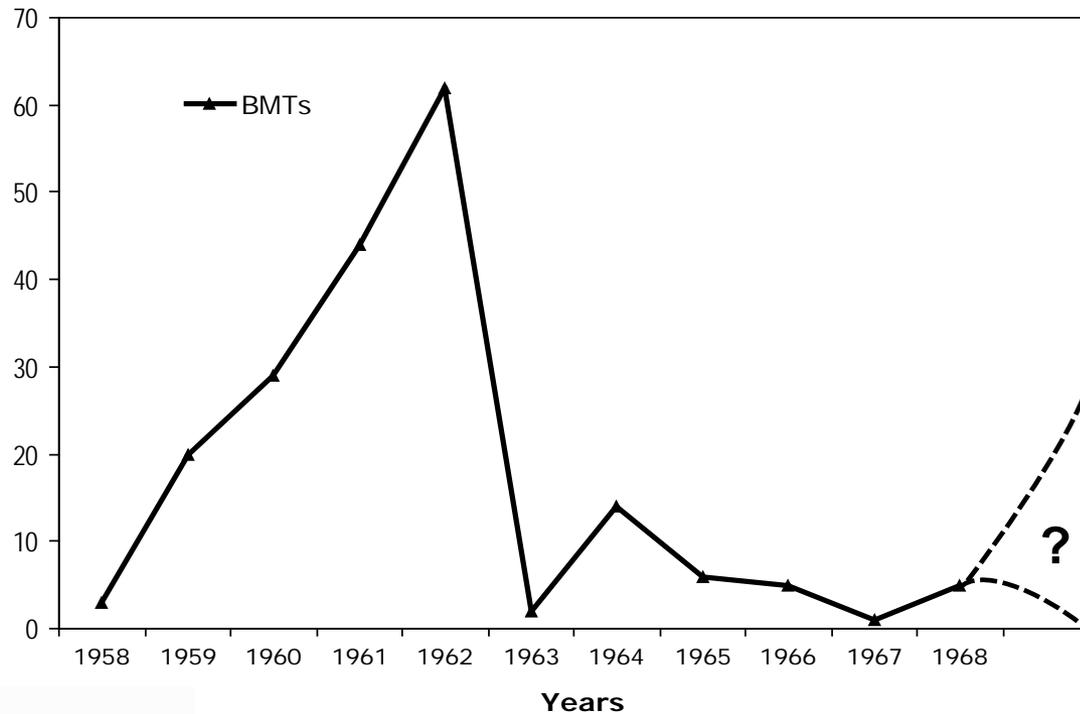
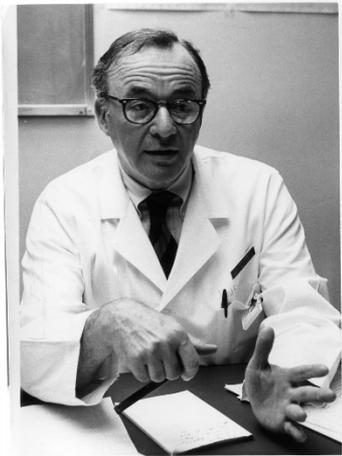


The Value of Outcomes Databases: Collaboration for Clinical Research in Blood and Marrow Transplantation

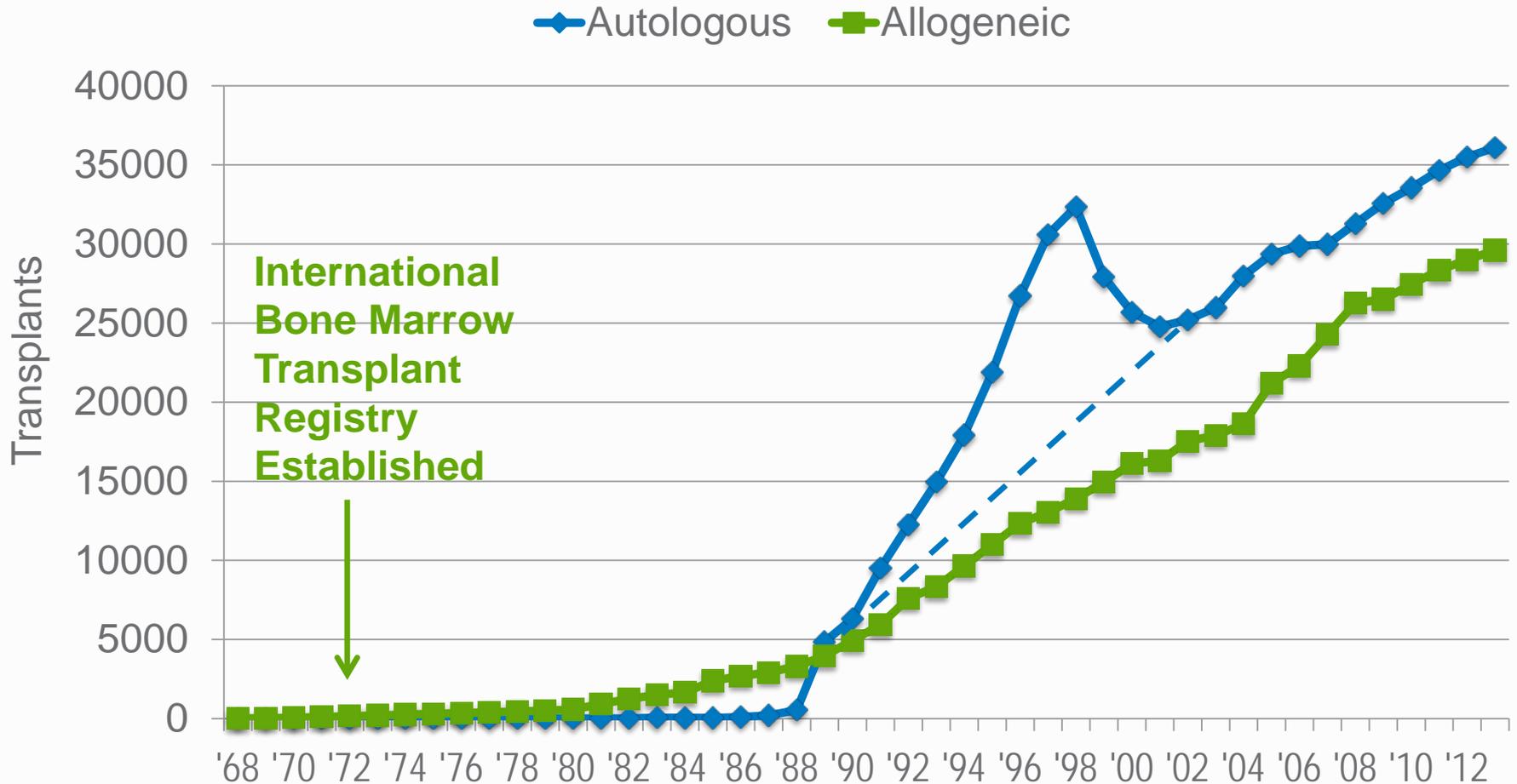
Mary M Horowitz, MD, MS
Chief Scientific Director, CIBMTR
Chief of Hematology and Oncology, Medical
College of Wisconsin, Milwaukee
January 2017

A Little History.....



Bortin, Transplantation, 1970

Transplant Activity Worldwide 1968-2014



In the Beginning.....

