

SUMMARY OF ACCOMPLISHMENTS

July 1, 2013 – June 30, 2014

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MISSION

The Center for International Blood and Marrow Transplant Research (CIBMTR) collaborates with the global scientific community to advance hematopoietic cell transplantation (HCT) and cellular therapy research worldwide to increase survival and enrich quality of life for patients. The CIBMTR facilitates critical observational and interventional research through scientific and statistical expertise, a large network of transplant centers, and a unique and extensive clinical database.

VALUE TO THE HCT COMMUNITY

The CIBMTR represents an international network of **>320** participating transplant centers that submit transplant-related data for patients. CIBMTR research involves **5** major programs:

- Outcomes Research
- Statistical Methodology Research
- Clinical Trials Support
- Health Services Research
- Immunobiology Research

The CIBMTR has been collecting HCT outcomes data worldwide for **>40** years, resulting in a Research Database with information on **>380,000** transplant recipients. These data are freely available to investigators with interest in HCT and treatments for cancer and other life-threatening diseases. The CIBMTR has become a respected leader in HCT research by providing a unique resource of information and expertise to the medical and scientific communities.

IMPROVING PATIENTS' LIVES

The CIBMTR is dedicated to improving survival, treatment, and quality of life for transplant patients. With **>900** publications, the CIBMTR conducts practice-changing research that helps patients and physicians:

SELECT DONORS AND GRAFTS

CIBMTR studies have established the paradigm for selecting the best donor and graft:

- Optimal HLA-matching
- Other important donor characteristics
- Cord blood vs. bone marrow vs. peripheral blood

EVALUATE PATIENT RISK

CIBMTR studies have shown which patients:

- Have the highest risk of GVHD and other complications
- Are most likely to benefit from transplant

IDENTIFY LONG-TERM EFFECTS OF TRANSPLANTATION

CIBMTR studies provide insight into:

- Long-term impact of transplant on patients and their families, including risk of second cancers and other late complications
- Survivors' quality of life

PROVIDE MEDICAL CARE GUIDANCE FOR SURVIVORS

The CIBMTR has worked with the medical community to develop guidelines for optimal long-term care of transplant survivors to:

- Decrease the rate of late complications
- Preserve patients' fertility as much as possible
- Identify post-transplant best practice preventive health behaviors

ADDRESS ACCESS TO CARE AND FUTURE WORKFORCE NEEDS

CIBMTR studies address the broad range of issues that influence access to transplant and long-term care after transplantation, including:

- Disparities in access and outcomes of specific populations
- Costs of care
- Future work force capacity

Publications establishing the CIBMTR's research in each of these areas are listed at <http://www.cibmtr.org/About/ProceduresProgress/Pages/SummaryPubs.aspx>

OUTCOMES RESEARCH

Clinical outcomes research using the CIBMTR's Research Database is a core activity of the organization.

Scientific Working Committees

Fifteen Scientific Working Committees oversee most of the CIBMTR's clinical outcomes research. Their accomplishments this year include:

- Consolidated 19 Working Committees into 15 in order to more efficiently utilize CIBMTR resources.
- Conducted the 208 ongoing studies that were in progress as of July 1, 2014.
- Received 156 new study proposals, 88 of which were presented and 40 of which were approved at the 2014 BMT Tandem Meetings.
- Published 45 manuscripts in peer-reviewed journals.
- Presented 41 abstracts (28 oral and 13 poster), including:
 - 21 (15 oral and 6 poster) at the American Society of Hematology Annual Meeting.
 - 16 (13 oral and 3 poster) at the BMT Tandem Meetings.
- Implemented an annual meeting of leadership across Working Committees to share best practices.

