From Data to Peer Reviewed Publication

Behind the scenes tour

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There are no conflicts of interest to disclose.
Outline

• What does CIBMTR do with the data we share? (eg “the data I worked so hard to provide”)

• How does CIBMTR transform data into a study?

• Why does CIBMTR ask me questions about my center’s data?
  – “Why is CIBMTR always looking for more data”

• What is CIBMTR doing to make it easier to get data back?
CIBMTR Number of Patients Registered, 1970-2016

Data are incomplete for 2016.
Facilitating Data to Knowledge

- Experience
- Interpretations
- Patterns
- Calculations
- Relationships
- Standardization
- Observations
- Facts

- Data
- Information
- Knowledge
- Publications

Collecting
Organizing
Validating
Summarizing
Analyzing
Interpreting
Decision-making

CIBMTR
CENTER FOR INTERNATIONAL BLOOD
& MARROW TRANSPLANT RESEARCH
Cumulative Publications 1972-2016
### 89 CIBMTR Presentations in 2016

<table>
<thead>
<tr>
<th>Conference</th>
<th>Oral</th>
<th>Poster</th>
<th>Total</th>
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<tbody>
<tr>
<td>American Society of Hematology</td>
<td>21</td>
<td>7</td>
<td>28</td>
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<tr>
<td>BMT Tandem Meetings</td>
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<td>6</td>
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<td>European Society for BMT</td>
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<td>8</td>
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<tr>
<td>European Immunogenetics and Histocompatibility</td>
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<tr>
<td>American Society of Clinical Oncology</td>
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<td>2</td>
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<tr>
<td>International Donor Registry Conference</td>
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<tr>
<td><strong>Other Scientific Meetings</strong></td>
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<td><strong>Total</strong></td>
<td>53</td>
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Outcomes Research (including Immunobiology Research) is Core Activity of CIBMTR Accounting for ~2/3 of our Publications
Who are we?

• The CIBMTR is a unique resource of data and statistical expertise to the scientific community for addressing important issues in HCT

• Network of >450 centers

• Clinical database with information for >450,000 HCT recipients

• Leading to: successful completion of hundreds of studies that have had an important impact on clinical practice!
Why so essential?

• These data are the core of our resource
• This is what US Gov pays us to do
• This is what centers, physician scientists, public hold us accountable for
• This is what we love to do – our mission, our passion

• This is the value proposition of the CIBMTR
Credits

- Kavita Bhavsar
- Waleska Perez
- Andrea Benoit
- Sue Logan
- Sharon Meiers
How does data become transformed into a published study?

• Who can/does propose studies that use data from CIBMTR?
• Who decides what studies are worth doing?
• What is the process of completing a study?
• How do we decide when to ask centers for data clarification?
  - And how much data
• What is the benefit?
Stages of a CIBMTR Research Study

1) Proposal
2) Protocol
3) Data File Preparation
4) Analysis
5) Manuscript Preparation
6) Submission
Proposal

• **Overview of the desired project**
  – Should include study objective, endpoints, brief scientific justification, patient selection criteria and variables
  – 1-2 pages – pre-specified format

• **Process:**
  – Submit to CIBMTR (relevant Working Committee)
  – WC leadership and statistician assess for feasibility, sufficient data, study overlap
  – BMT Tandem Meeting
    • PI / proposer presents study
    • WC review scientific merit
    • WC assigns a priority score
Who can propose a study?