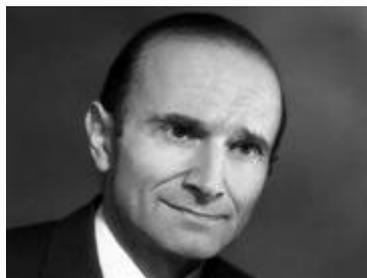


Don Thomas

First Advisory Committee of
the International Bone
Marrow Transplant Registry



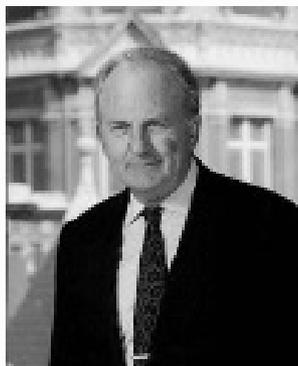
Dirk van Bekkum



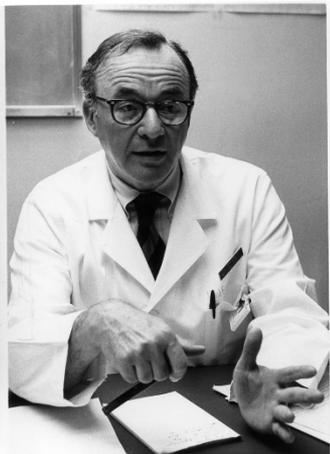
George Mathe



Bob Good



George Santos



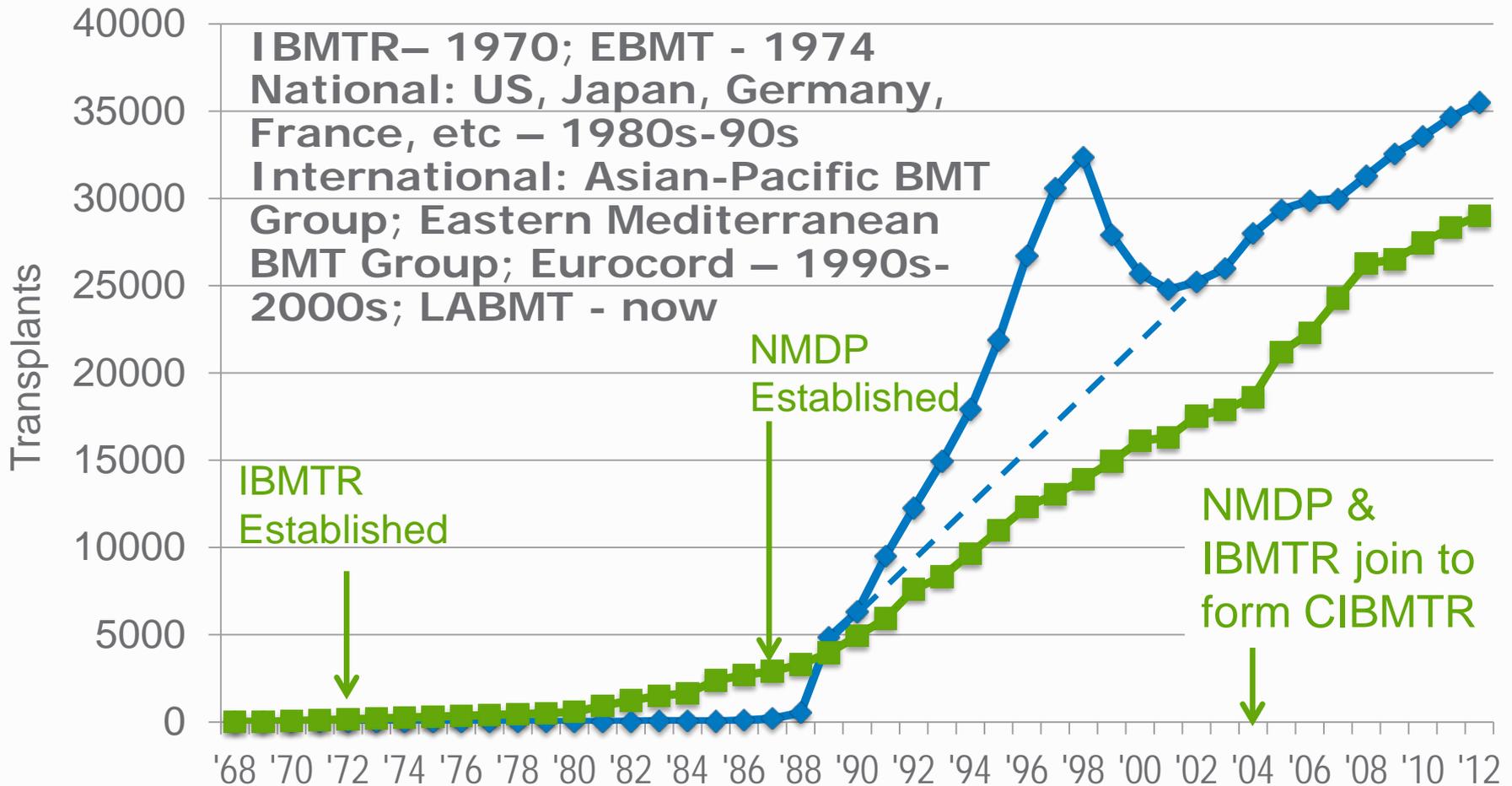
Mort Bortin



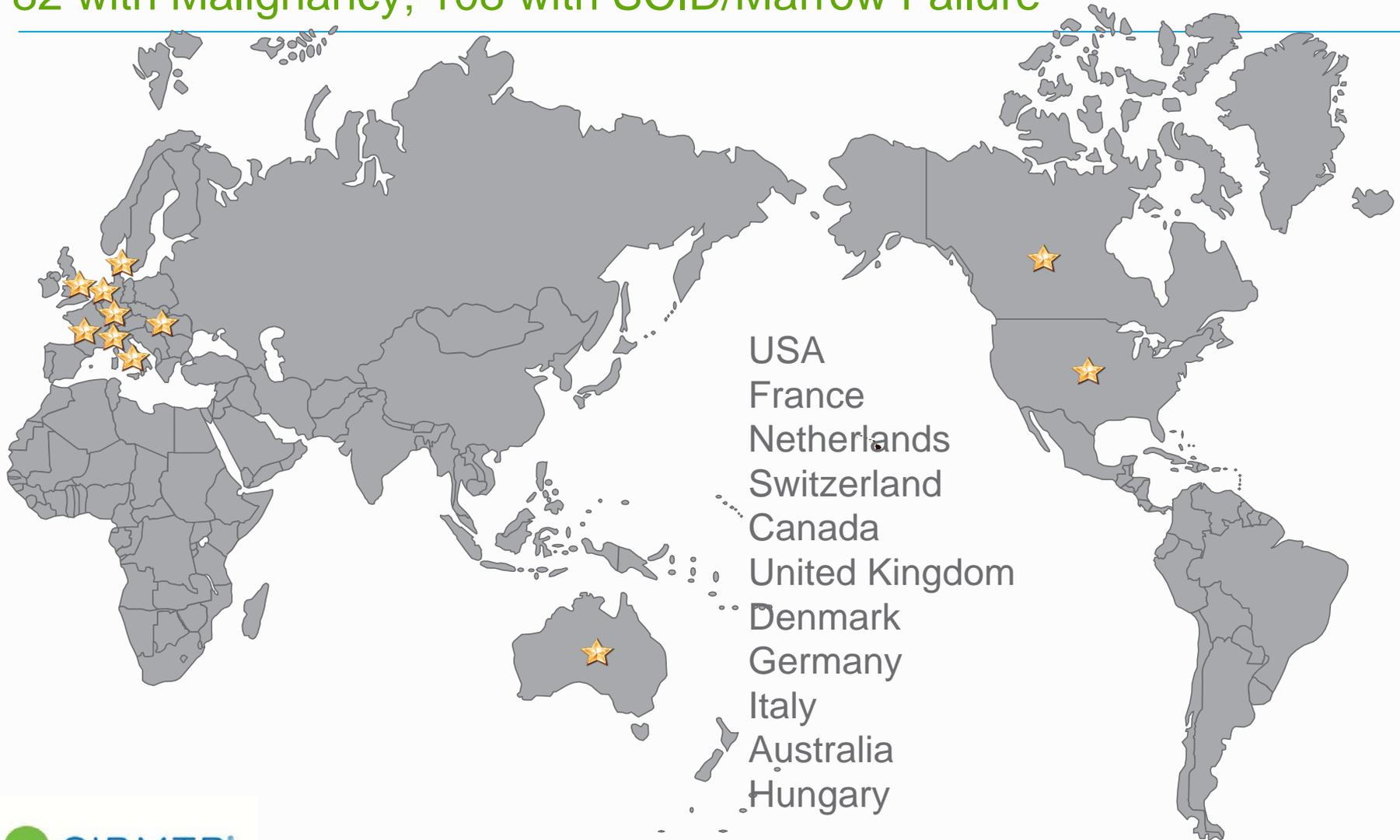
Fritz Bach

**JJ Bergan, JL Fahey,
Bob Levey, GN Rogentine**

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



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



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

