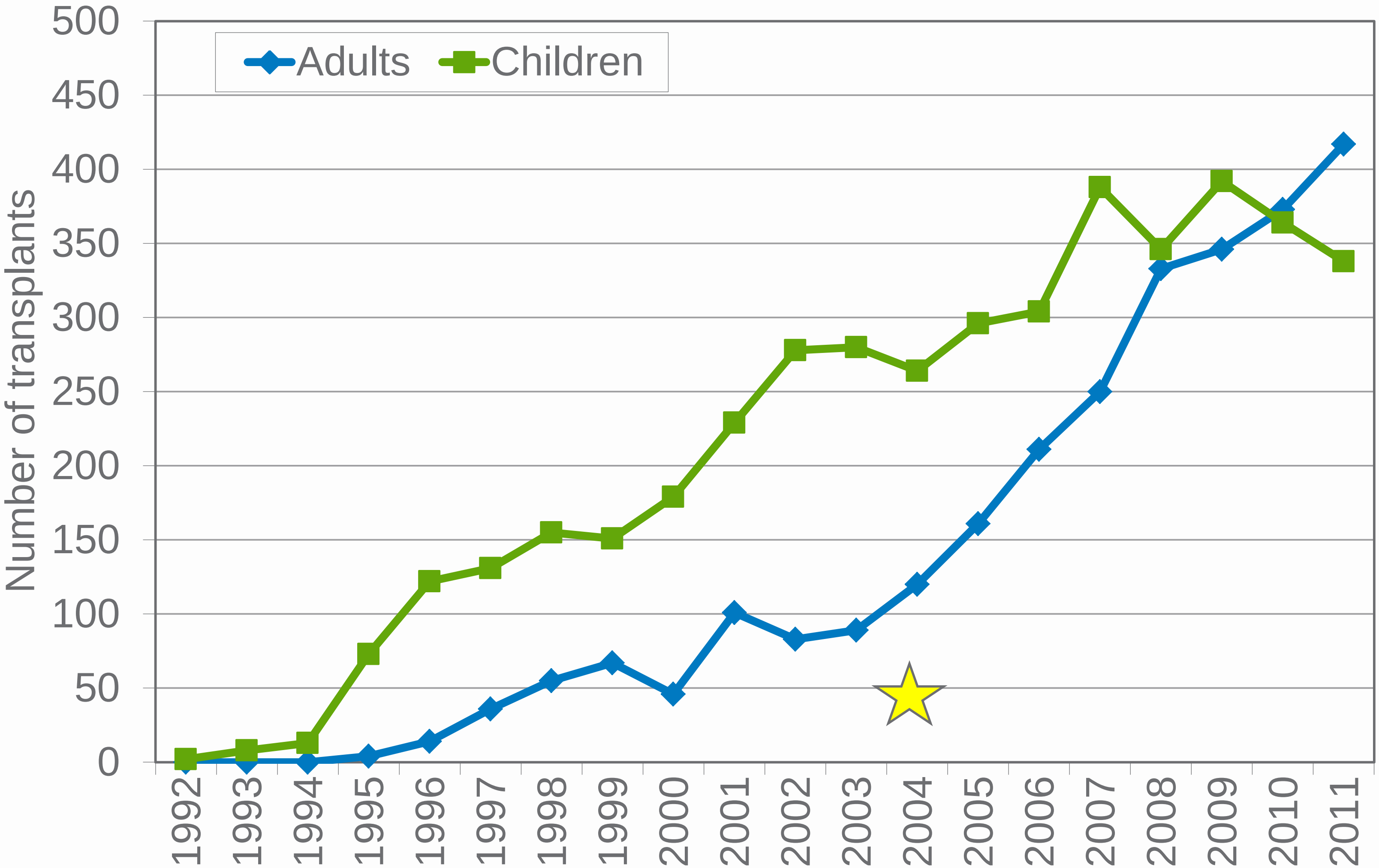
Mary J. Laughlin, M.D., Mary Eapen, M.B., B.S., Pablo Rubinstein, M.D., John E. Wagner, M.D., Mei-Jei Zhang, Ph.D.,
Richard E. Champlin, M.D., Cladd Stevens, M.D., Juliet N. Barker, M.D., Robert P. Gale, M.D., Ph.D.,
Hillard M. Lazarus, M.D., David I. Marks, M.D., Ph.D., Jon J. van Rood, M.D.,
Andromachi Scaradavou, M.D., and Mary M. Horowitz, M.D.