• Anyone from a participating CIBMTR center
• Anyone with a good idea, even if not from a participating center
Working Committee Structure

- Acute Leukemia
- Autoimmune Diseases and Cellular Therapies
- Chronic Leukemia
- Donor Health and Safety
- Graft Sources and Manipulation
- Graft-vs-Host Disease
- Health Services and International Studies
- Immunobiology
- Infection and Immune Reconstitution
- Late Effects and Quality of Life
- Lymphoma
- Non-Malignant Marrow Disorders and Inborn Errors of Metabolism
- Pediatric Cancer
- Plasma Cell Disorders and Adult Solid Tumors
- Regimen-Related Toxicity and Supportive Care
Working Committee Organization

• Leadership
  – 2-4 Chairs appointed by Advisory Committee
  – MD CIBMTR Scientific Director
  – PhD CIBMTR Statistical Director
  – MS CIBMTR Statistician

• Membership
  – Open to any investigator
  – Total number of members: >2,600
Working Committees

• Set priorities for observational outcomes studies
• Evaluate study proposals to ensure relevance and meaningful results
• Design and conduct relevant studies
• Assess and revise CIBMTR data collection forms
• Plan and conduct workshops at CIBMTR meetings
It Takes a Village

CIBMTR PUBLICATIONS by Federal U24 Grant Periods

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<thead>
<tr>
<th>Period</th>
<th>Peer-reviewed pubs</th>
<th># Different authors</th>
<th># Different institutions</th>
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<td>2003-2007</td>
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<td>357</td>
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<td>2008-2012</td>
<td>235</td>
<td>775</td>
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<tr>
<td>2013-2016*</td>
<td>327</td>
<td>1,403</td>
<td>542</td>
</tr>
</tbody>
</table>

~40% of studies led by junior investigators (paired with senior investigators)

* First 4 years of grant period 2013-2017
Why so much work at the beginning?

• Stewardship of valuable resources
• Maximize the value of data, CIBMTR staff and efforts to publish the most important, impactful research that benefits patients, researchers and the HCT community
• In other words – we take your work and investment seriously
Statistical Hours: MS Statistician Hours

- Average number of hours to complete a study: 310
  - Protocol: 60
  - Data File Preparation: 100
  - Analysis: 80
  - Manuscript Preparation/Journal Comments: 70
Protocol Development

- Clarifies the study objectives to Working Committee participants
- Ensures that these objectives will be met by the analyses conducted at the Statistical Center
- Utilized by statisticians to prepare data-files for analyses
- Essential to a high quality research study
- Substantial scrutiny by all members of study team and the Statistical Center
Protocol Outline

- **Objective**: the purpose for which the data will be analyzed
- **Scientific Justification**: summarize the rationale of the study
- **Study Population**: Selection criteria of the cases to be included in the analysis
- **Outcomes**
- **Variables to be analyzed**
- **Study Design**: specific statistical methodology
- **Table describing the population**
Data File Preparation

• Eligible subjects who are consecutively treated at participating centers

• **Requirements:**
  – Adequate follow-up
  – Minimal missing data items
  – Sufficient statistical power
  – Series of steps to ensure data quality

• **GOAL:** Complete, consistent, high quality research-ready data!
Data File Preparation
- Process -

• **Selection criteria**: restriction applied to the database. Examples are:
  – First auto *or* first twin HCT for MM
  – Year or transplant: 1988-2003
  – Available research information
  – Exclude planned tandem transplants

• **Creation of outcomes and variables to be analyzed**: At this stage, the statistician checks the following:
  – Adequate follow-up
  – Missing values
  – Data discrepancy/outliers
Data File Preparation

- **Adequate follow-up**: Request necessary follow-up to centers

- **Missing values**:
  - Not a key variable: Dropped if large percentage is missing
  - Key variable: Center must be contacted

- **Data discrepancy/outliers**:
  - Reviewed by Scientific Director and PI
  - Contact centers for further details
Data File Preparation
- Request -

Statistician → Study Coordinator → CRC → CIBMTR Centers
Data File Preparation
- Request -

**STEP 1:**
- Study protocol
- Study selection criteria
- Study file in Excel format with:
  - CRC Code
  - Patient identification (CCN, CRID, IUBMID, NMDP ID)
  - Team Number
  - Date of Birth
  - Date of Transplant
  - Type of request: data check, new data or form request
Data File Preparation
- Request -

**STEP 2:**

- The study coordinator reviews the study request and updates statistician
Data File Preparation
- Request -

**STEP 3:**

- E-mail request
- Excel file
- Due date set up
- Supplemental forms
- Retired CIBMTR forms
Data File Preparation
- Request -

**STEP 4:**
- Timeline for study request
STEP 4:

- Why so much pressure on deadlines?