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

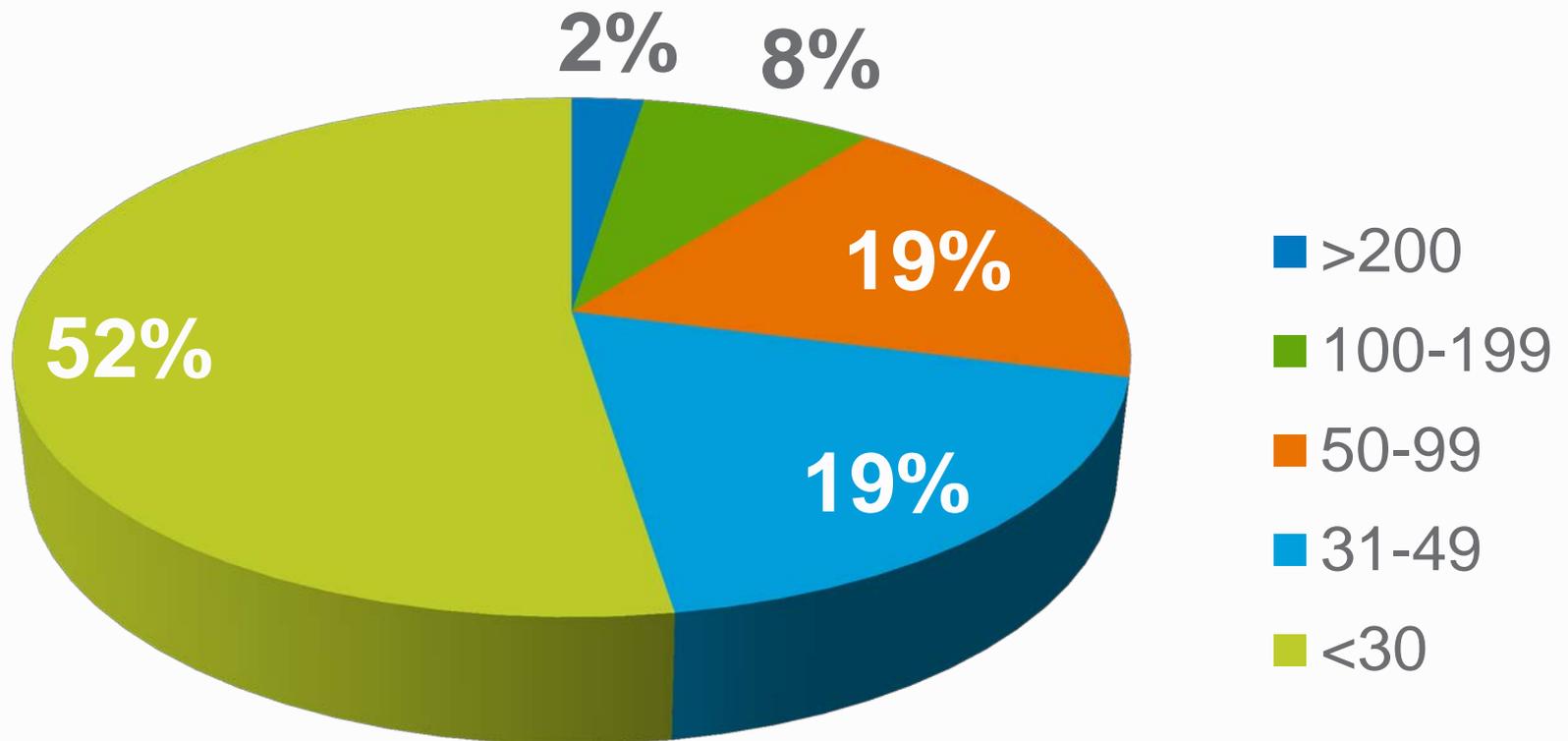
Risk Factors

- 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

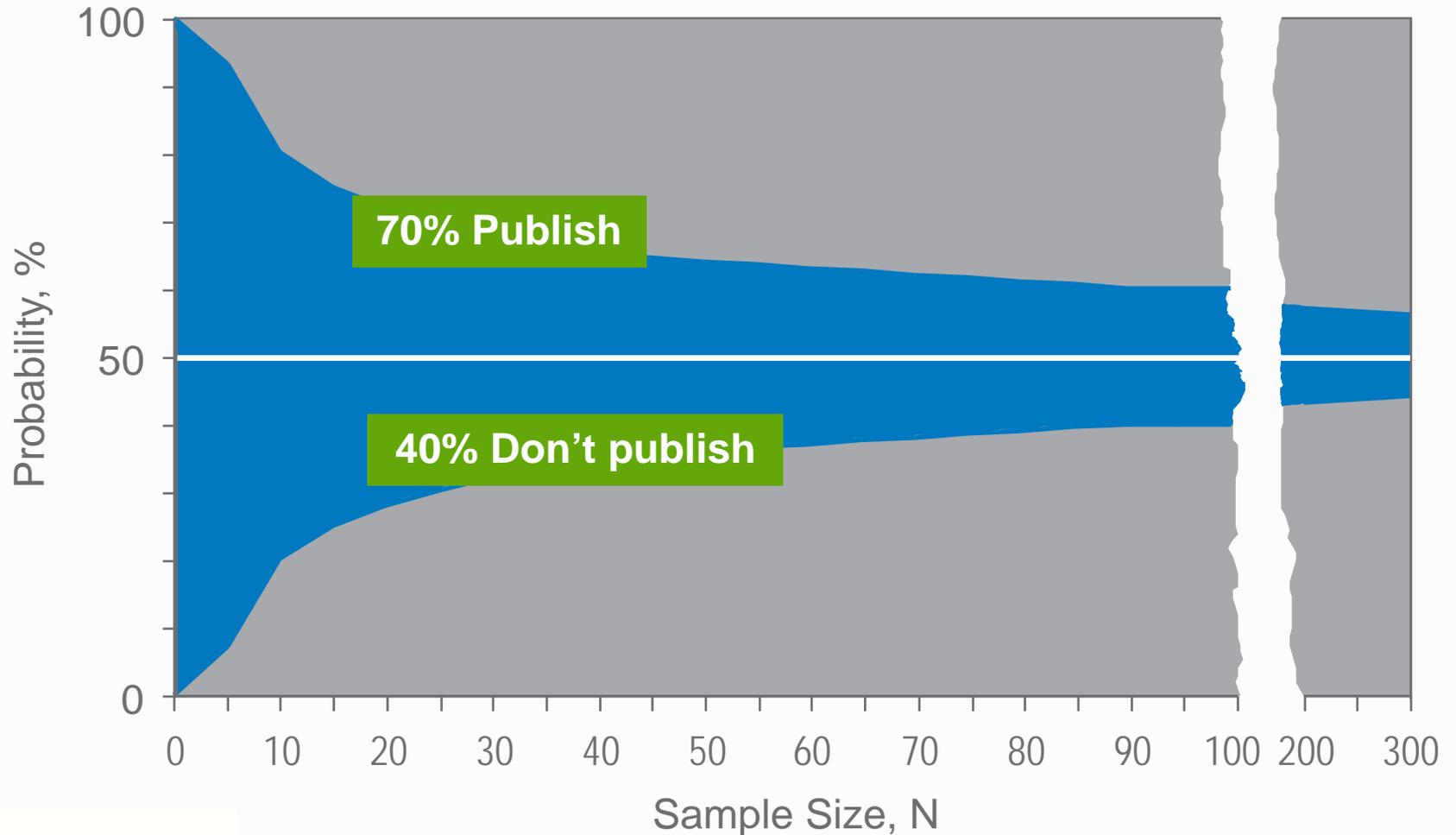
- Rimm AA, Bortin MM. HLA antigens and SCID. *Lancet*. 1977
- D'Amaro JD, van Rood JJ, Rimm AA, Bortin MM. HLA associations in Italian and non-Italian Caucasoid aplastic anaemia patients. *Tissue Antigens*. 1983
- D'Amaro JD, van Rood JJ, Bach FH, Rimm AA, Bortin MM. HLA C associations with acute leukaemia.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