CIBMTR Research Database

>380,000 Transplant Recipients
>320 Participating Transplant Centers
~19,500 New Transplant Recipients Annually
>250 Active Studies
>900 Peer-Reviewed Publications
~40 Presentations Annually

Additional Outcomes Research Initiatives

- Initiated development of innovative electronic tools that will enhance Data Sharing initiatives.
- Collaborated with industry partners on various studies, such as long-term follow-up of new therapies, drug comparisons, and assessment of target populations for new therapies.
- Continued collecting data for the Myelodysplastic Syndrome study, which qualifies for Coverage with Evidence Development under the Centers for Medicare and Medicaid Services; this mechanism allows eligible patients on the study to receive Medicare or Medicaid reimbursement for transplantation.

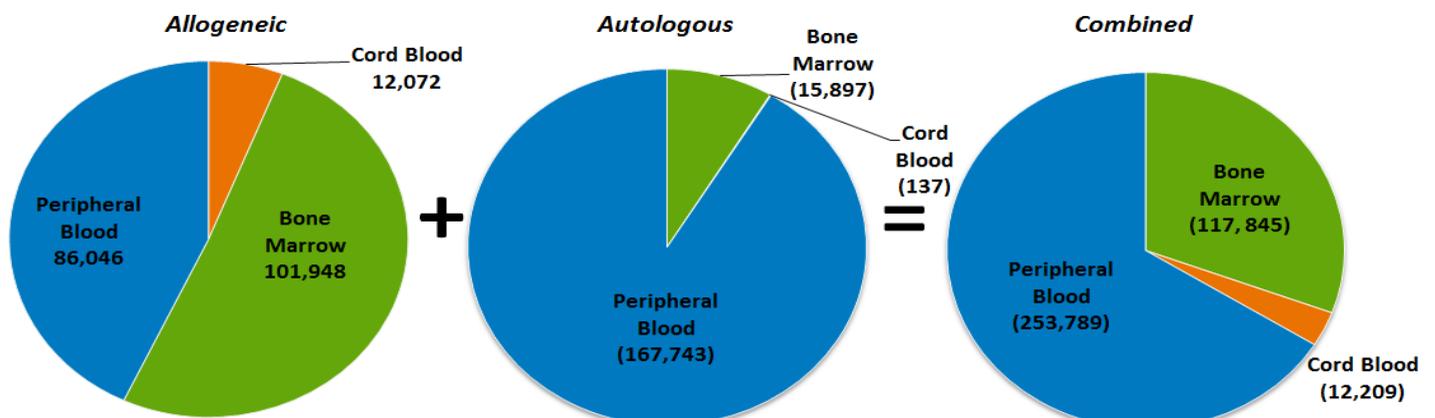
STATISTICAL METHODOLOGY RESEARCH PROGRAM

The Statistical Methodology Research Program's development goals are two-fold: develop statistical models to use in HCT research and compare the models with existing solutions using the Research Database.

This year the Statistical Methodology Research Program published 2 manuscripts in peer-reviewed journals:

- Comparison of statistics in association tests of genetic markers for survival outcomes.
- Pseudo-value approach for comparing survival medians for dependent data.

Distribution of Patients in the CIBMTR Research Database by Graft Type



CLINICAL TRIALS SUPPORT PROGRAM

The CIBMTR participates in and supports prospective research in various ways, including providing data management resources, access to its Research Database, and statistical expertise.

Blood and Marrow Transplant Clinical Trials Network (BMT CTN)

Along with the National Marrow Donor Program (NMDP) and The EMMES Corporation, a contract research organization, the CIBMTR serves as the Data and Coordinating Center for the BMT CTN. The BMT CTN's accomplishments over the past year include:

- Opened 4 new trials to accrual, bringing the total number of launched trials to 33.
- Accrued 1,166 patients to trials, increasing the total number of accrued patients to 6,618.
- Managed 16 open protocols with overall accrual for open studies at about 175% of projections.
- Published 9 peer-reviewed manuscripts and one editorial article.
- Presented 4 abstracts of study results at national and international meetings.