- CIBMTR has performance expectations for timely publications
  - Expectations of funding partners
  - Expectations of investigators
  - Timeliness of the research question
Advisory Committee Annual Metrics
Studies in Progress ≥3 years

Number of studies in progress ≥3y


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Data File Preparation
- Request -

STEP 5:
• CRCs send study request to centers

STEP 6:
❖ CRCs collect responses from centers

STEP 7:
❖ CRCs update study coordinator with responses

STEP 8:
❖ Study Coordinators combine responses

STEP 9:
❖ Study Coordinators update statistician and Database
Data File Preparation - Request -

**STEP 10:**

- Statistician makes decision on subsequent requests
  - cc: medical director on 2\textsuperscript{nd} request
  - phone call on 3\textsuperscript{rd}
  - a 4th request should not be necessary!
Data File Preparation
- Common Data Checks -

• Acute GVHD onset >120 days
• Negative intervals
• GVHD prophylaxis=none
• Primary COD=primary disease and no evidence of disease post transplant
• Primary COD=missing
• New malignancy
How are we trying to reduce our requests to centers

• Improve clarity and structure of questions and responses during forms revisions
• Increasing data quality/validation checks at time of data entry in FN
  – Sooner is better
• Streamline error correction process
  – Electronic requests when feasible
  – Electronic error corrections in FN for latest forms
• Data corrections for any given purpose improve quality across all use cases
Query Functionality: Overview

- CIBMTR staff will initiate queries on completed forms
- The center will review each queried form and work to resolve
- The resolution submitted by the center will be reviewed
- Once answers are approved, the form will go back to CMP status
Reasons for Queries

• Each query will have a comment category put on by CIBMTR staff
Data File Preparation

• **Adequate follow-up:** If adequate follow-up on survivors was not obtained, all patients in the center are **excluded** from analysis.

• **Handling of potentially eligible patients excluded from the study file:** Demographic characteristics must be compared between patients excluded and those included in the final study file.
Analyses

• Description of the population
  – Patient-, disease- and transplant characteristics

• Outcomes
  – Univariate (probabilities)
  – Multivariate (Relative Risk)

• Figures

• Review of final analyses by collective meeting of Statistical Center
Manuscript/Submission

- First draft manuscript
  - Minimal data request
- Final draft manuscript
- Submit to a peer-reviewed journal
- Address journal comments
What is the benefit?

- Peer reviewed publications with meaningful impact on the field
  - Benefit to participating centers
  - Benefit to participating investigators
  - Benefit to future patients
Peer-Reviewed Publications 2004-2016

CIBMTR®
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A ‘super-massive’ black hole
How can you get information back from CIBMTR?

• Publications
• Website
• Summary slides
• Information requests
• Calculators
  – Disease Risk Index, One year survival calculator
• CIBMTR Portal
  – eDBTC – electronic Data Back to Centers
  – Center performance analytics
Summary Slides – HCT Trends and Survival Data

- An annual report on data submitted to the CIBMTR by centers worldwide
- Describes information related to practices and general survival outcomes after hematopoietic cell transplantation
- Current edition includes transplants performed prior to 2015

The Disease Risk Index (DRI) is a validated tool to categorize groups of patients undergoing allogeneic stem cell transplantation (HCT) for hematologic malignancy by disease risk. It is intended for research purposes, to stratify patients in broad disease risk categories for retrospective or prospective studies.

The DRI considers only disease-related parameters (i.e., disease, stage and, for some diseases, cytogenetics) and was developed only for the primary outcome of overall survival after HCT.