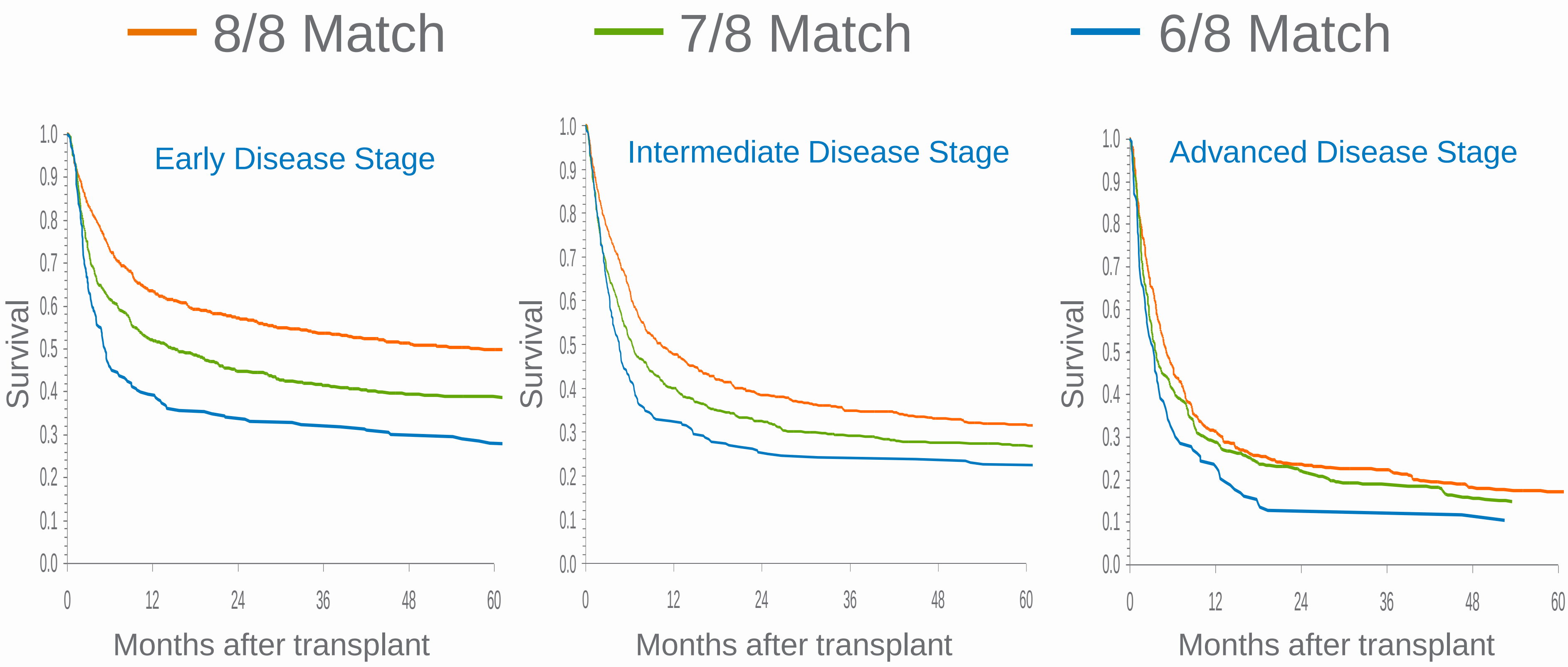
Transplants of Umbilical-Cord Blood or Bone Marrow from Unrelated Donors in Adults with Acute Leukemia

Vanderson Rocha, M.D., Ph.D., Myriam Labopin, M.D., Guillermo Sanz, M.D.,
William Arcese, M.D., Rainer Schwerdtfeger, M.D., Alberto Bosi, M.D.,
Niels Jacobsen, M.D., Tapani Ruutu, M.D., Marcos de Lima, M.D., Jürgen Finke, M.D.,
Francesco Frassoni, M.D., and Eliane Gluckman, M.D.,
for the Acute Leukemia Working Party of European Blood
and Marrow Transplant Group and the Eurocord–Netcord Registry*

The Value of Outcomes Registries: Changing Practice - US Cord Blood Transplants, 1990-2011



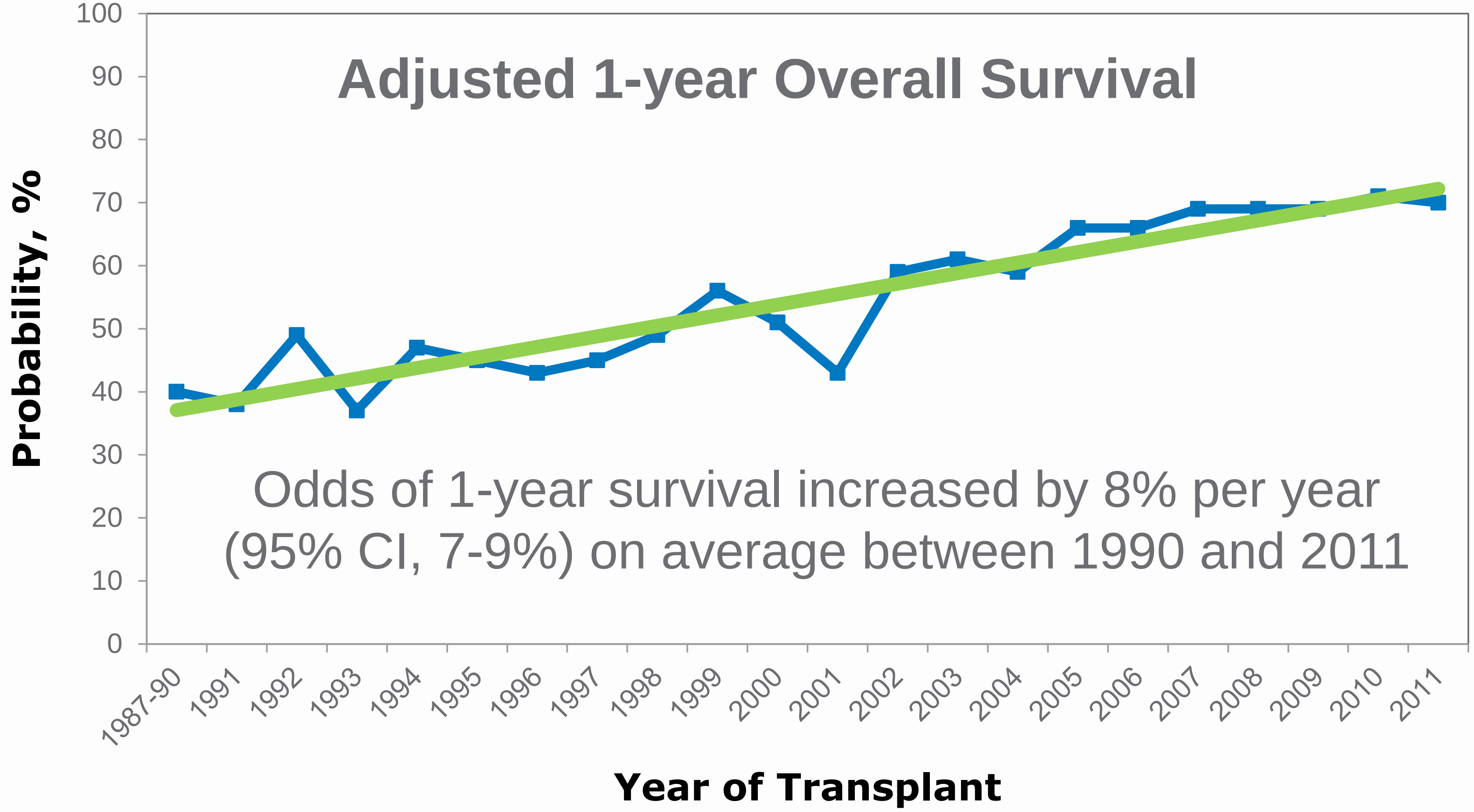
The Value of Outcome Registries: Understanding the Influence of HLA