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

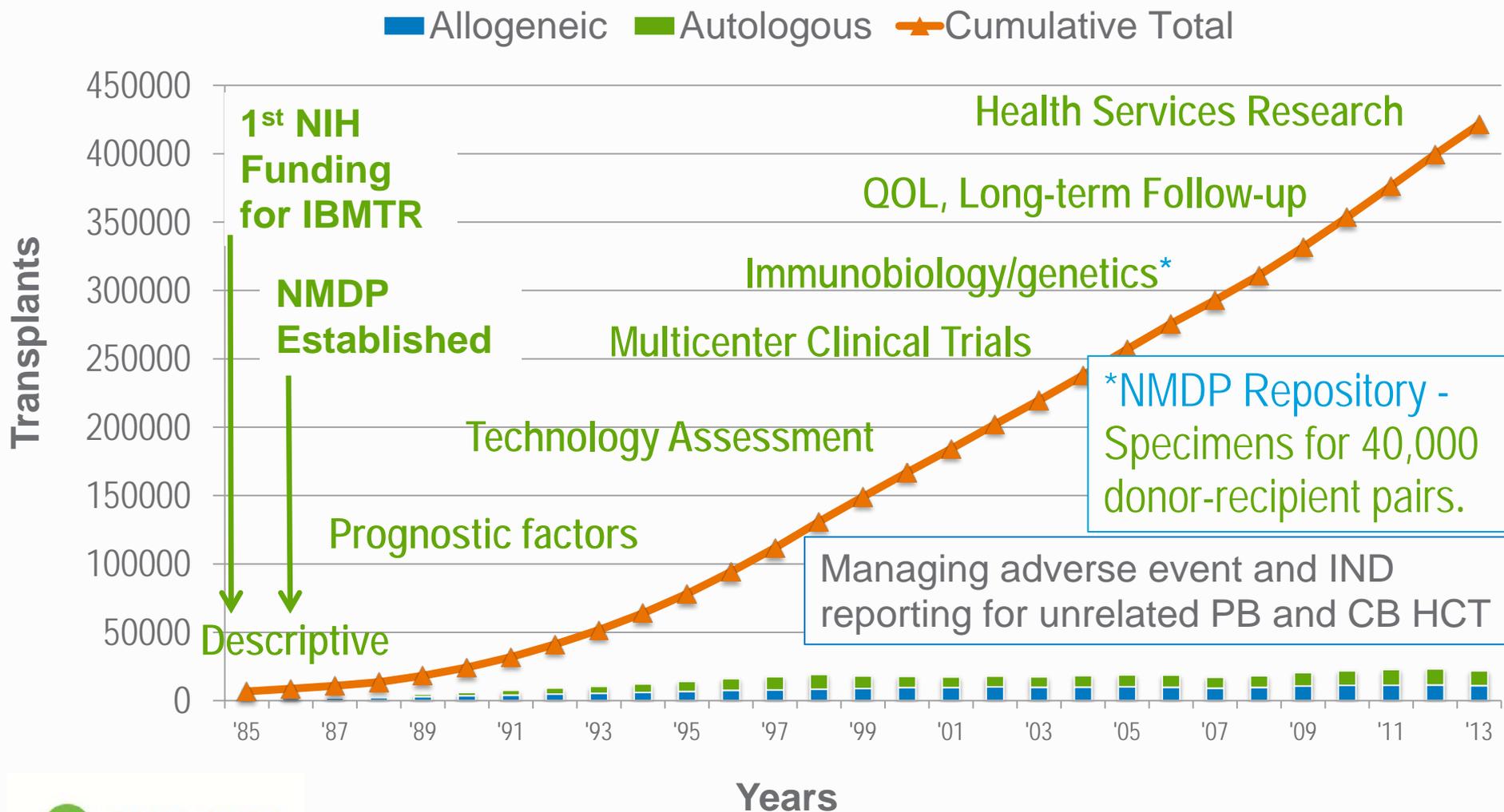


Individual transplant centers treat relatively few patients and these patients are heterogeneous in many factors that affect outcomes

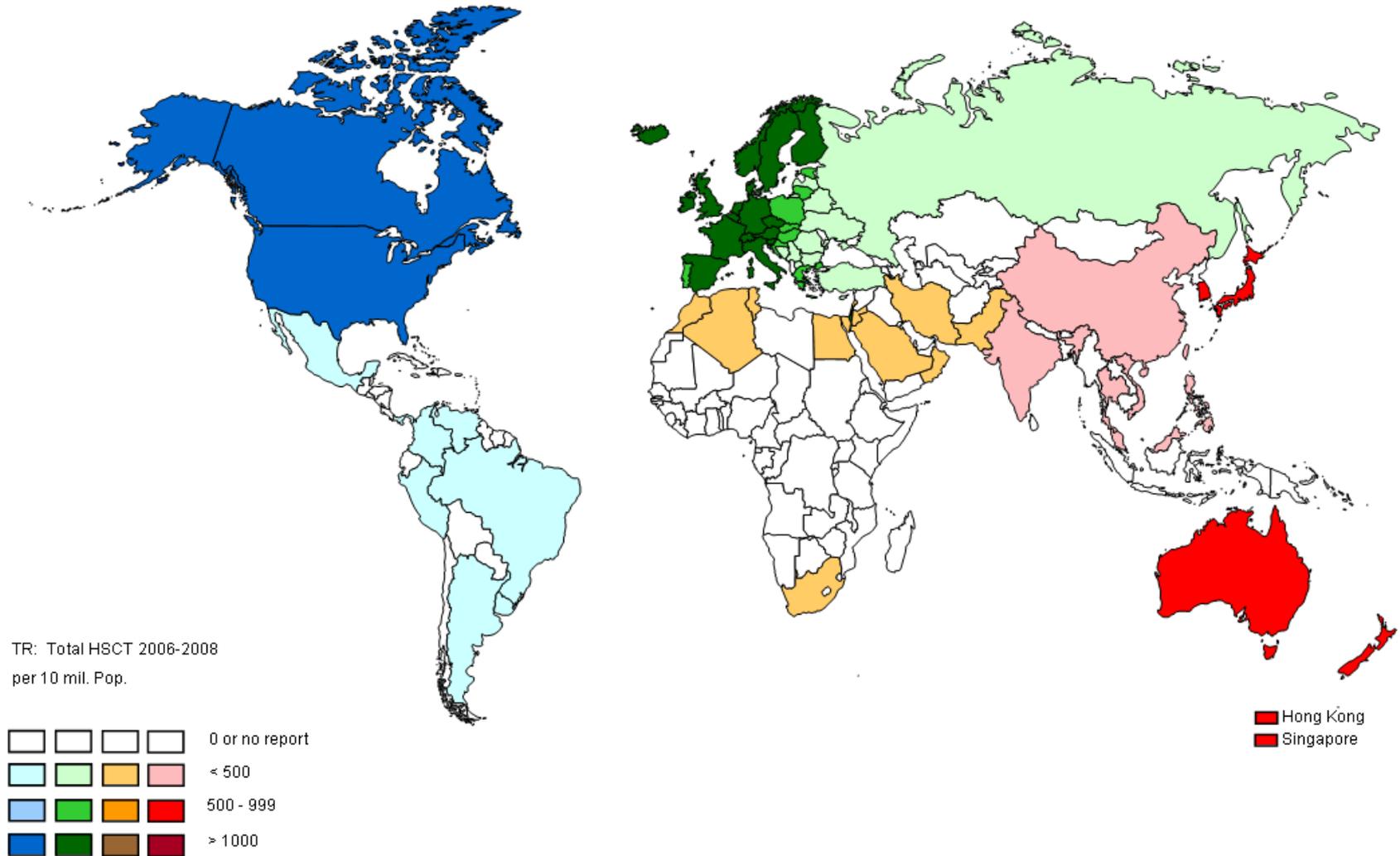
95% Confidence Intervals for Samples Drawn from a Population Receiving a Treatment Producing 50% Survival



