The Value of Outcomes Databases: Collaboration for Clinical Research in Blood and Marrow Transplantation

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January 2017

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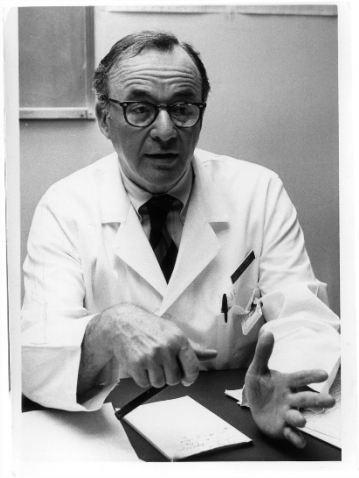
A research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin

A Little History…….



Bortin, Transplantation, 1970

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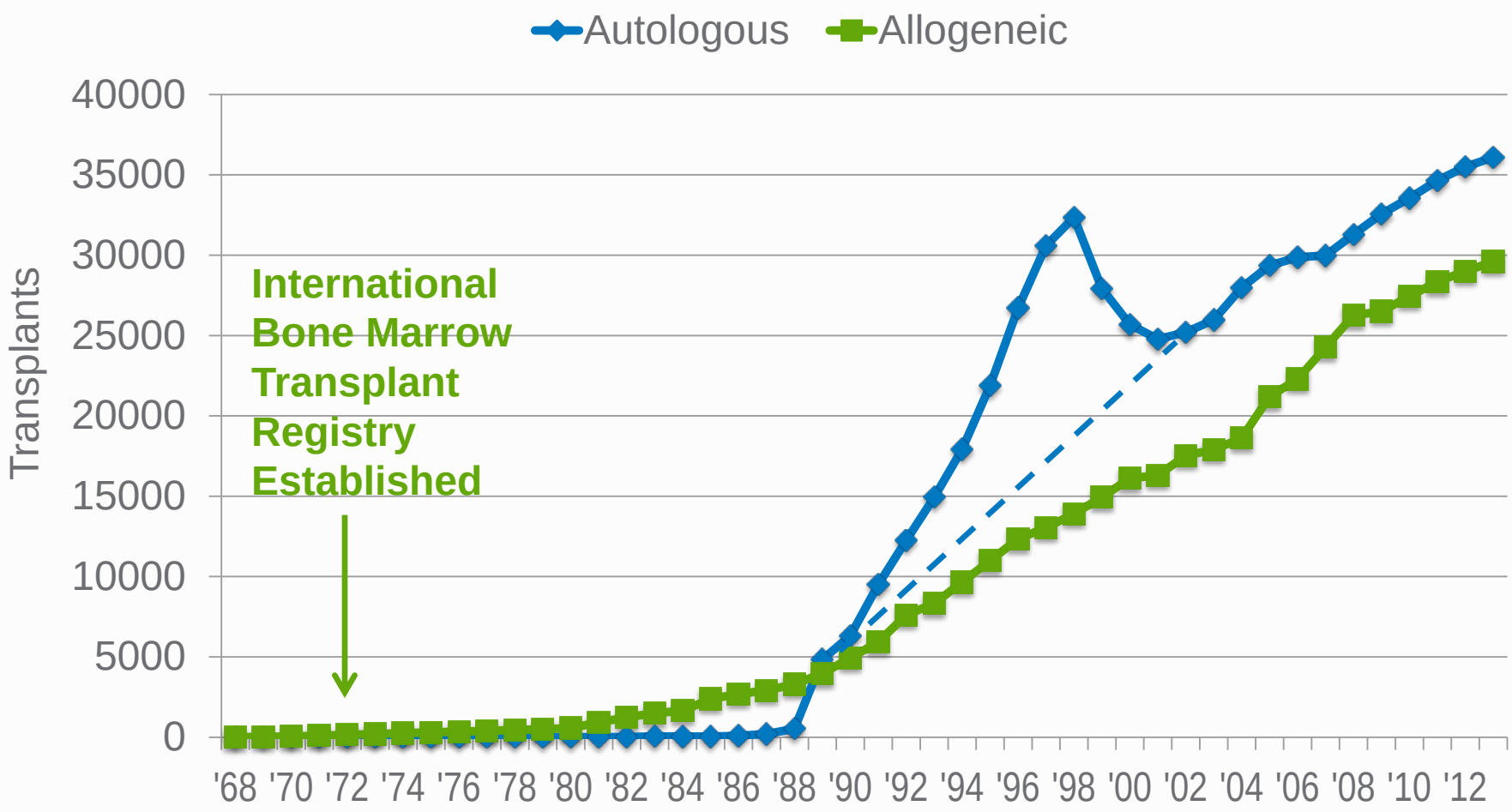
Transplant Activity Worldwide 1968-2014



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In the Beginning……

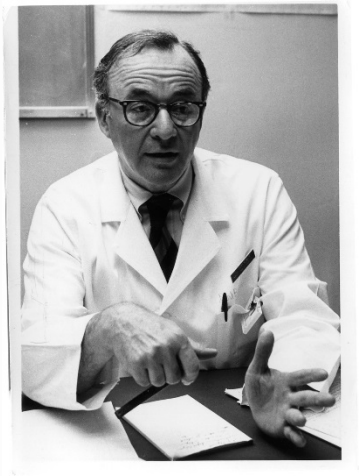
Don Thomas

First Advisory Committee of the International Bone Marrow Transplant Registry

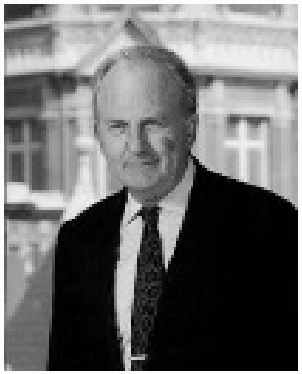
Dirk van Bekkum

George Mathe

Bob Good

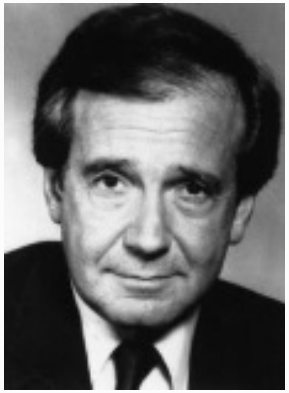


Mort Bortin



George Santos

JJ Bergan, JL Fahey,
Bob Levey, GN Rogentine



Fritz Bach

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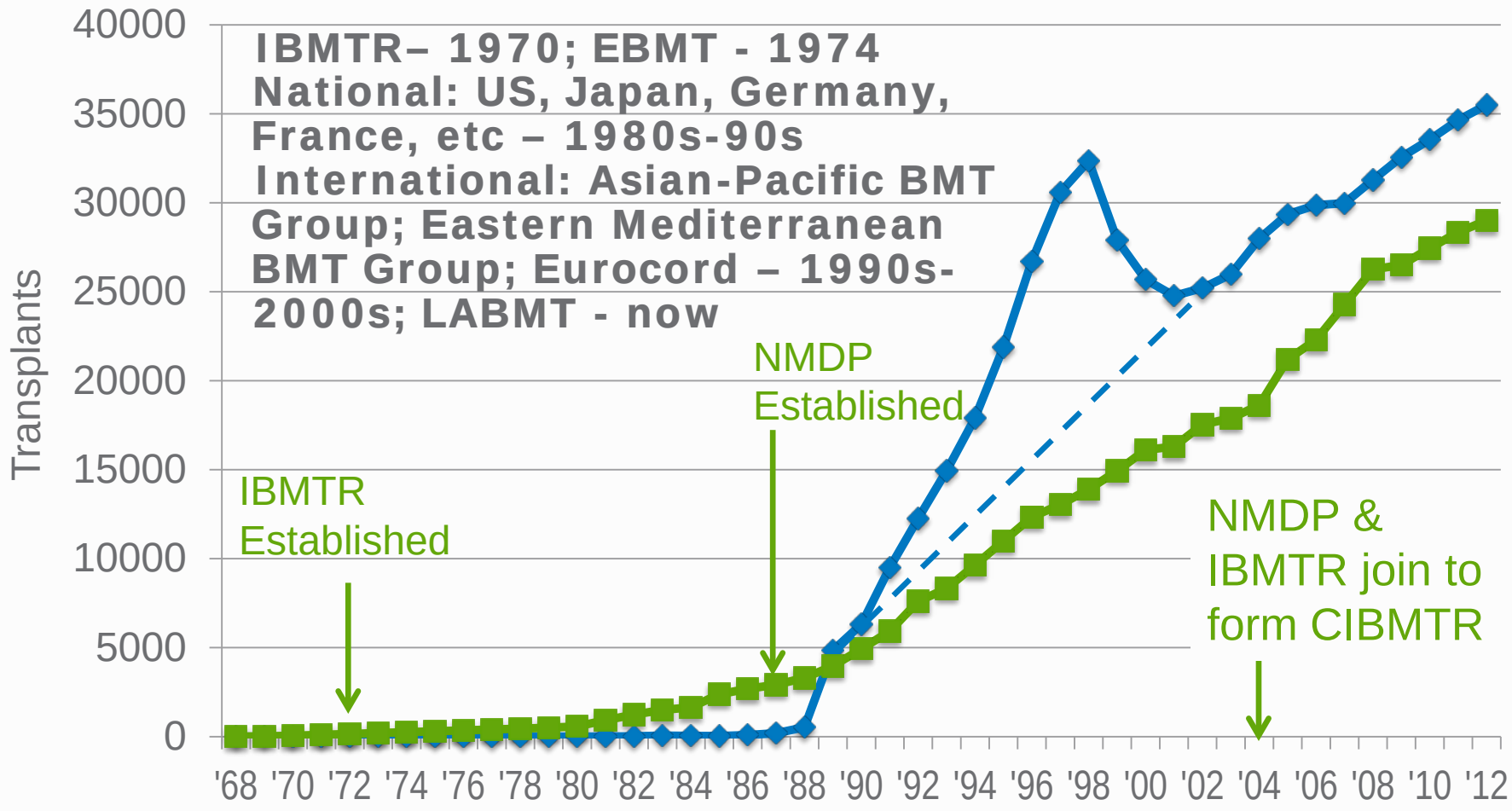
OUTCOMES REGISTRIES – A Part of the HCT Community Since the "Beginning" and Continuing to Grow