S. Lee, et al. Blood 2007 Showed impact of single allele mismatch at A, B, C and DRB1: *changed the paradigm for selecting adult donors*

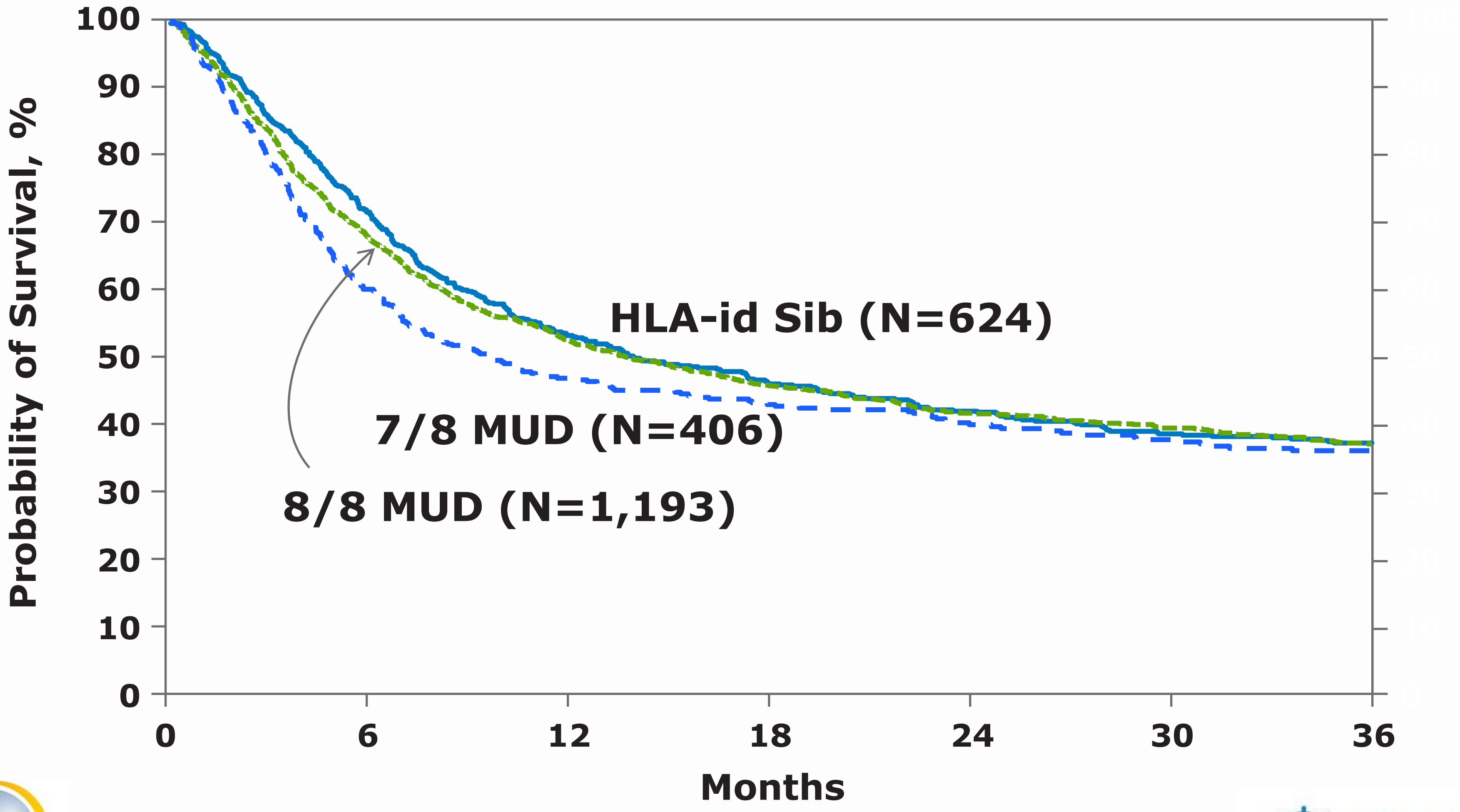
Survival After Unrelated Donor Transplantation