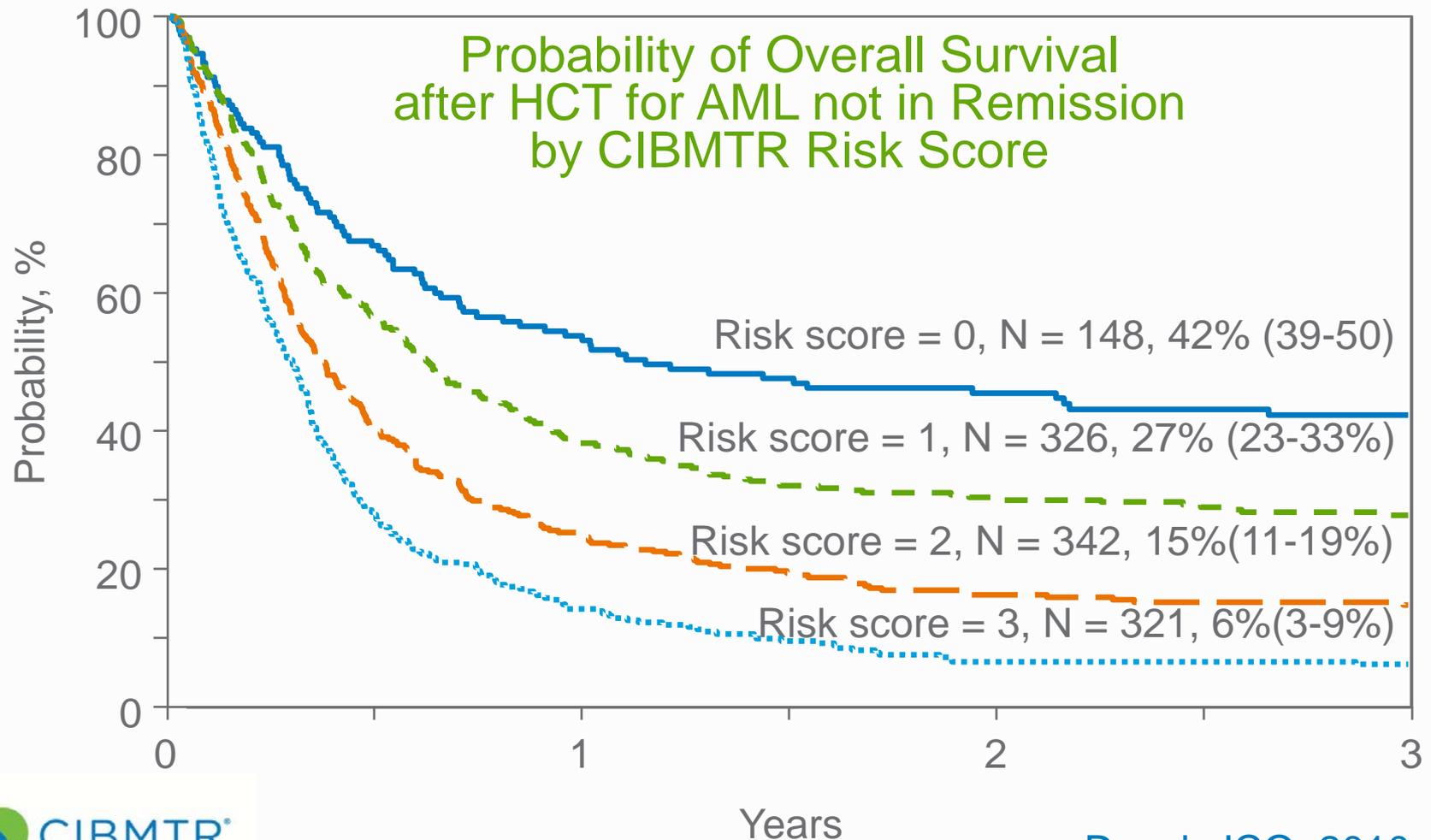
CIBMTR 440,000 Cases Registered, up to ~10,000 variables per person (most with repeated observations, some extending over >30 years), >1000 publications



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

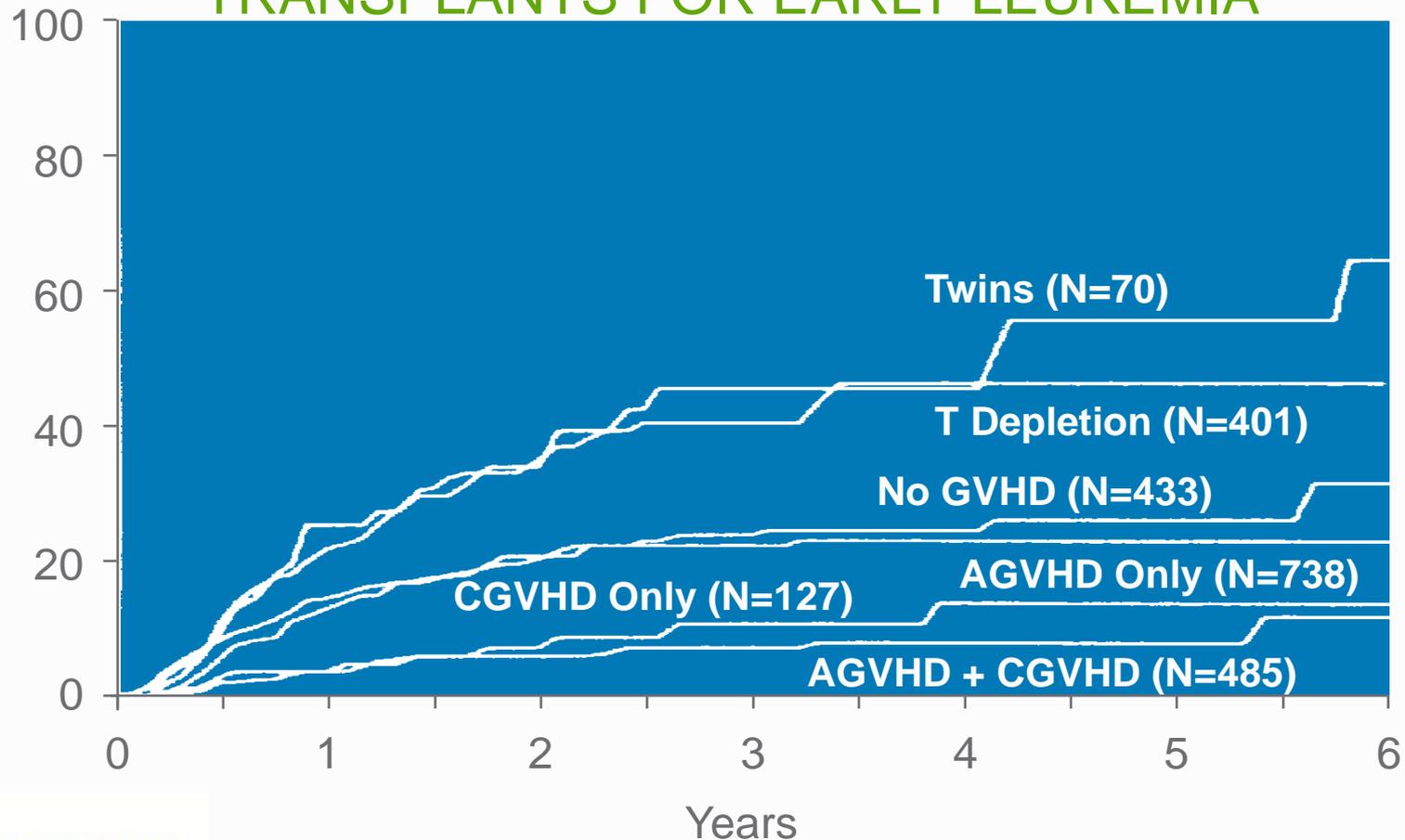


The Value of Outcome Registries: Identifying patients most likely to benefit from BMT