Resource for Clinical Investigations in Blood and Marrow Transplantation (RCI BMT)

The RCI BMT was developed to provide a multi-center clinical trials and prospective observational

research mechanism complementary to the BMT CTN. This year the RCI BMT's accomplishments include:

- Managed 6 open protocols, which accrued 883 patients.
- Completed analysis and submitted manuscripts, which were accepted, for 2 protocols.
- Completed accrual on 2 protocols.
- Continued the development of 2 other protocols.
- Supported 5 studies involving unrelated donor data or sample collection for investigators.

Survey Research

The Survey Research Group was created to assist HCT researchers in developing and conducting research involving questionnaires and patient interviews. The Group's accomplishments over the past year include:

- Supported 7 active studies.
- Participated in the development of 3 upcoming studies.

HEALTH SERVICES RESEARCH PROGRAM

The CIBMTR conducts research in health services issues, such as quality of care, survivorship, and disparities in as well as economic aspects of transplantation, through the Health Services Research Program.

- Completed the stakeholder focus group phase of a study of individualized care plans for HCT survivors.
- Completed a study comparing Medicaid coverage of HCT among the United States.
- Received a 2-year grant to conduct a research and educational intervention project regarding a payer-partnered approach to community-based referral for HCT.
- Conducted >35 evaluations for the Health Resources and Services Administration Office of Patient Advocacy / Single Point of Contact contract and Be The Match® patient programs.
- Presented research findings at the System Capacity Initiative Year IV Symposium, evaluated effectiveness of the program, and conducted research projects in response to prioritized recommendations from the participants.
- Provided technical writing support and

developed easy-to-read consent forms for 5 BMT CTN protocols.

- Published 2 manuscripts in peer-reviewed journals and presented 15 abstracts at national conferences.



IMMUNOBIOLOGY RESEARCH PROGRAM

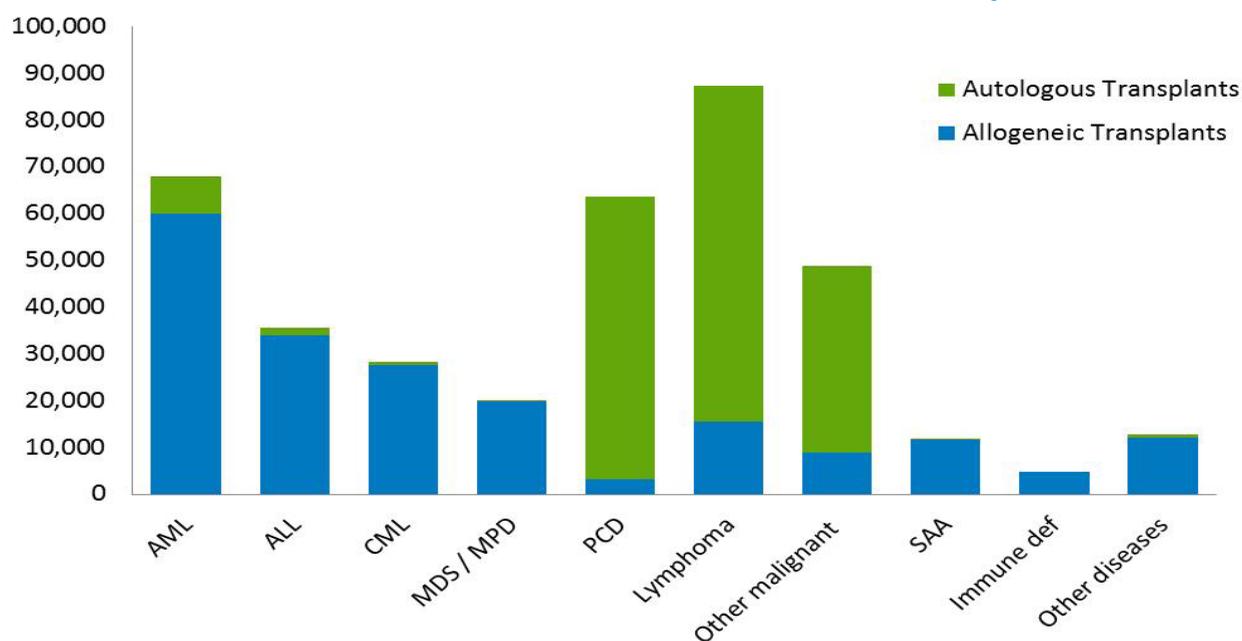
The CIBMTR's Immunobiology Research Program is facilitated by its Immunobiology Working Committee, functioning in collaboration with the NMDP Histocompatibility Advisory Group.