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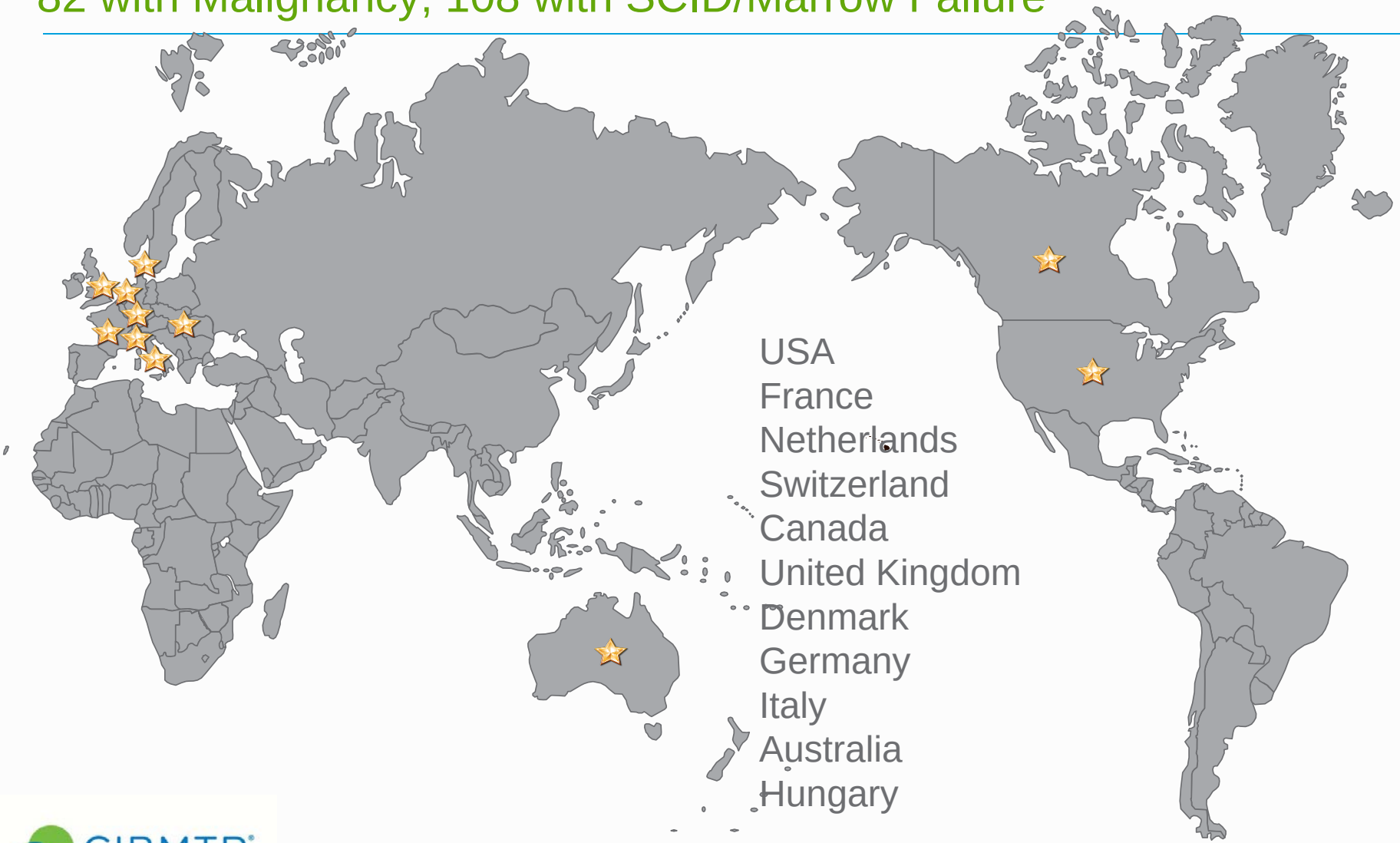
First 200 Patients Reported to IBMTR
1968-73, 11 Countries, 35 Centers
82 with Malignancy; 108 with SCID/Marrow Failure



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IBMTR – 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

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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