Age <50 years, myeloablative conditioning, acute leukemia in remission or MDS

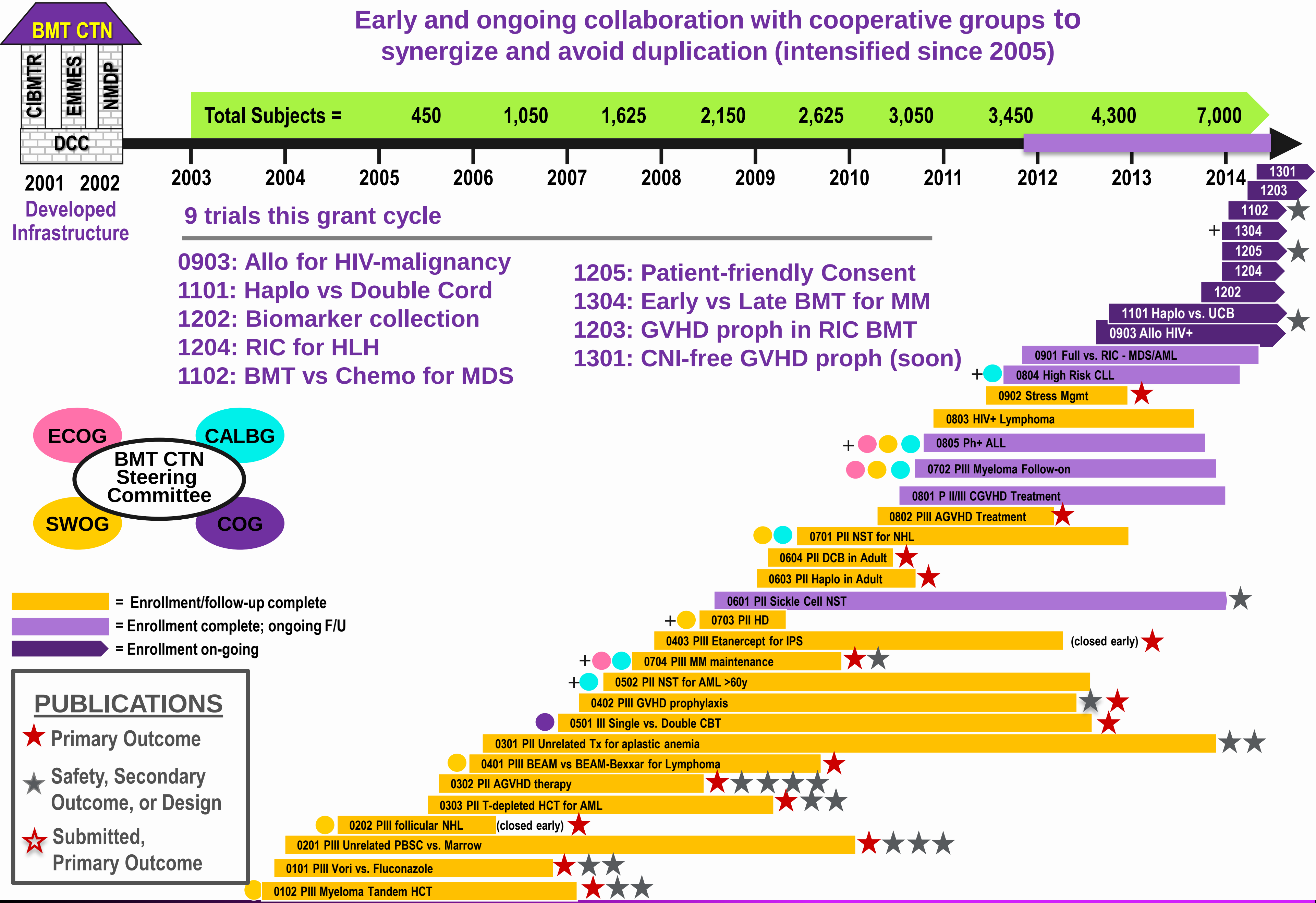


Odds of 1-year survival increased by 8% per year (95% CI, 7-9%) on average between 1990 and 2011

Adjusted Probability of Survival After Transplantation for AML, 2002-2006



Early and ongoing collaboration with cooperative groups to synergize and avoid duplication (intensified since 2005)



9 trials this grant cycle

0903: Allo for HIV-malignancy
1101: Haplo vs Double Cord
1202: Biomarker collection
1204: RIC for HLH
1102: BMT vs Chemo for MDS