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



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

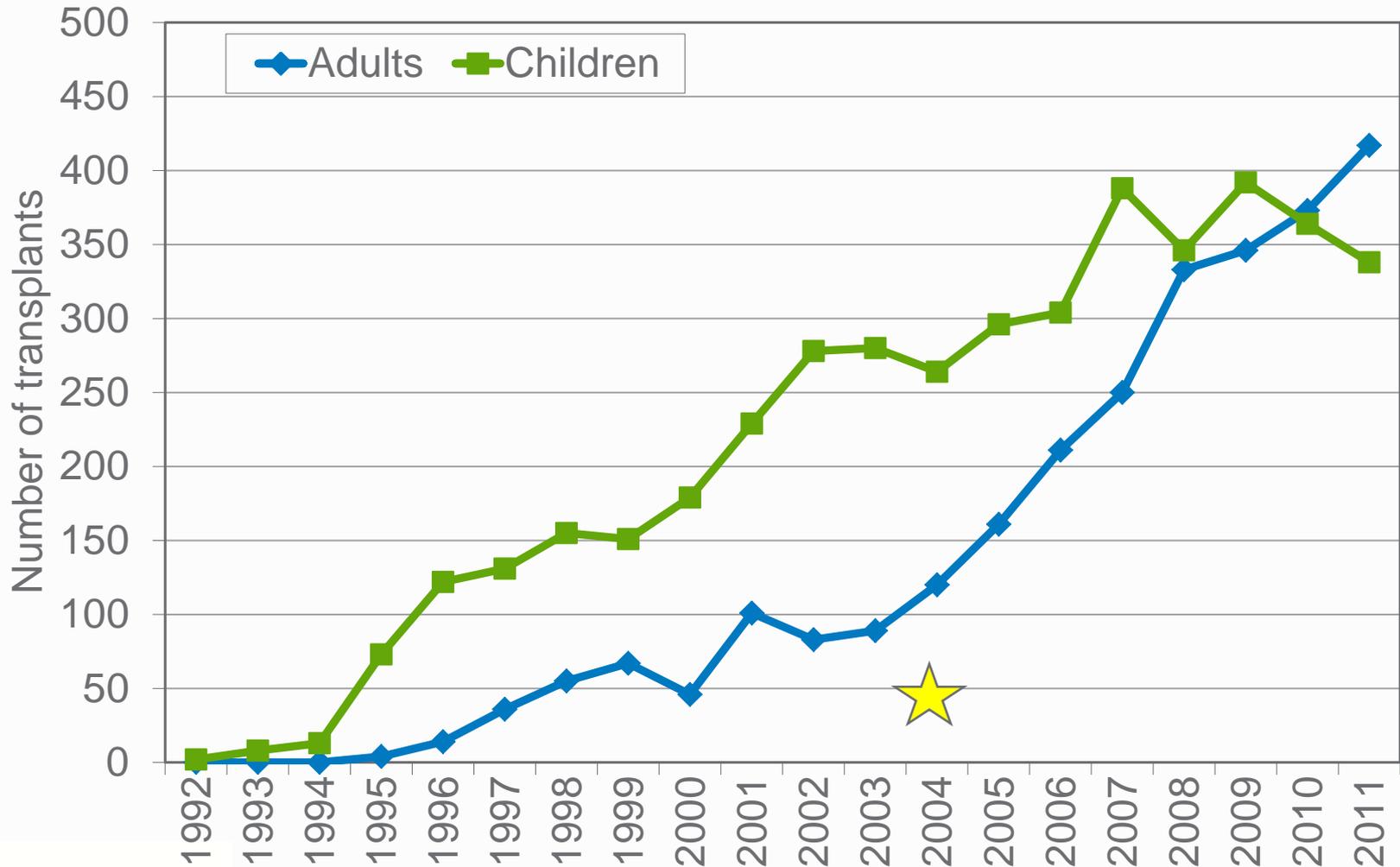
Outcomes after Transplantation of Cord Blood or Bone Marrow from Unrelated Donors in Adults with Leukemia