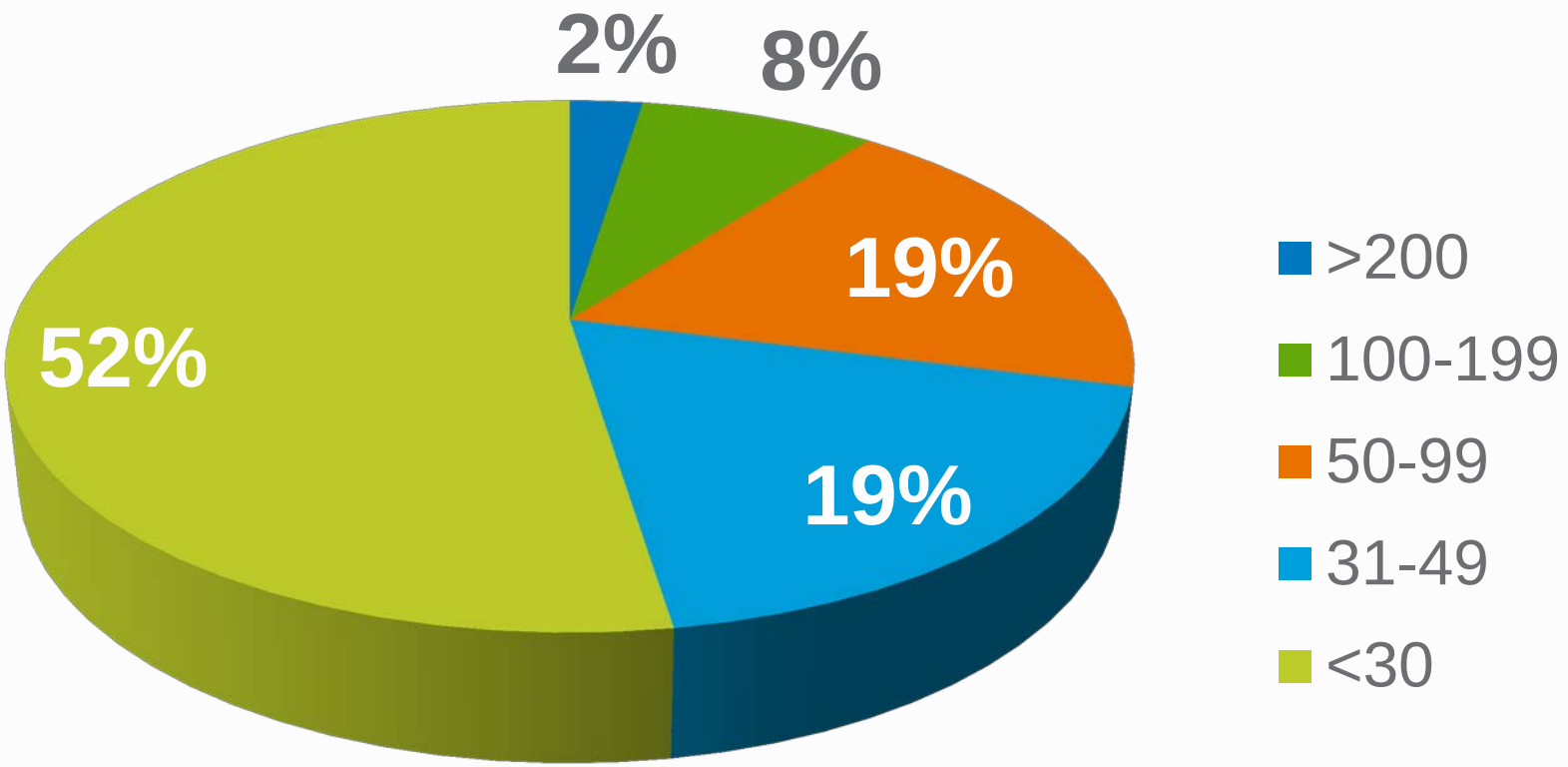
Risk Factors

- 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

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

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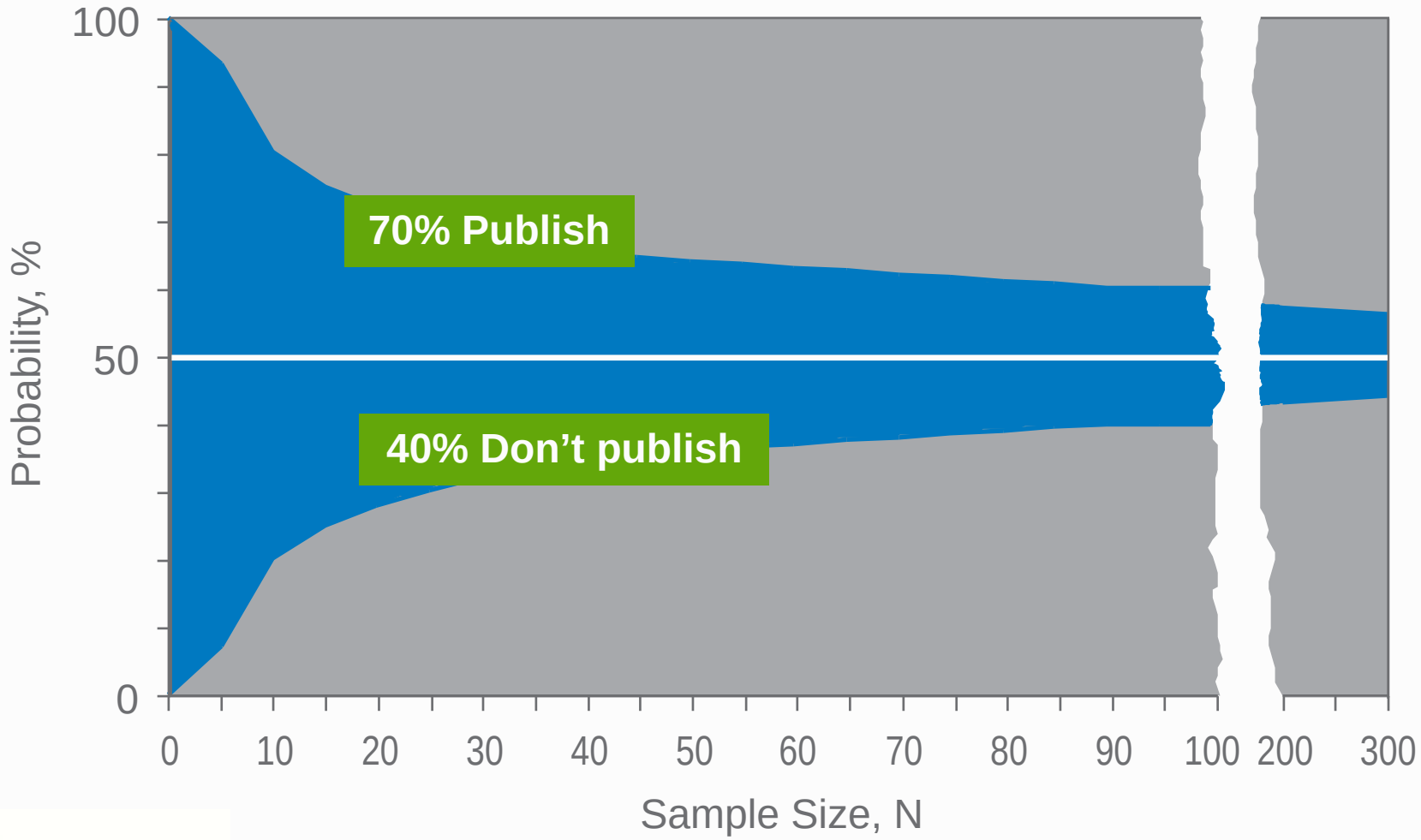
95% Confidence Intervals for Samples Drawn from a Population Receiving a Treatment Producing 50% Survival



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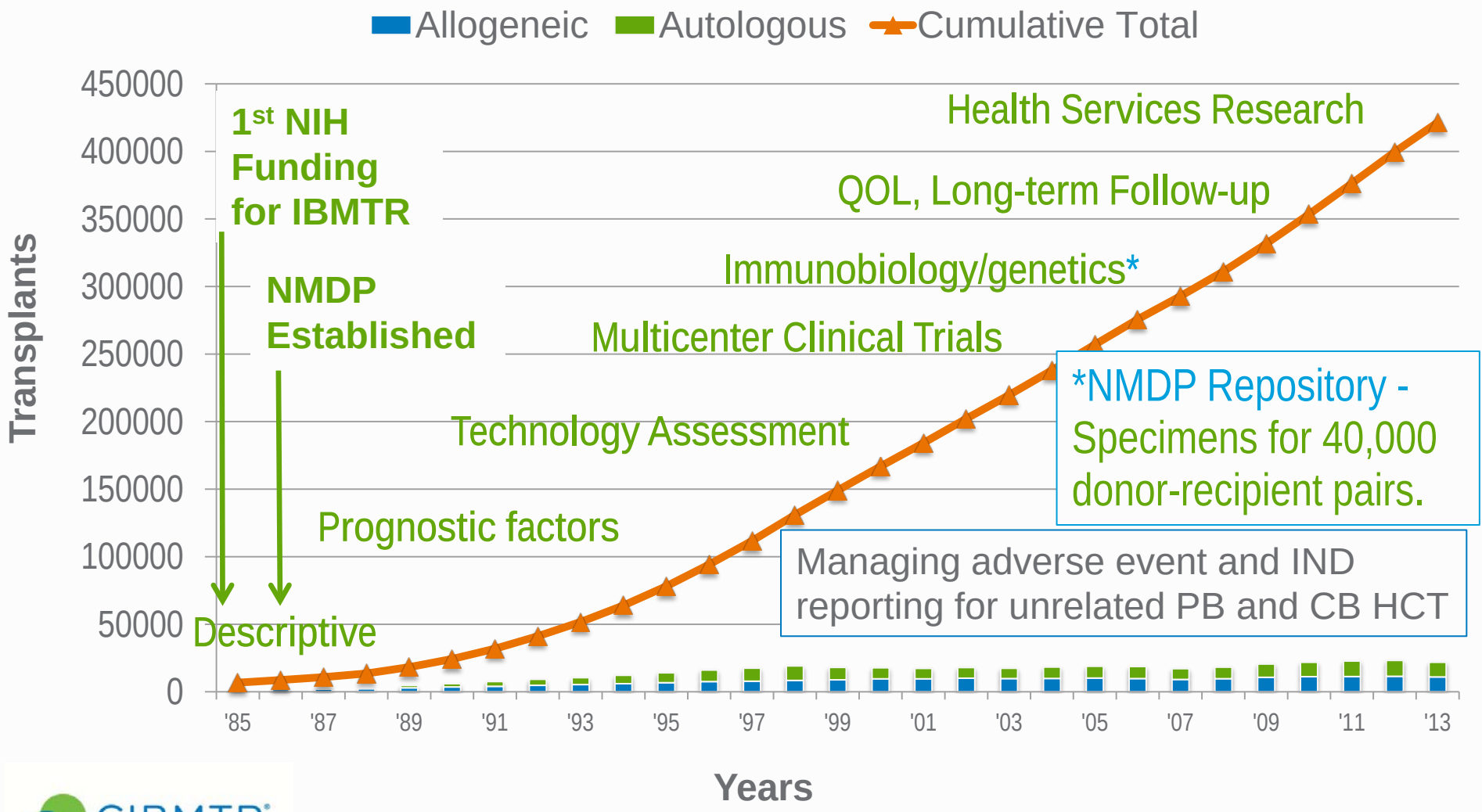
CIBMTR 440,000 Cases Registered, up to ~10,000 variables per person (most with repeated observations, some extending over >30 years), >1000 publications