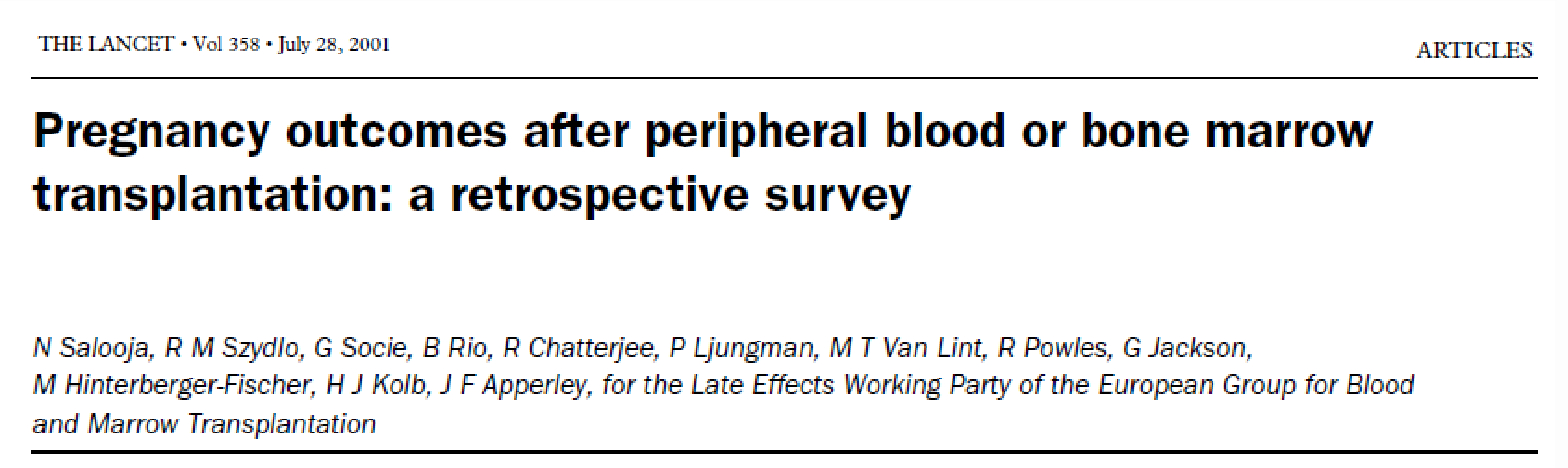
1205: Patient-friendly Consent
1304: Early vs Late BMT for MM
1203: GVHD proph in RIC BMT
1301: CNI-free GVHD proph (soon)

🟨 = Enrollment/follow-up complete
🟪 = Enrollment complete; ongoing F/U
▶ = Enrollment on-going

PUBLICATIONS

★ Primary Outcome
★ Safety, Secondary Outcome, or Design
☆ Submitted, Primary Outcome

The Value of Global Outcome Registries: Understanding Late Effects



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ARTICLES

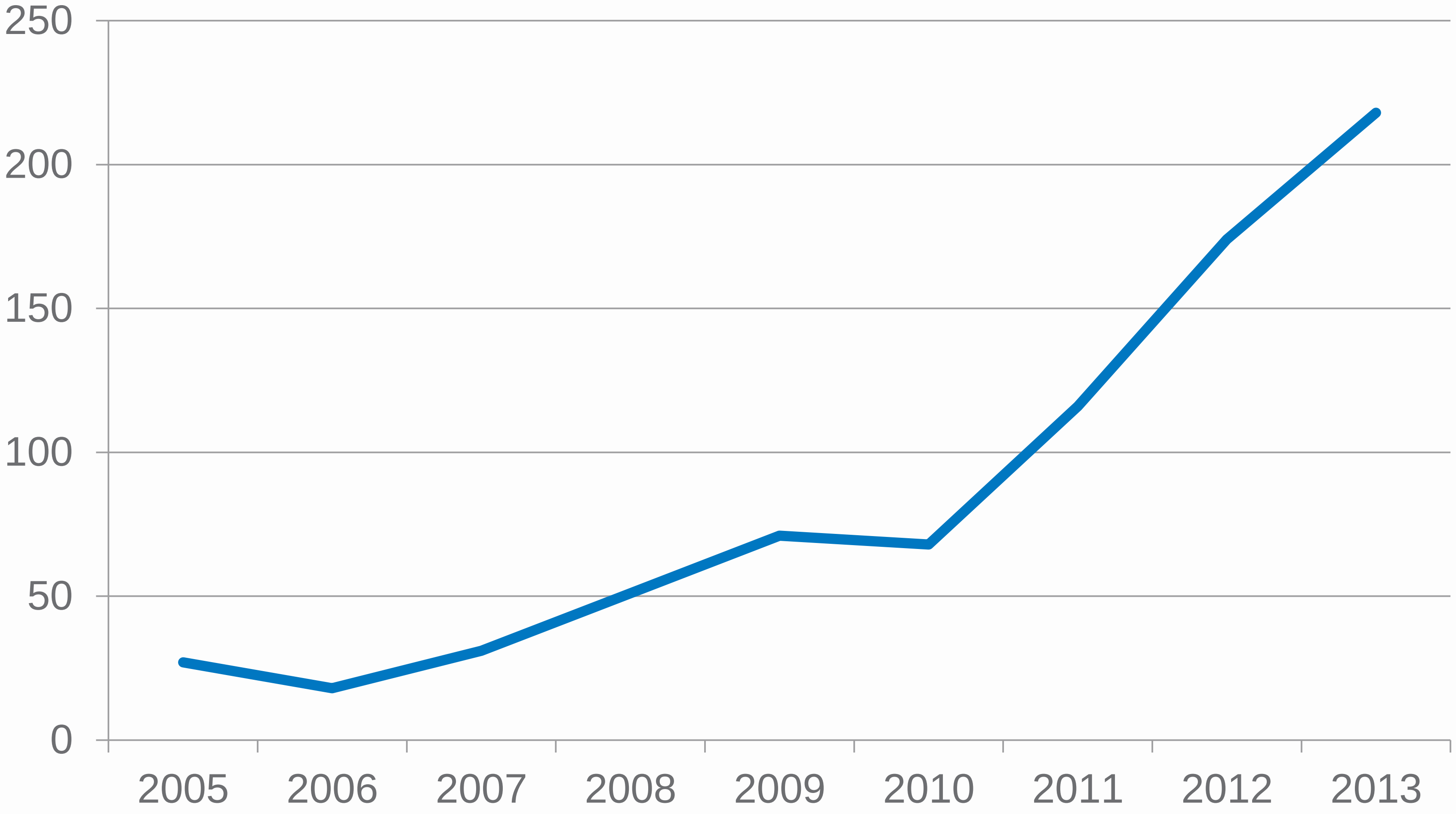
Pregnancy outcomes after peripheral blood or bone marrow transplantation: a retrospective survey