Publication Details

DRI Assignment Tool

<table>
<thead>
<tr>
<th>Disease*:</th>
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<table>
<thead>
<tr>
<th>Disease Stage*:</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>DRI Group:</th>
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https://www.cibmtr.org/ReferenceCenter/Statistical/Tools/Pages/DRI.aspx
CIBMTR Portal

Welcome to the CIBMTR Portal

The CIBMTR Portal is a specialized and secure, password-protected area for CIBMTR community users. As an authorized user, you may view, analyze, or download information for your center by accessing different applications:

- **CVDR (Center Volumes Data Report)** – View details regarding your center’s transplant volume in prior years.
- **Survival Calculator** – Create a one-year predicted survival for allogeneic transplants based on the three year transplant center specific survival dataset.
  - This application is only available to Medical Directors, Physicians, and Center Administrators.
- **DBtC (Data Back to Centers)** – Access TED-level data your center submitted through FormsNet.
- **eDBtC (enhanced Data Back to Centers)** – Analyze, filter, or download select center CRF- and TED-level data from 2008 to present.
- **CPA (Center Performance Analytics)** – Comparatively analyze your transplant center specific survival data relative to aggregated data from other US centers.

To access the Portal and its applications, you must have a Google account registered with the CIBMTR.
eDBtC (enhanced DBtC) using Qlikview

- Dramatically improved user interface
- Self service and easy access
- Visualization of center analytics and descriptive statistics
  - ~60 selectable data dimensions, TED and CRF variables
  - ~30 predefined filters
- Logical organization of data in tabs
- Ad Hoc analysis – explore your data, including outcomes
- Data will be refreshed monthly
- Export application source data will be retained on the CIBMTR Portal Site
  
Current DBtC data download capability retained
eDBtC Patient Level Data
Survival Calculator – 1 year

- Calculates probability of 1 year survival after allogeneic transplantation for individual patients
- Uses model developed for annual center-specific outcomes analysis for US transplant centers
What can centers expect in Center Performance Analytics (CPA)?

- Selectable data dimensions include key variables for first allogeneic transplants facilitated in the U.S. in 2011, 2012 & 2013
- Data is organized in category-specific tabs
- Predefined filters enable limited comparative analysis based on center size, patient population (adult, pediatric, both), center performance, and region
- Visualization of each center’s data relative to other centers in data set for selected dimensions
- Analyze center's own one-year observed survival rate
- Create center-specific query on data dimensions available in the data set
- Export filtered data in Excel file format
- Export the center's entire Center Specific data set
- Data refreshed annually
## Selectable Dimensions in CPA

<table>
<thead>
<tr>
<th><strong>Patient</strong></th>
<th><strong>Disease</strong></th>
<th><strong>Transplant</strong></th>
<th><strong>Outcomes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>Broad Disease</td>
<td>Year of Transplant</td>
<td>One year Survival Probability</td>
</tr>
<tr>
<td>Gender</td>
<td>Disease stage</td>
<td>Product Type</td>
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<tr>
<td>HCT CI</td>
<td>ALL Philadelphia chromosome</td>
<td>Donor Type/Graft Type/HLA</td>
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<tr>
<td>History of Malignancy</td>
<td>ALL T-cell lineage</td>
<td>Product Type Details</td>
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<td>KPS Category Score</td>
<td>CLL &amp; other chronic Leukemia stage</td>
<td>BM or PBSC HLA Match</td>
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<tr>
<td>KPS Score</td>
<td>NHL subtype</td>
<td>Single Cord Blood HLA Match</td>
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<tr>
<td>Race</td>
<td>HL Chemo sensitivity</td>
<td>Conditioning Regimen Drugs</td>
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<tr>
<td>Recipient CMV Status</td>
<td>Interval Between DX &amp; TX</td>
<td>TBI</td>
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</tr>
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</table>

**Ad-hoc Query**
Accessing the new RFI tool

• Accessible through eDBtC from the Center Dashboard or the Disease tabs (top right corner “ASBMT RFI” button).
• Only available to active, U.S.-based centers.
• Application embedded into the Qlikview® eDBtC application.
• Separate, independent filtering configuration that allows users to switch between eDBtC and the RFI module without having to clear or reconfigure filter variables.
Questions?