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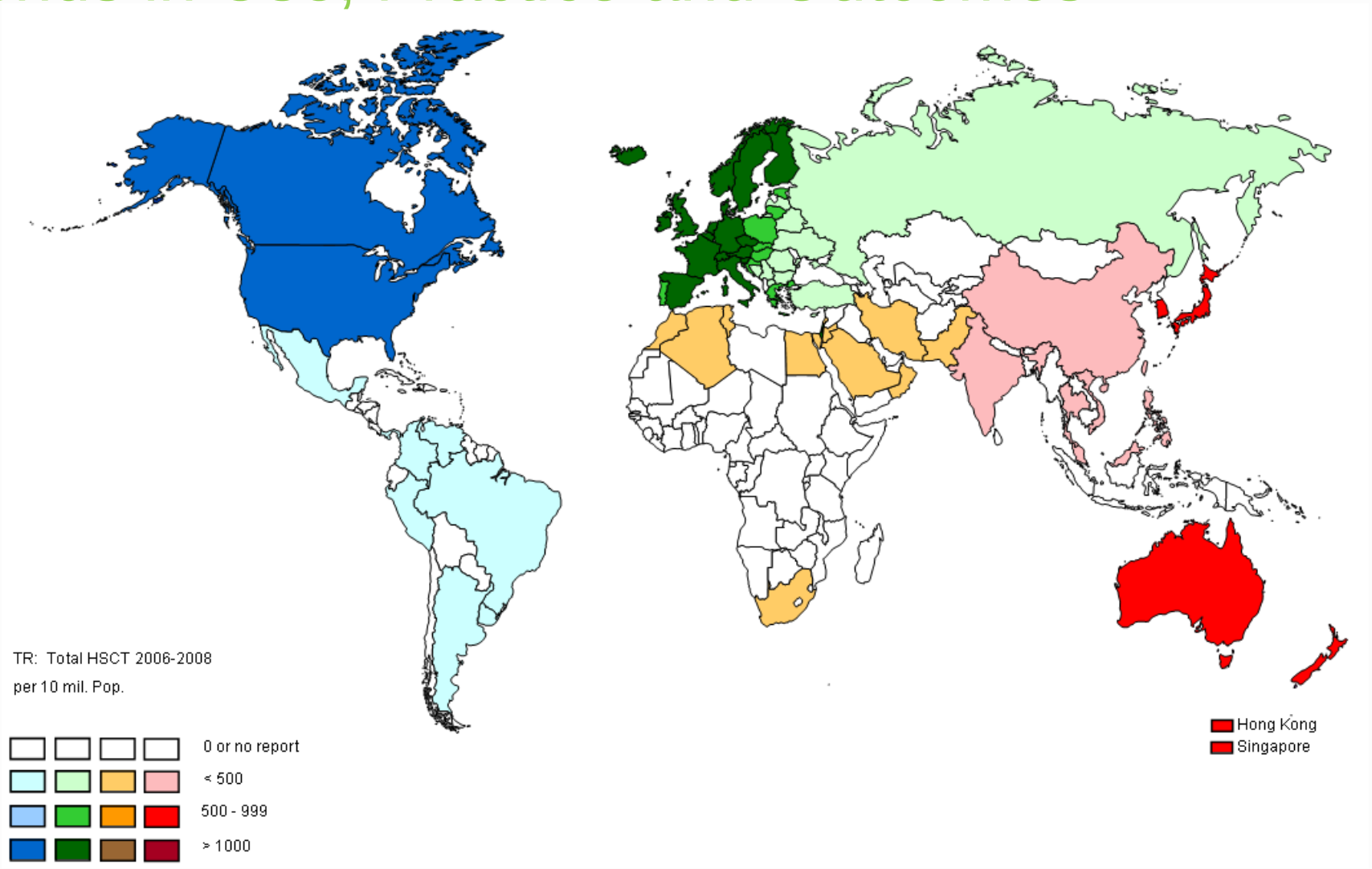
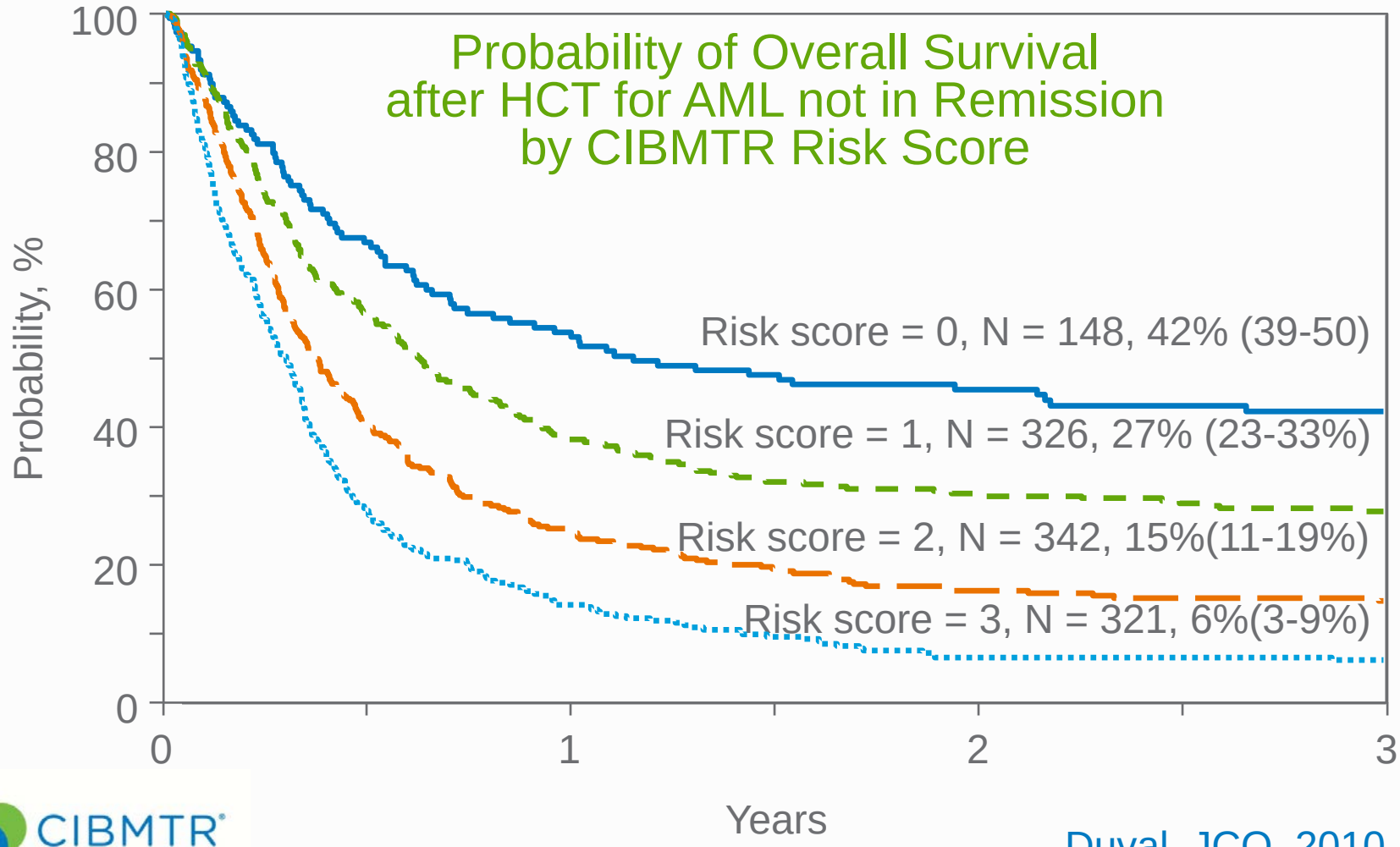
The Value of Outcome Registries: Understanding Trends in Use, Practice and Outcomes



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



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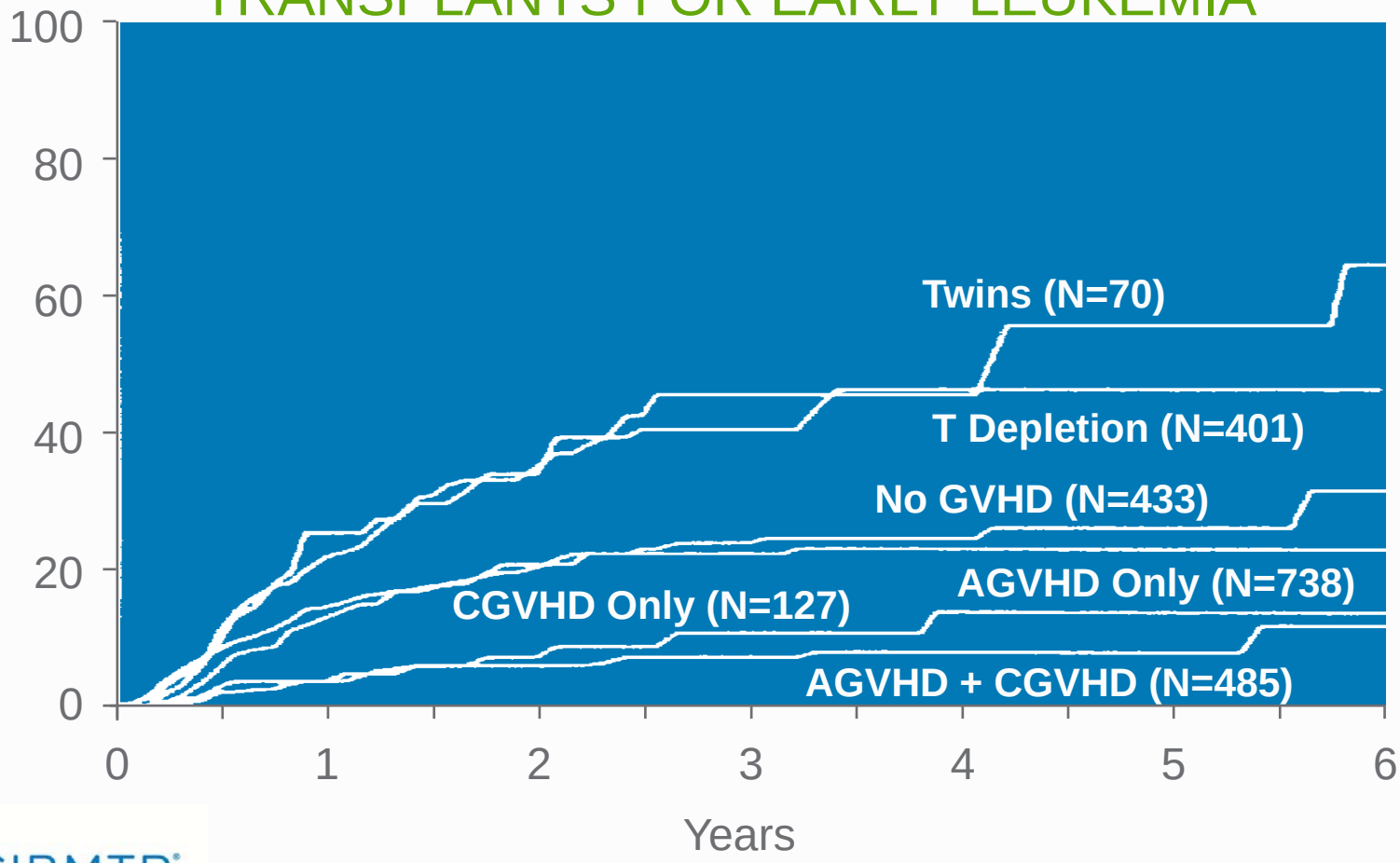
Duval, JCO, 2010