N Salooja, R M Szydlo, G Socie, B Rio, R Chatterjee, P Ljungman, M T Van Lint, R Powles, G Jackson, M Hinterberger-Fischer, H J Kolb, J F Apperley, for the Late Effects Working Party of the European Group for Blood and Marrow Transplantation

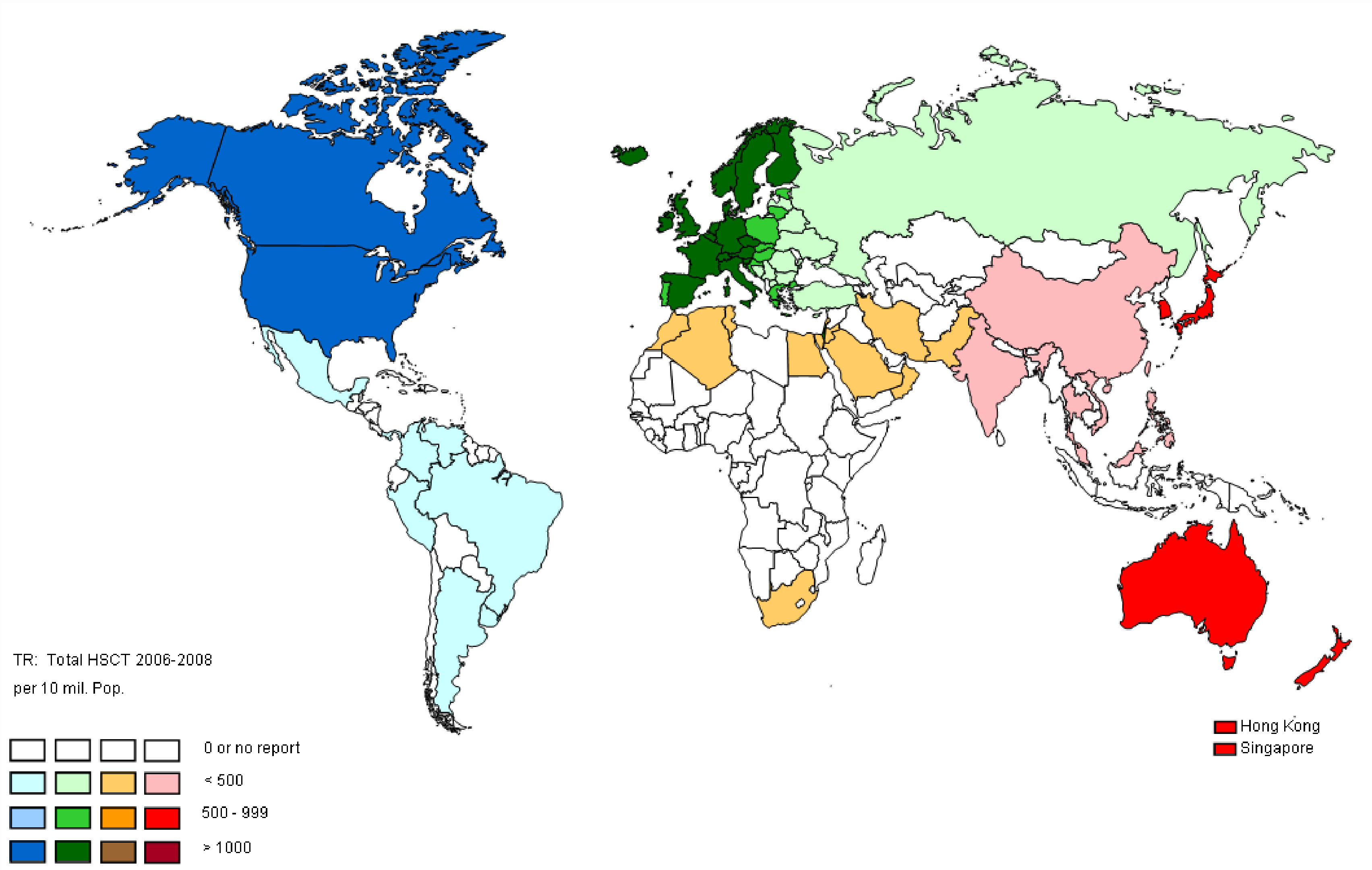
The Value of Outcome Registries: Influencing National Public Policy