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

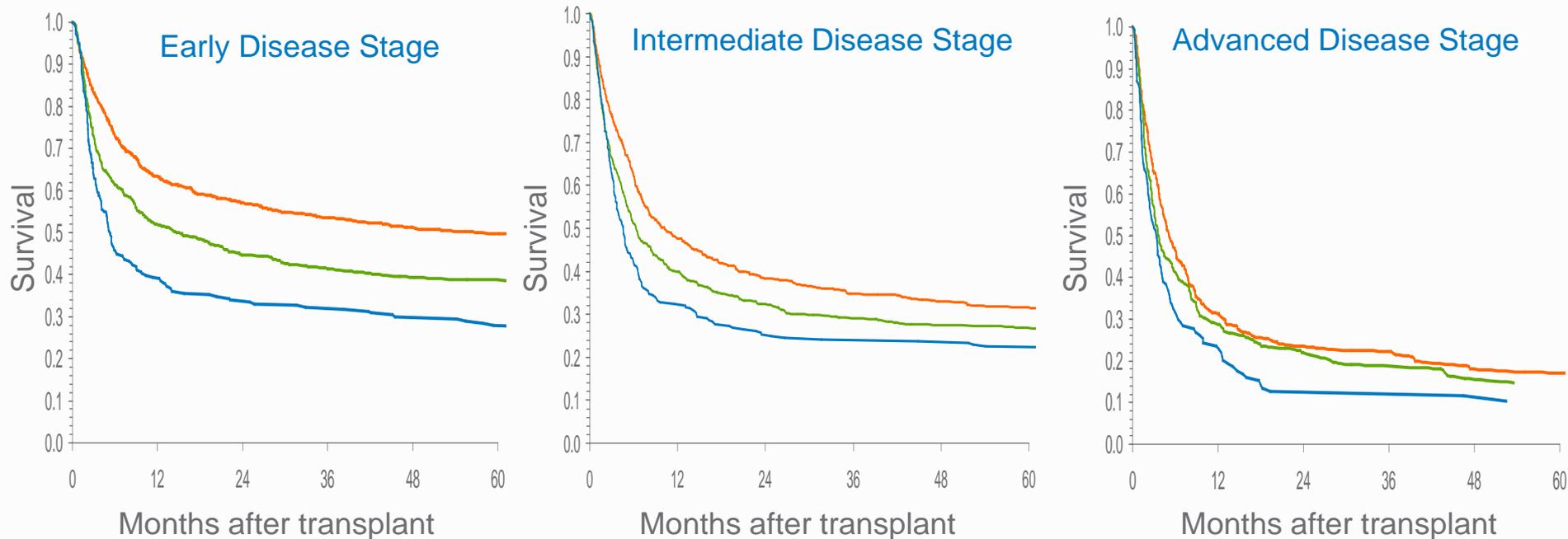


The Value of Outcome Registries: Understanding the Influence of HLA

— 8/8 Match

— 7/8 Match

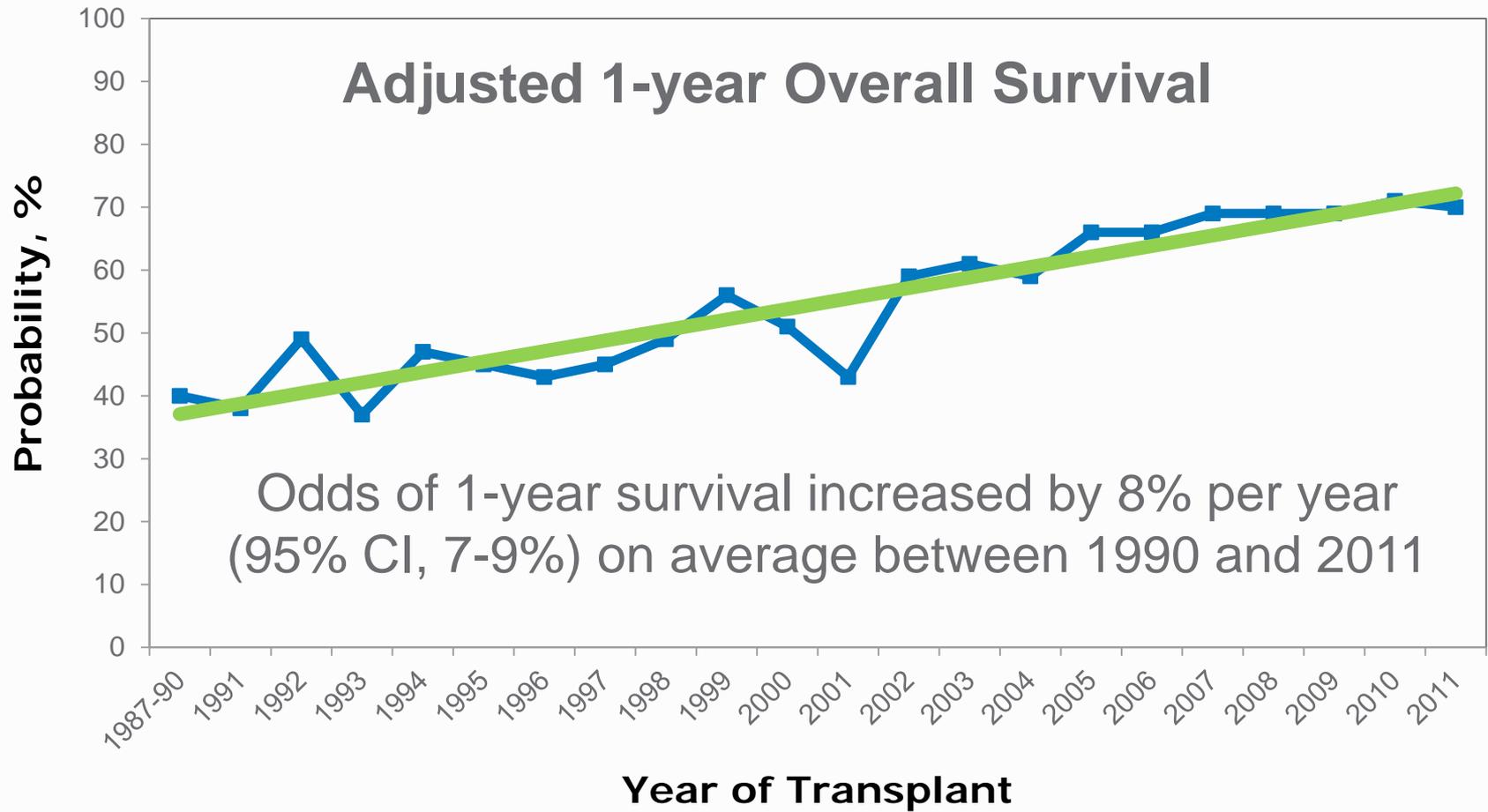
— 6/8 Match



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*

Survival After Unrelated Donor Transplantation

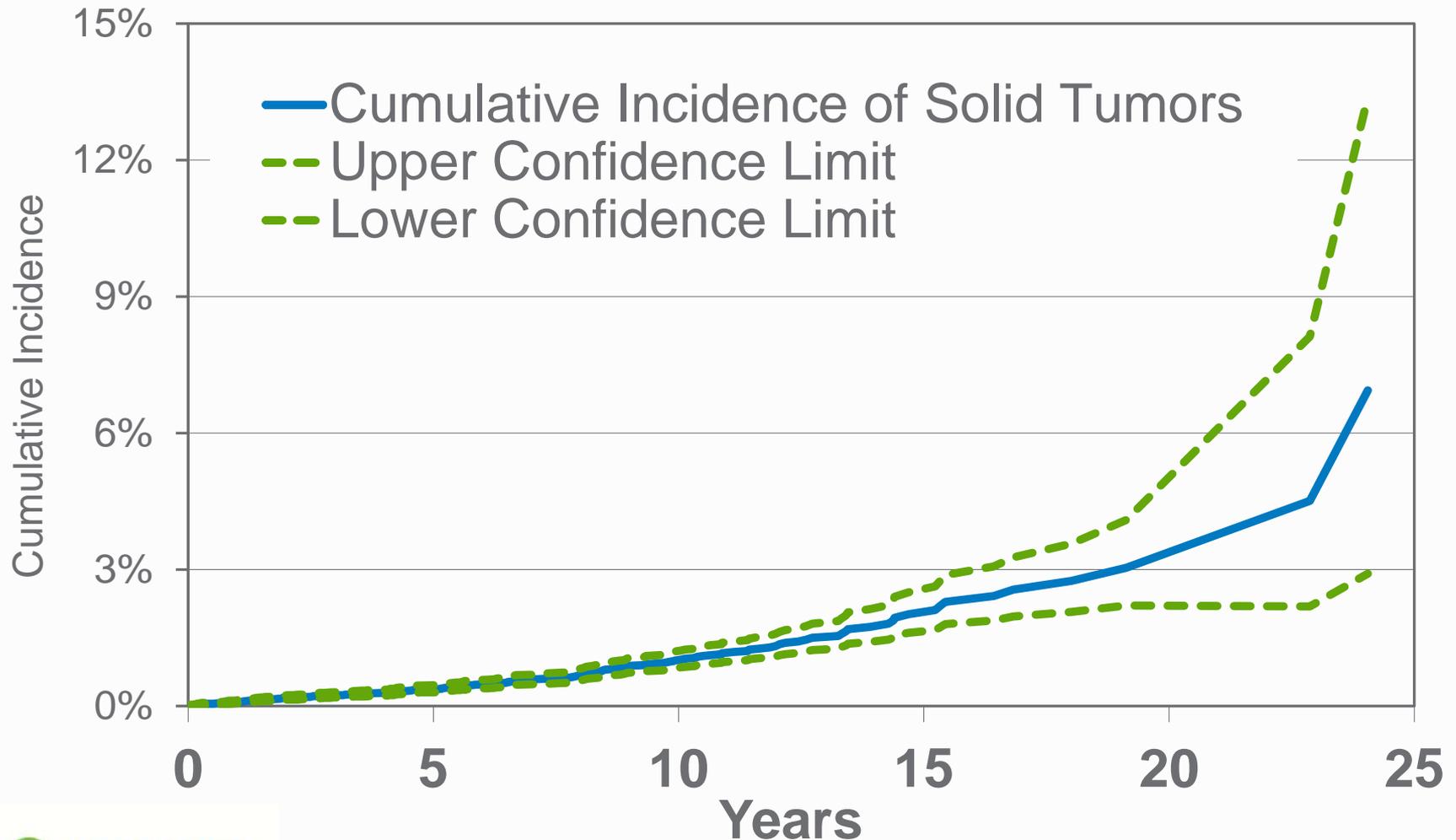
Age <50 years, myeloablative conditioning, acute leukemia in remission or MDS