The Value of Outcome Registries: Clinical Evidence of Biologic Effects (e.g. graft versus tumor effects)

RELAPSE AFTER 2,254 HLA-IDENTICAL SIB TRANSPLANTS FOR EARLY LEUKEMIA



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Horowitz, Blood, 1990

The Value of Outcomes Registries: Evaluating and Diffusing New Technologies

The NEW ENGLAND JOURNAL of MEDICINE

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

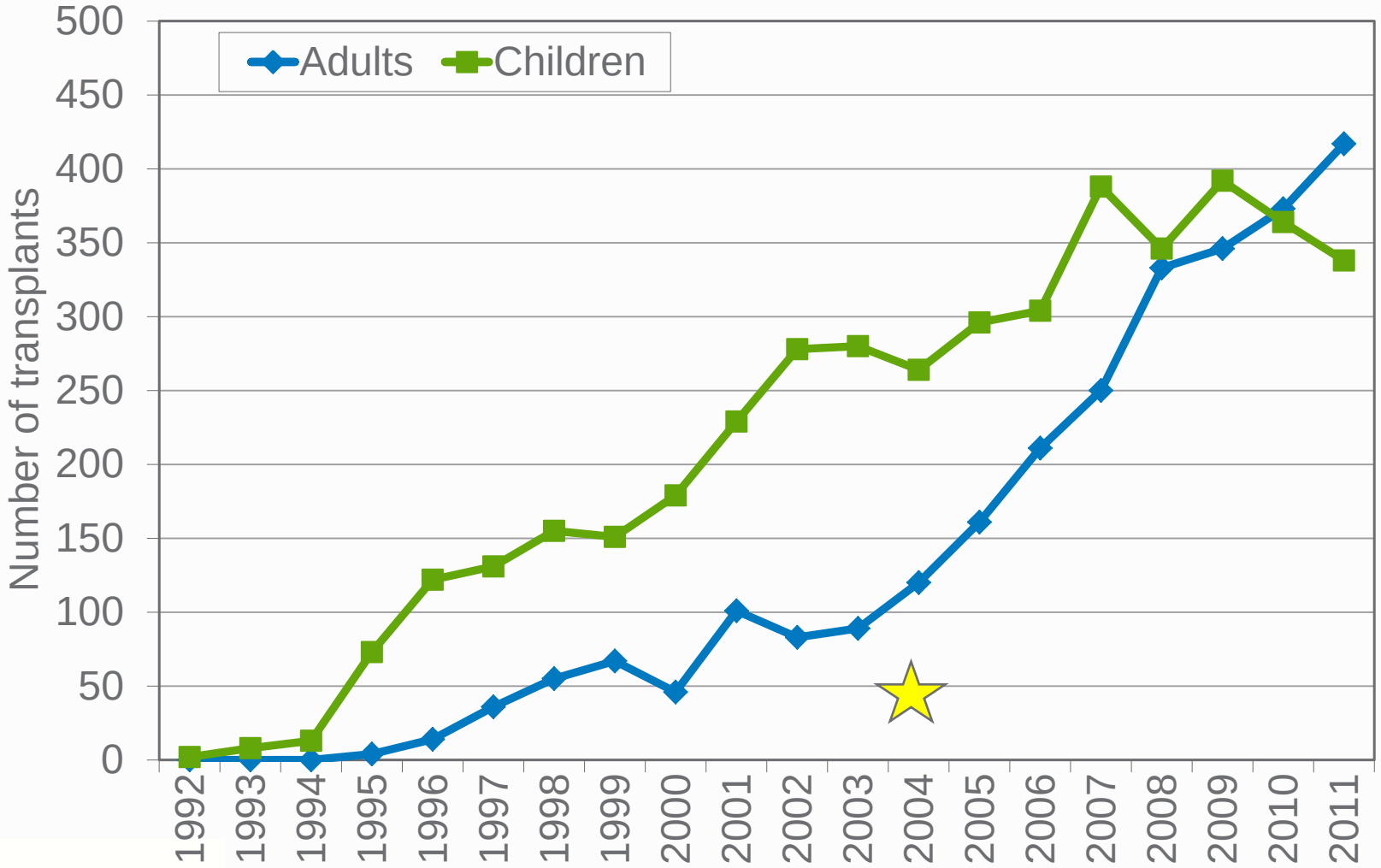
Outcomes after Transplantation of Cord Blood or Bone Marrow from Unrelated Donors in Adults with Leukemia

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



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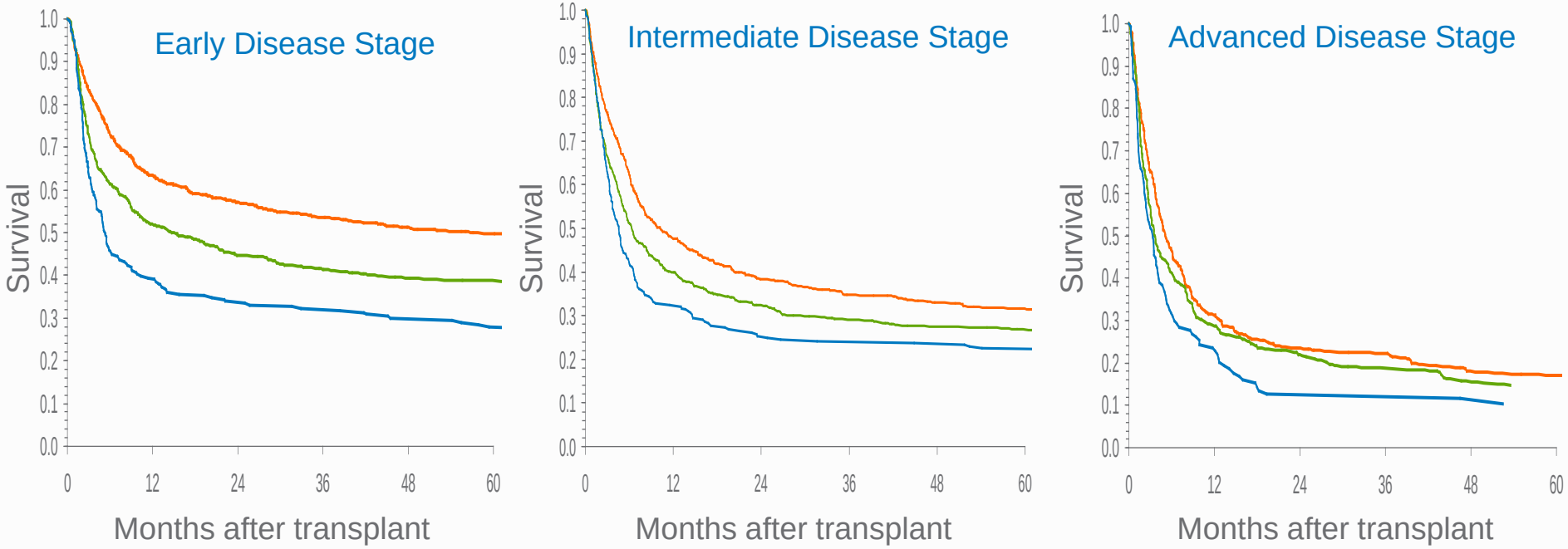
The Value of Outcome Registries: Understanding the Influence of HLA