- Most US patients 65+ years have health insurance through Medicare *which did not cover BMT for MDS*
- August 2010: Medicare, in part because of existing CIBMTR data, decided it would cover costs of BMT but ONLY if patients enrolled in an IRB-approved study that will provide CMS with data to determine the value of the procedure in the Medicare population
- CIBMTR used its infrastructure to open a study using EXISTING data collection mechanisms (minimal additional work of transplant centers)

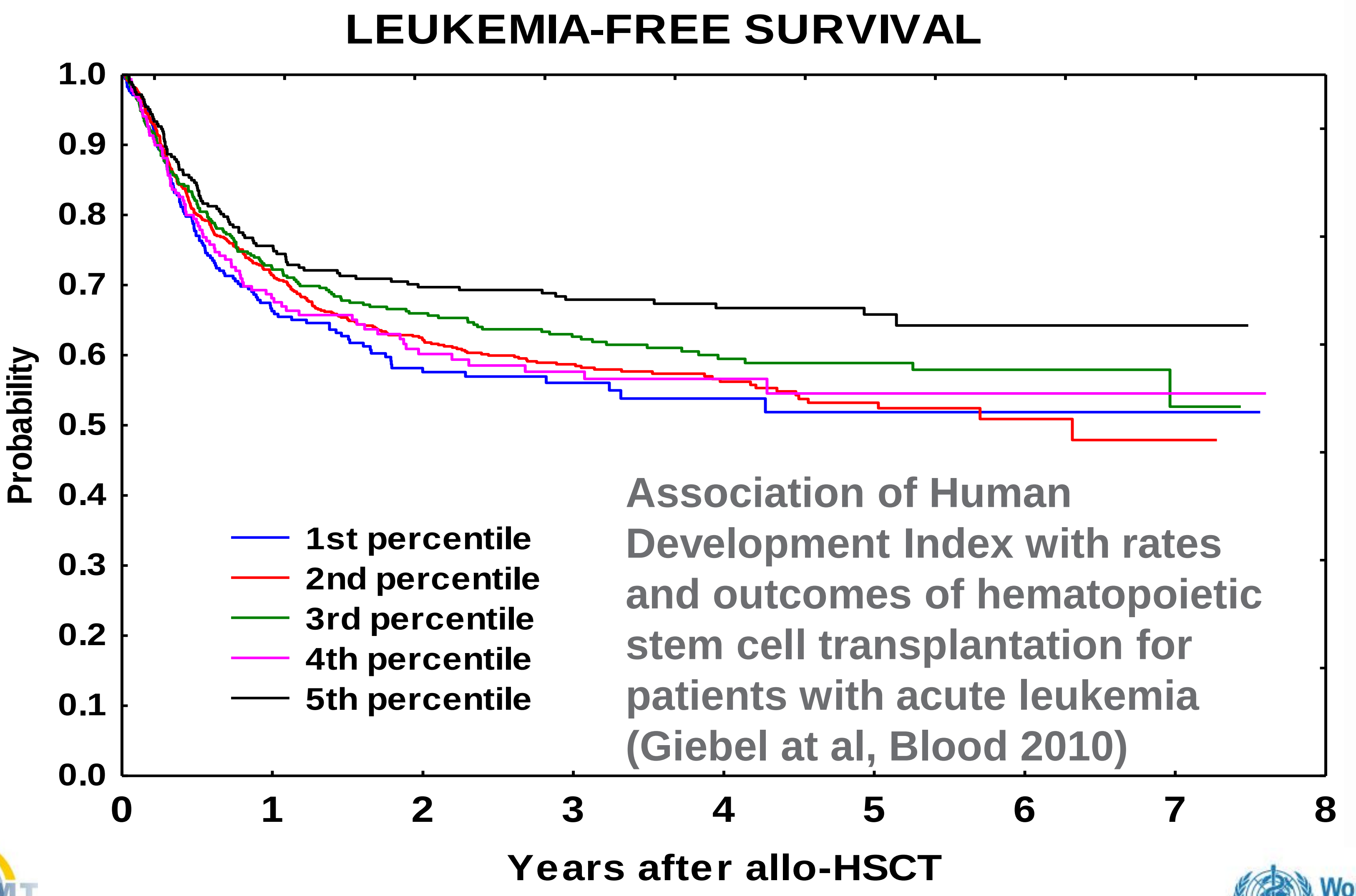
US Allogeneic Transplants for MDS in patients older than 65, 2005 - 2013



The Value of Global Outcome Registries: Understanding Trends in Use, Practice and Outcomes



The Value of Global Outcomes Registries: Understanding Macro-Economic Influences on Survival Globally



Association of Human Development Index with rates and outcomes of hematopoietic stem cell transplantation for patients with acute leukemia (Giebel at al, Blood 2010)

Why Should a Registry be Considered When BMT is Just Developing in a Country or a Region?