- Published 10 manuscripts in peer-reviewed journals.
- Presented 8 abstracts at scientific meetings.
- Reviewed and accepted 7 new project proposals.
- Distributed 10,245 samples to investigators for 13 different studies.
- Curated 12,923 samples in the NMDP Research Repository (119,711 overall).

NMDP Research Repository:

- 4,493 unrelated recipient samples (50,745 overall)
- 1,109 related recipient samples (3,889 overall)
- 4,707 adult unrelated donor samples (53,025 overall)
- 1,025 related donor samples (3,664 overall)
- 1,810 unrelated cord blood samples (7,490 overall)

Distribution of Patients in the CIBMTR Research Database by Disease



STEM CELL THERAPEUTIC OUTCOMES DATABASE

The Stem Cell Therapeutic Outcomes Database is a national outcomes registry for allogeneic transplants performed in the US as well as transplants performed elsewhere with products from the US.

Since 2006, the CIBMTR has held a Health Resources and Services Administration (HRSA) contract authorized by the C.W. Bill Young Cell Transplantation Program to manage the Stem Cell Therapeutic Outcomes Database. This year's accomplishments related to the contract include:

- Coordinated the fourth Center-Specific Outcomes Analysis Forum, which generated recommendations to improve risk adjustment, future collection of relevant data elements, and tools to enhance centers' quality improvement efforts.
- Published annual Center-Specific Outcomes Analyses.
- Continued to build the related sample repository by collecting pre-HCT biologic specimens of related donor-recipient pairs from 57 centers.
- Completed accrual on a quality of life pilot project, which is unique in that the CIBMTR collects data directly from patients after HCT.
- Engaged a task force with broad user perspective that provided recommendations for making CIBMTR data available on its public websites.
- Completed a manuscript, which was accepted for publication by the New England Journal of Medicine, based on the HRSA registry models report last updated through 2012, showing the likelihood of identifying a volunteer adult donor or cord blood from inventory for transplantation in the US. We are developing an updated HRSA registry models report that will evaluate impact of greater HLA match stringency and estimate match likelihoods for multi-race patients.

DATA MANAGEMENT

The CIBMTR collects data for approximately 19,500 new HCT recipients annually as well as follow-up data on previously reported transplants. To collect and share data in an efficient manner while ensuring data quality, this year the CIBMTR:

- Performed on-site audits of 47 centers.
- Continued the Continuous Process Improvement program with both US and international centers to ensure quality data is submitted within

specified time frames. As of the May 2014 report, 87% of US centers met Continuous Process Improvement standards.

- Maintained Institutional Review Board approval of the Research Database by 99% of active US transplant centers. Currently, there are only 2 centers that do not have Institutional Review Board approval for the Research Database.

INFORMATION TECHNOLOGY SERVICES

The CIBMTR IT team manages CIBMTR data and information, adapts commercial software products, develops custom software, and provides technical support.

FormsNet

More than 95% of data collected by the CIBMTR is submitted electronically via FormsNetSM, a comprehensive electronic data submission system containing >240 forms related to capturing HCT outcomes for donors and recipients. This year the IT team:

- Received 189,867 HCT recipient forms.
- Released the FormsNet3 Donor module, including an improved user interface and enhanced validations / navigations.
- Released major revisions for 26 recipient data collection forms to align forms with current treatment practices.
- Completed a Customer Satisfaction release, which consisted of performance enhancements and printing upgrades.
- Documented, produced, and released 8 new reports and 21 enhancements to the Management Reporting Website.