8/8 Match 7/8 Match 6/8 Match



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*

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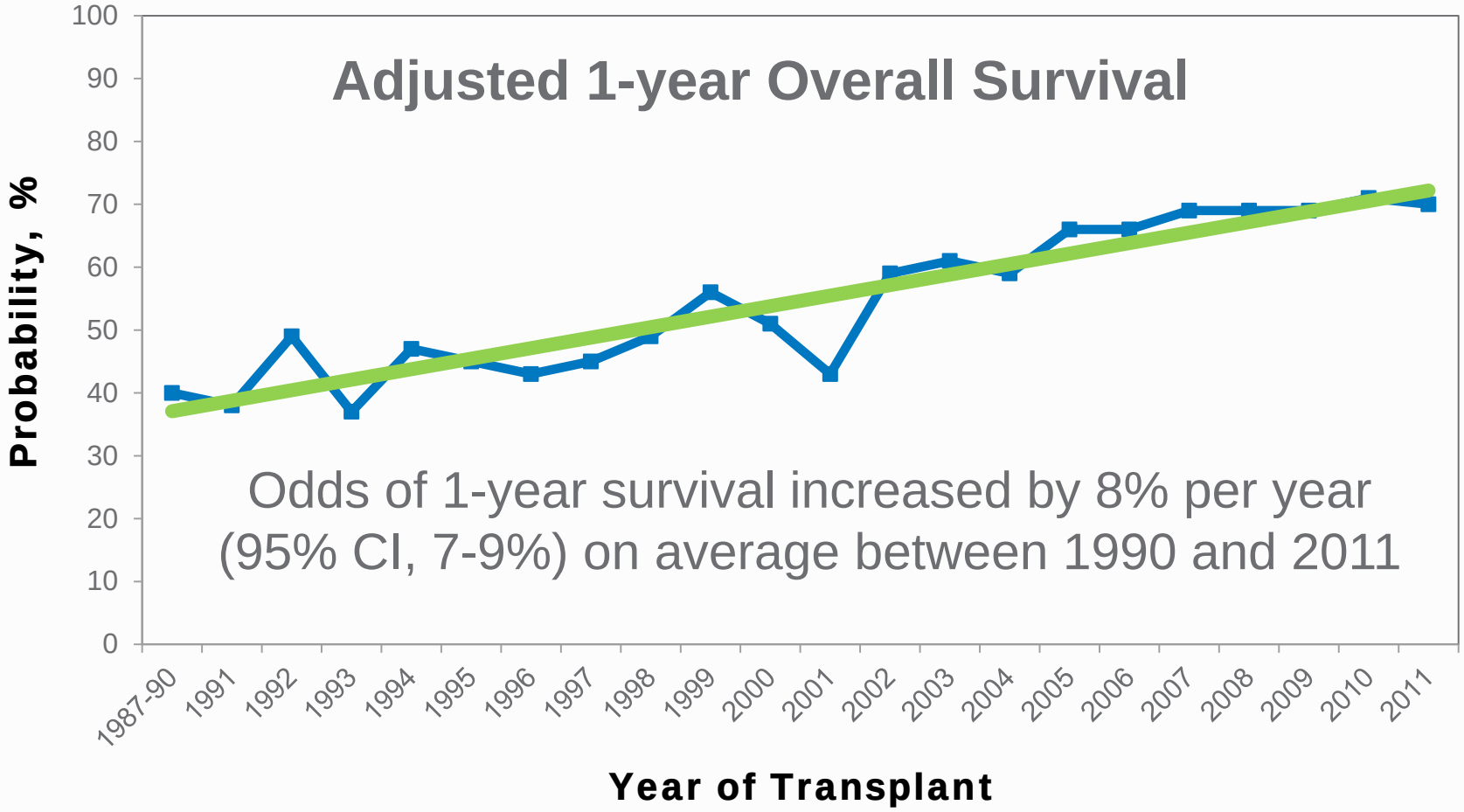
Survival After Unrelated Donor Transplantation

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



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Side Comment

- The importance of HLA and other donor characteristics will need re-evaluated in the setting of post-transplant cyclophosphamide for GVHD prophylaxis

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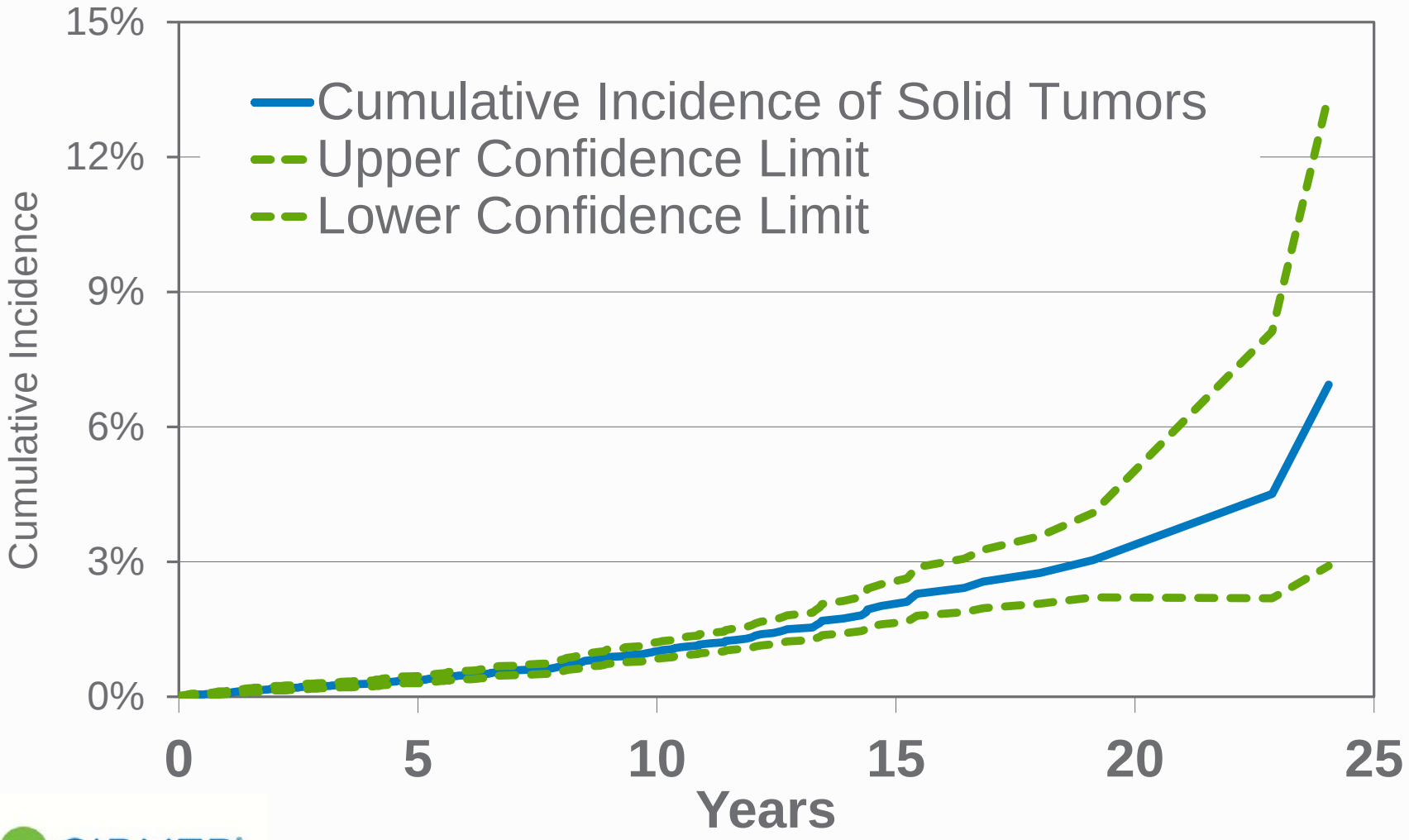
The Value of Outcomes Registries: Understanding Long-term Outcomes