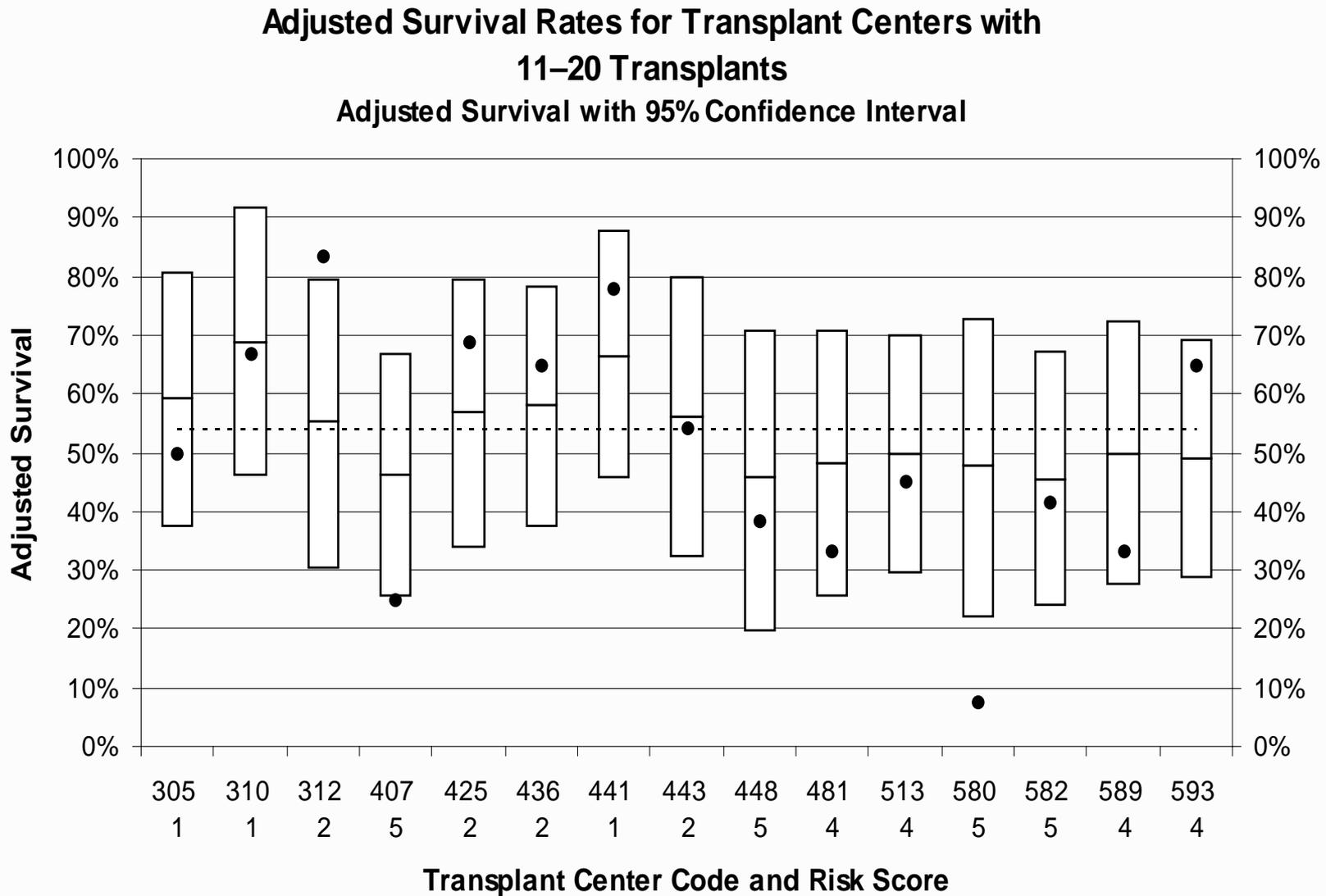
Side Comment

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

The Value of Outcomes Registries: Understanding Long-term Outcomes

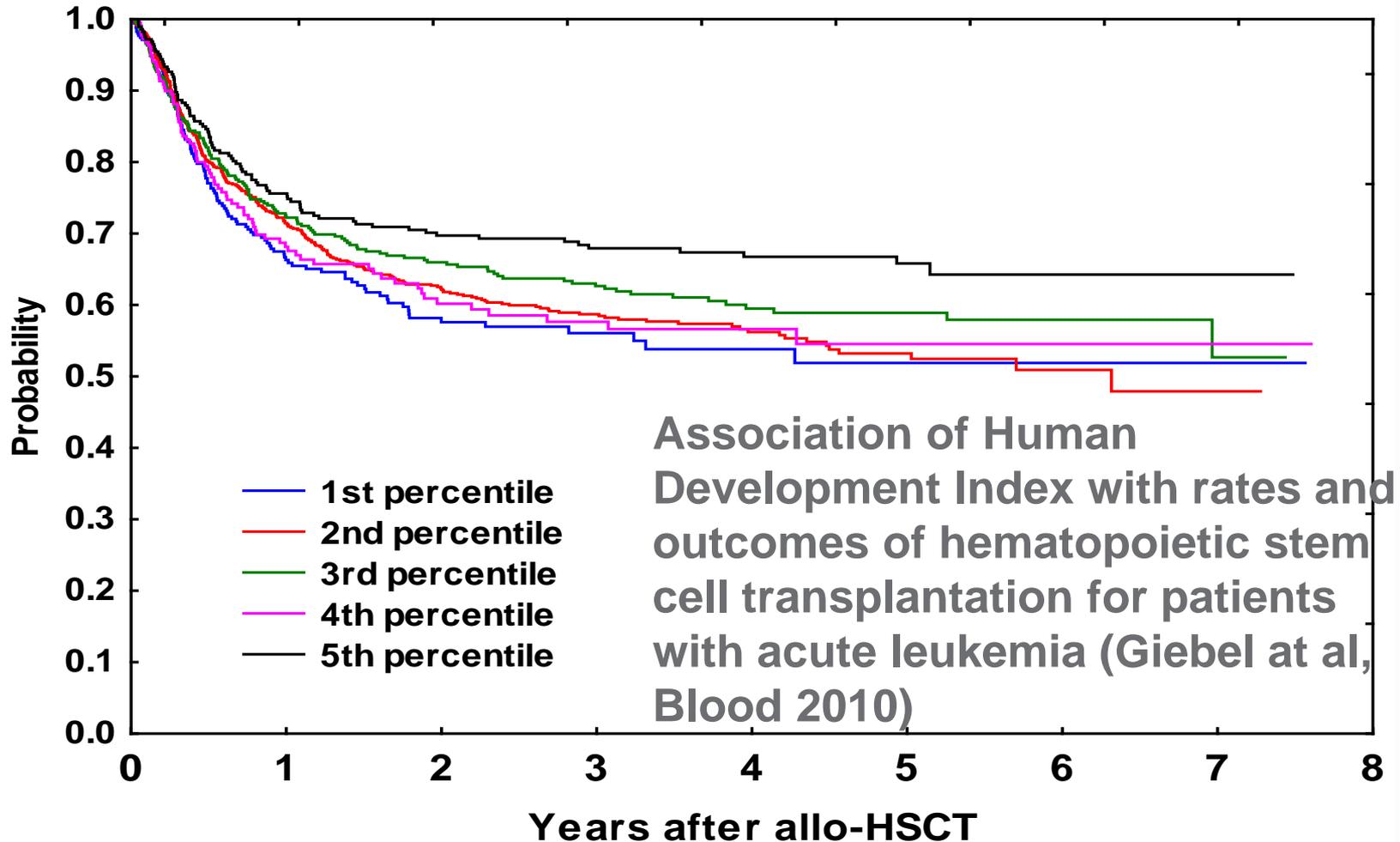


The Value of Outcomes Registries: Center-Specific Outcomes



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

LEUKEMIA-FREE SURVIVAL



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

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

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

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

How Might Existing Registries Help?

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

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

eDBtC: Enhanced Data Back to Centers

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

Intro **How To** Center Dashboard Patient Donor Type Disease Conditioning Intensity Survival Other Outcomes Ad-hoc Query Data Download

How To

 A video tutorial is available by clicking this 'Training Video' image

To Make Selections
To make a selection click on the data value you want to know more about. The selected data value turns green. Values compatible with the selection are white and unrelated values are gray.
To select more than one item in the same listbox, hold the CTRL key down while selecting additional values.

Clear Selections
To clear all selections click on the "Clear" button from the tool bar.
To clear selections in a specific field, click the eraser icon on the list box.

Search
Click on list box title bar, or click the magnifier icon. Start typing the value or number you wish to find. Press enter or click on a value to select. Also, use a search object.

Minimized Icons
Double click on minimized icons to launch. Hover with cursor over minimized icon to view entire title.

Cycle & Drill Buttons
If available, click on cycle button to display other dimensions, or drill down button to drill down to the next variable in the chart.

Printing and Exporting
Click the corresponding icon at the top right of the window.
(To print click to export, click XL)

To Navigate Between Sheets
To move between sheets click on the sheets tab at the top.

Selected Data (Green)
Associated Data (White)
Unrelated Data (Gray)

Quarter: Q1, Q2, Q3, Q4
Month: Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, Nov, Dec

Year: 2007, 2008, 2009, 2010

Title Bar >> Week: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15

Top Performers

Cycle	Drilldown
Sales	Sales
1,783,148	1,783,148
1,783,148	1,783,148

How to Dashboard Sales Customer Details

*** 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

eBIC Data Download

Data Download

Year: 2008 2009 2010 2011 2012 2013 2014 2015 **2016** Month: JUN AUG DEC NOV JUL SEP OCT JAN FEB MAR APR MAY

Welcome Portal | pgengler@cibmtr.org

Clear All Selections

CCN - Center's name

Data Dictionary Download

Current Selections

YEARTX: 2016
SEX: 2

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

You are viewing data for Center: 10128 - Froedtert Memorial Lutheran Hospital

Data Download

CRID	TXNUM	Center Number	NMDPRID	ASSIGNBY	TEDVSRES	TXTYPE	TXDATE	AUTOTX	UNRELATX	RELATX	SYNGENTX	BM	PB	CB	MULTICB	OPRODUCT	OPRODTP
4826410	1	10128	2895650	1	2	1	3/18/2016 12:00:00 AM	0	1	0	0	0	1	0	0	0	0
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4865982	1	10128	2604277	1	2	1	5/19/2016 12:00:00 AM	0	1	0	0	0	1	0	0	0	0
4725901	2	10128	-	1	4	1	2/9/2016 12:00:00 AM	0	0	1	0	0	1	0	0	0	0
4838308	1	10128	-	1	2	1	3/30/2016 12:00:00 AM	0	0	1	0	0	1	0	0	0	0
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4775633	1	10128	-	1	1	2	1/22/2016 12:00:00 AM	1	-	-	-	-	0	1	0	0	0

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

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

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?