Because to Develop a Therapy Effectively, We Need DATA

- Assessment – identify the most important problems and most promising solutions
- Analysis - determine efficacy – overall and for specific subgroups/regions; monitor long-term outcomes
- Advancing best practices - Optimize treatment strategies/improve outcome in the real world with real resource constraints
- Allocation of resources – research and clinical care

Data Are Needed:

- At the center level
  - Quality improvement
  - Understanding costs and resource needs (and making the case for them to hospital and local authorities)
  - Scientific study
- At the national level
  - Understanding access, costs and resource needs (and making the case for them)
  - To advance best practices

Data Are Needed:

- At the regional level
  - Facilitate research relevant to regional issues
  - The process of sharing data also creates opportunities for professional, educational and scientific collaboration in a community that faces similar challenges and affords the potential for sharing expertise and resources
- At the global level
  - To understand differences and commonalities in access, practice and outcomes
  - To advance the science and practice of HCT
  - To communicate with regulatory and funding bodies about needs

It is Important to Incorporate Careful Data Collection and Analysis Early

- Because building a culture of evaluating and understanding outcomes is critical for
  - effective quality management systems to improve patient care
  - building an effective clinical research infrastructure to improve patient care
- When numbers of transplants in individual centers and countries are small, sharing data allows examination of important issues with greater power

An African Registry Could Offer Some Unique Contributions to Global Understanding of BMT

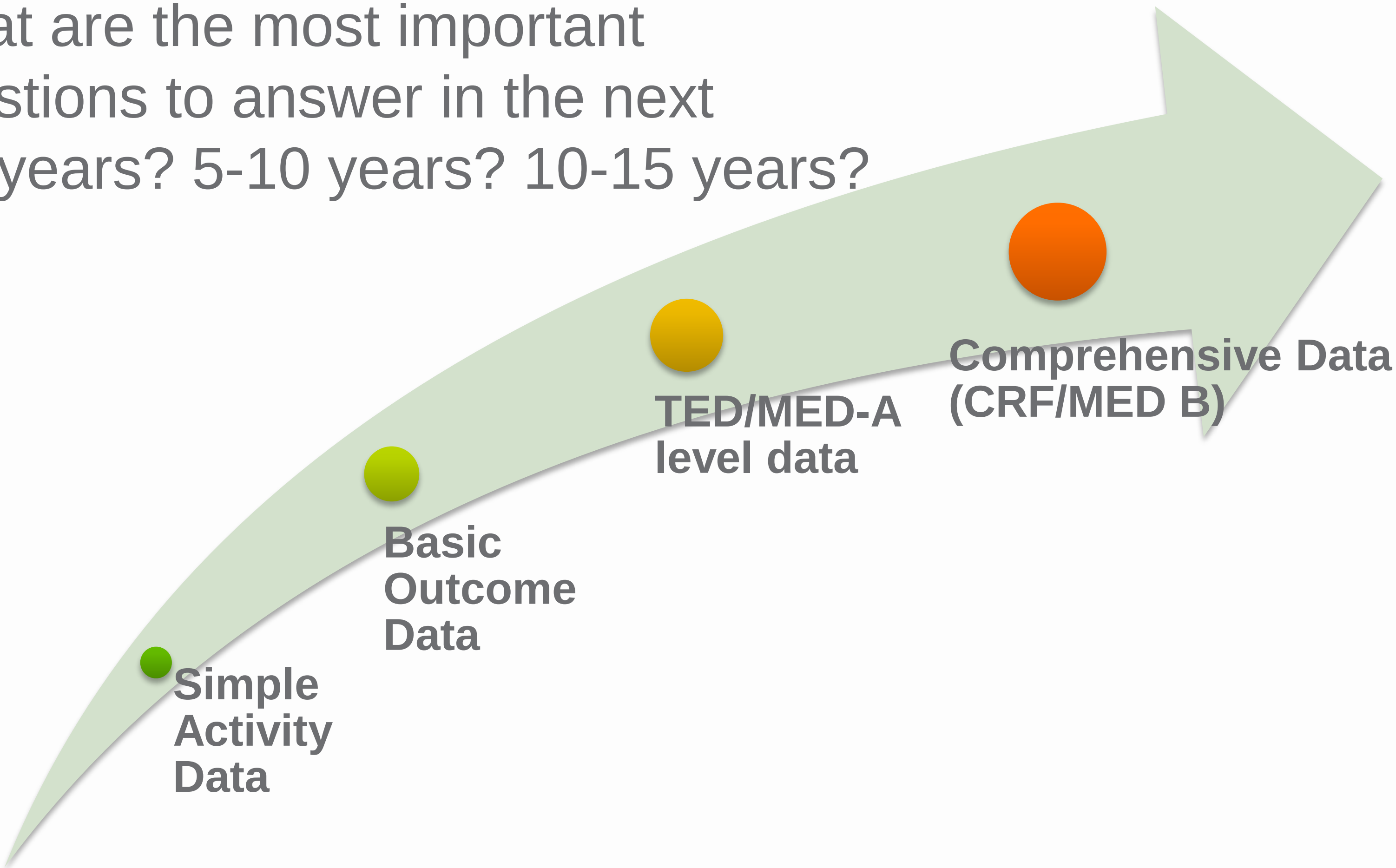
- High prevalence of non-malignant hematopoietic disorders
  - Development and evaluation of regimens that ensure engraftment and minimize GVHD
  - Studies of BMT vs non-BMT therapy; HLA-id sib vs haplo or other alternative graft sources
- Extremely diverse distribution of HLA and other genetic determinants of outcomes – insight into permissive vs non-permissive matches/variations
- Examination of cost-effective approaches to both autologous and allogeneic BMT

WBMT
worldwide network for blood and marrow transplantation
WWW.WBMT.ORG

World Health Organization

Levels of Data Collection

Start small but plan for growth:
What are the most important questions to answer in the next 3-5 years? 5-10 years? 10-15 years?



Simple Activity Data

Basic Outcome Data

TED/MED-A level data

Comprehensive Data (CRF/MED B)

Thank You

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If you want to go fast, go alone; if you want to go far, go with others.