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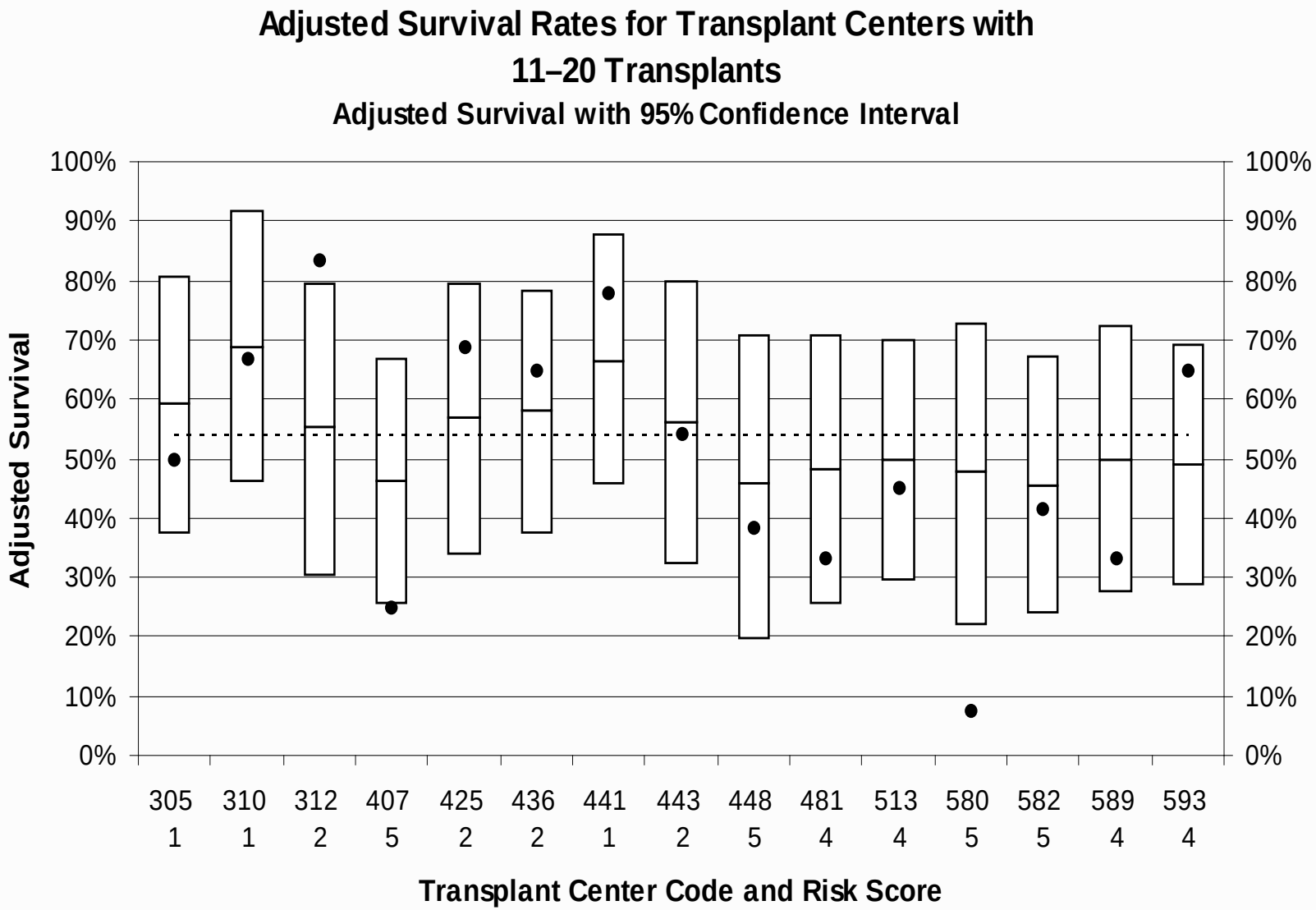
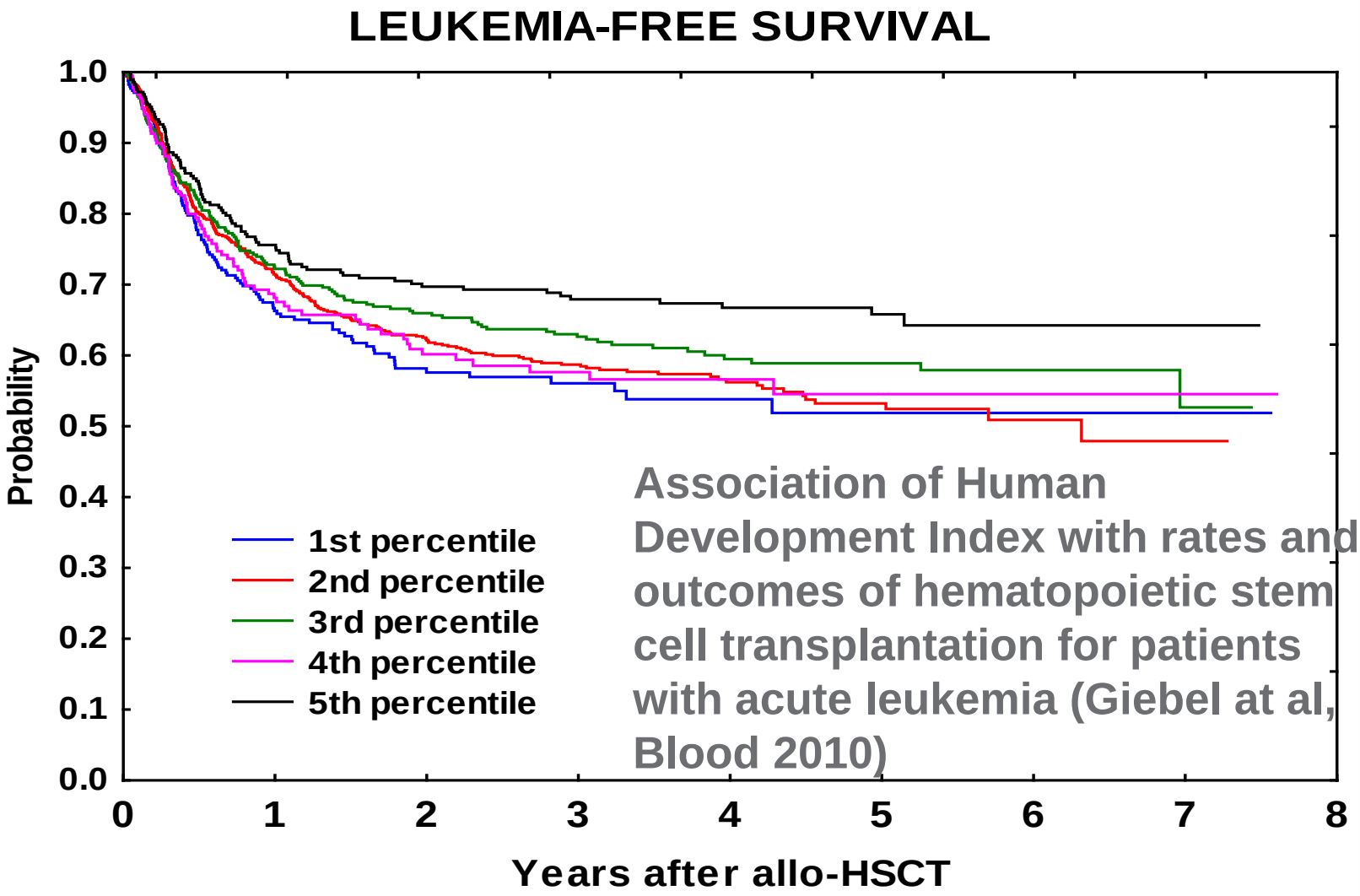
Rizzo JD, Curtis RE et al CIBMTR 2008

The Value of Outcomes Registries: Center-Specific Outcomes



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



Why Should A Registry Be Considered When BMT Is Just Developing in a Country or a Region or When Resources Are Limited?

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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

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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

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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
- Create and pursue a **scientific agenda** that is **relevant to the region**
  - Attract resources for clinical trials

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Data Are Needed:

- At the global level
  - To understand differences and commonalities in access, practice and outcomes
  - To communicate with regulatory and funding bodies about needs
  - To advance the science and practice of HCT: the region has the some unique opportunities to make important contributions

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Why Is It Important?

- 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

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How Might Existing Registries Help?

Making Use of Existing Resources May Make Data Sharing More Feasible Logistically and Financially

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CIBMTR Resources

- Existing electronic data collection system
- Existing database structure
- Existing quality control systems
- Existing training resources for data management staff
- Reimbursement for comprehensive data forms
- Available statistical expertise