Research Database

Over the previous year, the IT team enhanced the CIBMTR Research Database, and the retrievals that extract data from it, to integrate legacy data and synchronize changes to fields and values. Specifically, the team:

- Successfully migrated legacy data, including detailed outcomes information, to the Research Database.
- Integrated the first group of forms revision changes, including 1,808 changes across 8 major baseline and disease follow-up forms and 138 forms pages.
- Began integrating the second major group of revised forms, including >1,000 changes across 6 major pre-disease forms and 73 form pages.

Data Sharing

In April 2014, the CIBMTR formalized its Data Sharing Program to improve how data, as well as the information and knowledge produced from the data, is shared with and among stakeholders. Included within this scope are 3 existing data sharing solutions:

AGNIS

A Growable Network Information System (AGNIS) allows data to flow from other databases into FormsNet as well as back to centers. This functionality allows centers to submit data from a local database without manual re-entry. This year the IT team:

- Increased the number of AGNIS production users from 6 to 9.
- Released 3 new form revisions to support Phase 1 of the Forms Revision Project.
- Collected >15,000 forms from the European Group for Blood and Marrow Transplantation.

Data Back to Centers (DBtC)

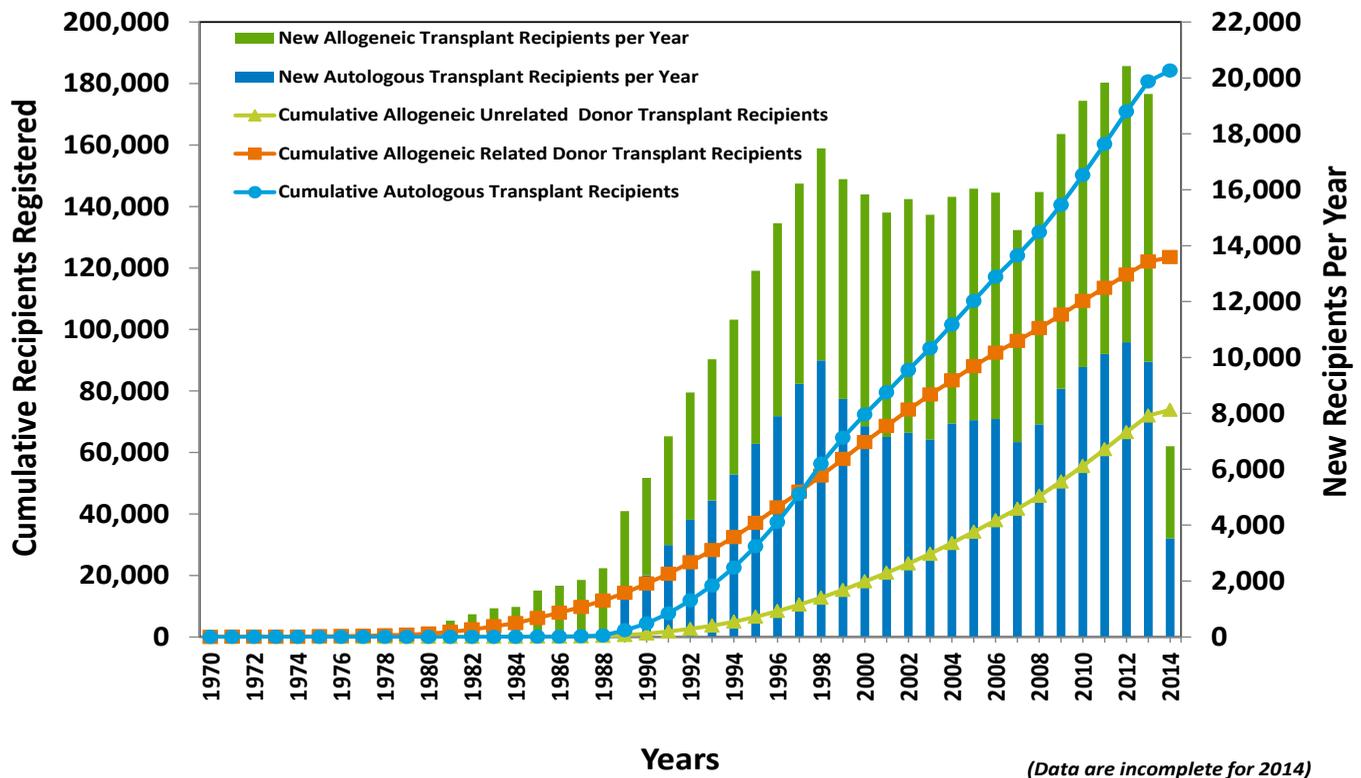
DBtC is a web-based application that allows the CIBMTR to securely share with transplant centers their own center-specific transplant essential data, which have been validated and processed into the Research Database. This year the IT team:

- Integrated DBtC with the CIBMTR's new contact management system (DISCO) to manage security of the Portal.
- Created the Tips for Centers document to improve use of downloaded files and increase time-savings.
- Reviewed and updated data dictionaries, code definition tables, and FAQs.

Information Requests

Requests for custom one-time analyses may be initiated through the public website. Requests may include descriptive statistics for the population of interest and / or a univariate analysis of overall survival. This year the CIBMTR provided data to support 623 requests.

Accession of Transplant Recipients Registered with the CIBMTR



RECENT PUBLICATIONS

The CIBMTR published 67 manuscripts, 2 editorials, and 2 other articles in peer-reviewed journals this year. Some of the CIBMTR's key findings were published in the following articles:

- Saber W et al. Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS). *Blood*. 2013 Sep 12; 122(11):1974-1982. Epub 2013 Jul 11.
- Lee SJ et al. Providing personalized prognostic information for adult leukemia survivors. *Biology of Blood and Marrow Transplantation*. 2013 Nov 1; 19(11):1600-1607. Epub 2013 Sep 6.
- Marks DI et al. Unrelated umbilical cord blood transplant for adult acute lymphoblastic leukemia in first and second complete remission: a comparison with allografts from adult unrelated donors. *Haematologica*. 2014 Feb 1; 99(2):322-328. Epub 2013 Sep 20.
- Eapen M et al. Impact of allele-level HLA matching on outcomes after myeloablative single unit umbilical cord blood transplantation for hematologic malignancy. *Blood*. 2014 Jan 2; 123(1):133-140. Epub 2013 Oct 18.
- Preussler J et al. Variation in Medicaid coverage for hematopoietic cell transplantation. *Journal of Oncology Practice*. 2014 Jul 1; 10(4):e196-e200. Epub 2014 Apr 8.
- Armand P et al. Validation and refinement of the disease risk index for allogeneic stem cell transplantation: a study from the CIBMTR. *Blood*. 2014 Jun 5; 123(23):3664-3671. Epub 2014 Apr 17.
- Alsina M et al. Lenalidomide maintenance for high risk multiple myeloma after allogeneic hematopoietic cell transplantation. *Biology of Blood and Marrow Transplantation*. 2014 Aug 1; 20(8):1183-1189. Epub 2014 Apr 21.
- Jacobsen PB et al. Exercise and stress management training prior to hematopoietic cell transplantation: Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0902. *Biology of Blood and Marrow Transplantation*. Epub 2014 Jun 6.
- Cutler C et al. Tacrolimus / sirolimus versus tacrolimus / methotrexate as GVHD prophylaxis after matched, related donor allogeneic hematopoietic cell transplantation. *Blood*. Epub 2014 Jun 30.

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