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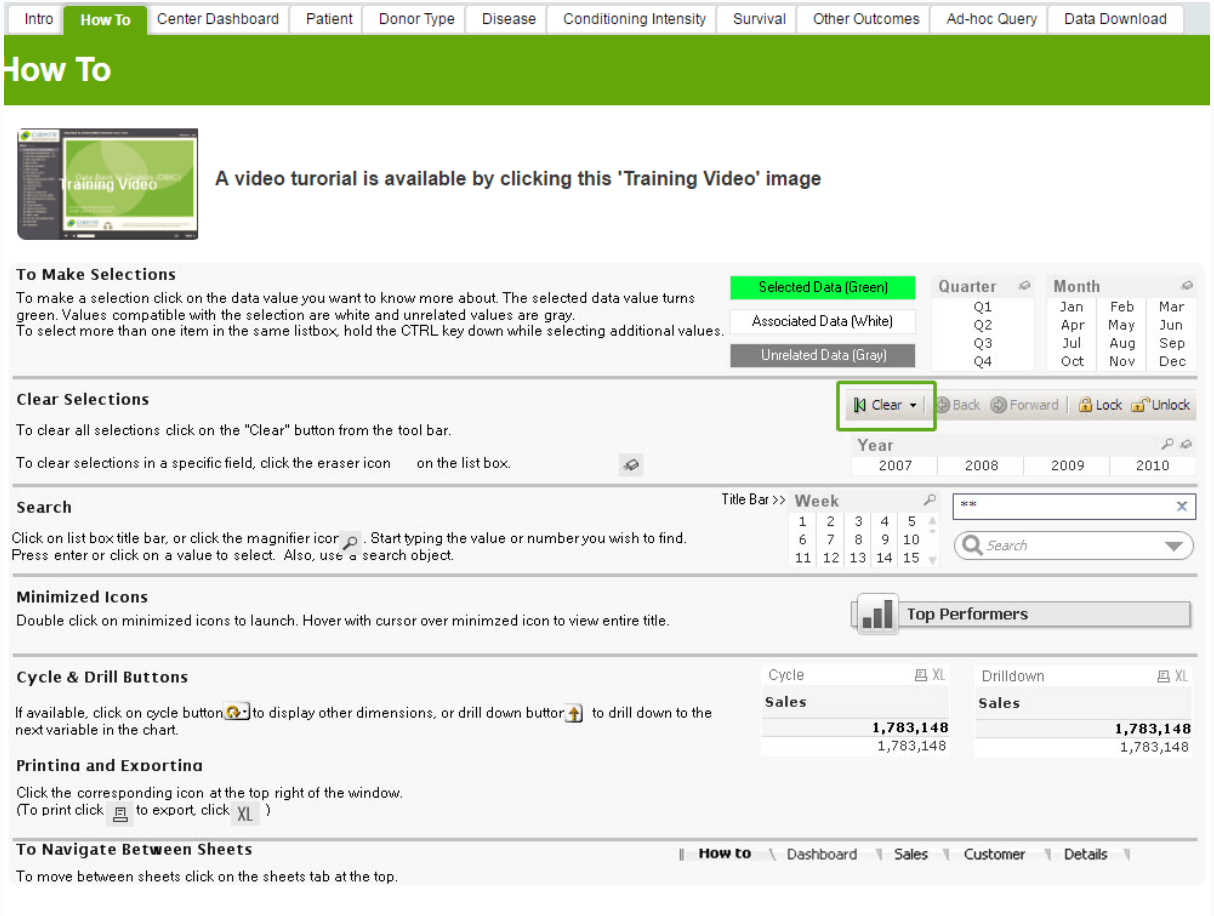
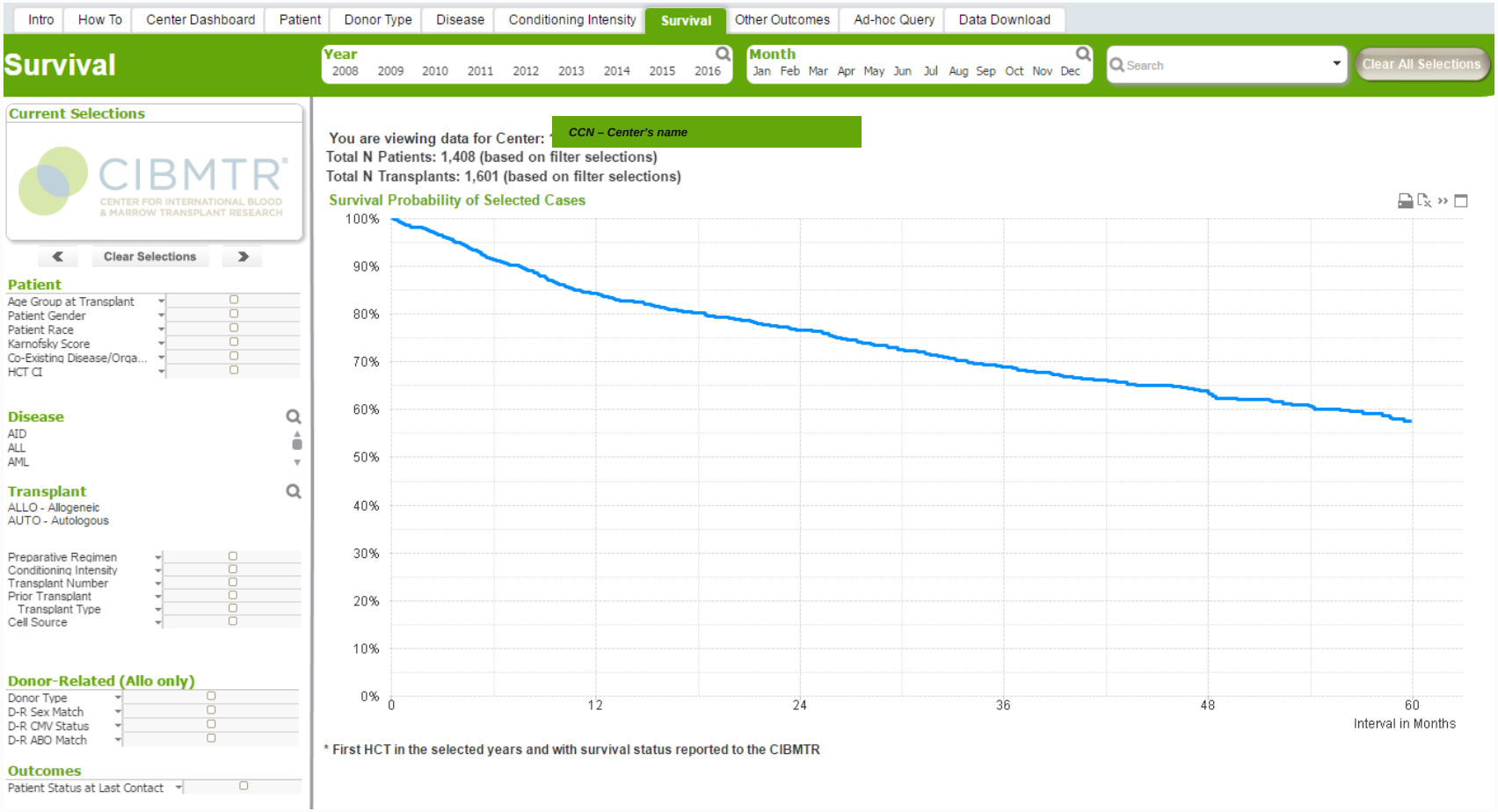
eDBtC: Enhanced Data Back to Centers

- Make selections
- Clear selections
- Minimized icons
- Cycle and drill buttons
- Printing and exporting
- Navigate between tabs



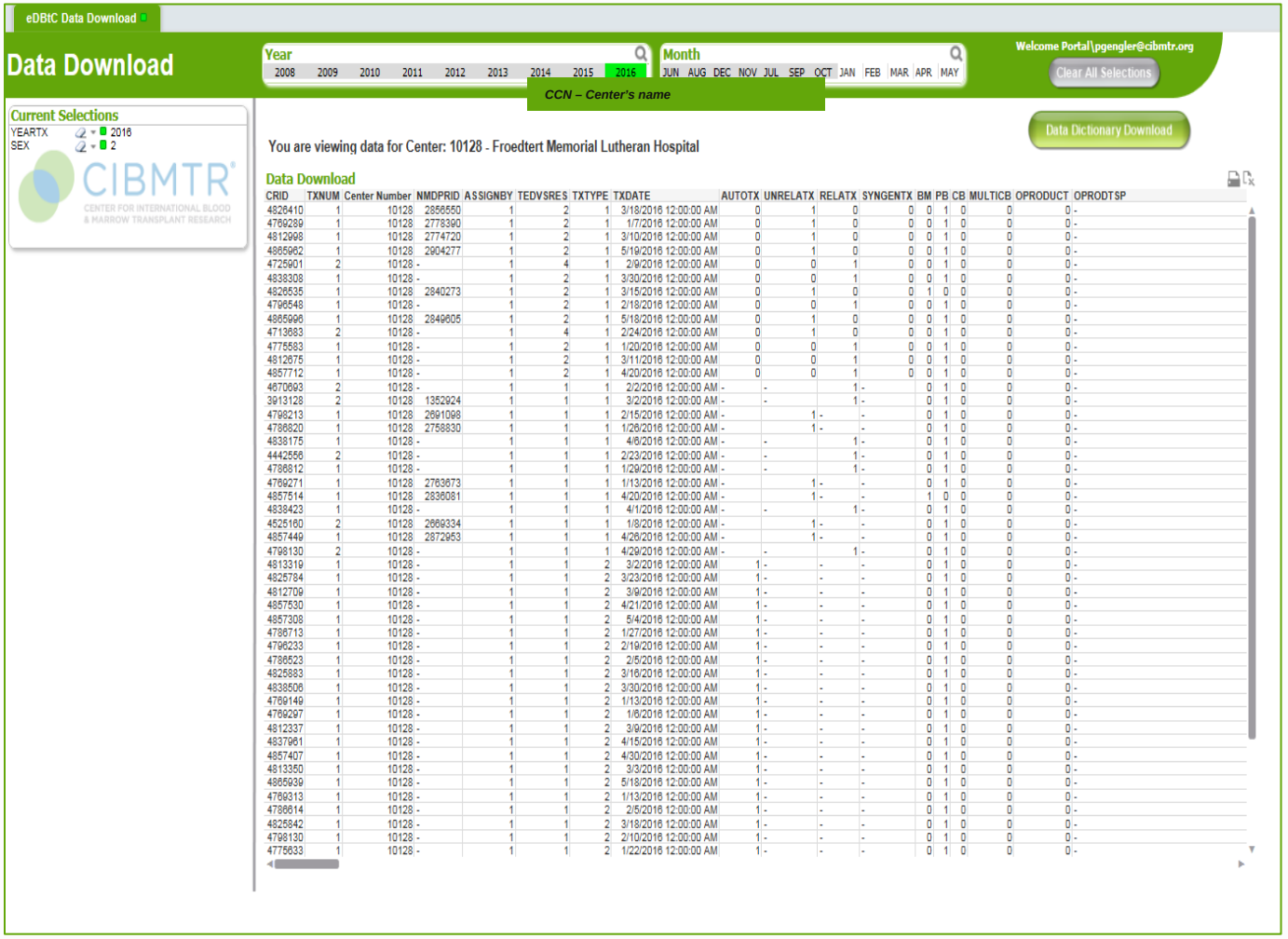
**** A video tutorial is also available***

Tab: Survival



Data Download

- Validated data
- Data dictionary
- Differentiate between TED or CRF data
- Future: Expand scope of data



Data Retrieval for Statistical Analyses

- Quarterly retrieval of validated data into SAS analysis files
  - These are the files used by CIBMTR statisticians for all CIBMTR studies
  - Shared with BMT CTN for patients on BMT CTN trials
  - Subset could be shared with other groups
  - Easily converted into EXCEL and other formats

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Summary

- Outcomes Registries can
  - Allow assessment and improvement of HCT
  - Facilitate scientific collaboration; attract research funds
  - Change practice
- Regional Outcomes Registries can foster pursuit of a scientific agenda that is relevant to regional issues
- Collaboration with existing international registries can allow development of a regional registry in a cost-effective manner

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Questions

1. What are the potential benefits of expanding the EMBMT registry?
2. What are the challenges in expanding the registry?
3. What can existing international registries do to support the EMBMT?

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